IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
CINCINNATI DIVISION

HUNTER DOSTER, *et al.*,

Plaintiffs,

v.

FRANK KENDALL, *et al.*,

Defendants.

No. 1:22-cv-00084
Hon. Matthew W. McFarland

DEFENDANTS' OPPOSITION TO PLAINTIFFS' EMERGENCY MOTION FOR TEMPORARY RESTRAINING ORDER AND PRELIMINARY INJUNCTION

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INTRODUCTION

In warfare, disease has historically accounted for more service member deaths than battlefield injuries. The current Department of Defense ("DoD") immunization program, which has been in place for decades, requires that all service members obtain nine immunizations, and an additional eight may be required depending on circumstances like deployment. In the midst of a deadly pandemic that has killed more than 870,000 Americans, DoD added vaccination against COVID-19 to this long list of immunizations already required for service members.

Plaintiffs—18 members of the Air Force—challenge the Air Force's COVID-19 vaccination requirement as inconsistent with their religious beliefs. Plaintiffs request not only that this Court overturn the Air Force's decision to deny their religious accommodation requests, but also that the Court to grant the religious accommodation requests of all other service members of the Air Force, and to supervise the ongoing accommodation process as to thousands of other service members not before the Court. Such an injunction would be wholly improper, particularly as the Supreme Court has consistently cautioned against judicial interference in military affairs.

This Court should deny Plaintiffs' request, as it fails to satisfy the standard for preliminary injunctive relief. First, Plaintiffs are unlikely to succeed on the merits of their claims. For those Plaintiffs whose military processes are still ongoing, the Plaintiffs have neither ripe nor exhausted claims. For all Plaintiffs, their RFRA claims fail on the merits. The challenged vaccine requirement explicitly contemplates the possibility of a religious accommodation, and the military assesses such requests under the standards set forth in the Religious Freedom Restoration Act ("RFRA"). The Air Force's interest in protecting the health of its service members to carry out its mission is indisputably compelling, and there is no basis for the Court to conclude that Plaintiffs' proposed alternatives would protect the military's compelling interests as effectively as

immunization. The Court should defer to the military's judgment that vaccination is necessary for readiness. For much the same reasons, Plaintiffs' First Amendment claim also fails because the vaccine mandate does not infringe upon the free exercise of religion. The remaining factors weigh heavily against the entry of any injunctive relief. Plaintiffs cannot show that they face irreparable harm or that the balance of equities tilts in their favor. But the entry of an injunction granting Plaintiffs' exemption requests and imposing judicial supervision over the Air Force's exemption process would greatly harm the Air Force, its vital mission, the national security of the United States, and the public interest.

Seven other courts have declined to grant service members' similar motions for preliminary injunctions.[1,2] Another Court within this district denied a motion for a temporary restraining order against the military's vaccine directive. *See* Order, Doc. No. 3, *Poffenbarger v. Kendall*, No. 3:22-cv-00001-TMR (S.D. Ohio Jan. 3, 2022). The Court should likewise deny Plaintiffs' motion for a preliminary injunction. The Court should also reject Plaintiffs' attempt to receive a nationwide injunction of the COVID-19 vaccine requirement pertaining to the entire Air Force. Every court that has considered a request for such sweeping relief in this context has denied the request. *See supra* notes 1, 2. Indeed, a Court in this district denied a request for a nationwide injunction against

[1] *See Church v. Biden*, ---F. Supp. 3d---, 2021 WL 5179215 (D.D.C. Nov. 8, 2021); *Doe #1 -#14 v. Austin*, ---F. Supp. 3d---, 2021 WL 5816632 (N.D. Fla. Nov. 12, 2021); *Guettlein v. U.S. Merch. Marine Acad.*, ---F. Supp. 3d---, 2021 WL 6015192 (E.D.N.Y. Dec. 20, 2021); *Oklahoma v. Biden*, ---F. Supp. 3d---, 2021 WL 6126230 (W.D. Okla. Dec. 28, 2021); *Robert v. Austin*, No. 21-cv-02228, 2022 WL 103374 (D. Colo. Jan. 11, 2022), *appeal filed*, No. 22-1032 (10th Cir. Feb. 22, 2022); Order, Doc. No. 25, *Short v. Berger*, No. 2:22-cv-1151 (C.D. Cal. Mar. 3, 2022); Transcript of Order, Doc. No. 25, *Dunn v. Austin*, No. 22-cv-0028 (E.D. Cal. Feb. 22, 2022).

[2] The district court in *Navy SEALs 1–26 v. Biden*, ---F. Supp. 3d---, 2022 WL 34443, at *14 (N.D. Tex. Jan. 3, 2022), recently granted a motion for a preliminary injunction which enjoined the Department of Defense and the U.S. Navy from applying certain COVID-19 vaccination policies to the 35 plaintiffs in that case or taking any adverse action against those plaintiffs on the basis of their requests for religious accommodation. Similarly, the district court in *Navy SEAL 1 v. Biden*, *see* Order, Doc. No. 67, No. 8:21-cv-02429 (M.D. Fla. Feb. 2, 2022), granted in part a motion for a preliminarily injunction, enjoining the Department of Defense from "altering in any manner and for any reason" the current employment status of two plaintiffs. The Government strongly disagrees with these decisions, for the reasons set forth herein, and has filed a notice of appeal in both cases. *See also Air Force Officer v. Austin*, ---F. Supp. 3d---, 2022 WL 468799 (M.D. Ga. Feb. 15, 2022) (denying plaintiff's request for nationwide injunction of Air Force vaccine requirement but granting "narrowly tailored" relief).

the Air Force and instead issued a "relatively limited preliminary injunction" based on a finding that honorably discharging the plaintiff (rather than taking punitive measures) is a less restrictive means of accomplishing the military's vaccination goals. *See Poffenbarger*, ---F. Supp. 3d---, 2022 WL 594810, at *1, 14–15, 19–20.[3]

BACKGROUND

I. The COVID-19 Pandemic

The virus SARS-CoV-2 causes a disease known as COVID-19 that "spreads when an infected person breathes out droplets and very small particles that contain the virus." Centers for Disease Control and Prevention ("CDC"), *How COVID-19 Spreads*, https://perma.cc/4ZBC-8WYQ.[4] In July 2021, the United States began to experience "a rapid and alarming rise in . . . COVID-19 case[s] and hospitalization rates," driven by the Delta variant. *See* CDC, *Delta Variant: What We Know About the Science* (updated Aug. 26, 2021), https://perma.cc/4RW6-7SGB. Community transmission rates remain high in all 50 states. *See* CDC, *COVID Data Tracker*, https://perma.cc/ZKQ5-W8QC. And daily case rates recently and rapidly surpassed the previous peak. *Id*. To date, more than 79,000,000 Americans have been infected, and nearly 955,000 Americans have died from COVID-19. *Id*.

In DoD alone, as of March 1, 2022, "there have been 387,621 cases" of COVID-19 in service members, which have led to 94 deaths." Ex. 10 (Decl. of Major Scott Stanley) ¶ 3. Of those 94 service members, all but five were unvaccinated, and of those five, two had received a single dose of a two-dose mRNA vaccine. *Id*. Moreover, many "otherwise healthy Service

[3] The Government contends that even a "relatively limited preliminary injunction" should not have issued in *Poffenbarger*, *inter alia*, because there was no indication that the Air Force intended to initiate punitive measures such as court-martial against plaintiff, *see* Order at 28, Doc. No. 32, *Poffenbarger v. Kendall*, No. 3:22-cv-0000-TMR (S.D. Ohio Jan. 3, 2022), thus it was not necessary to enjoin them from doing so in that case.

[4] The Court may take judicial notice of factual information available on government websites. *See Tellabs, Inc. v. Makor Issues & Rts., Ltd.*, 551 U.S. 308, 322–23 (2007).

members have developed 'long-haul' COVID-19, potentially impacting their long-term ability to perform their missions." Ex. 9 (Decl. of Col. Tonya Rans, M.D.) ¶ 10.

II. Department of Defense Vaccination Directives

The U.S. military instituted its first immunization program in 1777 when General Washington directed the inoculation of the Continental Army for smallpox. Stanley Lemon, et al., *Protecting Our Forces: Improving Vaccine Acquisition and Availability in the U.S. Military*, National Academies Press, 2002, https://perma.cc/E545-TQ9G. Deaths due to infectious diseases outnumbered those due to direct combat injuries until World War II, when vaccines became widespread. *Id*. at 3. More recently, disease accounted for nearly 70% of U.S. Army hospital admissions during the Persian Gulf War. *Id*. at 10, Figure 1-1. Military-mandated vaccines have played a key role in reducing infectious disease morbidity and mortality among military personnel. *Id*. (highlighting the historical use of vaccines in armed conflict). For decades, the military has implemented a variety of enduring or situational inoculation measures to maintain the readiness of the force. *See* Ex. 3 (Congressional Research Report Defense Health Primer).

DoD's current immunization program is governed by DoD Instruction ("DoDI") 6205.02. Nine vaccines are required for all service members, including the annual influenza vaccine, while eight others are required when certain elevated risk factors are present, such as deployment to certain parts of the world. *See* Ex. 5 (Air Force Instruction ("AFI") 48-110_IP), Table D-1. In general, DoD aligns its immunization requirements and eligibility determinations for service members with recommendations from the CDC's Advisory Committee on Immunization Practices. Ex. 4 (DoDI 6205.02) at 3. The Military Services have separately issued regulatory guidance for the administration of vaccines to service members, including processes to seek medical and religious exemptions. *See* Ex. 5, Chapter 2.6.

On August 9, 2021, the Secretary of Defense, noting the impact COVID-19 has on military readiness, announced that he would add the COVID-19 vaccine to the list of vaccines required for all service members by the earlier of mid-September or upon approval by the Food and Drug Administration ("FDA"). *See* Ex. 1 (Mem. for all Defense Employees (Aug. 9, 2021)). On August 24, 2021, after FDA announced the approval of the Pfizer COVID-19 vaccine, *see* Ex. 8 (Decl. of Peter Marks, M.D., Ph.D) ¶ 6,[5] the Secretary directed the Secretaries of the Military Departments to immediately vaccinate all members of the armed forces under DoD authority who were not already fully vaccinated, *see* Ex. 2 (Mem. For Senior Pentagon Leadership, Commanders of the Combatant Commands, Defense Agency and DoD Field Activity Directors (Aug. 24, 2021)).

III. The Air Force's Implementation of DoD's COVID-19 Vaccination Directive

Shortly after the Secretary of Defense issued the vaccine directive, the Air Force issued implementing guidance. *See* Ex. 6 (Mem. for Dep't of the Air Force Commanders). The Secretary of the Air Force directed all reservists to be fully vaccinated by December 2, 2021. *Id*. As with other vaccine requirements, the Air Force has guidance that establishes processes for seeking medical, administrative, and religious exemptions. *See* Ex. 11 (Decl. of Col. Artemio Chapa) ¶¶ 3–9; Ex. 12 (Decl. of Major Matthew Streett) ¶ 3; Ex. 15 (Decl. of Lt. Col. Nekitha Little) ¶¶ 3–4. Members may seek a temporary medical exemption if, for example, they currently have COVID-19, are pregnant, or are allergic to an ingredient in the vaccine. Ex. 11 ¶¶ 4–6. Members who are on terminal leave (i.e., they are no longer coming into their workspace and are taking leave until the date they retire or separate from service) or otherwise retiring or separating (that is, leaving military service) in the near future may also seek an exemption, as they will be leaving military

[5] The Marks Declaration was prepared and submitted in connection with separate litigation. Here, it provides useful background on the safety and efficacy of COVID-19 vaccines.

service imminently. Ex. 15 ¶¶ 3–4; Ex. 23.

Members may seek a religious exemption by submitting a written request to the approval authority. Ex. 12 ¶ 4.[6] The service member then consults with a chaplain, his commander, and a military medical provider, who "each provide written memoranda of their respective meetings to include in the request package." *Id.* ¶ 9. Although chaplains may make recommendations, they are not authorized to approve or deny exemption requests. *Id.* ¶ 10. A separate legal review of the package is also conducted. *Id.* ¶ 11.

The package is then routed through each commander in the chain of command, who each provide an endorsement with a recommendation to approve or disapprove the request. *Id.* ¶ 12. Endorsements must address if there is a compelling government interest; any effect the accommodation will have on readiness, unit cohesion, good order and discipline; health, or safety, and impact on the duties of the member; and whether "less restrictive means can be used to meet the government's compelling government interest.'" *Id.* (quoting DAFI 52-501 ¶ 6.6.1.5). The commanders are not authorized to approve or deny requests. *See id.* ¶¶ 12–13.

In addition, a multidisciplinary Religious Resolution Team at the approval authority level reviews the package in order to advise the approval authority regarding resolution of religious liberty matters.[7] *Id.* ¶¶ 7, 13. After reviewing the request package, the team provides a written recommendation that includes any dissenting views of any members of the team. *Id.* ¶ 11. The team is not authorized to approve or deny requests. *See id.*

[6] The approval authority indicated in DAFI 52-201 is the Major Command (MAJCOM), Field Command (FIELDCOM), Direct Reporting Unit (DRU), or Field Operating Agency (FOA) commander over the service member. *Id.* ¶ 4.

[7] The team is composed of a representative from the Deputy Chief of Staff for Manpower, Personnel, and Services, as well as from the Chaplains Corps, Air Force Public Affairs, a representative from the Air Force Surgeon General, and from the Air Force Judge Advocate General's Corps. Ex. 12 ¶ 8 n.10. Due to the part-time nature of the Reserves and the logistical difficulties in assembling members to address the numerous religious accommodation packages submitted, the Air Force Reserve Command ("AFRC") temporarily waived the requirement for AFRC units to hold a Religious Review Team, in accordance with applicable Department of the Air Force regulations, which authorize such waivers. *Id.* ¶ 8. The AFRC-level Religious Review Team fulfills the requirement instead.

Once each commander in the chain of command has provided an endorsement and the Religious Review Team has provided its recommendation, the package is submitted to the approval authority. *Id.* ¶ 13. The approval authority assesses each request individually "to determine (1) if there is a sincerely held religious (as opposed to moral or conscience) belief, (2) if the vaccination requirement substantially burdens the applicant's religious exercise based upon a sincerely held religious belief, and if so, (3) whether there is a compelling government interest in requiring that specific requestor to be vaccinated, and (4) whether there are less restrictive means in furthering that compelling government interest." *Id.* ¶ 5. For active duty service members within the continental United States, the approval authority must review and make a decision on the exemption request within 30 business days of the date the service member submitted an exemption request. *Id.* ¶ 15. For service members overseas or in the Air Force Reserves, the timeline is extended to 60 business days. *Id.* If the approval authority denies the request, the service member may appeal to the Air Force Surgeon General, who reviews each package individually, is advised by another Religious Resolution Team, and renders a final decision on the request taking into account these same four criteria. *Id.* ¶¶ 1, 4, 5, 16. The Air Force Surgeon General must reach a final decision on the appeal within 30 business days from the date the service member provided notice of an intent to appeal. *Id.* ¶ 16.[8]

Air Force commanders have a variety of administrative and disciplinary actions that may be taken against service members who do not have an exemption and who refuse the COVID-19 vaccination. Ex. 13 (Decl. of Col. Elizabeth Hernandez) ¶¶ 3–14. However, to ensure consistency and uniformity in disposition, before any administrative or disciplinary action can be taken based

[8] These timelines may not be met if there is a large influx of religious accommodation requests. Ex. 12 ¶ 15. Even if the timelines are not met, a service member faces no harm, as he or she is temporarily exempted from the immunization requirement while the request or appeal is pending and does not face any administrative or disciplinary action for failure to comply with the vaccination requirement during that period. *Id.*

on a COVID-19 vaccine refusal, the case must be reviewed by a high-ranking official. *Id.* ¶ 3.

Regular service members who refuse to comply with the COVID-19 vaccination mandate, absent an exemption, will be subject to initiation of administrative discharge proceedings. *Id.* ¶ 10. The processes differ slightly for enlisted and officer members, but in general the process starts when the service member's immediate commander notifies the service member of a recommendation administrative discharge. *Id.* The service member may respond, with the support of free defense counsel provided to service members, before the discharge recommendation goes to the separation authority. *Id.* Depending on the characterization of the service separations and the service member's time in office, the decision may move to a higher level and the service member may be entitled to a formal administrative hearing. *Id.*

For members of the Air Force Reserve who refuse to comply with the COVID-19 vaccination mandate, absent an exemption, discipline may include an administrative action, such as the issuance of a Letter of Reprimand, which is a "non-punitive tool[], intended to improve, correct, and instruct service members who violate established Department of Air Force standards." *Id.* ¶ 6. If a Letter of Reprimand is issued, the member is given the opportunity to consult with a free defense counsel, provide a response, and provide other relevant information to the issuing authority. *Id.* The issuing authority then decides whether to uphold the Letter of Reprimand, which would result in the letter being filed in the service member's personnel records. *Id.* The service member may appeal to the issuing authority or superior authority for removal of the reprimand from the personnel record. *Id.* They may also be placed in a "no pay/no points status and involuntarily reassigned to the Individual Ready Reserve" ("IRR"). Ex. 7 (Secretary of the Air Force Mem. (Dec. 7, 2021)) at Attach. 1; Ex. 14 (Decl. of Lt. Col. Ethel Watson) ¶ 8. Reassigning a member to the IRR is not a discharge or separation. Ex. 17 (Decl. of Col. Ashley

Heyen) ¶ 5. Rather, it is an assignment action which places the member in a "resource pool of reservists" who are unable to meet readiness standards or need to manage other commitments in their personal lives. *Id*. ¶ 3. The service member remains a member of the Air Force, but is not drilling with his unit, is not earning pay as a reservist, and is not getting credit toward retirement. *Id*.; Ex. 14 ¶ 8. Once a member is reassigned to the IRR, that member loses his eligibility for health insurance at a reduced rate. Ex. 17 ¶ 3.

IV. Procedural Background

On February 16, 2022, Plaintiffs filed a purported class-action complaint against the Secretary of the Air Force, the Air Force Surgeon General, multiple commanders, and the United States, alleging two claims: (1) a violation of RFRA "in light of [the] vaccine mandates" and for alleged failure to "timely process" some of Plaintiffs' exemption requests; and (2) a violation of the First Amendment for "refusing to accommodate religious exemptions." Compl. ¶¶ 65–75, Doc. No. 1, PageID 17–18. On February 22, 2022, Plaintiffs filed a Motion for an Emergency Temporary Restraining Order and Preliminary Injunction seeking (1) a temporary restraining order to prevent the imposition of punitive action against four Plaintiffs for their refusal to get vaccinated and (2) a preliminary injunction granting all of Plaintiffs' religious accommodation requests and enjoining Defendants from taking punitive action against them. Pls.' Mot. 1, Doc. No. 13, PageID 578. Plaintiffs also appear to seek nationwide, class-wide relief—although no class has been certified—for all Air Force service members.[9]

LEGAL STANDARDS

[9] Plaintiffs' request for relief is inconsistent across their motion, memorandum supporting their motion, and proposed order. In their motion, Plaintiffs seek (1) "a temporary restraining order as to four of the Plaintiffs, who face imminent adverse punitive actions," and (2) "as to all of the Plaintiffs, a request for a preliminary injunction that their religious accommodations be granted . . . , including enjoining the Government Defendants from taking punitive actions against all Plaintiffs." Pls.' Mot. 1, Doc. No. 13, PageID 578. But Plaintiffs' memorandum supporting their motion and their proposed order also appear request a nationwide injunction as to all Air Force Service members. Pls.' Mem. 18–19, Doc. No. 13, PageID 598–99; Proposed Order, Doc. No. 13-6, PageID 814–15.

"A preliminary injunction is an extraordinary remedy never awarded as of right." *Winter v. Nat. Res. Def. Council, Inc.*, 555 U.S. 7, 24 (2008). Plaintiffs must "*by a clear showing*" establish that (1) they have a substantial likelihood of success on the merits; (2) they will suffer irreparable harm without an injunction; (3) the balance of equities tips in their favor; and (4) preliminary relief serves the public interest. *Mazurek v. Armstrong*, 520 U.S. 968, 972 (1997); *Thompson v. DeWine*, 976 F.3d 610, 615 (6th Cir. 2020), *cert. denied*, 141 S. Ct. 2521 (2021). The Sixth Circuit has cautioned against the entry of mandatory preliminary injunctions that alter the status quo and "which would finally dispose of the case on its merits." *Dunn v. Retail Clerks Int'l Ass'n, AFL-CIO, Loc. 1529*, 299 F.2d 873, 874 (6th Cir. 1962); *see also Gaines v. NCAA*, 746 F. Supp. 738, 742 (M.D. Tenn. 1990).

Additionally, judicial review of claims involving the "complex[,] subtle, and professional decisions as to the composition, training, equipping, and control of a military force[,]" *Gilligan v. Morgan*, 413 U.S. 1, 10 (1973), is highly constrained, *Rostker v. Goldberg*, 453 U.S. 57, 66 (1981) (explaining that because of the "healthy deference to legislative and executive judgments in the area of military affairs," courts employ a relaxed scrutiny in reviewing military policy); *Hartmann v. Stone*, 68 F.3d 973, 984 (6th Cir. 1995) ("Clearly the courts must grant the military wide latitude in its operations."). "The Supreme Court has explained that courts 'give great deference to the professional judgment of military authorities concerning the relative importance of a particular military interest.'" *Poffenbarger*, 2022 WL 594810, at *17 (quoting *Winter*, 555 U.S. at 25). Such deference extends to constitutional claims and military decisions about the health and welfare of the troops, *see Solorio v. United States*, 483 U.S. 435, 448 (1987); *Mazares v. Dep't of Navy*, 302 F.3d 1382, 1385 (Fed. Cir. 2002), and in the RFRA context, *see also Poffenbarger*, 2022 WL 594810, at *17 (citing S. Rep. No. 103-111, *reprinted in* 1993 U.S.C.C.A.N. 1892, 1901 (1993)

("S. Rep. No. 103-111")) (noting that deference to the military applies in RFRA).

ARGUMENT

I. Plaintiffs Are Unlikely to Succeed on the Merits of Their Claims.

Plaintiffs have failed to establish that this Court has jurisdiction over their claims. Plaintiffs also fail to establish either their RFRA or First Amendment claims.

A. Plaintiffs Have Failed to Establish That This Court Has Jurisdiction Over Their Claims Because Their Claims Are Not Ripe and They Have Failed to Exhaust Their Administrative Remedies.

For all but two Plaintiffs, their claims are neither ripe nor exhausted because they have not completed the process for requesting exemptions or exhausted their intra-military remedies.[10]

1. Plaintiffs' Claims Are Not Ripe.

The ripeness doctrine "prevent[s] the courts, through premature adjudication, from entangling themselves in abstract disagreements." *Thomas v. Union Carbide Agric. Prods. Co.*, 473 U.S. 568, 580 (1985) (citation omitted). To determine whether a claim is ripe, courts evaluate "both the fitness of the issues for judicial decision and the hardship to the parties of withholding court consideration." *Airline Pros. Ass'n of Int'l Bhd. of Teamsters, Loc. Union No. 1224, AFL-CIO v. Airborne, Inc.*, 332 F.3d 983, 988 (6th Cir. 2003) (quoting *Abbott Lab'ys v. Gardner*, 387 U.S. 136, 149 (1967)). Plaintiffs' claims fail to satisfy either prong. Plaintiffs' claims are not fit for judicial resolution because "matters 'still pending before [an agency] . . . [are] not yet ripe for judicial review.'" *Shrimpers & Fisherman of the RGV v. U.S. Army Corps of Eng'rs*, 849 F. App'x 459, 462 (5th Cir. 2021) (quoting *La. Power & Light Co. v. Fed. Power Comm'n*, 526 F.2d 898, 910 (5th Cir. 1976)). Only four Plaintiffs have completed the appeal process. Pls.' Mem. 2–3, Doc. No. 13, PageID 582–83. Addressing Plaintiffs' claims before their

[10] Plaintiffs Dills and Schuldes, both Reservists who have completed the appeal process, are the only two Plaintiffs with ripe claims and who have arguably exhausted their intra-military remedies. However, what they are facing a reassignment action, not discharge or separation from the Air Force.

religious accommodation requests are finally adjudicated "would require the Court to adjudicate internal military affairs before the military chain of command has had full opportunity to consider the accommodation requests at issue." *Church v. Biden*, No. 21-2815 (CKK), --- F. Supp. 3d ---, 2021 WL 5179215, at *11 (D.D.C. Nov. 8, 2021); *see also Poffenbarger*, 2022 WL 594810, *9 (citing *Church*, 2021 WL 5179215, at *10); *see also Reno v. Cath. Soc. Servs., Inc.*, 509 U.S. 43, 59 (1993) ("[T]he promulgation of the challenged regulations did not itself give each . . . class member a ripe claim; a class member's claim would ripen only once he took the affirmative steps that he could take before the [agency] blocked his path by applying the regulation to him.").[11]

Even for the three active-duty Plaintiffs (Doster, Colantonio, and Theriault) who have completed the appeal process for their religious accommodation requests, their claims are unripe because the Air Force has not yet made a final determination on separation. The Supreme Court in *Toilet Goods Association v. Gardner*, 387 U.S. 158 (1967), held a challenged regulation unripe for review when the regulation was permissive rather than mandatory—*i.e.*, one it did not compel the agency to act but only authorized the agency to exercise a discretionary power to act. Similarly, here, Air Force regulations provide that "[i]n the case of a refusal to comply with the COVID-19 vaccination mandate, absent an exemption, regular service members will be subject to initiation of administrative discharge proceedings." Ex. 13 ¶ 10. But the Air Force's "initiation of separation proceedings is a tentative action not fit for judicial review; one can only speculate as to the final outcome of any proceedings." *Smith v. Harvey*, 541 F. Supp. 2d 8, 13 (D.D.C. 2008); *see also* Order, *Short*, No. 2:22-cv-01151, Doc. No. 25 at 5 (holding that plaintiff challenging denial of

[11] The court in *Poffenbarger* recognized this exhaustion requirement. Although exhaustion was not at issue in that case—like the two Reservists here, Plaintiffs Dills and Schuldes—the court noted the importance of "exhaust[ing] [] available intraservice corrective remedies." *Poffenbarger*, 2022 WL 594810, at *9 (citation omitted). The court compared the plaintiff to the plaintiffs in *Church*, who had failed to exhaust their remedies because their "appeals of denials for religious accommodations to the Department of Defense vaccine mandate remained pending, and [they] had not been disciplined nor separated from the Marine Corps." *Id.* (citing *Church*, 2021 WL 5179215, at *10).

religious accommodation request for COVID-19 vaccine had "not exhausted administrative remedies" despite receiving a decision on his appeal because "he still must undergo separation proceedings before any permanent adverse consequences are imposed"). The service member has an opportunity to respond before the discharge recommendation goes to the separation authority, and—depending on the type of separation and the service members' time in service—the decision may move to a higher level, and the service member may be entitled to a formal administrative hearing before a decision is made regarding their discharge. Ex. 13 ¶ 10.

Plaintiffs also fail to establish the second prong of hardship from delay. As discussed in more detail below, *see infra* Section II, Plaintiffs will suffer no harm between now and when the Air Force finally decides whether to pursue adverse administrative action against any Plaintiff whose religious accommodation request is finally denied.

2. Plaintiffs Have Failed to Exhaust Their Administrative Remedies.

For similar reasons, Plaintiffs have failed to exhaust available administrative remedies. "The basic purpose of the exhaustion doctrine is to allow an administrative agency to perform functions within its special competence—to make a factual record, to apply its expertise, and to correct its own errors so as to moot judicial controversies." *Parisi v. Davidson*, 405 U.S. 34, 38 (1972). This is especially true in the military context, "given the judiciary's lack of expertise in areas of military judgment and its long-standing policy of non-intervention in internal military affairs." *Heidman v. United States*, 414 F. Supp. 47, 48 (N.D. Ohio 1976) (citing *Schlesinger v. Councilman*, 420 U.S. 738 (1975); *Parker v. Levy*, 417 U.S. 733 (1974); *Gilligan*, 413 U.S. 1); *see also Seepe v. Dep't of the Navy*, 518 F.2d 760, 764 (6th Cir. 1975) (holding that service members failed to exhaust his remedies in regard to discharge, and explaining that exhaustion could not be excused where facts were "entirely service-oriented" and therefore "demanded military expertise"); *Von Hoffburg v. Alexander*, 615 F.2d 633, 637–38 (5th Cir. 1980) ("The strict

application of the exhaustion doctrine in military discharge cases serves to maintain the balance between military authority and the power of federal courts."); *Bois v. Marsh*, 801 F.2d 462, 468 (D.C. Cir. 1986) ("The salutary rule [is] that an aggrieved military officer must first exhaust his administrative remedies . . . prior to litigating his claims in a federal court." (citation omitted)); *Doe v. Ball*, 725 F. Supp. 1210, 1211 (M.D. Fla. 1989) (requiring exhaustion before bringing facial challenge to Navy regulations), *aff'd sub nom. Doe v. Garrett*, 903 F.2d 1455 (11th Cir. 1990). "Evaluating the risks to the health and safety of other soldiers, as well as to the combat readiness of the force, posed by the inclusion of unvaccinated [service members] in the ranks necessarily involves 'complex, subtle, and professional decisions as to the composition, training, equipping, and control of a military force[, which] are essentially professional military judgments.'" Order, *Short*, No. 2:22-cv-01151, Doc. No. 25 at 6 (quoting *Gilligan*, 413 U.S. at 10)).

The Air Force provides Plaintiffs many opportunities to present their arguments and for the Air Force to respond. *See supra* pp. 5–7. Anyone subject to discipline may challenge the lawfulness of the vaccine requirement in those proceedings. *See, e.g.*, *United States v. Kisala*, 64 M.J. 50, 53-55 (C.A.A.F. 2006) (allowing a challenge to the lawfulness of an anthrax vaccination requirement). Yet only four Plaintiffs have completed the appeal process. Pls.' Mem. 2–3, Doc. No. 13, PageID 582–83. Ten Plaintiffs have not even received an initial decision on their requests. *Id*. None have had discharge procedures initiated against them. No Plaintiffs have therefore had opportunity to complete the specialized military administrative procedures granted to them. Plaintiffs seek to have this Court order the Air Force to grant them a religious exemption to the COVID-19 vaccination requirement before the Air Force has fully adjudicated most of those requests. Further, they ask this Court to intrude into the management of the military by forcing

the Air Force to consider Plaintiffs medically qualified for continued service in units eligible for worldwide deployability.

B. Plaintiffs' RFRA Claims Fail Because The Military Has a Compelling Governmental Interest in Maintaining a Medically Fit Force and the Vaccine Requirement is the Least Restrictive Means of Doing So.

The Air Force's conduct with regard to the vaccine directive comports with RFRA—both as applied to Plaintiffs and to "other[s] similarly situated." *See* Pls.' Mem. 10, Doc. No. 13, PageID 590. "Under RFRA, the Federal Government may not . . . substantially burden a person's exercise of religion, 'even if the burden results from a rule of general applicability.'" *Gonzales v. O Centro Espirita Beneficente Uniao do Vegetal*, 546 U.S. 418, 424 (2006) (quoting 42 U.S.C. § 2000bb–1(a)).[12] "The only exception recognized by the statute requires the Government to satisfy the compelling interest test—to 'demonstrat[e] that application of the burden to the person—(1) is in furtherance of a compelling governmental interest; and (2) is the least restrictive means of furthering that compelling governmental interest.'" *Id.* (quoting 42 U.S.C. § 2000bb–1(b)). As the military has found, a uniform vaccination requirement for members in Plaintiffs' positions furthers the compelling governmental interest of military readiness and is the least restrictive means of furthering that interest.

1. The COVID-19 Vaccination Requirement Furthers the Government's Compelling Interest in Military Readiness.

The Supreme Court has held that "[s]temming the spread of COVID–19 is unquestionably a compelling interest." *Roman Cath. Diocese of Brooklyn v. Cuomo*, 141 S. Ct. 63, 67 (2020). Plaintiffs themselves acknowledge, Pls.' Mem. at 10, Doc. No. 13, PageID 590, the Sixth Circuit's

[12] The "substantial burden" in this case is not forcing the Plaintiffs to choose between their religious beliefs and their jobs, but rather the significantly lesser burden related to traveling internationally to receive one of the several vaccines that does not involve fetal cell testing and therefore does not violate Plaintiffs' religious beliefs. *See* Ex. 24 (Letter from SSgt. Adam P. Theriault) ("It is my sincerely held belief that the Novavax vaccine differs from the currently available COVID-19 [vaccines] in the fact that I am aware of no data that directly ties [it] to the practice of abortion . . . .").

recognition of the Government's "compelling interest in preventing the spread of a novel, highly contagious, sometimes fatal virus," *Maryville Baptist Church, Inc. v. Beshear*, 957 F.3d 610, 613 (6th Cir. 2020). This interest is especially compelling in the military context, because "when evaluating whether military needs justify a particular restriction on religiously motivated conduct, courts must give great deference to the professional judgment of military authorities concerning the relative importance of a particular military interest." Order, *Short*, No. 2:22-cv-01151, Doc. No. 25 at 10 (quoting *Goldman v. Weinberger*, 475 U.S. 503, 507 (1986)). Indeed, the Supreme Court has repeatedly emphasized that the government's interest in "maximum efficiency" of military operations is paramount, *cf. United States v. O'Brien*, 391 U.S. 367, 381 (1968), and that "[f]ew interests can be more compelling than a nation's need to ensure its own security," *Wayte v. United States*, 470 U.S. 598, 611 (1985). Although Plaintiffs argue that deference principles do not apply here, *see* Pls.' Mem. 11 n.20, Doc. No. 13, PageID 591, Congress expressly intended for courts to apply long-standing principles of military deference under RFRA, *see* S. Rep. No. 103-111, 12 ("The courts have always recognized the compelling nature of the military's interest in [good order, discipline, and security] in the regulations of our armed services [and] have always extended to military authorities significant deference in effectuating these interests. The committee intends and expects that such deference will continue under this bill.").

Here, after consulting with "medical experts and military leadership," Ex. 2, including the "Chairman of the Joint Chiefs of Staff, the Secretaries of the Military Departments, [and] the Service Chiefs," and considering the rise in infection rates due to the Delta variant, Ex. 1, the Secretary of Defense "determined that mandatory vaccination against [COVID-19] is necessary to protect the Force and defend the American people," Ex. 2 ("To defend this Nation, we need a healthy and ready Force"). The Secretary of the Air Force likewise found that COVID-19

vaccination of each service member is necessary to ensure military readiness and the health and safety of airmen. Ex. 7 at 1. The Court must "give great deference" to the "professional military judgments" of these leaders when it comes to what is needed to ensure military readiness and the welfare of service members.[13] *See Winter*, 555 U.S. at 24–25; *Goldman*, 475 U.S. at 507. And "when executive officials 'undertake to act in areas fraught with medical and scientific uncertainties' their judgments 'should not be subject to second-guessing by an unelected federal judiciary, which lacks the background, competence, and expertise to assess public health.'" Order, *Short*, No. 2:22-cv-01151, Doc. No. 25 at 7 (quoting *S. Bay United Pentecostal Church v. Newsom*, 140 S. Ct. 1613, 1613–14 (2020) (Roberts, C.J., concurring)).

These professional military judgments are supported by the evidence showing COVID-19's harmful impact on the military. *See Church*, 2021 WL 5179215, at *18 (requiring vaccination is "supported by a lengthy record replete with data demonstrating the necessity of a general vaccine mandate"). COVID-19 has "impacted exercises, deployments, redeployments, and other global force management activities," Ex. 10 ¶ 6; caused the cancellation of "19 major training events, many of which involved preparedness and readiness training with our foreign partners," *id.* ¶ 9; and "required significant operational oversight" by the most senior military leaders, *id.* ¶ 4. Further, vaccination requirements of other nations restrict the ability of unvaccinated service members to participate in joint training exercises, which are "vital to the preservation of national security and the protection of our foreign interests." *Id.* ¶¶ 10–11. And because health care providers have had to care for COVID-19 patients, certain service members have not been able to "address non-emergency conditions and undergo routine medical and health assessments that are

[13] In finding that the Navy had no compelling interest in vaccinating the 35 Navy SEALs and members of the Navy's Special Warfare Community, the court in *Navy SEALs 1–26* ignored Supreme Court precedent such as *Goldman*, 475 U.S. at 507, and *Winter*, 555 U.S. at 24–25, and failed to consider either the Secretary of Defense's or the Secretary of the Navy's determinations that vaccination is necessary for military readiness, or the declarations from military leaders concerning the military's interest in vaccination. *See Navy SEALs 1–26*, 2022 WL 34443, at *9–11.

required under military directives to maintain medical readiness." *Id.* ¶¶ 12–13.

Vaccinations have promoted readiness by reducing the risk of infections, hospitalizations, and deaths of service members. *Id.* ¶ 20. Since the onset of the COVID-19 pandemic, hundreds of thousands of service members have been infected, thousands have been hospitalized, and 94 have died. *Id.* ¶ 3. None of the service members who died had both doses of an mRNA vaccine. *See id.* In addition, "[b]etween July and November of 2021, non-fully-vaccinated active-duty service members had a 14.6-fold increased risk of being hospitalized when compared to fully vaccinated active-duty service members," "[i]n December 2021 unvaccinated adults were 16-times more likely to be hospitalized than vaccinated adults," *id.* ¶ 18, and "the hospitalization rate during Omicron dominance in the unvaccinated active duty population was 65 times higher than the hospitalization rate in those fully vaccinated," Ex. 9 ¶ 39. "Given the tangible protection the vaccines afford service members against infection, serious illness, hospitalization, and death, it is clear that COVID-19 vaccines improve readiness and preserve the DoD's ability to accomplish its mission." Ex. 10 ¶ 20. Not only have vaccinations reduced the risk of infections, hospitalizations, and deaths of service members, they have reduced the number of service members required to quarantine, permitted the military to return to higher levels of occupancy in DoD facilities and hold in-person training, and allowed service members to participate in joint training exercises with countries that have vaccine requirements. *Id.* ¶ 14.

Even the risk of a single Plaintiff going unvaccinated is serious. Unvaccinated individuals have five times the risk of testing positive for COVID-19. Ex 14 ¶ 15. Accordingly, each Plaintiff who refuses to immunize against COVID-19 exponentially increases the rate of transmission in the Services and has a "realistic possibility" of infecting other service members with COVID-19. *Cf. United States v. Christie*, 825 F.3d 1048, 1057 (9th Cir. 2016). Additionally, given the many

thousands of religious objections, DoD would be required to grant exemptions to others similarly situated. Thus the calculus necessarily includes the government's interest in vaccinating not only the 18 Plaintiffs at issue here, but the thousands of others who would subsequently request exemptions. Regardless, Plaintiffs' obligations necessitate vaccination because their duties require close physical contact with other individuals. *See, e.g.*, Ex. 18 ¶¶ 3–7; Ex. 19 ¶¶ 3–10; Ex. 20 ¶¶ 4–9; Ex. 21 ¶¶ 5–9; Ex. 22 ¶¶ 3–7.

Vaccination also furthers the military's interest in having service members ready to "deploy on a few days' notice." *Id.* ¶ 13. Service members must "stay deployment-ready in the event that not only they get individually tasked with a deployment, but in the event the entire [unit] gets activated due to current world events." *Id.*; Ex. 16 (Decl. of Col. James Poel) ¶ 31. The vaccine is necessary for members to stay deployment-ready because a member's illness or an outbreak in a deployed environment "create an unacceptable risk to personnel and substantially increase the risk of mission failure." Ex. 22 ¶ 6. Deployed environments frequently do not have extensive medical facilities, such that a critically ill service member may not receive the same level of care they would receive in the United States and caring for that ill member may take away the unit's medical capacity to treat battle injuries. *Id.* Moreover, because deployments are "by design, minimally manned," "[i]f one service member were to get sick, contract long-COVID, get hospitalized, or die, that section may only have one extra person performing similar duties, leaving little redundancy and backup to support the mission." *Id.* "An outbreak impacting multiple service members could potentially risk support to the mission altogether." *Id.*

Plaintiffs rely on the opinion of Dr. Peter McCullough to argue that the military has no compelling interest in vaccination because "[t]he current vaccinations are not preventing the spread" of the coronavirus. Pls.' Mem. 16, Doc. No. 13, PageID 596. Plaintiffs' reliance on this

putative expert is misplaced for several reasons. First, Dr. McCullough's opinion is exactly the type of "expert testimony" the Supreme Court has dismissed in the military context as "quite beside the point." *Goldman*, 475 U.S. at 509 (explaining that military decisions are "decided by the appropriate military officials" who "are under no constitutional mandate to abandon their considered professional judgment"). The Supreme Court has chastised district courts for "palpably exceed[ing] [their] authority" for "relying on [such] testimony." *Rostker*, 453 U.S. at 81 (explaining that "[i]t is not for this Court" to impose its own calculations "in the context of military preparedness and the exigencies of a future mobilization"). Second, three courts have already rejected Dr. McCullough's opinions concerning COVID-19 vaccines. *See Harris v. Univ. of Mass., Lowell*, ---F. Supp. 3d---, 2021 WL 3848012, at *3 n.5 (D. Mass. Aug. 27, 2021); *Klaassen v. Trs. of Ind. Univ.*, ---F. Supp. 3d---, 2021 WL 3073926, at *28–32 (N.D. Ind. July 18, 2021), *vacated & remanded on mootness grounds*, 24 F.4th 638 (7th Cir. 2022); *United KP Freedom All. v. Kaiser Permanente*, No. 21-cv-07894, 2021 WL 5370951, at *2 (N.D. Cal. Nov. 18, 2021) (finding that, in a case where plaintiffs submitted a declaration by Dr. McCullough (Doc. No. 27-8), "plaintiffs have submitted declarations contesting the safety and efficacy of COVID-19 vaccines . . . , but it appears unlikely that much of this testimony would stand up under Rule 702 of the Federal Rules of Evidence"). Third, the military generally aligns its immunization requirements and eligibility determinations for service members with recommendations from the CDC, Ex. 4 at 3, and the CDC has reviewed studies and found that although vaccinated people "can still become infected and have the potential to spread the virus to others," they do so "at much lower rates than unvaccinated people," CDC, *Science Brief: COVID-19 Vaccines and Vaccination* (updated Sept. 15, 2021), https://perma.cc/KGN4-QRUX. Finally, Plaintiffs ignore that the military has an interest not only in preventing the spread of COVID-19 among its ranks, but also

in ensuring that individual members who do contract COVID-19 do not get seriously ill, hospitalized, or die. *See* Ex. 9 ¶¶ 7–12; Ex. 16 ¶¶ 3–7.

Plaintiffs also rely heavily on the Air Force's granting of medical and administrative exemptions to assert that the Air Force must not have a compelling interest in vaccinating the 18 named Plaintiffs. Pls.' Mem. 5, 12, Doc. No. 13, PageID 585, 592. But the Air Force grants medical exemptions and administrative exemptions only when doing so comports with the Air Force's compelling governmental interest in ensuring service members remain fit for duty. First, medical exemptions are granted when necessary to protect the service members' health. *See Does 1-6 v. Mills*, 16 F.4th 20, 31 (1st Cir. 2021) ("[P]roviding healthcare workers with medically contraindicated vaccines would threaten the health of those workers and thus compromise both their health and their ability to provide care."), *cert. denied*, 2022 WL 515892 (U.S. Feb. 22, 2022); *We the Patriots USA, Inc. v. Hochul*, 17 F.4th 266, 285 (2d Cir. 2021) (explaining that vaccinating a service member "who is known or expected to be injured by the vaccine would harm her health"), *clarifying*, 17 F.4th 368 (2d Cir. 2021); *see also* Ex. 7 at 1; Ex. 16 ¶ 7; Ex. 11 ¶ 13. Medical exemptions are temporary, lasting as short as 30 days or as long as one year depending on the reason for the exemption. Ex. 11 ¶ 6 (noting that there no permanent medical exemptions to the COVID-19 vaccine because new COVID-19 immunizations products may be approved in the future). Thus, for example, a service member may be granted a temporary medical exemption for pregnancy, current COVID-19 infection, or an allergic reaction to a previous dose or a known allergy component of the COVID-19 vaccine. Ex. 11 ¶ 5. The temporary nature of medical exemptions ensures that members with temporary medical conditions get vaccinated once their condition is resolved; or, alternatively, it allows the Air Force to reassess members with contraindications for the vaccine to determine whether a vaccine has been approved with

constituents the member can safely take. Ex. 16 ¶ 7. Moreover, a medical exemption "does not permit the recipient to continue to freely perform any and all duties without" limitation. Ex. 11 ¶ 14. Rather, a service member who receives a medical exemption "may be reassigned and/or likely categorized as non-deployable just as any other unvaccinated person with or without a pending religious accommodation," and "may require an additional medical waiver in order to deploy overseas, go on sea duty, or engage in other special duties or assignments." *Id*.

Similarly, the Air Force grants administrative exemptions to certain service members on terminal leave, separating, or retiring because it "has assessed that its interest in military readiness and mission accomplishment is not served by requiring members to be vaccinated when they are no longer anticipated to return to duty." Ex. 15 ¶ 3; *see also* Ex. 23 ¶ 5 (Decl. of Col. Justin L. Long). The Air Force also grants administrative exemptions for service members actively participating in COVID-19 vaccine clinical trials. Ex. 11 ¶ 17. Participation in a clinical trial does not necessarily mean that the service member is unvaccinated, *id*. ¶ 20, and the exemption is limited temporally to the duration of the trial. *Id*. ¶ 17. It is unknown how many exemptions, if any, have been granted for vaccine trials. *Id*. ¶ 19. The Air Force has assessed that its interest in military readiness and mission accomplishment is best served by allowing some service members to *temporarily* forego vaccination so as to better the vaccine itself.

Thus, contrary to Plaintiffs' allegations, there is no "double standard" for exemption requests indicating that the Secretary of the Air Force ordered the implementation of a vast, discriminatory scheme. Pls.' Mem. 5, Doc. No. 13, PageID 585. Rather, the interest behind granting medical and administrative exemptions is the same interest driving the denial of religious accommodation requests: the need to maintain a medically fit force ready to deploy at a moment's notice. *See* Order, *Short*, No. 2:22-cv-01151, Doc. No. 25 at 12 ("To the extent the [military]

accommodates medical exemptions but not religious ones, that is therefore not a sign of underinclusiveness or discriminatory treatment, but rather is simply a reflection of what is feasible while still maintaining the government's interest"); Transcript of Order, *Dunn*, No. 2:22-cv-00288, Doc. No. 22 at 44 (noting that medical and administrative "exemptions do not undermine the government's interests the way a religious exemption would").

2. Vaccination is the Least Restrictive Means of Furthering the Government's Compelling Interest in Military Readiness.

As other courts have found in non-military settings, a uniform practice of vaccination is the least restrictive means in accomplishing the government's interest in preventing the spread of infectious diseases in the workforce. *See, e.g.*, *Does 1-6 v. Mills*, ---F. Supp. 3d---, 2021 WL 4783626, at *14 (D. Me. Oct. 13, 2021), *aff'd*, 16 F.4th 20 (1st Cir. 2021); *see also F.F. ex rel. Y.F. v. New York*, 65 Misc. 3d 616, 634 (N.Y. Sup. Ct. 2019) (concluding same in schools); *Burwell v. Hobby Lobby Stores, Inc.*, 573 U.S. 682, 733 (2014) (recognizing that vaccines "may be supported by" the government's compelling interest in "the need to combat the spread of infectious diseases"). This reasoning has even greater force in the military setting, where health of service members is paramount to military readiness. *See* Order, *Short*, No. 2:22-cv-01151, Doc. No. 25 at 10 (noting that "deference [to military judgments] is layered on top of the deference that courts must give to expert policymakers on matters involving complex medical or scientific uncertainties"). Indeed, "the acceptable level of risk is a military decision that deserves great deference." Transcript of Order, *Dunn*, No. 22-cv-00288, Doc. No. 22 at 36.

After careful consideration of each of Plaintiffs' respective request for a religious accommodation and their appeals, the Air Force Surgeon General concluded that there are no lesser restrictive means than vaccination of these individual service members to further the military's compelling interests in readiness and ensuring the health and safety of all service members. *See,*

e.g., Ex. 18 ¶ 21 (Decl. of Col. Richard M. Heaslip); Ex. 19 ¶ 16 (Decl. of Col. Donald F. Wren); Ex. 20 ¶ 15 (Decl. of Col. Paul K. Harmer); Ex. 21 ¶ 16 (Decl. of Col. Deedrick L. Reese); Ex. 22 ¶ 9 (Decl. of Lt. Col. Nicholas M. Pulire). None of Plaintiffs' suggested alternatives to vaccination, *see* Pls.' Mem. 6–7, Doc. No. 13, PageID 586–87, are sufficient lesser restrictive means of furthering that interest because they fail to serve the military's compelling interests "equally well" relative to vaccination. *See Burwell*, 573 U.S. at 731 (examining whether alternative served stated interest "equally well").

First, Plaintiffs propose that the Air Force use "[t]emperature checks" and "testing" in lieu of vaccination. Pls.' Mem. 6, Doc. No. 13, PageID 586. Temperature checks can identify only if a member has a fever; they do not detect COVID-19. Ex. 16 ¶ 16. And although "[s]erial testing will curtail the exposure in the unit after the infection is detected," it "is not as effective as preventing the original infection." *Id.* ¶ 20. Indeed, the military experienced multiple COVID-19 outbreaks when it merely required service members to undergo routine testing requirements, rather than requiring vaccination. Ex. 10 ¶¶ 7–8; *see Does 1-6*, 16 F.4th at 33 (noting same was true of Maine). Nor do testing and temperature checks prevent a service member who tests positive from suffering serious health outcomes, such as long COVID, hospitalization, and death. Ex. 16 ¶ 21. Moreover, the "virus can be easily transmitted to others prior to symptom development and therefore may infect significant numbers before being identified." Ex. 9 ¶ 10; Ex. 16 ¶¶ 16–20.

Second, Plaintiffs suggest that the Air Force simply "[p]ermit[] the Plaintiffs to demonstrate they have robust and long-lasting natural immunity" to COVID-19. Pls.' Mem. 6, Doc. No. 13, PageID 586. But DoD policy mandates vaccination in accordance with the CDC's recommendations, Ex. 4, ¶ 1.2, and the CDC currently recommends COVID-19 vaccination for individuals five and over "regardless of a history of symptomatic or asymptomatic [COVID-19]

infection," and "serological testing to assess for prior infection is not recommended for the purpose of vaccine decision-making." CDC, *Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the United States* (last updated Feb. 22, 2022), https://perma.cc/4KTU-6EZX. Indeed, "[c]ontrary to [Plaintiffs'] assertion, there is no 'recognized, long standing, natural immunity' against COVID-19." Ex. 16 ¶ 22; *see also* Ex. 9 ¶ 28 (noting that "[t]he body of evidence for infection-induced immunity is more limited than that for vaccine-induced immunity in terms of the quality of evidence . . . and types of studies"). Individuals who have been infected with the virus have had "diverse or varying immune responses which, when compared to the subsequent response of those receiving the COVID-19 vaccine, are not as reliable or consistent." Ex. 9 ¶ 20; Ex. 16 ¶ 23. "Conversely, the immune response following COVID-19 vaccination is more reliable, consistent, and predictable." Ex. 9 ¶ 20. Furthermore, "[n]umerous immunologic studies have consistently shown that vaccination of individuals who were previously infected enhances their immune response, and growing epidemiologic evidence indicates that vaccination following infection further reduces the risk of subsequent infection, including in the setting of increased circulation of more infectious variants." *Id.*[14] For these reasons, Plaintiffs' assertions that some of them previously had COVID-19 is irrelevant. *See* Pls.' Mem. 5, Doc. No. 13, PageID 585.

Third, Plaintiffs suggest that the Air Force "[p]rovide an exemption" to the COVID-19 vaccination requirement because "vaccination will not guarantee immunity" and service members are permitted to serve and deploy even if they "are not immune to diseases they were vaccinated for." Pls.' Mem. 6–7, Doc. No. 13, PageID 586–87. This is not an alternative to vaccination so

[14] Plaintiffs suggest that if the Air Force truly wanted to protect its airmen, it would "require[e] its airmen to become infected *and* vaccinated to have this robust immunity." Pls.' Mem. 5, Doc. No. 13, PageID 585 (emphasis added). Of course, this would require the Air Force to intentionally spread COVID-19 throughout its units, which is flatly contrary to the Air Force's interest in ensuring service members do not get sick themselves or transmit the virus to others.

much as merely an argument against vaccination in general. Regardless, no vaccines "guarantee immunity"; instead, they are meant to "reduce the risk of infection" and reduce symptoms from possible infection. CDC, *Understanding How Vaccines Work*, https://perma.cc/9H29-DMWM. As discussed above, the military requires vaccination because vaccines are the most effective way of mitigating the risk of service members getting seriously ill, being hospitalized, and dying, or spreading diseases to other members. *See* Ex. 16 ¶¶ 3–6, 31, 38; Ex. 9 ¶¶ 26, 39; *see also* Ex. 8 ¶ 21 (discussing the efficacy of the Pfizer COVID-19 vaccine).

Fourth, Plaintiffs' proposal to "isolat[e]" them "to keep [them] away from those with the disease" is not a feasible option based on Plaintiffs' respective job responsibilities. Pls.' Mem. 7, Doc. No. 13, PageID 587; *see, e.g.*, Ex. 18 ¶¶ 3–10; Ex. 19 ¶¶ 4–7; Ex. 20 ¶¶ 4–9; Ex. 21 ¶¶ 5–9; Ex. 22 ¶¶ 3–7. Nor is it feasible for service members deployed in support of operations.

Fifth, Plaintiffs' proposal that the Air Force reassign them each to a "position and/or Air Force Specialty Code that is available for remote work or telework, and not in contact with other airmen" is also not a viable option. Pls.' Mem. 7, Doc. No. 13, PageID 587. For the Reserve Plaintiffs, "Reserve units have openings based on the needs of the particular mission and unit." Ex. 18 ¶ 15; Ex. 19 ¶ 11. Plaintiffs fail to even allege that any of them qualify for another Air Force occupation as an officer, that such a need or opening exists in their respective unit (or any other unit), that they would be the best fit for any such openings, or that such other positions are available for remote work or telework. *Cf.* Transcript of Order, *Dunn*, No. 22-cv-00288, Doc. No. 22 at 38 (noting that plaintiffs "obviously cannot telework when [they]'re deployed"). Plaintiffs' speculation that they might be qualified for and assigned to some other hypothetical military occupation, which somehow may not entail serving in close proximity to other service members, does not remotely establish that the denial of their RFRA exemption was unlawful. *Cf. Harkness*

v. Sec'y of Navy, 858 F.3d 437, 443 (6th Cir. 2017) ("[C]ourts are generally reluctant to review claims involving military duty assignments."); *Cargill v. Marsh*, 902 F.2d 1006, 1007 (D.C. Cir. 1990) (Courts should not "second-guess the Secretary's decision about how best to allocate military personnel in order to serve the security needs of the Nation." (quoting *Kreis v. Sec'y of Air Force*, 866 F.2d 1508, 1511 (D.C. Cir. 1989))). The court should not accept Plaintiffs' invitation to dictate to the military what career fields its service members should be assigned or to interfere in how the military chooses to allocate its personnel and priorities.

Similarly, Plaintiffs' sixth proposal to place them each in a "non-deployable status and/or assignment to a unit that does not deploy overseas" is not a feasible alternative. Pls.' Mem. 7, Doc. No. 13, PageID 587. Plaintiffs' units "cannot afford to place [them] in a non-deployable status because of the ever-increasing need and dependence on an already short-staffed requirement." Ex. 18 ¶ 15; Ex. 19 ¶ 11. "Having a member non-deployable places a larger burden on the other members within the section, hurts [] overall unit readiness and degrades [the unit's] ability to complete the mission." Ex. 19 ¶ 11; Ex. 18 ¶ 15. If the unit is activated and all the members but the respective Plaintiff deploys, the unit "would be unable to provide the full support required for the deployment, degrading [its] mission capabilities, or would have to maintain an additional person to backfill his position should it deploy, making his position unnecessarily redundant." Ex. 18 ¶ 15; Ex. 19 ¶ 11.

Seventh, Plaintiffs contend that "honorably discharg[ing]" them would be a lesser restrictive means than enforcing the Air Force's vaccination policy. Pls.' Mem. 7, Doc. No. 13, PageID 587. For active-duty Plaintiffs, Air Force policy for a service member who continues to refuse vaccination is to initiate discharge proceedings, which may result in either an honorable or general service characterization. Ex. 13 ¶ 10. As such, the Court should not enjoin the military

from initiating administrative proceedings that could result in the exact outcome Plaintiffs accuse the Air Force of withholding. For reservist Plaintiffs, it is unclear how honorable discharge would reduce the burden on their religious exercise relative to the current Air Force policy of involuntarily reassigning them to the IRR to complete their service obligations. *See id*. Indeed, reassignment to the IRR "is a less significant step than discharge" because it allows members "to remain a part of the Air Force and return to a participating Reserve status should [they] choose to vaccinate on a future date." Ex. 18 ¶ 16; Ex. 19 ¶ 18. Discharging a service member, in contrast, means that the member could not return to a participating reserve status if, for example, vaccines become available that they did not object to taking.

Finally, Plaintiffs contend that the Air Force should grant the "few numbers of religious exemption requests" because there is a "significant level of vaccine compliance within the military." Pls.' Mem. 7, Doc. No. 13, PageID 587. The premise of this "herd immunity" argument is flawed. Although the Air Force has high vaccination rate, its members usually live in and interact with individuals in communities surrounding military bases, which may not have as high of a vaccination rate. Ex. 16 ¶ 28. Indeed, the five Plaintiffs who are reservists, Compl. ¶¶ 17–21, Doc. No. 1, PageID 5–6, work only one weekend per month at their respective Air Force bases, and likely spend the majority of their time in the counties surrounding the base, which may have much lower vaccination rates. Interactions with less-vaccinated populations increases the risk of contracting the disease and spreading it to other members. Ex. 16 ¶ 26. Even if herd immunity had been achieved, it is not as effective as vaccination at protecting a member from infection, spreading the disease, or combatting the disease. *Id*. ¶¶ 28, 32; Ex. 9 ¶ 23. Unvaccinated service members are at an increased risk of infection and may spread the virus (particularly new variants) to other service members, and thus still pose a risk of significant harm to maintaining a healthy

force. Ex. 16 ¶¶ 31–32. For these reasons, the military has not set any benchmark to cease any of its immunization requirements based on herd immunity. *See* Ex. 9 ¶¶ 23–27. The military has determined that maximum vaccination for all of the mandatory ten vaccines minimizes the risk to service members of illness and outbreaks. *See id*. The Court should defer to the military's assessment of the acceptable level of risk. *See Gilligan*, 413 U.S. at 10.

It is also worth noting that more than 10,000 airmen have submitted religious accommodation requests. U.S. Air Force, *DAF processes religious accommodations requests* (Dec. 22, 2021), https://perma.cc/V7KD-ZJHX. Like many of the named Plaintiffs here, many of these service members likely work in deployable units or in close physical contact with other service members for extended periods of time in facilities that are not well-ventilated. Under Plaintiffs' proposed less restrictive alternatives, the Air Force would be forced to allow thousands of unvaccinated service members to serve, risking the spread of disease, hospitalizations, and death within multiple units for both unvaccinated personnel, as well as vaccinated personnel at risk of breakthrough infections. *See* Ex. 16 ¶ 4 ("As the number of unvaccinated people increases, the risk of resurgence of such diseases and their associated morbidity and mortality, increases.").

In sum, the military's vaccine policy is narrowly tailored to serve compelling military interests. The military is best situated to assess whether a specific unvaccinated individual puts the military mission at risk, or whether feasible, less restrictive alternatives are available. *See Orloff v. Willoughby*, 345 U.S. 83, 94 (1953) ("Orderly government requires that the judiciary be as scrupulous not to interfere with legitimate Army matters as the Army must be scrupulous not to intervene in in judicial matters."); *Bryant v. Gates*, 532 F.3d 888, 899 (D.C. Cir. 2008) (Kavanaugh, J., concurring) ("[T]he Supreme Court has indicated" that "military decisions and assessments of morale, discipline, and unit cohesion . . . are well beyond the competence of

judges."). The Air Force has considered whether there are any lesser restrictive means of achieving its interest in military readiness and concluded that there are none. RFRA does not compel the military to adopt a measure that is inferior in the military context to requiring the use of safe and effective vaccines. Therefore, Plaintiffs have not shown a likelihood of success on their RFRA claims to warrant the extraordinary preliminary injunctive relief he seeks.

C. Plaintiffs' First Amendment Claim Is Unlikely to Succeed on the Merits.

Plaintiffs' facial challenge to the Air Force's COVID-19 vaccination requirement under the First Amendment also fails.[15] A regulation will withstand a free exercise challenge under the First Amendment when it is "a generally applicable law that incidentally burdens religious practices." *Roberts v. Neace*, 958 F.3d 409, 413 (6th Cir. 2020). The Supreme Court has emphasized that it "hardly ever strikes down a policy as illegitimate under" such "rational basis scrutiny." *Trump v. Hawaii*, 138 S. Ct. 2392, 2420 (2018). The vaccine requirement is neutral and generally applicable because it applies to all service members. *Cf. Cuomo*, 141 S. Ct. at 67 (finding challenged regulation was not neutral or generally applicable where it limited attendance only at houses of worship but not secular businesses). The vaccine requirement mandate survives rational basis scrutiny because its "terms . . . do not make any reference to religion, and [P]laintiff[s] ha[ve] not claimed . . . that the mandate was implemented with the aim of suppressing religious belief." Transcript of Order, *Dunn*, No. 2:22-cv-00288, Doc. No. 22 at 44; *see also Trump*, 138 S. Ct. at 2420 ("On the few occasions where" the Supreme Court has struck down a law under rational basis scrutiny, "a common thread has been that the laws at issue lack any purpose other than a 'bare . . . desire to harm a politically unpopular group." (quoting *Dep't of*

[15] There is no need for the Court to address Plaintiffs' First Amendment claim separately. If the Government prevails on Plaintiffs' RFRA claim, then the Government would necessary prevail under Plaintiffs' First Amendment claim. Conversely, if Plaintiffs prevail under RFRA, they would necessarily prevail under their First Amendment theory as well. In any event, Plaintiffs' First Amendment claims fail for the same reasons as their RFRA claim, *see supra* Part I.B, and for additional reasons as well.

Agric. v. Moreno, 413 U.S. 528, 534 (1973))). Rather, the vaccine mandate is intended to keep all service members medically fit for service, including ready to immediately deploy as needed.

Contrary to Plaintiffs' assertions, the Air Force's allowance of medical exemptions and administrative exemptions does not trigger strict scrutiny. *See* Pls.' Mem. 12–13, Doc. No. 13, PageID 592–593. Plaintiffs cite *Fulton v. City of Philadelphia*, 141 S. Ct. 1868 (2021), and *Dahl v. Board of Trustees of Western Michigan University*, 15 F.4th 728 (6th Cir. 2021), but neither case is availing. Preliminarily, both cases arose in the civilian context, which does not implicate the longstanding principle that "review of military regulations challenged on First Amendment grounds is far more deferential than constitutional review of similar laws or regulations designed for civilian society." *Goldman*, 475 U.S. at 507. Plaintiffs "cite no authority for [their] proposition that the more free-ranging inquiry [they] propose[] is appropriate in the national security and foreign affairs context." *Trump*, 138 S. Ct. at 2420 n.5. Indeed, "'when it comes to collecting evidence and drawing inferences' on questions of national security, 'the lack of competence on the part of the courts is marked.'" *Id.* at 2419 (citation omitted). "'Any rule of constitutional law that would inhibit the flexibility' of the President 'to respond to changing world conditions should be adopted only with the greatest caution,' and [judicial] inquiry into matters of . . . national security is highly constrained." *Id.* at 2419–20 (citation omitted).

Additionally, Plaintiffs misunderstand the underlying principle of both cases. *Fulton* and *Dahl* are premised on the notion that "[a] law is not generally applicable if it 'invite[s]' the government to consider the particular reasons for a person's conduct by providing 'a mechanism for individualized exemptions.'" *Fulton*, 141 S. Ct. at 1877 (quoting *Emp. Div., Dep't of Hum. Res. of Or. v. Smith*, 494 U.S. 872, 884 (1990)); *see Dahl*, 15 F.4th at 733 (citing *Fulton*, 141 S. Ct. at 1877). But "an exemption is not individualized simply because it contain[s] express

exceptions for objectively defined categories of persons." *303 Creative LLC v. Elenis*, 6 F.4th 1160, 1187 (10th Cir. 2021) (citation omitted), *cert. granted in part*, 2022 WL 515867 (U.S. Feb. 22, 2022); *see also Kane v. De Blasio*, 19 F.4th 152, 165 (2d Cir. 2021) (quoting *We the Patriots USA*, 17 F.4th at 288) (same); *Lighthouse Inst. for Evangelism, Inc. v. City of Long Branch*, 510 F.3d 253, 276 (3d Cir. 2007) (same). It is "not the mere existence of an exemption procedure" that triggers strict scrutiny, but rather the existence of a generalized, discretionary exemption procedure that allows the government to determine that the mere "religious *motivation* of [a requestor's] conduct[] justified the unavailability of an exemption." *Lighthouse Inst. for Evangelism, Inc.*, 510 F.3d at 276. Put another way, in order to trigger strict scrutiny, "there must be some showing that the exemption procedures allow secularly motivated conduct to be favored over religiously motivated conduct." *Kane*, 19 F.4th at 165.

Thus, the single "'good cause' standard" in *Fulton* triggered strict scrutiny because it "'invit[ed]' the government to decide which reasons for not complying with the policy are worthy of solicitude." 141 S. Ct. at 1877, 1879 (citation omitted). Similarly, in *Dahl*, the University considered religious exemptions "on an individual basis," thereby allowing them to discretionarily reject such exemptions merely because they were religious in nature. 15 F.4th at 734. In contrast, here, Plaintiffs make no showing that the religious accommodation procedures allow secularly motivated conduct to be favored over religiously motivated conduct. The mandate applies with equal force to all service members. The only exceptions are for medical exemptions and administrative exemptions—which, as discussed above, are not comparable to religious accommodations because they apply only in the very limited circumstance in which *not* granting an exemption would be actively harmful to the Air Force's interest in maintaining a medically fit force, and in any event may still involve reassignment or categorization as non-deployable as

necessary in order to protect the force. *See* Transcript of Order, *Dunn*, No. 2:22-cv-00288, Doc. No. 22 at 36 ("The fact that the Air Force has granted medical and administrative exemptions does not render the mandate not generally applicable" because "these exemptions do not undermine the government's interests the way a religious exemption would[.]"); Ex. 11 ¶ 14.

Thus, especially given the deference to military judgments in the First Amendment context, the vaccine mandate easily survives rational basis review. Even if strict scrutiny applied, the vaccine mandate still comports with the First Amendment for all the reasons described above. *See supra* Part I.A. Indeed, the Sixth Circuit in *Dahl* expressly recognized that the defendant-University's "interest in fighting COVID-19 is compelling" and that "COVID-19 vaccines are the most effective and reasonable way to guard against the virus." *Dahl*, 15 F.4th at 735. And here, unlike in *Dahl*, Defendants present substantial analysis on their interest in vaccinating the individual Plaintiffs. *See generally* Exs. 18–22; *cf. Dahl*, 15 F.4th at 735 (noting that "[d]efendants present neither evidence nor argument" regarding their interest in denying an exception to the particular plaintiffs at issue).

II. Plaintiffs Do Not Face Irreparable Harm.

Plaintiffs are also not entitled to a preliminary injunction because they fail to show a likelihood of irreparable harm, an "indispensable" requirement for a preliminary injunction. *D.T. v. Sumner Cnty. Schs.*, 942 F.3d 324, 327 (6th Cir. 2019). "To merit a preliminary injunction, an injury must be both certain and immediate, not speculative or theoretical." *Id.* (citation omitted). And "[i]n the context of 'military personnel decisions, . . . courts have held that the showing of irreparable harm must be *especially strong* before an injunction is warranted, given the national security interests weighing against judicial intervention in military affairs.'" *Church*, 2021 WL 5179215, at *17 (quoting *Shaw v. Austin*, 539 F. Supp. 3d 169, 183 (D.D.C. 2021)).

None of Plaintiffs' alleged harms are irreparable. First, Plaintiffs argue that they suffer irreparable harm because their constitutional and statutory rights have been infringed. *See* Pls.' Mem. 9, Doc. No. 13, PageID 589. But, as shown above, Plaintiffs have failed to establish a violation of law—so any infringement is neither "threatened [nor] occurring" and thus cannot establish irreparable harm. *Elrod v. Burns*, 427 U.S. 347, 374 (1976); Order, *Short*, No. 22-cv-01151, Doc. No. 25 at 14 ("[B]ecause this Court has found that Plaintiff failed to demonstrate a sufficient likelihood of success on the merits of his religious freedom claims, there is no presumption of irreparable harm."). Second, Plaintiffs appear to allege that involuntary reassignment to the Individual Ready Reserve and loss of retirement constitutes irreparable harm. *See* Pls.' Mem. 2, 4, Doc. No. 13, PageID 579, 584. But any such contention is meritless, as military administrative and disciplinary actions, including separation, are not *irreparable* injuries because the service member could later be reinstated and provided back pay if he prevailed on his claim. *See, e.g.*, *Hartikka v. United States*, 754 F.2d 1516, 1518 (9th Cir. 1985); *Chilcott v. Orr*, 747 F.2d 29, 34 (1st Cir. 1984); *Guitard v. U.S. Sec'y of Navy*, 967 F.2d 737, 742 (2d Cir. 1992); *Church*, 2021 WL 5179215, at *17. Finally, although Plaintiffs allege that they may be subject to court-martial for non-compliance with the COVID-19 vaccine directive, Pls.' Mem. 6, Doc. No. 13, PageID 586, such action is speculative given the potential range of disciplinary consequences that may be pursued for service members who do not have an exemption (or pending exemption request) and who do not get vaccinated, *see* Ex. 13 ¶¶ 3–14. This is particularly so in light of Air Force policy to reassign reserve members to the IRR and discharge active duty members. Such speculation cannot establish irreparable harm. *See D.T.*, 942 F.3d at 327; *see also Church*, 2021 WL 5179215, at *17. In any event, subjecting a service member to court-martial proceedings does not constitute an irreparable injury. *See Schlesinger*, 420 U.S. at 755.

III. The Equities and the Public Interest Weigh Against a Preliminary Injunction.

The third and fourth requirements for issuance of a preliminary injunction—the balance of harms and whether the requested injunction will disserve the public interest—"merge when the Government is the opposing party." *Nken v. Holder*, 556 U.S. 418, 435 (2009). These factors tilt decisively against granting a preliminary injunction here.

The public has an exceptionally strong interest in national defense, *see Winter*, 555 U.S. 7, and, for all of the reasons explained above, the military has a compelling interest in requiring its fighting forces to be vaccinated, healthy, and ready to deploy. An injunction that allows Plaintiffs to serve in a military setting without being vaccinated against COVID-19 would, as detailed above, threaten harm to each Plaintiff and to other service members serving alongside them in the execution of their job duties, in training facilities, or on deployment, and would risk accomplishment of each Plaintiffs' respective unit's mission. *See supra* Part I.A; *see also* Ex. 9 ¶ 10; Ex. 10 ¶¶ 16–20; Ex. 19 ¶¶ 6, 8; Ex. 20 ¶¶ 4–5. Such an injunction also would encourage other members with exemption requests to attempt to bypass the military's process and ask courts to enter similar injunctive relief, which "'in the aggregate' present the possibility of substantial disruption and diversion of military resources" and is contrary to the public interest. *Parrish v. Brownlee*, 335 F. Supp. 2d 661, 669 (E.D.N.C. 2004) (citation omitted).

Plaintiffs request that the Court not only grant their own respective exemption requests prematurely or retrospectively, but that the Court grant all other religious exemption requests, direct the Air Force to rescind any adverse or disciplinary action (including discharges) against airmen whose requests were denied, and monitor the Air Force's processing of exemption requests for non-parties. *See* Pls.' Mem. 18–19, Doc. No. 13, PageID 598–99; Proposed Order, Doc. No. 13-5, PageID 812–13. Particularly in a military setting, enjoining vaccination requirements would

harm the public interest (and the national security interests of the United States), as vaccination is necessary to protect the health of individual service members and curb transmission of COVID-19 among service members to ensure the military is ready to "defend this Nation." Ex. 2; *see also* Ex. 7; *Oklahoma*, 2021 WL 6126230, at *14; *Church*, 2021 WL 5179215, at *18–19. Moreover, the military has clear discretion to handle matters of good order and discipline—which includes compliance with lawfully issued orders—without interference from the Judiciary. *Chappell v Wallace*, 462 U.S. 296 300–01 (1983); *Church*, 2021 WL 5179215, at *18. An injunction granting all religious exemption requests, rescinding all adverse action or discipline taken against those who have refused vaccination after their exemption requests were denied, and monitoring the Air Force's processing of exemptions, "would be a disruptive force as to affairs peculiarly within the jurisdiction of the military authorities," *Orloff*, 345 U.S. at 95, and contrary to the public interest, *see Chilcott*, 747 F.2d at 33 (noting the "strong judicial policy against interfering with the internal affairs of the armed forces"); *Shaw*, 539 F. Supp. 3d at 184 (same); *Reinhard v. Johnson*, 209 F. Supp. 3d 207, 221 (D.D.C. 2016) (same).

IV. Any Relief Should Be Narrowly Tailored.

Even if the Court were to disagree with Defendants' arguments, the law is clear that any injunctive relief should be no broader than necessary to provide relief to the plaintiffs before the Court. "A plaintiff's remedy must be tailored to redress the plaintiff's particular injury." *Gill v. Whitford*, 138 S. Ct. 1916, 1934 (2018); *see also Trump*, 138 S. Ct. at 2425 (Thomas, J., concurring) (explaining the harm of nationwide injunctions). "Narrower injunctive relief is especially appropriate here considering the deference given to military authorities concerning the importance of a particular military interest, the significant public interest in ensuring a strong national defense, and the potential for a wide array of bases for a religious accommodation

request." *Poffenbarger*, 2022 WL 594810, at *20 (citing *Winter*, 555 U.S. at 25).

Here, Plaintiffs request a nationwide, Air Force–wide injunction. But "[j]udges are not given the task of running the [military]." *Chappell*, 462 U.S. at 301; *Larsen v. U.S. Navy*, 486 F. Supp. 2d 11, 36 (D.D.C. 2007) (declining to consider relief that would "assign the Court the role of monitoring [the Navy's chaplaincy program]"). Plaintiffs' reliance on *Califano v. Yamasake*, 442 U.S. 682, 702 (1979), to seek military-wide relief is misplaced. *See* Pls.' Mem. 18, Doc. No. 13, PageID 598. There, the Supreme Court determined that class certification of a nationwide class was permissible—here, however, "[t]his Court has not determined that class certification—of a nationwide class or otherwise—is appropriate." *Poffenbarger*, 2022 WL 594810, at *20 (rejecting plaintiff's reliance on *Califano*). The programmatic relief Plaintiffs seeks for all airmen would regulate the Air Force's day-to-day procedures for making personnel and assignment decisions intended to protect the health of the force. Such universal or class-wide injunctive relief would be clearly improper, even if the Court determined that Plaintiffs were entitled to some individual relief at this stage. *See, e.g.*, *id.* ("[T]he Court will only enter a relatively limited preliminary injunction and one that only applies to [the plaintiff.]").

Far from being tailored to address their own purported injuries, Plaintiffs' request—that the Court grant thousands of religious exemption requests, order the Air Force to rescind disciplinary actions for other airmen, and impose judicial supervision over the Air Force's exemption process—is wholly improper and must be rejected, along with any individual injunctive relief for the Plaintiffs themselves.

CONCLUSION

For the foregoing reasons, the Court should deny Plaintiffs' motion for a preliminary injunction.

Dated: March 8, 2022

Respectfully submitted,

BRIAN M. BOYNTON
Principal Deputy Assistant Attorney General
Civil Division

ALEXANDER K. HAAS
Director, Federal Programs Branch

ANTHONY J. COPPOLINO
Deputy Branch Director
Federal Programs Branch

/s/ Cassandra Snyder
ANDREW E. CARMICHAEL
AMY E. POWELL
Senior Trial Counsel
STUART J. ROBINSON
Senior Counsel
ZACHARY A. AVALLONE
COURTNEY D. ENLOW
LIAM HOLLAND
CATHERINE YANG
CASSANDRA SNYDER
Trial Attorneys
Department of Justice, Federal Programs Branch
1100 L Street, N.W., Washington, DC 20005
Tel: (202) 451-7729
Email: cassandra.m.snyder@usdoj.gov

Attorneys for Defendants

CERTIFICATE OF SERVICE

I hereby certify that on March 8, 2022, I electronically filed the foregoing paper with the Clerk of Court using this Court's CM/Doc. system, which will notify all counsel of record of such filing.

/s/ Cassandra Snyder
CASSANDRA M. SNYDER
Trial Attorney
United States Department of Justice
Civil Division, Federal Programs Branch
1100 L Street, N.W.
Washington, DC 20005
Tel: (202) 451-7729
Fax: (202) 616-8460
Email: cassandra.m.snyder@usdoj.gov

Table of Exhibits

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1.	Secretary of Defense Message to the Force (Aug. 9, 2021)
2.	Secretary of Defense Memorandum For Senior Pentagon Leadership, Commanders of the Combatant Commands, Defense Agency and DoD Field Activity Directors (Aug. 24, 2021)
3.	Congressional Research Service, Defense Health Primer: Military Vaccinations
4.	Department of Defense Instruction ("DoDI") 6205.02
5.	Air Force Instruction ("AFI") 48-110_IP
6.	Secretary of the Air Force Memorandum for Department of the Air Force Commanders (Sept. 3, 2021)
7.	Secretary of the Air Force Memorandum for ALMAJCOM-FLDCOM-FOA-DRU/CC (Dec. 7, 2021)
8.	Declaration of Peter Marks (filed in *Robert v. Austin*, 21-cv-02228 (D. Colo.))
9.	Declaration of Colonel Tonya Rans
10.	Declaration of Major Scott Stanley
11.	Declaration of Colonel Artemio C. Chapa
12.	Declaration of Major Matthew J. Streett
13.	Declaration of Colonel Elizabeth M. Hernandez
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16.	Declaration of Colonel James R. Poel
17.	Declaration of Colonel Ashley Heyen
18.	Declaration of Colonel Richard M. Heaslip
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21.	Declaration of Colonel Deedrick L. Reese
22.	Declaration of Lieutenant Colonel Nicholas M. Pulire
23.	Declaration of Lieutenant Colonel Justin L. Long
24.	Letter from SSgt. Adam P. Theriault

Exhibit 1

SECRETARY OF DEFENSE
1000 DEFENSE PENTAGON
WASHINGTON, DC 20301-1000

AUG 09 2021

MEMORANDUM FOR ALL DEPARTMENT OF DEFENSE EMPLOYEES

SUBJECT: Message to the Force

As many of you know, President Biden asked me to consider how and when we might add the coronavirus disease 2019 (COVID-19) vaccines to the list of those required for all Service members. So, over the last week, I have consulted closely with the Chairman of the Joint Chiefs of Staff, the Secretaries of the Military Departments, the Service Chiefs, and medical professionals. I appreciate greatly the advice and counsel they provided.

Based on these consultations and on additional discussions with leaders of the White House COVID Task Force, I want you to know that I will seek the President's approval to make the vaccines mandatory no later than mid-September, or immediately upon the U.S. Food and Drug Agency (FDA) licensure, whichever comes first.

By way of expectation, public reporting suggests the Pfizer-BioNTech vaccine could achieve full FDA licensure early next month.

The intervening few weeks will be spent preparing for this transition. I have every confidence that Service leadership and your commanders will implement this new vaccination program with professionalism, skill, and compassion. We will have more to say about this as implementation plans are fully developed.

In the meantime, we will comply with the President's direction regarding additional restrictions and requirements for unvaccinated Federal personnel. Those requirements apply to those of you in uniform as well as our civilian and contractor personnel.

We will also be keeping a close eye on infection rates — which are on the rise now due to the Delta variant — and the impact these rates might have on our readiness. I will not hesitate to act sooner or recommend a different course to the President if I feel the need to do so.

To defend this Nation, we need a healthy and ready force. I strongly encourage all DoD military and civilian personnel — as well as contractor personnel — to get vaccinated now and for military Service members to not wait for the mandate.

All FDA-authorized COVID-19 vaccines are safe and highly effective. They will protect you and your family. They will protect your unit, your ship, and your co-workers. And they will ensure we remain the most lethal and ready force in the world.

Get the shot. Stay healthy. Stay ready.

Lloyd J. Austin

Exhibit 2

SECRETARY OF DEFENSE
1000 DEFENSE PENTAGON
WASHINGTON, DC 20301-1000

AUG 24 2021

MEMORANDUM FOR SENIOR PENTAGON LEADERSHIP
COMMANDERS OF THE COMBATANT COMMANDS
DEFENSE AGENCY AND DOD FIELD ACTIVITY DIRECTORS

SUBJECT: Mandatory Coronavirus Disease 2019 Vaccination of Department of Defense Service Members

To defend this Nation, we need a healthy and ready force. After careful consultation with medical experts and military leadership, and with the support of the President, I have determined that mandatory vaccination against coronavirus disease 2019 (COVID-19) is necessary to protect the Force and defend the American people.

Mandatory vaccinations are familiar to all of our Service members, and mission-critical inoculation is almost as old as the U.S. military itself. Our administration of safe, effective COVID-19 vaccines has produced admirable results to date, and I know the Department of Defense will come together to finish the job, with urgency, professionalism, and compassion.

I therefore direct the Secretaries of the Military Departments to immediately begin full vaccination of all members of the Armed Forces under DoD authority on active duty or in the Ready Reserve, including the National Guard, who are not fully vaccinated against COVID-19.

Service members are considered fully vaccinated two weeks after completing the second dose of a two-dose COVID-19 vaccine or two weeks after receiving a single dose of a one-dose vaccine. Those with previous COVID-19 infection are not considered fully vaccinated.

Mandatory vaccination against COVID-19 will only use COVID-19 vaccines that receive full licensure from the Food and Drug Administration (FDA), in accordance with FDA-approved labeling and guidance. Service members voluntarily immunized with a COVID-19 vaccine under FDA Emergency Use Authorization or World Health Organization Emergency Use Listing in accordance with applicable dose requirements prior to, or after, the establishment of this policy are considered fully vaccinated. Service members who are actively participating in COVID-19 clinical trials are exempted from mandatory vaccination against COVID-19 until the trial is complete in order to avoid invalidating such clinical trial results.

Mandatory vaccination requirements will be implemented consistent with DoD Instruction 6205.02, "DoD Immunization Program," July 23, 2019. The Military Departments should use existing policies and procedures to manage mandatory vaccination of Service members to the extent practicable. Mandatory vaccination of Service members will be subject to any identified contraindications and any administrative or other exemptions established in Military Department policy. The Military Departments may promulgate appropriate guidance to carry out the requirements set out above. The Under Secretary of Defense for Personnel and

Readiness may provide additional guidance to implement and comply with FDA requirements or Centers for Disease Control and Prevention recommendations.

The Secretaries of the Military Departments should impose ambitious timelines for implementation. Military Departments will report regularly on vaccination completion using established systems for other mandatory vaccine reporting.

Our vaccination of the Force will save lives. Thank you for your focus on this critical mission.

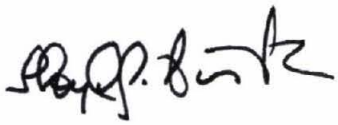

Exhibit 3

Congressional Research Service
Informing the legislative debate since 1914

IN FOCUS

Updated August 6, 2021

Defense Health Primer: Military Vaccinations

The Department of Defense (DOD) administers a variety of force health protection (FHP) measures to "promote, protect, improve, conserve, and restore" the health and well-being of servicemembers. These measures include health promotion and education programs, periodic health assessments, preventive therapies, medical countermeasures, and vaccinations. The U.S. military instituted its first vaccination program in 1777 when General George Washington directed the inoculation of the Continental Army to protect personnel from smallpox. Since then, DOD has implemented a variety of enduring or situational FHP measures to protect servicemembers from health threats. Certain vaccines are required for all servicemembers, while others may only be required for those deploying to particular locations. Other vaccines may be available based on public health recommendations or on a voluntary basis.

Since at least the late 1990s, Congress has expressed interest in DOD vaccination policies, specifically those on compulsory vaccinations. Similar interest among certain Members of Congress has arisen as DOD administers the Coronavirus Disease 2019 (COVID-19) vaccine to servicemembers on a voluntary basis. This In Focus describes DOD's military vaccination policies and immunization program, and offers issues for congressional consideration.

DOD Policies on Military Vaccinations

DOD Instruction 6205.02 establishes the DOD Immunization Program. The policy generally directs combatant commands and the military departments (MILDEPs) to identify and define "mandatory immunization requirements" for servicemembers. The *Joint Regulation on Immunization and Chemoprophylaxis for the Prevention of Infectious Diseases* outlines specific vaccination requirements for servicemembers, as well as service-specific procedures for administering such requirements. In general, DOD vaccination requirements follow the recommendations of the U.S. Centers for Disease Control and Prevention (CDC) and the Advisory Committee on Immunization Practices (ACIP). DOD vaccination requirements fall into one of three categories:

- vaccinations during initial entry or basic training;
- routine adult vaccinations; and
- special risk-based, or occupation-specific vaccinations.

Table 1 lists the mandatory vaccinations required for all servicemembers upon entering initial entry or basic training. In addition to these vaccinations, combatant commands establish further requirements for servicemembers, other DOD personnel, and certain family members, based on specific health threats in a geographic region.

Table 1. Mandatory Vaccinations for All Servicemembers

Adenovirus	Meningococcal
Hepatitis A & B	Poliovirus
Influenza	Tetanus-Diphtheria
Measles/Mumps/Rubella	Varicella

Source: Joint Service Regulation on Immunizations and Chemoprophylaxis for the Prevention of Infectious Diseases, October 7, 2013, p. 29.

DOD Immunization Program

The Defense Health Agency (DHA) manages the DOD Immunization Program. Based on the MILDEPs' and combatant commands' vaccination requirements, as well as CDC and ACIP recommendations, DHA coordinates the administration of vaccines to servicemembers and other DOD beneficiaries. Vaccinations are typically available in military treatment facilities, certain military-specific settings (e.g., basic training), or from participating TRICARE providers. DHA is also responsible for relevant medical documentation, patient safety surveillance, and coordination with the Defense Logistics Agency and commercial manufacturers to procure such vaccines. DOD health care providers typically document servicemember vaccinations and any related adverse health events in the electronic health record system (e.g., MHS Genesis), paper medical records, and the respective MILDEPs' medical readiness information system.

Opting Out of a Vaccination

A servicemember may request to opt out of a mandatory vaccination. Upon request by a servicemember, DOD may authorize a temporary or permanent medical or administrative exemption to a required vaccine. DOD health care providers may authorize a *medical exemption* when a servicemember has an underlying health condition or known adverse reaction contraindicated with a certain vaccine. Unit commanders may authorize an *administrative exemption* for a servicemember who is within 180 days from separating or retiring from the military or within 30 days of departing a permanent assignment location. Pursuant to the Religious Freedom Restoration Act (42 U.S.C. §2000bb-1), administrative exemptions for religious reasons may also be granted. DOD policy requires that:

- the unit commander seek input from medical, legal, and chaplain representatives;
- the unit commander counsel the servicemember on potential adverse impact to "deployability, assignment, or international travel"; and
- a military physician counsel the servicemember on the benefits and risks of forgoing a required vaccination.

Unit commanders may revoke a religious exemption "if the individual and/or unit are at imminent risk of exposure to a disease for which an immunization is available." Commanders may also administratively separate, or initiate disciplinary proceedings under the Uniform Code of Military Justice, servicemembers without an authorized exemption, if they are non-compliant with a mandatory vaccination.

Authority to Waive Informed Consent

DOD Instruction 6205.02 directs the "preferential use of immunizations approved by the U.S. Food and Drug Administration" (FDA); however, non-FDA approved drugs, biologics (e.g., vaccines), or medical products may be administered for FHP purposes. DOD may administer an "investigational new drug" or "drug unapproved for its applied use" to servicemembers after obtaining *prior consent* (also referred to as *informed consent*). Under 21 U.S.C. §355(i)(4) and related regulations, the informed consent process typically requires human subjects to agree to the receipt of drug, biologic, or medical product upon a disclosure that the product in question is not yet FDA approved and that the receipt of such product is voluntary.

In certain instances, DOD may request a waiver to statutory and regulatory informed consent requirements in order make an investigational drug, biologic, or medical product mandatory for servicemembers participating "in a particular military operation." Section 1107 of Title 10, U.S. Code:

- authorizes the Secretary of Defense to request a waiver;
- assigns approval authority to the President of the United States; and
- if a waiver is approved, directs a congressional notification process.

If a waiver of informed consent is approved, the statute also requires DOD, prior to administering the investigational product, to notify servicemembers that a non-FDA approved product is being administered, the reasoning for such use, information on known side effects, and other information that the "Secretary of Health and Human Services may require to be disclosed." For products subject to emergency use authority (EUA), as is the case for several COVID-19 vaccines, Section 1107a of Title 10, U.S. Code grants the President the authority to waive certain EUA conditions "designed to ensure that individuals are informed of an option to accept or refuse administration" of the product.

A waiver of informed consent does not abrogate the *Feres* doctrine. If a servicemember is harmed from an administered drug, biologic, or medical product, *Feres* generally prohibits active duty servicemembers from filing medical malpractice lawsuits against the United States. However, servicemembers may seek alternative recourse through a DOD administrative process, the National Vaccine Injury Compensation Program, the Countermeasures Injury Compensation Program, or disability compensation administered by the Department of Veterans Affairs.

Issues for Congress

The following lines of inquiry may assist Congress in obtaining further clarification on the administration of compulsory vaccinations and may support congressional oversight of the DOD Immunization Program.

Program Administration

- Are the MILDEPs receiving adequate support from DHA to meet their medical readiness requirements?
- How do DOD and CDC share pertinent health information documented in the Vaccine Adverse Event Reporting System?
- What health communication strategies are used to educate or solicit feedback from servicemembers on DOD's vaccination or other FHP requirements?

Military Readiness

- Does DOD have adequate authorities and processes in place to protect the health and well-being of servicemembers and other DOD personnel conducting the full range of military operations?
- What were the lessons learned from the Anthrax Vaccine Immunization Program and how were those lessons used to improve the DOD Immunization Program?

COVID-19 Vaccinations

- What is DOD's long-term strategy to mitigate risks from COVID-19 and of future pandemics?
- Will DOD's COVID-19 mitigation strategy require compulsory vaccination of servicemembers? Is DOD considering requesting a waiver of informed consent for the COVID-19 vaccine?

Relevant Statutes and Policies

10 U.S.C. §1107 – Notice of use of an investigational new drug or a drug unapproved for its applied use

10 U.S.C. §1107a – Emergency use products

21 U.S.C. §355 – New drugs

DOD Directive 6200.04 – *Force Health Protection (FHP)*

DOD Instruction 6200.02 – *Application of Food and Drug Administration Rules to Department of Defense Force Health Protection Programs*

DOD Instruction 6205.02 – *DoD Immunization Program*

Joint Service Regulation on Immunizations and Chemoprophylaxis for the Prevention of Infectious Diseases

CRS Products

CRS In Focus IF10530, *Defense Primer: Military Health System*, by Bryce H. P. Mendez

CRS Report R46745, *State and Federal Authority to Mandate COVID-19 Vaccination*, by Wen W. Shen

CRS In Focus IF11102, *Military Medical Malpractice and the Feres Doctrine*, by Bryce H. P. Mendez and Kevin M. Lewis

CRS Legal Sidebar LSB10584, *Compensation Programs for Potential COVID-19 Vaccine Injuries*, by Kevin J. Hickey and Erin H. Ward

CRS In Focus IF10745, *Emergency Use Authorization and FDA's Related Authorities*, by Agata Bodie

Bryce H. P. Mendez, Analyst in Defense Health Care Policy

IF11816

Disclaimer

Exhibit 4

DoD Instruction 6205.02

DoD Immunization Program

Originating Component:	Office of the Under Secretary of Defense for Personnel and Readiness
Effective:	July 23, 2019
Releasability:	Cleared for public release. Available on the Directives Division Website at https://www.esd.whs.mil/DD
Incorporates and Cancels:	DoD Directive 6205.02E, "Policy and Program for Immunizations to Protect the Health of Service Members and Military Beneficiaries," September 19, 2006 DoD Directive 6205.3, "DoD Immunization Program for Biological Warfare Defense," November 26, 1993 DoD Instruction 6205.4, "Immunization of Other Than U.S. Forces (OTUSF) for Biological Warfare Defense," April 14, 2000
Approved by:	James N. Stewart, Assistant Secretary of Defense for Manpower and Readiness, Performing the Duties of the Under Secretary of Defense for Personnel and Readiness

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Purpose: In accordance with the authority in DoD Directive (DoDD) 5124.02, this issuance:

- Establishes policy, assigns responsibilities, and provides procedures to establish a uniform DoD immunization program, in accordance with the authority in DoDD 6200.04 and DoD Instruction (DoDI) 1010.10.
- Reflects the cancellation of the Secretary of the Army as the DoD Executive Agent for the DoD Immunization Program, including the functions of the former Military Vaccine Agency, in accordance with the July 9, 2014 Deputy Secretary of Defense Memorandum.

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SECTION 1: GENERAL ISSUANCE INFORMATION

1.1. APPLICABILITY. This issuance applies to:

a. OSD, the Military Departments (including the Coast Guard at all times, including when it is a Service in the Department of Homeland Security by agreement with that Department), the Office of the Chairman of the Joint Chiefs of Staff (CJCS) and the Joint Staff, the Combatant Commands (CCMDs), the Office of the Inspector General of the Department of Defense, the Defense Agencies, the DoD Field Activities, and all other organizational entities within the DoD (referred to collectively in this issuance as the "DoD Components").

b. DoD Immunization Program support to other than U.S. forces (OTUSF) in regions designated as high-threat by the CJCS in consultation with the geographic Combatant Commanders (CCDRs) and the Director, Defense Intelligence Agency.

1.2. POLICY. It is DoD policy that:

a. All DoD personnel and other beneficiaries required or eligible to receive immunizations will be offered immunizations in accordance with recommendations from the Centers for Disease Control and Prevention and its Advisory Committee on Immunization Practices.

b. All health-care personnel (HCP) working in DoD medical treatment facilities are required to receive the annual seasonal influenza immunization or obtain an exemption (i.e., medical or administrative). During an outbreak, pandemic influenza immunizations will be required or recommended for HCP, as appropriate, depending on the immunization's regulatory status at the time of the outbreak. Pandemic influenza immunization is an additional requirement or recommendation during an outbreak, regardless of seasonal influenza immunization status.

(1) The Military Health System (MHS) will provide influenza vaccines for DoD employees and volunteers who are eligible for medical care in the MHS and for OTUSF as approved or directed by the Secretary of Defense.

(2) For HCP working under contract to any DoD Component, seasonal influenza immunizations may be provided by the DoD medical treatment facilities, if stated in the contract agreement. Otherwise, contracting companies will provide influenza vaccines to their employees.

c. All Active Duty and Selected Reserve (including National Guard) personnel are required to receive the annual seasonal influenza immunization or obtain an exemption (i.e., medical or administrative), with a goal of 90 percent immunized by January 15th of each year. During an outbreak, pandemic influenza immunizations will be required or recommended as appropriate, depending on the immunization's regulatory status at the time of the outbreak.

d. As part of the total force, DoD civilian employees are highly encouraged to receive the annual seasonal influenza vaccine.

e. Designated at-risk individuals among the total force and other eligible beneficiaries will be provided the best available immunizations against biological hazards; infectious diseases of military or national importance; and other health threats.

(1) The DoD Components will make preferential use of immunizations approved by the U.S. Food and Drug Administration (FDA) and, when applicable, recommended by the Advisory Committee on Immunization Practices for their intended use, when available, to provide the needed medical protection.

(2) Under certain circumstances, the DoD may administer medical products for force health protection purposes that are not FDA-approved, or not approved for the particular use involved, in accordance with DoDI 6200.02.

(3) Smallpox and anthrax immunizations, when used as a force health protection measure, are restricted to DoD personnel or groups identified by the Office of the Secretary of Defense, in consultation with the CJCS, the Under Secretary of Defense for Intelligence, and the geographic CCDRs. This identification is based on information received from the CJCS, in consultation with the DoD Components.

(4) When there is a threatened or actual use of biological warfare agents, or naturally occurring infectious diseases of military or national significance, geographic CCDRs, in consultation with the CJCS, will recommend to the Secretary of Defense immunization requirements for OTUSF category 1-3 personnel. Coordination with the Secretary of State is required before providing immunization to OTUSF category 4 personnel.

SECTION 2: RESPONSIBILITIES

2.1. ASD(HA). Under the authority, direction, and control of the Under Secretary of Defense for Personnel and Readiness (USD(P&R)), and in accordance with DoDD 5136.01, the ASD(HA):

a. Serves as the principal advisor to the Secretary of Defense and the USD(P&R) for all DoD health policies, programs, and force health protection activities.

b. Oversees the DoD Immunization Program and addresses requests from the DoD Component heads for changes to guidance or exceptions via the procedures in Section 3.

c. In coordination with the Under Secretary of Defense for Policy (USD(P)) and the General Counsel of the Department of Defense, recommends the initiation, modification, or termination of immunizations for deliberately released biological agents or naturally occurring infectious diseases of military or national importance beyond CCMD-defined requirements and associated Service-specific implementation plans to the Secretary of Defense. Depending on the scope of the intended changes to immunization activities against such health threats, and in coordination with the Office of the General Counsel of the Department of Defense, the ASD(HA) may recommend the approval be made by the USD(P&R) or the Secretary of Defense.

2.2. DEPUTY ASSISTANT SECRETARY OF DEFENSE FOR HEALTH READINESS POLICY AND OVERSIGHT (DASD(HRP&O)). Under the authority, direction, and control of the ASD(HA), the DASD(HRP&O):

a. Identifies the military-unique clinical needs for immunization-related medical products against deliberately released biological agents and naturally occurring infectious disease threats that impact force health protection, in coordination with the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs (ASD(NCB)), in accordance with DoDD 6200.04 and DoDD 5160.05E.

b. Reviews, evaluates, and provides policy and execution management oversight of the DoD Immunization Program.

c. Serves as the DoD representative for interagency efforts related to immunization policy.

d. Develops, in collaboration with the Secretaries of the Military Departments; the Commandant, U.S. Coast Guard (USCG); the CJCS; and the Director, Defense Health Agency (DHA), operational use guidance that reflects mandatory immunization requirements and availability of immunizations against deliberately released biological agents and naturally occurring infectious diseases of military or national importance.

2.3. DIRECTOR, DHA. Under the authority, direction, and control of the USD(P&R), through the ASD(HA), and in accordance with DoDD 5136.13, the Director, DHA:

a. Serves as the manager for the DoD Immunization Program.

(1) Develops standardized clinical and implementation guidance for the DoD Immunization Program.

(2) Publishes procedural instructions necessary to implement the DoD Immunization Program.

b. Synchronizes, integrates, and coordinates immunization policies and guidelines for the DoD Components, including applicable DoD civilian personnel and eligible health care beneficiaries.

c. Oversees DoD Components' post-immunization patient safety surveillance procedures and publishes guidance on the detection, reporting, investigation, and management of immunization-associated adverse events.

d. Develops and implements DoD-wide immunization communication strategies and activities.

e. In conjunction with the Secretaries of the Military Departments, provides recommendations to the ASD(HA) through the DASD(HRP&O) on DoD immunization policy and operational use guidance necessary to protect the total force, eligible beneficiaries, and OTUSF listed in this issuance against diseases affecting public health.

f. Serves as the primary medical consultation resource for clinical immunization healthcare issues including suspected immunization-associated adverse events and fatalities.

g. Maintains and centrally manages a comprehensive program for DoD healthcare providers and beneficiaries to provide worldwide, continuously accessible, military, travel, and routine immunization healthcare-specific information, educational resources, training support, and specialized consultative services, and complete case management for immunization-associated adverse events.

h. Collects and maintains historical DoD vaccine usage data, including quantities of vaccines acquired, administered, and unused, and supports the Secretaries of the Military Departments; the Commandant, USCG; and the CCDRs in identifying and defining future immunization requirements.

i. Serves as the primary coordinator between DoD and commercial immunization-related medical product manufacturers for all applicable immunization safety studies following FDA approval or when otherwise authorized for use.

j. Publishes procedural instructions requiring MHS enterprise-level immunization information management systems to meet national standards for storage of individual immunization data to facilitate safe and effective administration of immunization-related medical products.

k. In collaboration with the Secretaries of the Military Departments, the Defense Agencies, and DoD Field Activities operating medical clinics, and the Commandant, USCG:

(1) Establishes clinical standards for the quality delivery of immunizations, including education and training of individuals involved in immunization healthcare.

(2) Establishes procedures for, and monitors compliance with, mandatory annual seasonal influenza immunization of HCP at DoD medical treatment facilities, and provides a consolidated report to the ASD(HA) no later than May 1st of each year.

(3) Establishes standards for the Military Departments for immunization-related product distribution and administration; risk communication; clinical services; patient safety surveillance; research; and program evaluation.

(4) Publishes procedural instructions and other supporting DHA execution guidance required for immunization healthcare operations to include immunization procedures and processes for MHS-eligible beneficiaries under DHA jurisdiction and OTUSF. See Section 3 for immunization guidance.

(5) Establishes an immunization distribution schedule to reduce impacts on operational requirements during periods of immunization shortage.

(6) Develops pandemic vaccination prioritization guidance in coordination with the Department of Health and Human Services, tailored to DoD operational requirements.

(7) Assesses the DoD Immunization Program no less than annually, and provides recommendations for improvement to the ASD(HA) through the DASD(HRP&O).

l. Identifies and defines requirements, and provides resources, including logistical support, through the DoD planning, programming, budgeting, and execution process for immunizations required to protect eligible beneficiaries.

m. Manages a single, standardized DoD immunization registry compliant with DoDIs 5400.11 and 6025.18, and coordinates health information exchange with state and territorial immunization registries.

n. Serves as primary coordinator for DoD support of the U.S. Government (USG) efforts to modernize influenza vaccine manufacturing.

2.4. ASSISTANT SECRETARY OF DEFENSE FOR MANPOWER AND RESERVE AFFAIRS. Under the authority, direction, and control of the USD(P&R), the Assistant Secretary of Defense for Manpower and Reserve Affairs:

a. Requires that immunization policy, operational use, clinical and administrative guidance, and related plans and programs pertaining to all Reserve Component forces are consistent with the immunization policies of the Active Components.

b. Develops, in coordination with the ASD(HA), immunization policy and clinical and administrative guidance pertaining to the Reserve Component forces that enhance the readiness and capabilities of Reserve Component units and personnel.

c. In conjunction with the ASD(HA) and the Secretaries of the Military Departments, develops operational use guidance and related plans and programs pertaining to the Reserve Component forces that enhance the readiness and capabilities of Reserve Component units and personnel.

2.5. ASSISTANT SECRETARY OF DEFENSE FOR READINESS. Under the authority, direction, and control of the USD(P&R), the Assistant Secretary of Defense for Readiness develops medical guidance for the Military Departments' occupational and environmental health programs in coordination with the Director, DHA, pursuant to DoDI 6055.05. This guidance may include providing immunizations to prevent or lessen the effects of diseases associated with occupational and environmental exposures to biological hazards.

2.6. UNDER SECRETARY OF DEFENSE FOR INTELLIGENCE. In coordination with the CJCS, provides required intelligence support necessary for the validation of deliberately released biological agents, and the validation and assessment of infectious diseases of military or national importance, as well as biological agent threats to DoD personnel, pursuant to DoDD 5160.05E and DoDD 6490.02E.

2.7. ASD(NCB). Under the authority, direction, and control of the Under Secretary of Defense for Acquisition and Sustainment, the ASD(NCB):

a. Coordinates and integrates the DoD Immunization Program with all acquisition-related elements of the DoD Chemical and Biological Defense Program, in accordance with DoDD 5160.05E.

b. Coordinates the development of chemical, biological, radiological, and nuclear defense concepts of operation and proposes immunization concepts for medical products under development for use as immunizations against deliberately released biological agents, in coordination with the ASD(HA).

2.8. USD(P). The USD(P):

a. Reviews and approves the implementation guidance for immunization of OTUSF.

b. Approves requests for exceptions to policy for immunization of OTUSF, in coordination with the CJCS, the Under Secretary of Defense for Acquisition and Sustainment, and the USD(P&R).

c. Coordinates with the ASD(HA) on the recommendation to immunize OTUSF.

d. Represents the Secretary of Defense and DoD with the National Security Council, USG departments and agencies, and other countries requesting vaccine, immunization assistance, or other related capabilities, in coordination with the USD(P&R), the ASD(HA), the CJCS, other senior DoD officials, and the Department of State.

2.9. ASSISTANT SECRETARY OF DEFENSE FOR HOMELAND DEFENSE AND GLOBAL SECURITY. Under the authority, direction, and control of the USD(P), the Assistant Secretary of Defense for Homeland Defense and Global Security receives, coordinates with the ASD(HA) and other DoD officials, and responds to USG department or agency requests for DoD vaccine, immunization assistance, or related capabilities in accordance with DoDD 3025.18, DoDD 5111.13, and DoDI 3025.24.

2.10. ASSISTANT SECRETARY OF DEFENSE FOR SPECIAL OPERATIONS AND LOW-INTENSITY CONFLICT. Under the authority, direction, and control of the USD(P), the Assistant Secretary of Defense for Special Operations and Low-Intensity Conflict:

a. Serves as the DoD representative for international requests for vaccine, immunization assistance, or related capabilities.

b. Evaluates and advises the USD(P) on interagency support requests for use of DoD immunizations in special operations or low-intensity conflict.

c. In consultation with the Office of the General Counsel of the Department of Defense, monitors interagency use of DoD immunizations in such activities, in accordance with DoDD S-5210.36.

d. Provides input to recommendations to the Secretary of Defense for immunization of OTUSF.

2.11. SECRETARIES OF THE MILITARY DEPARTMENTS, DIRECTORS OF DEFENSE AGENCIES AND DOD FIELD ACTIVITIES THAT OPERATE MEDICAL CLINICS, AND THE COMMANDANT, USCG. The Secretaries of the Military Departments, Directors of Defense Agencies and DoD Field Activities that operate medical clinics, and the Commandant, USCG:

a. Develop, implement, and maintain immunization procedures or processes for personnel and beneficiaries under their jurisdiction. See Section 3 for immunization guidance.

b. Comply with procedural instructions published by the Director, DHA.

c. Require that properly identified and defined mandatory immunization requirements are provided in operational use guidance.

d. In conjunction with the Joint Requirements Office for Chemical, Biological, Radiological, and Nuclear Defense and CCMDs, develop risk assessments and impact projections for

deliberately released biological agents and unique CCMD requirements to inform Service-specific immunization policies.

e. Identify and define requirements, and provide resources, including logistical support through the planning, programming, budgeting, and execution process for immunizations required to protect eligible beneficiaries.

f. Provide requested information to the Director, DHA, to support annual status reviews of the DoD Immunization Program.

2.12. CHIEF, NATIONAL GUARD BUREAU. The Chief, National Guard Bureau:

a. Serves as a channel of communications for matters pertaining to immunization readiness of National Guard personnel, coordination of resources, and decisions regarding priorities of immunization activities for National Guard personnel.

b. In coordination with the Adjutants General of the States, and consistent with Service regulations and policies, ensures National Guard personnel pre-designated for immediate response missions or deployment receive required immunizations. This includes provision of smallpox, anthrax, and other appropriate immunizations to chemical, biological, radiological, and nuclear response personnel.

2.13. CJCS. The CJCS:

a. Validates and prioritizes chemical, biological, radiological, and nuclear threats to DoD personnel, equipment, and weapon systems in coordination with the DoD Components in accordance with DoDD 5160.05E.

b. Requires that current geographic CCDR threat and risk assessments for deliberately released biological agents and infectious diseases of military or national importance are coordinated with the ASD(NCB), the ASD(HA), and the Assistant Secretary of Defense for Homeland Defense and Global Security.

c. Provides CCMD-specific immunization requirements to the Secretaries of the Military Departments and the ASD(HA).

d. Forwards CCMD requests for use of medical products and changes to immunization activities against deliberately released biological agents or naturally occurring infectious diseases of military or national concern to the ASD(HA) for approval.

e. Reviews geographic CCDRs' implementation guidance for immunizations of OTUSF.

2.14. CCDRS.

a. Geographic CCDRs:

(1) Use Defense Intelligence Agency assessments and Armed Forces Health Surveillance Branch-Integrated Biosurveillance Section updates to continually identify and reduce risk to the force and other eligible beneficiaries from infectious diseases of military or national importance, as well as deliberately released biological agents.

(2) Identify and define mandatory immunization requirements and establish policy and programs for the protection of Service members and deployable civilian employees within each respective CCMD in accordance with DoDD 6200.04. These requirements will apply to:

(a) Individuals assigned to the CCMD.

(b) Individuals pre-designated for immediate deployment (e.g., crisis response) to the CCMD.

(c) Individuals identified and scheduled for deployment on an imminent or ongoing contingency operation to the CCMD.

(d) OTUSF personnel within the CCMD, as defined by CCMD-specific guidance, and in accordance with procedures outlined in Section 3.

(3) Submit requests through the CJCS to the ASD(HA) for approval to initiate, modify, or terminate mandatory immunizations of personnel and voluntary immunizations of other eligible beneficiaries determined to be at risk from the effects of deliberately released biological agents or naturally occurring infectious diseases of military or national importance.

(4) Determine, at least every 3 years, the estimated quantity of vaccines required to immunize DoD non-uniformed beneficiaries or other individuals should there be a deliberate release of, or significantly elevated threat of release of, a biological agent or a naturally occurring infectious disease of military or national importance. Non-U.S. military personnel include, but are not limited to, DoD civilian and contractor support employees, including associated family members, and USG agency employees and family members. Include estimated total quantities of individuals in operational plans along with distribution and mass immunization contingency plans.

b. Functional CCDRs:

(1) Identify and define mandatory immunization requirements in addition to those of the geographic CCDRs for specific occupations or billets within their commands.

(2) Submit requests through the CJCS, through the ASD(HA) to the Secretary of Defense for approval to initiate, modify, or terminate mandatory immunizations of personnel and voluntary immunizations of other eligible beneficiaries determined to be at risk from the effects of deliberately released biological agents.

SECTION 3: PROCEDURES

3.1. IMMUNIZATION GUIDANCE. Individual immunization delivery decisions will be based on nationally recognized standards of U.S. medical care or clinical practice guidelines to customize care or respond to specific clinical situations for each individual. All immunization programs must include, at a minimum, procedures that:

a. Provide clinical immunization services for vaccine-preventable diseases, including occupation-specific immunizations for personnel exposed to preventable hazards as part of their work environment.

b. Implement patient safety surveillance following immunizations that detects, evaluates, reports, investigates, and clinically manages vaccine-associated adverse events.

c. Document all immunizations electronically with systems interfacing with the DoD Immunization Registry.

d. Assess individual and unit medical readiness and effectiveness, in accordance with DoDI 6025.19.

e. Implement clinical guidelines and quality of care for the delivery of immunizations, including education and training of personnel involved in immunization healthcare.

f. Monitor and keep Service member and deployable civilian employee immunization requirements current.

g. To the maximum extent practicable, provide for the immunization of personnel for protection against deliberately released biological agents and naturally occurring infectious diseases of military or national importance, in time to develop sufficient immunity before deployment. These programs will provide specific immunizations identified by CCDRs and the Services.

h. When the types of immunizations provides indications of an impending deployment, especially to a sensitive location, the five-step operations security process will be used to protect this information in accordance with DoDD 5205.02E. Use of the operations security process helps planners develop measures to prevent exposing critical information and indicators associated with a deployment to our adversaries.

i. Advise eligible DoD beneficiaries of the availability and uses of immunizations for disease prevention, including the personal and collective (e.g., military or community) benefits, potential health risks, and the indications for providing an immunization.

j. Identify the overseas locations where beneficiaries are subject to Service- and CCMD-specific immunization requirements and recommendations and provide the immunizations in accordance with these recommendations.

3.2. IMMUNIZATIONS AGAINST BIOLOGICAL WARFARE AGENTS AND NATURALLY OCCURRING INFECTIOUS DISEASES OF MILITARY OR NATIONAL IMPORTANCE FOR OTUSF.

a. The Secretary of Defense, upon the advice of the geographic CCDRs, the CJCS, and senior officials within the Office of the Secretary of Defense, will decide whether or not to provide immunizations for OTUSF.

b. All immunizations provided or supported in accordance with this section will be consistent with the medical procedures, requirements, and standards defined in Paragraph 3.1.

c. For all immunizations carried out by the DoD Components in accordance with this issuance, a full information and communications program must be implemented to ensure that recipients receive accurate and complete information regarding the vaccine or other immunization product and the immunization program involved. With the exception of those personnel for whom the immunization is determined to be mandatory, information provided must include a clear explanation that the immunization is voluntary.

d. For all immunizations carried out by entities other than the DoD Components in accordance with this issuance, the DoD will provide all necessary information to the receiving entity to allow it to carry out a comparable information and communication program for the benefit of its immunization recipients.

e. The responsibility for record-keeping rests with the DoD Component, other USG agency, allied or coalition government agency, or other organizational entity that receives the immunization and has responsibility for providing it. Record-keeping requirements will be consistent with the standards defined in Paragraph 3.1.

f. OTUSF Categories.

(1) Category 1: Emergency-Essential and Combat-Essential DoD Civilian and Contractor Personnel. This category includes emergency-essential and combat-essential U.S. national civilian employees of the DoD, in accordance with DoDI 1400.32 and DoD contractors (or subcontractors) or employees of DoD contractors (or subcontractors) performing mission essential DoD contractor services, in accordance with DoDI 3020.41.

(2) Category 2: Other DoD or U.S. National Personnel and Other U.S. Citizens. This category includes U.S. military family members; non-emergency-essential DoD civilian employees; non-combat essential DoD civilian employees; family members of DoD civilian employees; DoD contractor and subcontractor employees not covered by Paragraph 3.2.f.(1); family members of DoD contractor and subcontractor employees; employees of other USG agencies; family members of employees of other USG agencies; other USG contractor and subcontractor employees; and family members of other USG contractor and subcontractor employees.

(3) Category 3: Non-U.S. National Civilian Personnel Supporting U.S. Military Operations. This category includes non-U.S. national personnel who are employees of the DoD or a DoD contractor or subcontractor not included in categories 1 or 2 and their family members;

and foreign personnel employed by the host-nation government or contractors of the host-nation government and their family members.

(4) Category 4: Allied/Coalition Nation Personnel. This category includes host-nation and third-country personnel the United States may assist pursuant to an international agreement or as directed by the Secretary of Defense, such as allied or coalition military forces, government officials, and emergency response personnel.

g. Immunization Guidance for OTUSF.

(1) Unless otherwise directed by the ASD(HA), immunization requirements, tracking, and documentation applicable under Paragraph 3.1. apply to category 1 personnel assigned or designated to be deployed with those military personnel in a high-threat area.

(2) The Secretary of Defense, may direct immunizations as mandatory for category 1 personnel. DoD Components that employ emergency-essential DoD U.S. national civilian employees or that maintain contracts performing mission essential DoD contractor services, will comply with all administrative and procedural actions necessary to implement such a requirement. When immunizations are mandatory for DoD contractors (or subcontractor) employees, components will modify contracts as necessary to implement this requirement.

(3) Category 2 personnel will be removed from threat areas in accordance with standard inter-agency procedures for crisis situations. If there is an imminent threat of hostilities, the USG will attempt to evacuate category 2 personnel from the threat area. Evacuation, rather than immunization, is the primary means of addressing the threat for category 2 personnel.

(4) CCDRs may request authority to provide immunization for one or more designated groups of category 2, 3, or 4 personnel. The Secretary of Defense reserves the authority to approve such a request. The decision will be based on the feasibility of evacuation, availability of vaccine, impact on mission and other pertinent factors. For category 2, 3, and 4 personnel to whom immunization is offered, the following additional requirements apply:

(a) Receipt of immunization will be on a voluntary basis.

(b) For category 2 personnel, the DoD Component is responsible for implementation, including administering the vaccine and maintaining medical and other records. The medical records will be updated, maintained, and stored in accordance with DoD Component policies and procedures for medical records of DoD personnel.

(c) For category 3 personnel, implementation of the immunization initiative will be the responsibility of the DoD Component for DoD employees, contractors, and family members; and the host-nation for foreign personnel and family members employed by the host-nation government.

(d) For category 4 personnel, the foreign government is responsible for implementation of the immunization initiative. Coordination with the U.S. Secretary of State is required before providing immunization to category 4 personnel.

(5) Heads of other USG agencies may decide to immunize their employees and family members. When another USG agency requests vaccine, immunization assistance, or other relevant capabilities, the Secretary of Defense reserves the authority to approve such a Defense Support of Civil Authorities request in accordance with DoDDs 5111.1, 5111.13, 3025.18, and DoDI 3025.24. In cases under this policy in which vaccine, immunization assistance, or other related capability is provided to another USG Agency pursuant to Section 1535 of Title 31, U.S.C (the Economy Act), the receiving agency will agree to indemnify the DoD for any DoD liability arising from personal injury, death, or other damage associated with the use of the vaccine, immunization assistance, or related capabilities provided.

(6) In cases where vaccine, immunization assistance, or other related DoD capability is provided to a foreign government, in accordance with DoDDs 5111.1 or 5111.10, or under the Arms Export Control Act (Chapter 39 of Title 22, United States Code), or the Foreign Assistance Act (Chapter 32 of Title 22, United States Code), the receiving government, absent a contrary requirement under treaty or international agreement, agrees to indemnify the DoD and the USG for any liability of the DoD arising from personal injury, death, or other damage associated with the use of the vaccine, immunization assistance, or other DoD capabilities provided.

3.3. EXCEPTIONS TO POLICY. The following procedures apply to initiate or increase immunizations against deliberately released biological agents beyond those specified by the geographic CCDRs:

a. FDA-approved immunizations.

(1) The requested use must be consistent with product's labeling. This includes indications, route of administration, dosing schedule, and dose of immunization.

(2) A risk/benefit analysis must accompany the request to justify use as a general readiness measure (i.e., use beyond geographic CCDR-identified threats). In addition to the justification, the request must include the units or unit types, personnel or personnel types, or individuals, and the number of such personnel or other individuals affected by the request.

(3) Requests will be routed from the requesting component to the ASD(HA) for approval or disapproval.

b. Requests to use non-FDA-approved immunizations will be processed as outlined in DoDI 6200.02.

c. Requests will be routed from the geographic CCDR through the CJCS to the Secretary of Defense for OTUSF.

(1) Requests that include non-DoD category 2 personnel will be coordinated with the head of the appropriate USG agency.

(2) Requests that include category 4 personnel will be coordinated with the U.S. Secretary of State.

d. For changes to immunization activities that terminate such measures, the request must justify the reason for termination and a risk/benefit analysis must accompany the request. The request must also state the unit or unit types, personnel or personnel types, or individuals to no longer be immunized and the number of such personnel or other individuals affected by the request.

GLOSSARY

G.1. ACRONYMS.

ASD(HA)	Assistant Secretary of Defense for Health Affairs
ASD(NCB)	Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs
CCDR	Combatant Commander
CCMD	Combatant Command
CJCS	Chairman of the Joint Chiefs of Staff
DASD(HRP&O)	Deputy Assistant Secretary of Defense for Health Readiness Policy and Oversight
DHA	Defense Health Agency
DoDD	DoD directive
DoDI	DoD instruction
FDA	U.S. Food and Drug Administration
HCP	health-care personnel
MHS	Military Health System
OTUSF	other than U.S. forces
USCG	U.S. Coast Guard
USD(P)	Under Secretary of Defense for Policy
USD(P&R)	Under Secretary of Defense for Personnel and Readiness
USG	U.S. Government

G.2. DEFINITIONS. Unless otherwise noted, these terms and their definitions are for the purpose of this issuance.

beneficiaries. Designated Active and Reserve Component military personnel, including the National Guard, U.S. Army, Navy, Air Force, Marine Corps, and USCG; non-military persons under military jurisdiction; selected federal employees; eligible DoD civilian employees and DoD contractor personnel, as specified by operational use guidance and subject to applicable civilian personnel system or acquisition system procedural requirements, respectively; dependents, retirees, and other individuals eligible for care within the MHS; and family members of contracted workers under military sponsorship in foreign-duty settings.

biological agent. Defined in the DoD Dictionary of Military and Associated Terms.

dependent. Defined in Section 1072 of Title 10, United States Code.

DoD Immunization Program. A single, uniform program, administered by the DHA, that the DoD Components will use to provide educational, public health, and clinical services to deliver and assess the effect of immunizations for eligible beneficiaries.

This program includes immunizations to protect the total force and other eligible beneficiaries against both naturally occurring diseases and biological threats.

Clinical services include disease surveillance, vaccine supply monitoring, pre-immunization education and screening, clinical administration of immunizations, post-immunization follow-up, and patient safety surveillance for effectiveness, and patient advocacy and care following adverse events following immunization.

force health protection. Defined in the DoD Dictionary of Military and Associated Terms.

HCP. All paid and unpaid persons working in healthcare settings who have the potential for exposure to patients or to infectious materials including body substances, contaminated medical supplies and equipment, contaminated environmental surfaces, or contaminated air.

HCP include both persons who provide direct or indirect care to patients and those not directly involved in patient care but potentially exposed to infectious agents that can be transmitted to and from other HCP and patients. HCP required to receive annual influenza vaccination will be identified by the Director, DHA, and published in procedural instructions.

immunization. The process by which a person becomes protected or resistant to an infectious disease, typically by the administration of a vaccine.

infectious diseases of military or national importance. Naturally occurring infectious diseases with high potential to adversely affect U.S. or coalition forces, particularly during deployment. This term may also be called infectious diseases of operational concern.

OTUSF. Collectively refers to noncombatant, non-uniformed U.S. citizens, as well as other select non-U.S. citizens. The specific categories of OTUSF covered by this issuance are defined in Paragraph 3.2.

Reserve Components. Refers collectively to the Army National Guard of the United States, the Army Reserve, the Navy Reserve, the Marine Corps Reserve, the Air National Guard of the United States, the Air Force Reserve, and the Coast Guard Reserve at all times, including when the Coast Guard is operating as a Service of the Department of the Navy or when it is a Service in the Department of Homeland Security by agreement with that Department.

total force. The organizations, units, and individuals that comprise DoD resources for implementing the National Security Strategy. It includes DoD Active and Reserve Component military personnel, military retired members, DoD civilian personnel (including foreign national direct- and indirect-hire, as well as non-appropriated fund employees), contractor personnel, and host-nation support personnel.

vaccination. The administration of a vaccine to an individual for inducing immunity.

vaccine. A preparation that contains one or more components of a biological agent or toxin and induces a protective immune response against that agent when administered to an individual.

REFERENCES

Deputy Secretary of Defense Memorandum, "Transfer of Executive Agent Responsibilities to the Defense Health Agency," July 9, 2014

DoD Directive 3025.18, "Defense Support of Civil Authorities (DSCA)," December 29, 2010, as amended

DoD Directive 5111.1, "Under Secretary of Defense for Policy," December 8, 1999

DoD Directive 5111.10, "Assistant Secretary of Defense for Special Operations and Low-Intensity Conflict (ASD(SO/LIC)," March 22, 1995, as amended

DoD Directive 5111.13, "Assistant Secretary of Defense for Homeland Defense and Global Security (ASD(HD&GS))," March 23, 2018

DoD Directive 5124.02, "Under Secretary of Defense for Personnel and Readiness (USD(P&R))," June 23, 2008

DoD Directive 5136.01, "Assistant Secretary of Defense for Health Affairs (ASD(HA))," September 30, 2013, as amended

DoD Directive 5136.13, "Defense Health Agency (DHA)," September 30, 2013

DoD Directive 5160.05E, "Roles and Responsibilities Associated with the Chemical and Biological Defense Program (CBDP)," September 8, 2017, as amended

DoD Directive 5205.02E, "DoD Operations Security (OPSEC) Program," June 20, 2012, as amended

DoD Directive S-5210.36, "Provision of DoD Sensitive Support to DoD Components and Other Departments and Agencies of the U.S. Government (U)," November 6, 2008, as amended

DoD Directive 6200.04, "Force Health Protection (FHP)," October 9, 2004

DoD Directive 6490.02E, "Comprehensive Health Surveillance," February 8, 2012, as amended

DoD Instruction 1010.10, "Health Promotion and Disease Prevention," April 28, 2014, as amended

DoD Instruction 1400.32, "DoD Civilian Work Force Contingency and Emergency Planning Guidelines and Procedures," April 24, 1995

DoD Instruction 3020.41, "Operational Contract Support (OCS)," December 20, 2011, as amended

DoD Instruction 3025.24, "DoD Public Health and Medical Services in Support of Civil Authorities," January 30, 2017

DoD Instruction 5400.11, "DoD Privacy and Civil Liberties Programs," January 19, 2019

DoD Instruction 6025.18, "Privacy of Individually Identifiable Health Information in DoD Health Care Programs," March 13, 2019

DoD Instruction 6025.19, "Individual Medical Readiness (IMR)," June 9, 2014

DoD Instruction 6055.05, "Occupational and Environmental Health (OEH)," November 11, 2008, as amended

DoD Instruction 6200.02, "Application of Food and Drug Administration (FDA) Rules to Department of Defense Force Health Protection Programs," February 27, 2008

Office of the Chairman of the Joint Chiefs of Staff, "DoD Dictionary of Military and Associated Terms," current edition

United States Code, Title 10

United States Code, Title 14

United States Code, Title 22

United States Code, Title 31, Section 1535

United States Code, Title 32

Exhibit 5

Army Regulation 40–562
BUMEDINST 6230.15B
AFI 48–110_IP
CG COMDTINST M6230.4G

Medical Services

Immunizations and Chemoprophylaxis for the Prevention of Infectious Diseases

Headquarters
Departments of the Army,
the Navy,
the Air Force,
and the Coast Guard
Washington, DC
7 October 2013

UNCLASSIFIED

SUMMARY of CHANGE

AR 40–562/BUMEDINST 6230.15B/AFI 48–110_IP/CG COMDTINST M6230.4G
Immunizations and Chemoprophylaxis for the Prevention of Infectious Diseases

This major revision, dated 7 October 2013--

- Changes the regulation title to "Immunizations and Chemoprophylaxis for the Prevention of Infectious Diseases" (cover).

- Describes the responsibilities of the privileged physician with medical oversight of any clinic or activity that administers immunizations (para 1-4*c*(2)).

- Describes the responsibilities of the privileged health care provider, who is under the direction of the privileged physician of any clinic or activity that administers immunizations (para 1-4*c*(3)).

- Changes a reference to five-injection thresholds to reflect current evidence-based practices (para 2-1*e*(1)).

- Adds a description of procedures for vaccine storage and handling (para 2-3).

- Adds a description of military indications for required and recommended vaccines (paras 4-2 through 4-19).

- Makes changes to chemoprophylaxis recommendations (chap 5).

- Adds a description of procedures for documenting immunizations and immunization recordkeeping (para B-5).

- Establishes and recommends immunization personnel training (para B-6 and table B-1).

- Establishes criteria for determining required immunizations for military personnel (app D).

- Makes administrative revisions (throughout).

Headquarters
Departments of the Army,
the Navy,
the Air Force,
and the Coast Guard
Washington, DC
7 October 2013

***Army Regulation 40–562**
***BUMEDINST 6230.15B**
***AFI 48–110_IP**
***CG COMDTINST M6230.4G**

Medical Services

Effective 7 November 2013

Immunizations and Chemoprophylaxis for the Prevention of Infectious Diseases

By Order of the Secretary of the Army, Navy, Air Force, and Coast Guard:

RAYMOND T. ODIERNO
General, United States Army
Chief of Staff

Official:

GERALD B. O'KEEFE
Administrative Assistant to the Secretary of the Army

M. L. NATHAN
Vice Admiral, Medical Corps
United States Navy
Surgeon General of the Navy

THOMAS TRAVIS
Lieutenant General, U.S. Air Force
Surgeon General

MAURA K. DOLLYMORE
Rear Admiral, U.S. Coast Guard
Director, Health, Safety and Work-Life

History. This publication is a major revision.

Summary. This regulation for immunization and chemoprophylaxis updates quality standards for immunization delivery; establishes electronic immunization tracking systems as the preferred immunization record; provides guidance for lost immunization records, immunization credit for pre-existing immunity, and complying with regulations for vaccines and other products administered in investigational, new drug status or in accordance with emergency use authorization; describes dividing initial entry immunization into two clusters; and describes the role of the Military Vaccine Office.

Applicability. This regulation applies to the Active Army, the Army National Guard/Army National Guard of the United States, and the U.S. Army Reserve, unless otherwise stated. It also applies to the following: uniformed Departments of the Navy, Air Force, and Coast Guard (including the active and reserve components of each Service); nonmilitary persons under military jurisdiction; selected Federal employees; selected employees of Department of Defense contractors; and Family members and other health care beneficiaries eligible for care within the military health care system. This regulation is applicable during mobilization.

Proponent and exception authority. The proponent of this regulation is The Surgeon General. The proponent has the authority to approve exceptions or waivers to this regulation that are consistent with controlling law and regulations. The proponent may delegate this approval authority, in writing, to a division chief within the proponent agency or its direct reporting unit or field operating agency, in the grade of colonel or the civilian equivalent. Activities may request a waiver to this regulation by providing justification that includes a full analysis of the expected benefits and must include formal review by the activity's senior legal officer. All waiver requests will be endorsed by the commander or senior leader of the requesting activity and forwarded through their higher headquarters to the policy proponent. Refer to AR 25–30 for specific guidance.

Army internal control process. This regulation contains internal control provisions and identifies key internal controls that must be evaluated (see appendix E).

Supplementation. Supplementation of this regulation and establishment of command and local forms are prohibited without prior approval from The Surgeon General (DASG–ZA), 7700 Arlington Blvd., Falls Church, VA 22041–5143.

Suggested improvements. Users are invited to send comments and suggested improvements on DA Form 2028 (Recommended Changes to Publications and Blank Forms) directly to The Surgeon General (DASG–ZA), 7700 Arlington Blvd., Falls Church, VA 22041–5143. Air Force users are invited to send comments and suggested improvements on AF Form 847 (Recommendations for Change of Publication) through channels to Headquarters, AFMSA/SGOP, 7700 Arlington Blvd., Falls Church, VA 22041–5143.

Distribution. This publication is available in electronic media only and is intended for command levels A, B, C, D, and E for the Active Army, the Army National Guard/Army National Guard of the United States, and the U.S. Army Reserve. Navy/Marine Corps: Ships, units, and stations having medical department personnel. Air Force: Active Air Force, the Air National Guard, and Air Force Reserve. Coast Guard: Active Coast Guard and Coast Reserves.

*This regulation supercedes AR 40–562/BUMEDINST 6230.15A/AFJI 48–110/CG COMDTINST M6230.4F, dated 29 September 2006.

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Appendixes

Table List

Glossary

Chapter 1
Introduction

1–1. Purpose
This publication provides directive requirements for the Military Vaccination Program; establishes general principles, procedures, policies, and responsibilities for the immunization program; and implements military and international health regulations and requirements.

1–2. References
Required and related publications and prescribed and referenced forms are listed in appendix A.

1–3. Explanation of abbreviations and terms
Abbreviations and special terms used in this regulation are explained in the glossary.

1–4. Responsibilities
a. Command medical authority. The command medical authority will prescribe specific immunization and chemoprophylactic requirements for their units per requirements established by this publication and additional guidance provided by the appropriate surgeon general or the U.S Coast Guard (USCG), Director of Health, Safety, and Work-Life (USCG, CG–11).

b. Command leaders. Combatant commanders, major command commanders, unit commanding officers, commanders of special operations and forces, and officers-in-charge will:

(1) Ensure military and nonmilitary personnel under their jurisdiction receive required immunizations and chemoprophylaxis. Ensure immunizations and immunization exemption codes (medical or administrative) are documented in an approved Department of Defense (DOD) or USCG Service Immunization Tracking System (ITS), as described in paragraph 2–7*a*.

(2) Maintain appropriate international, Federal, State, and local records of all immunizations and chemoprophylaxis.

(3) Ensure personnel transferred to another command or unit, including advanced instructional training or technical school, receive proper screening for, and administration of, appropriate immunizations and chemoprophylaxis for the area assigned, and are timed to provide immunity before deployment or exposure or to complete a vaccine series.

(4) Ensure immunization exemptions are documented in the Service ITS.

(5) Ensure vaccine doses or boosters are administered to complete a started series or maintain immunity.

(6) Ensure deviations from specified immunizations are cleared or authorized by the appropriate combatant commander; surgeon general; or USCG, CG–11.

(7) Observe international military standardization agreements (STANAGs).

c. Medical commanders, commanding officers, and command surgeons. Medical commanders, commanding officers, and command surgeons will:

(1) Ensure individuals administering immunizations are properly trained in accordance with DOD, Service, and Centers for Disease Control and Prevention (CDC) guidelines and act within their scope of practice as determined by each Service. A training checklist is found in appendix B, paragraph B–6 and table B–1.

(2) Appoint, in writing, a privileged physician with medical oversight over any clinic or activity that administers immunizations. This physician will:

(a) Complete appropriate training in immunization science in residence or via distance learning.

(b) Be available to address immunization issues, although it is not required that the privileged physician be present for administration of vaccines. The USCG requires a privileged health care provider to administer immunizations to civilians who are eligible for care in a medical treatment facility.

(c) Establish and sign vaccine and chemoprophylaxis standing orders for clinics or other locations where immunizations or chemoprophylaxis medications are administered.

(d) Ensure standard operating procedures (SOPs) are established that implement current national standards for adult and pediatric immunizations and chemoprophylactic practices and promote appropriate quality improvement mechanisms. Incorporate local practices and requirements of policies contained in references listed at appendix A.

(3) Appoint, in writing, a privileged health care provider, who is under the direction of the privileged physician appointed in paragraph 1–4*c*(2), to have oversight over the daily activities of any clinic or activity that administers immunizations. The privileged physician may serve as the health care provider if no one is available to assume the position of privileged health care provider.

(4) Ensure patients are evaluated for preexisting immunity, screened for administrative and medical exemptions, and/or evaluated for the need for medical exemptions to immunizations or chemoprophylaxis medications. Exemptions are granted per paragraph 2–6; document any exemptions.

(5) Monitor the immunization status of personnel and ensure compliance with policies and procedures for creating and maintaining immunization records in accordance with Title 42, United States Code, Chapter 300aa-25.

(6) Ensure emergency medical response is available and that personnel who administer immunizations receive

training on: basic cardiopulmonary resuscitation, administration of epinephrine, and emergency response to immunization-adverse events, at a minimum.

(7) Ensure health care providers are available to respond to and report adverse events resulting from immunization.

(8) Ensure patients needing evaluation of adverse events after immunization are referred to appropriate health care providers, such as medical subspecialists (including specialists in immunization health care) for evaluation, consultation, or indicated intervention.

d. The Army, as Executive Agent for the Military Vaccination Program. The Army, as Executive Agent for the Military Vaccination Program and in cooperation with the Military Services, will:

(1) Operate a Military Vaccine (MILVAX) Office to provide the Military Services with a coordinated source for information and education of vaccine-related activities needed in order to implement Department of Defense Directive (DODD) 6205.3, DODD 6205.02E, and Department of Defense Instruction (DODI) 6205.4.

(2) Synchronize, integrate, and coordinate immunization policies and other immunization-related activities for all DOD components.

(3) Facilitate and promote the quality of immunization policy, implementation, education, distribution, risk communication, administration, clinical services, safety surveillance, research, and program evaluation.

(4) Provide a comprehensive access point to provide information, education resources, safety surveillance, and uniform procedures to identify, report, and evaluate vaccine-associated adverse events.

(5) Maintain historical vaccine usage data as well as identify future vaccine requirements as needed.

(6) Provide primary coordination between DOD and vaccine manufacturers for all applicable post-licensure vaccine studies.

(7) Coordinate with other Secretaries of the Military Departments and the Commandant, USCG to:

(a) Establish joint clinical quality standards for immunization delivery and education and training to personnel involved in immunization healthcare. The goals of these standards are to promote clinical excellence and decrease practice variability.

(b) Assess the DOD Immunization Program by developing metrics to measure individual medical readiness, vaccine effectiveness and safety, and compliance with overall immunization policies.

(c) Regularly update the Joint Regulation on Immunization and Chemoprophylaxis for the Prevention of Infectious Diseases.

(8) Promote scholarly immunization study activities through the Army's Medical Infectious Disease Research Program using funds both from the Defense Health Program and the Research, Development, Test, and Evaluation.

e. Each of the Military Services. Each of the Military Services will provide an immunization health care capability to deliver medical specialty consultation, case management, and clinical investigation. The U.S. Navy provides medical services for the U.S. Marine Corps.

Chapter 2
Program Elements and Clinical Considerations

2–1. Standards

a. Department of Defense and U.S. Coast Guard policy. The Military Service policy concerning immunizations follows the recommendations of the CDC and the Advisory Committee on Immunization Practices (ACIP) and the prescribing information on the manufacturer's package inserts, unless there is a military-relevant reason to do otherwise. Any vaccine or drug licensed by the U.S. Food and Drug Administration (FDA) or the U.S. Department of Health and Human Services (DHHS) may be used, as well as vaccines or drugs compliant with applicable DOD investigational new drug (IND) or emergency use authorization (EUA) processes. Privileged health care providers may make clinical decisions for individual beneficiaries to customize medical care or to respond to an individual clinical situation that is compliant with IND or EUA processes.

b. Standards for delivery of military vaccines. Standards for delivery of military vaccines are provided in appendix B. Military Services will abide by these standards in routine immunization delivery.

c. Expiration date. Vaccines or drugs will not be used beyond the manufacturer's potency expiration date, unless the appropriate surgeon general or USCG, CG–11, authorizes extension in exceptional circumstances.

d. Screening for contraindications. Screen all potential vaccines for contraindications, precautions, or warnings per the prescribing information on the manufacturer's package insert.

e. Immunization schedules and intervals.

(1) *Initial series.* Once an immunization series has been started, it must be completed, unless a medical or administrative exemption exists. Restarting an immunization series or adding extra doses is not necessary when an initial series of a vaccine or toxoid is interrupted; instead, give delayed doses as soon as feasible.

(2) *Doses.* Vaccine doses in an initial series will not be administered at intervals less than the recommended minimum intervals or earlier than the minimum age unless the doses are part of a CDC catch-up schedule or during an

outbreak. Doses in an initial series administered 5 or more days earlier than the minimum interval should not be counted as valid doses. The next valid dose is calculated after the last invalid dose.

(3) *Booster doses.* After the initial series of a vaccine is complete, a booster dose may be recommended for specific vaccines. For vaccines that do not provide lifetime immunity, the booster dose is usually recommended or required to increase immunity back to protective levels.

f. Simultaneous immunizations.

(1) When simultaneous vaccine injections are necessary, administer vaccines in different limbs. The anatomical site may depend on the age of the individual, and the degree of muscle development. If different anatomical sites are not possible, then separate the injections by at least 1 inch. Refer to the ACIP General Recommendations on Immunizations for proper needle lengths.

(2) Priority of immunization is based on the relative likelihood of various microbial threats and the existence of any vaccine-vaccine, vaccine-antibody, or vaccine-drug interactions and is best performed by the health care provider. In military training centers, contagious diseases typically represent the most imminent threats.

(3) Spacing of live and inactivated vaccines.

(a) Two or more inactivated vaccines can be administered simultaneously or at the prescribed interval and restrictions indicated in the package insert for each vaccine.

(b) Inactivated and live vaccines can be administered simultaneously or at the prescribed interval and restrictions indicated in the package insert for each vaccine.

(c) Two or more live virus vaccines must be administered simultaneously or separated by at least 28 days (4 weeks). Refer to ACIP guidelines for exceptions.

g. Screening for immunity. For some vaccine-preventable diseases, serologic or other tests can be used to identify pre-existing immunity from prior infections or immunizations that may eliminate unnecessary immunizations.

h. Live virus vaccines and tuberculosis testing. Vaccinations with live vaccines may affect tuberculosis (TB) testing. This includes both the Mantoux tuberculin skin test and the Intereferon-Gamma Release Assays test whole-blood test. To avoid interference:

(1) Administer live virus vaccines and TB test on the same day.

(2) Perform TB test 4 to 6 weeks after administration of live virus vaccines, or

(3) Administer live virus vaccines, once the TB test is read.

2–2. Logistics

a. Requisitioning of immunizing and chemoprophylaxis agents. Immunizing and chemoprophylaxis agents are requisitioned in accordance with medical supply procedures. However, vaccinia immune globulin—also known as VIG-intravenous—is available only by ordering through the MILVAX Office.

b. Transportation, storage, and handling. All personnel will maintain the cold chain in vaccine delivery during transportation, storage, and handling. Shipping and storage advice is available from Services medical logistics centers.

c. Small stations, ships, and cutters. To minimize the shipment of vaccines that must be stored at frozen temperatures, small stations, ships, and cutters may requisition these items from a nearby military medical activity stocking the items. Requisitioning procedures and reimbursement are prescribed by the supplying activity.

2–3. Storage and handling

a. Safety and efficacy of vaccines. Failure to adhere to recommended specifications for storage and handling of vaccines may reduce potency, resulting in inadequate immune responses in the recipients and inadequate protection against disease. To maintain the safety and efficacy of vaccines, ensure immunizing and chemoprophylaxis agents are stored, shipped, and handled in accordance with the pharmaceutical manufacturer's instructions as outlined in the product package insert or other guidance.

b. Policies for maintaining vaccines. All locations that maintain and administer vaccines will develop and implement policies and procedures for maintaining cold chain management of vaccines.

c. Shelf-life after opening.

(1) Administer vaccines shortly after withdrawal from single-dose or multi-dose vials, in accordance with the manufacturer's package insert.

(2) Single dose vials are meant for one-time use only. At the end of the clinic day, discard all single-dose vials without protective caps.

(3) For multi-dose vaccine vials that do not require reconstitution, doses that remain after withdrawal of a dose can be administered until the expiration date printed on the vial or vaccine packaging, so long as the vial has been stored correctly and the vaccine is not visibly contaminated and the manufacturer has not specified otherwise.

(4) Multi-dose vials that require reconstitution must be used within the interval specified by the manufacturer. After reconstitution, the new expiration date should be written on the vial.

d. Diluents.

(1) Diluents are not interchangeable, unless specified by the manufacturer.

(2) Transport diluents at room temperature in validated containers, but not in direct contact with shipping gel packs.

(3) Store diluents according to the manufacturer's package insert.

(4) Discard diluents when stored inappropriately or expired.

e. Filling syringes and attaching needles.

(1) Never mix individual vaccines in the same syringe. Different vaccines should never be mixed in the same syringe unless specifically licensed for such use. Do not transfer vaccine between syringes.

(2) Use a separate needle and syringe for each injection.

(3) Label filled syringes with the type of vaccine, lot number, and date of filling, unless the vaccine is administered immediately after being drawn into the syringe by the same person administering the vaccine.

(4) Attach needles to manufactured filled syringes just prior to administration. Discard needle and syringe if the vaccine is not administered before the end of the clinic day or vaccination session in accordance with the manufacturer's package insert. If no time line is provided, discard after 8 hours.

f. Prefilling syringes.

(1) Prefilling syringes is highly discouraged because of the increased risk of administration errors and possible bacterial growth in vaccines that do not contain preservatives. Syringes other than those filled by the manufacturer are designed for immediate use and not for vaccine storage.

(2) In certain circumstances in which a single vaccine type is being used, such as during an influenza vaccination campaign, filling a small number of syringes may be considered.

(3) Discard unused syringes filled by the end user (that is, not filled by the manufacturer) in accordance with the manufacturer's package insert. If no time line is provided, discard after 8 hours.

g. Storing vaccine.

(1) Ensure that only vaccines are stored in the vaccine storage unit (refrigerator or freezer).

(2) Store refrigerated vaccines at temperatures of 35°F to 46°F (2°C to 8°C). Do not expose refrigerated vaccines to freezing temperatures.

(3) Store frozen vaccines at temperatures of 5°F (-15°C) or lower.

(4) Store all reconstituted lyophilized (freeze-dried) vaccines in accordance with the manufacturer's temperature and light condition parameters.

h. Vaccine storage equipment. Ensure that vaccine storage units are carefully selected, used properly, and consistently monitored to maintain recommended vaccine storage temperatures.

(1) Stand-alone refrigerators and freezers are recommended for storage of vaccines. A combination refrigerator/frost-free freezer for home use is acceptable if only the refrigerator compartment of the combination unit is used to store refrigerated vaccines. A separate stand-alone freezer should then be used to store frozen vaccine. Dormitory style refrigerators are not authorized for vaccine storage.

(2) Use certified and calibrated thermometers in all vaccine storage units. Uncertified liquid (mercury or alcohol) thermometers and uncertified dial-type household refrigerator/freezer thermometers are not authorized.

(3) Ensure alarm systems are incorporated as part of the vaccine storage unit to alert staff of power failures or indicate whether or not vaccine temperatures have been maintained.

i. Temperature tracking.

(1) Ensure temperatures are documented for each vaccine storage unit. Physically confirm the temperature of all vaccine refrigerators and freezers at a minimum of two times per day. Document the date, time, and temperature of the vaccine storage unit on a temperature log. Vaccine outside of a refrigerator or freezer must have the temperature checked and documented every hour.

(2) Keep temperature logs for at least 3 years. State and/or local requirements may require longer recordkeeping.

(3) Record date and time of any mechanical malfunction or power outage on the temperature log or on another equipment-tracking document.

j. Vaccine storage alarms.

(1) Ensure alarm systems are capable of monitoring vaccine storage 24 hours a day, 7 days per week. Ensure the system either notifies an accountable person when a failure is detected, or the system is capable of indicating that the vaccine temperature integrity was maintained during the storage period (or notes any deviations).

(2) Ensure current personnel contact information exists on auto-dialers, and that appropriate coverage occurs during periods of leave, holiday weekends, and so forth.

(3) Monitor alarms electronically and physically 24 hours a day, 7 days per week.

(4) Test the entire alarm system, to include refrigerator-freezer-unit sensor to the remote monitoring station and telephone or pager, at least monthly. Maintain test records for at least 3 years.

(5) For vaccine storage units within restricted access areas, ensure the temperature can be checked and a light or audible alarm is installed to indicate when the storage unit temperature is out of range without having to physically enter the restricted area.

k. Transporting vaccines.

(1) Always transport vaccines in properly insulated containers to maintain the recommended temperatures.

(2) Ensure containers used for transporting vaccines are capable of maintaining the vaccine at the correct temperatures. Validated storage devices include the Vaxicool, Vaxipac, manufacturer shipping containers, Styrofoam(tm) coolers with at least 2-inch thick walls, or Endurotherm insulating shipping containers.

(3) Pack containers to appropriately maintain the proper temperature while vaccine is transported or shipped. Refrigerated or frozen packs are authorized for use to maintain the cold chain when used according to the U.S. Army Medical and Materiel Agency (USAMMA) Distribution Operations Center instructions.

(4) Include calibrated thermometers to track temperatures in all transportation and off-site storage containers.

(5) Pack vaccines in their original packaging. Do not remove vaccine vials from boxes.

(6) Document vaccine type, quantity, date, time, and originating facility on the outside of the transportation containers.

(7) Ensure temperatures are tracked during transportation and any deviations in temperature are readily identifiable.

l. Vaccine disposal or disposition.

(1) Discard syringes or vials that contain live virus vaccines per installation policy.

(2) Contact the pharmacy or logistics office for specific policies regarding the disposition of unopened vials, expired vials, unused doses, and potentially compromised vaccine.

(3) Label potentially compromised vaccines with the words “Do not use” and place in the refrigerator or freezer based on the manufacturer’s instructions as if they were not compromised. Report all compromised anthrax, smallpox, and influenza vaccines to USAMMA for validation before destruction. Contact the manufacturer for all other potentially compromised vaccines for disposition or destruction instructions.

(4) Report all confirmed compromised vaccine losses through Service-specific channels to the Military Vaccine Office. The report must include the following: description of the reason for the loss, vaccines compromised, total vials/doses lost, and cost of lost or compromised vaccines.

2–4. Hypersensitivity or allergy

a. Before administration of any medication, including vaccines, determine if the individual has previously shown any unusual degree of adverse reaction or allergy to it or any specific component of the vaccine or its packaging (for example, eggs, gelatin, preservatives, latex). Review the manufacturers’ package inserts and reference materials for product-specific information.

b. Defer individuals with reported hypersensitivity to a particular vaccine or its components from immunization.

c. Refer individuals with a hypersensitivity to an appropriate medical specialist for evaluation, unless the health record contains documentation of a prior consultation or a specialist’s recommendations. Document hypersensitivity and any recommended exemption(s) in the electronic ITS and the appropriate sections of the health record.

2–5. Immunizing women of childbearing potential

A pregnancy screening test for women of childbearing potential is not routinely required before administering vaccines, including live virus vaccines. Take the following precautions to avoid unintentional immunization with contraindicated products during pregnancy—

a. Display signs asking pregnant women to identify themselves. Discreetly ask her if she is, or might be, pregnant. Document responses in the health record. If the answer is “yes,” and the ACIP does not recommend the vaccine for use in pregnancy, then defer her from immunization or refer to an obstetric healthcare provider to determine whether the benefits of immunization outweigh risks in pregnancy. If the vaccine is recommend for use in pregnancy by ACIP, the vaccine may be administered. If pregnancy status is uncertain, defer immunization until after a negative pregnancy evaluation (for example, urine, or serologic test).

b. With regard to smallpox (vaccinia) vaccine, a specific pre-immunization screening form (available at http://www.smallpox.mil/resource/forms.asp) that assesses the date of the last menstrual period is required. For women whose last menstrual period was more than 28 days ago, a pregnancy test is recommended.

c. Breastfeeding women may be immunized in accordance with the current ACIP guidelines. At present, no immunization products are medically contraindicated in breastfeeding women. Smallpox vaccine is withheld from breastfeeding women, except in an outbreak, primarily due to the potential for contact transmission of vaccinia virus to the child.

d. If a live virus vaccine is administered, counsel her to avoid becoming pregnant for the appropriate interval as recommended by CDC or the vaccine manufacturer. Document the counseling in the health record.

e. If she is pregnant and immunization is indicated, immunize in consultation with her obstetric health care provider.

f. If a contraindicated vaccine is inadvertently administered to a pregnant woman, report the event upon discovery to the preventive medicine point of contact and obstetric services and complete appropriate quality assurance documents. Report such cases to any applicable registry. For assistance with registry referral procedures, contact the preventive medicine service or MILVAX.

2–6. Exemptions

There are two types of exemptions from immunization-medical and administrative. Granting medical exemptions is a medical function. Granting administrative exemptions is a nonmedical function.

a. Medical exemptions. A medical exemption includes any medical contraindication relevant to a specific vaccine or other medication. Health care providers will determine a medical exemption based on the health of the vaccine candidate and the nature of the immunization under consideration. Medical exemptions may be temporary (up to 365 days) or permanent. Standard exemption codes appear in appendix C.

(1) General examples of medical exemptions include the following—

(a) Underlying health condition of the vaccine candidate (for example, based on immune competence, pharmacologic or radiation therapy, pregnancy and/or previous adverse response to immunization).

(b) Evidence of immunity based on serologic tests, documented infection, or similar circumstances.

(c) An individual's clinical case is not readily definable. In such cases, consult appropriate medical specialists, including specialists in immunization health care.

(2) Providers who are assessing medical exemptions may seek a second opinion from a provider experienced in vaccine adverse event management, such as specialists in immunization health care at a medical center, or seek additional consultation from MILVAX.

(3) Annotate electronic ITS and paper-based service treatment records with exemption codes denoting evidence of immunity, severe adverse event after immunization (except for the Medical Readiness Reporting System), other temporary or permanent reasons for medical exemption, and other appropriate categories.

(4) Report cases warranting permanent medical exemptions due to a vaccine related adverse event to the Vaccine Adverse Events Reporting System (VAERS) at the Web site at http://www.vaers.hhs.gov and as discussed in paragraph 2–10.

(5) Revoke medical exemptions when they are no longer clinically warranted.

b. Administrative exemptions. Standard exemption codes appear in appendix C.

(1) *Separation or retirement.* Within 180 days before separation or retirement, Service personnel may be exempt from deployment (mobility) immunizations, if one of the following conditions are met:

(a) They are not currently assigned, deployed, or scheduled to perform duties in a geographical area where an immunization is indicated.

(b) The commander has not directed immunization because of overriding mission requirements. Personnel who meet separation or retirement requirements and desire an immunization exemption must identify themselves to their commander. The member must have approved retirement or separation orders. Active duty personnel continuing duty in the reserve component are not exempted on this basis.

(2) *Thirty days or fewer of service remaining.* Applies to civilian employees and contractor personnel who will leave a permanent (other than OCONUS deployments) assignment subject to immunization within 30 days or fewer.

(3) Religious exemptions.

(a) Servicemembers. Immunization exemptions for religious reasons may be granted according to Service-specific policies to accommodate religious beliefs of a Service member. This is a command decision made with medical, judge advocate, and chaplain input.

1. Requests for religious exemption must comply with the provisions of the applicable policy and/or regulation for the Servicemember requesting religious accommodation. For the Army, religious accommodation policy is provided in AR 600–20. For the Navy and Marine Corps, waivers are granted on a case-by-case basis by the Chief, Bureau of Medicine, and Surgery. For the Air Force, permanent exemptions for religious reasons are not granted; the MAJCOM commander is the designated approval and revocation authority for temporary immunization exemptions. For the Coast Guard, CG–122 is the designated approval and revocation authority for religious immunization exemptions. USCG requests must be forwarded through the appropriate chain to Commandant CG–122 via CG–112.

2. A military physician must counsel the applicant. The physician should ensure that the Servicemember is making an informed decision and should address, at a minimum, specific information about the diseases concerned; specific vaccine information including product constituents, benefits, and risks; and potential risks of infection incurred by unimmunized individuals.

3. The commander must counsel the individual that noncompliance with immunization requirements may adversely impact deployability, assignment, or international travel.

4. Per DODI 1300.17 and applicable service regulations will be provided whether Servicemembers with pending active requests for religious exemption are temporarily deferred from immunizations, pending outcome of their request.

5. Religious exemptions may be revoked, in accordance with Service-specific policies and procedures, if the individual and/or unit are at imminent risk of exposure to a disease for which an immunization is available.

(b) Civilian employees. Civilian employees submit requests for immunization exemption for religious reasons to their supervisors. Civilian requests are processed in accordance with Part 1605, Title 29, Code of Federal Regulations and component policies.

(c) Bargaining units. Civilian personnel affected by this document who are members of bargaining units will be

considered for exemption consistent with applicable personnel management policies and applicable labor relations obligations.

(d) Other exemption categories. Administrative or medical personnel will appropriately annotate electronic ITS with exemption codes denoting separation, permanent change of station, emergency leave, missing or prisoner of war, deceased, and other appropriate categories.

2–7. Immunization and chemoprophylaxis records

a. Electronic immunization tracking systems.

(1) Document all immunizations in a DOD and USCG-approved ITS. Include date, immunization given, dose, anatomical location of administration, lot number, manufacturer, Vaccine Information Sheet (VIS) date, and the identification of the person administering the vaccine.

(2) Electronic ITS must—

(a) Comply with the requirements of the National Vaccine Injury Compensation (NVIC) Program as provided in 42 USC 300aa-25, Report and Recording of Information, and 42 USC 300aa-26. NVIC information is outlined in paragraph 2–7*d*.

(b) Incorporate DOD-directed levels of security, certification, and redundancy, and the requirements of the Health Insurance Portability and Accountability Act to preclude unauthorized access to personal medical information and to survive hardware or software malfunction.

(c) Be capable of generating printed reports of immunization status and exemption information on both an individual and unit basis.

(3) A printed report from the electronic ITS, in CDC Form 731 (International Certificate of Vaccination or Prophylaxis) 731, SF 601 (Health Record-Immunization Record), or DD Form 2766C (Adult Preventive and Chronic Care Flowsheet) (Continuation Sheet) format, accompanied by an official clinic stamp and the authorized signature and printed name of an authenticating official, will qualify as an official paper immunization record.

(4) A printed report as identified in preceding paragraph 2–7*a*(3) will suffice as a valid certificate of vaccination for international travel (except for yellow fever which is documented on the CDC Form 731) for active duty members of the Armed Forces as outlined in Article 36 (Annex 6) of the World Health Organization (WHO) International Health Regulations.

b. Non-electronic immunization and chemoprophylaxis records.

(1) *Deployment records.* Transfer information regarding immunizations and chemoprophylaxis including date, product given, dose, and initials of person administering to the deployable health record (DD Form 2766) or comparable approved form, either by computer-generated report or by hand. Upon return from deployment, transfer entries on the deployment record into the appropriate ITS or other electronic record system.

(2) *Abbreviations.* Use abbreviations for vaccines and their manufacturers conforming to the nomenclature adopted by the CDC Vaccine Identification Standards Initiative. When annotating the date a vaccine is administered, the day, month, and year are listed in that order. The day is expressed in Arabic numerals, the month spelled out or abbreviated using the first three letters of the word, and the year expressed in Arabic numerals either by four digits or by the last two digits (for example, 14 June 1994 or 14 Jun 94).

(3) *Transcribed records.* Entries based on prior official records will include the following statement: “Transcribed from official records.” Alternately, the statement may cite the specific source (for example, “Transcribed from SF 601”). When entries are transcribed onto paper records, include the initials of the transcriber on each entry.

(4) *SF 601 (Navy, Marine Corps, and U.S. Coast Guard).* Prepare SF 601 in accordance with this directive and chapter 16 of NAVMED P–117.

(5) *DD Form 2766C.* Initiate DD Form 2766C for all personnel at the time of entry into Military Service.

(6) *Paper-based immunization and chemoprophylaxis records.* Individuals preparing paper-based immunization and chemoprophylaxis records will ensure that paper records match the electronic ITS. If paper-based immunization or chemoprophylaxis records are used, electronic ITS will be updated within 24 hours.

(7) *CDC Form 731.* Required for yellow fever documentation and or prepared upon request for each member of the Armed Forces and for nonmilitary personnel receiving immunizations, including date, immunization given, dose, and the initials of the person administering the vaccine. The form contains valid certificates of immunization for international travel and quarantine purposes in accordance with WHO international health regulations. CDC Form 731 remains in the custody of the individual who is responsible for its safekeeping and for keeping it in his or her possession when traveling internationally. Data are entered by hand, rubber stamp, or by typewriter.

(a) Supply. CDC Form 731 is obtained through normal publication supply channels.

(b) Stamps. Use in accordance with instructions received from the Division of Global Migration and Quarantine; the appropriate surgeon general; Chief, Bureau of Medicine and Surgery; or CG–11.

1. Army. USAHRC (AHRC–PDR), 1600 Spear Head Division Avenue, Fort Knox, KY 40122.

2. Navy. Bureau of Medicine and Surgery (BUMED), Washington, DC 20372.

3. Air Force. HQ AFPC/DPMDB, Randolph AFB, TX 78148.

4. Marine Corps. Headquarters, U.S. Marine Corps, Washington, DC 20380.

5. Coast Guard. Commandant, CG–11, USCG Headquarters, 2100 Second Street SW, Washington, DC 20593–0001.

(c) Written signatures. Written signatures must appear in appropriate spaces on each certificate; signature stamps are not valid.

c. Lost immunization records. If an individual's immunization records are lost, assume the individual received standard immunizations administered at entry into Military Service by the individual's accession source (for example, enlisted, Service academy, direct commission) unless there is an objective reason to believe otherwise. Do not repeat such immunizations. Base decisions for future immunizations on assumed date of last immunization (for example, individual assumed to have received tetanus-diphtheria toxoid in July 1995 would next be immunized in July 2005).

d. National Vaccine Injury Compensation Program.

(1) The statute 42 USC 300aa-1 to 300aa-34 (The National Childhood Vaccine Injury Act of 1986) and other regulations set standards for certain immunizations. These requirements apply to U.S. vaccines as indicated by the CDC after the DHHS Secretary publishes a notice of coverage. Document the patient's name; identifying number (for example, sponsor's SSN); type of vaccine; date of administration; manufacturer; lot number; and the name, address, and title of person administering the vaccine in a permanent health record or permanent office log or file, in either paper or electronic format. The electronic immunization tracking systems are the primary method of immunization documentation. Other records and management reports may be generated from the electronic immunization database, as described above.

(2) Personnel who administer any vaccine covered under the NVIC program, to either children or adults, will provide a written copy of the VIS to the vaccinee and allow sufficient opportunity to read the most recent VISs provided by the DHHS and an opportunity to ask questions about the vaccine. Copies of VISs are available through the CDC Web site (http://www.cdc.gov/vaccines). The VIS should be supplemented with an oral explanation or video presentation, or in the appropriate language, when the patient or guardian does not appear to be literate in English. Provide printed copies to any individual who requests one. Translations of VISs into languages other than English are available from nongovernmental organizations.

(3) Personnel who administer vaccines are not required to obtain the signature of the military member, patient, or legal representative acknowledging receipt of a VIS. However, to create a record that the materials were provided, health care personnel who administer vaccines will annotate each patient's health record that the VISs were provided at the time of immunization.

(4) The statute 42 USC 300aa-1 to 300aa-34 (The National Childhood Vaccine Injury Act of 1986), requires that the following events be reported to VAERS, a public health activity administered by the FDA and CDC:

(a) Any event listed in the NVIC program's vaccine injury table (at http://www.hrsa.gov/vaccinecompensation/table.htm) occurring within the time period specified.

(b) Any contraindicating event listed in a vaccine's package insert (product labeling).

(5) The VAERS accepts all reports by any interested party of real or suspected adverse events occurring after the administration of any vaccine.

(6) All DOD and USCG health care beneficiaries are eligible to file claims with the NVIC program, according to the program's procedures.

2–8. Jet-injection immunization devices

These devices must be used in accordance with FDA-approved manufacturer's recommendations. Only vaccines with FDA approval for jet injectors use may be used in these devices.

2–9. Emergency response requirements

a. Written plan. Clinics or activities administering immunizations will develop and maintain a written plan for emergency response, including standing orders for the management of anaphylaxis and fainting.

b. Training. Whenever vaccines are administered, at least one person present must be trained and current in basic cardiopulmonary resuscitation, oropharyngeal airway management, and recognition and initial treatment of anaphylaxis with epinephrine.

c. Anaphylaxis management. For the medical management of an anaphylaxis event whenever vaccines are administered, the following must be immediately accessible on scene: stethoscope, blood pressure cuff (sphygmomanometer), minimum of three adult doses of epinephrine (1:1000), oral airway, bag valve mask or equipment to administer oxygen by positive pressure, and the equipment and ability to activate an emergency medical system. Other equipment and/or medications (for example, injectable antihistamines, corticosteroids, vasopressors, glucagon, albuterol, and IV fluids with administration sets), depending on the clinical setting and local policy, may be included beyond the minimum requirements listed above.

d. Observation. The ACIP general recommendations suggest that persons be observed for 15 to 20 minutes after

being immunized. Manufacturer's guidance must be followed when the manufacturer's package insert exceeds this requirement.

2–10. Adverse events

a. Describe in the individual's health record a detailed account of adverse events after administering immunizing agents or other medications. Mandatory information consists of identification, lot number, and manufacturer of the vaccine or other medication; date of administration; name and location of the medical facility; the type and severity of the event; treatment provided; and any exemption from additional doses. Consultation through MILVAX's Vaccine Healthcare Centers network is available 24 hours a day, 7 days a week, for providers who require additional support for clinical evaluation of possible vaccine adverse events.

b. Health care providers will report adverse events involving vaccines via the VAERS Web site http://www.vaers.hhs.gov or by faxing or mailing a VAERS–1 form. Obtain VAERS forms and information by calling 1–800–822–7967 or by accessing the VAERS Web site.

c. Health care providers will report adverse events involving chemoprophylaxis agents to MedWatch via the Web site at http://www.fda.gov/Safety/MedWatch/default.htm or on FDA Form 3500. MedWatch forms and information are available by calling 1–888–463–6332 or on the MedWatch Web site.

d. Reporting requirements are as follows:

(1) Report adverse events resulting in hospitalization, a life-threatening event (for example, anaphylaxis), time lost from duty more than one duty shift, or an event related to suspected contamination of a vaccine vial. Reports are also required for all events listed on the VAERS Table of Reportable Events Following Vaccination (available at http://vaers.hhs.gov/resources/vaersmaterialspublications).

(2) Further, health care providers are encouraged to report other adverse events considered unexpected in nature or severity.

(3) Reports of mild expected reactions are not required (for example, low-grade, self-limited fever of less than 24 hours duration, temporary local soreness, redness, or minor swelling at the site of immunization), but such reports may be submitted if the clinician or patient wishes.

e. Patients may also submit a VAERS or MedWatch report directly. If a patient wishes to submit a VAERS report, health care personnel will assist the patient in completing the form, regardless of professional judgment about causal association to immunization.

f. Record pertinent information from the recipient's health record on the VAERS or MedWatch report. Submit copies of the report within 7 days of adverse event recognition as follows:

(1) Send the original report form to the VAERS or MedWatch office.

(2) File a copy of the VAERS or MedWatch report in the patient's individual health record or annotate the relevant information on the report within the health record.

g. Immediately notify USAMMA or the vaccine manufacturer if contamination or other serious problem with a vaccine vial or lot is suspected. Suspend usage, but quarantine and retain all such opened or unopened vials or lots under appropriate storage conditions pending further investigation and disposition instructions.

h. An adverse reaction to a DOD-directed immunization in Service personnel is a line-of-duty condition.

(1) Medical treatment facility (MTF) commanders will provide full access to reserve component (National Guard and Reserve) members for evaluation and treatment of adverse events potentially related to DOD-directed immunizations.

(2) Reserve component (National Guard and Reserve) unit commanders will inform their members that they may seek medical care for such adverse events, with the unit providing assistance and information related to pay status and compensation issues. Any necessary documentation, including line-of-duty determinations, will be completed after the Reserve component Servicemember is evaluated and, if required, treated. In no case will such evaluation or treatment be denied or delayed pending line-of-duty determination. If additional health care is required after the initial visit and a line-of-duty determination has established a Service connection, a notice of eligibility must be completed in accordance with DODD 1241.01.

(3) DOD will provide an immunization health care capability to deliver medical specialty consultation, case management, and clinical investigation.

2–11. Program evaluation

MTF facilities and commands storing service treatment records will review immunization and chemoprophylaxis practices at least annually to ensure compliance with current standards of care and documentation and as a measure of medical readiness and health promotion. Program evaluation includes internal and external assessments of the standards for military immunization (see app B). Program evaluation is focused at the clinic level, regardless of Service, to include both fixed facilities and field units. The Continuous Quality Immunization Improvement Process Tool is one of several tools available to assist with program evaluation and is described at http://www.vaccines.mil/cqiip. MILVAX

can assist with guidance and implementation of the Continuous Quality Immunization Improvement Process Tool. Other tools may be available depending on the Service.

2–12. Blood donation

For timing of immunization with regard to blood donations, clinicians will consider the policies of the Armed Services Blood Program Office (http://www.militaryblood.DOD.mil) and the specific Service Blood Program Offices. In some situations, such as accession sites where blood donations are scheduled, regularly coordinate the administration of live vaccine immunizations after scheduled blood donation activities, when possible.

Chapter 3
Personnel Subject to Immunization

3–1. Military accessions

a. Military accessions. Accessions include Service personnel in enlisted initial entry training, Reserve Officers Training Corps (ROTC), Officer Candidate School, academy preparatory school, Service academy, Officer Indoctrination School, other officer accession programs, and officers who are directly commissioned.

(1) When determining the immunization needs of accessions, give credit for immunizations appropriately documented earlier in life (for example, data from electronic immunization registries maintained by State health departments).

(2) Immunize if the primary series is incomplete, if a booster immunization is needed, or if the Service personnel has no serologic or documented evidence of immunity. Complete multiple-dose immunization series according to the recommended schedule as soon as possible.

(3) Before immunizing, conduct serologic testing where available. At a minimum, conduct serologic testing for antibodies for measles, rubella, hepatitis A, hepatitis B, and varicella. Document medical exemptions for immunity (MI) in Service ITS. Documented medical exemptions for immunity will be accepted as evidence of immunity in lieu of vaccination.

(4) Except in an outbreak setting or for individual clinical purposes, immunization records will not be screened after completion of initial training with regard to measles, mumps, and rubella (MMR), poliovirus, or varicella vaccines.

(5) Document immunizations and immunization exemption codes (medical or administrative) in a DOD-approved Service ITS.

b. Enlisted accessions. Enlisted accessions may be scheduled for immunizations in two or more clusters, as long as all appropriate immunizations are administered or seroimmunity is determined. Pregnancy screening or testing for female accessions must be verified prior to administration of any live virus vaccines.

(1) *First cluster.* The first cluster of immunizations is administered, if susceptible, before or at the beginning of collective training (initial entry training, basic military training) to protect against pathogens that represent an imminent risk of contagious disease in settings of close contact: adenovirus; influenza; meningococcal; MMR; tetanus-diphtheria-pertussis; and varicella. Pneumococcal vaccine may be administered if warranted epidemiologically. Ensure live virus vaccines are given on the same day or at least 28 days apart (see ACIP guidelines for exceptions).

(2) *Second cluster.* The second cluster of immunizations may be administered, if susceptible, in the first or second half of basic military training, during advanced individual training, or upon arriving at the first duty station to protect against travel and other military risks. These immunizations include hepatitis A, hepatitis B, influenza (if not administered in first cluster), and poliovirus. Live virus immunizations follow at least 28 days after earlier live virus immunizations (see ACIP guidelines for exceptions).

c. Reserve Officers' Training Corps cadets and midshipmen. ROTC cadets and midshipmen and similar officer candidates who are ordered or called to active duty or active duty for training will require immunizations. Cadets and midshipmen may be scheduled for immunizations in two or more clusters:

(1) *First cluster.* Assess immunization or immunity status and administer immunizations, if susceptible, before or at the beginning of collective training to protect against pathogens that represent an imminent risk of contagious disease in settings of close contact. These immunizations include: influenza; meningococcal; MMR; tetanus-diphtheria-pertussis; and varicella. Ensure live virus vaccines are given on the same day or at least 28 days apart (see ACIP guidelines for exceptions).

(2) *Second cluster.* The second cluster of immunizations may be administered, if susceptible, in the first or second half of collective training to protect against travel and other military risks. These immunizations include hepatitis A, hepatitis B, influenza (if not administered in first cluster), and poliovirus. Live virus immunizations follow at least 28 days after earlier live virus immunizations (see ACIP guidelines for exceptions). ROTC cadets or midshipmen who travel overseas as part of their training will receive immunizations according to geographic risk assessments.

d. Service academy cadets and midshipmen. Service academy cadets and midshipmen will require immunizations as follows:

(1) *First cluster.* Assess immunization or immunity status and administer immunizations, if susceptible, before or at the beginning of collective training to protect against pathogens that represent an imminent risk of contagious disease in settings of close contact. These immunizations include: influenza, meningococcal, MMR, tetanus-diphtheria-pertussis, and varicella. Ensure live virus vaccines are given on the same day or at least 28 days apart (see ACIP guidelines for exceptions).

(2) *Second cluster.* The second cluster of immunizations may be administered, if susceptible, in the first or second half of collective training to protect against travel and other military risks. These immunizations include hepatitis A, hepatitis B, influenza (if not administered in first cluster), and poliovirus. Live virus immunizations follow at least 28 days after earlier live virus immunizations (see ACIP guidelines for exceptions). Cadets and midshipmen who travel overseas as part of their training will receive immunizations according to geographic risk assessments.

e. Entry-level officers. Upon accession, screen commissioned and warrant officers for immunization or immunity status and vaccinate as required.

3–2. Military personnel

a. Active duty personnel. Immunize active duty personnel in accordance with appendix D or as supplemented in official notices posted at the Military Vaccine Office Web site, http://www.vaccines.mil. During Military Service, active duty personnel will receive or be up-to-date on adult routine immunizations.

b. Reserve component (National Guard and Reserve). Immunize Reserve component Servicemembers in accordance with appendix D or as supplemented in Service-specific policies and notices posted at http://www.vaccines.mil. Reserve component Servicemembers receive the same immunizations as active duty personnel, but must be in a duty status to receive required immunizations.

c. Aviation personnel. Typically, aviation personnel are grounded for 12 hours (Air Force: access to medical care 4 hours post vaccination unless operational needs dictate otherwise; Navy: refer to "Aeromedical Reference and Waiver Guide" (ARWG) for vaccine specific information) after immunization, or as specified by their flight surgeon. No formal grounding documents are required for uncomplicated immunization. Personnel who previously experienced urticaria, hypersensitivity phenomena, or other unusual phenomena after an immunization are restricted from flying duty for an appropriate interval (for example, 72 hours) as determined by the flight surgeon. Additional temporary grounding may be necessary until significant side effects resolve.

d. Occupational risk. Military members at occupational risk for specific disease threats will receive appropriate vaccines per appendix D or as supplemented in Service-specific policies posted at http://www.vaccines.mil. Immunize special populations at occupational risk for vaccine-preventable diseases not listed in appendix D per Service, Federal, State, or local occupational medicine guidance.

e. Geographic travel requirements.

(1) Each Service's preventive medicine authority maintains current health threat assessments based on disease prevalence in specific geographical regions using Federal, DOD, USCG, and other relevant sources of information. These assessments are disseminated to units within their respective jurisdictions. Special Operations may determine additional area-specific immunization requirements.

(2) Installations and deployed units report disease occurrence through appropriate unit and/or medical lines of communication.

(3) Combatant commanders, in coordination with the appropriate surgeons general or CG–11, establish specific immunization requirements based on a disease threat assessment. These requirements may differ from standard Service immunization policies for personnel entering their area of responsibility to participate in exercises or other operational missions. Immunize personnel on official deployment or travel orders in accordance with the specific guidance established by the combatant commander before departure.

(4) For short notice travel or deployments requiring vaccines given in a multi-dose series, administer the first dose of the basic series. Administer as many of the subsequent doses as time permits. Completion before departure is the goal. If the series cannot be completed before departure, complete it upon arrival. Inform the patient that in order to obtain optimal immunity, the series must be completed by receiving all the required doses at the recommended intervals.

(5) For quarantine, entry, and reentry requirements, follow the provisions of the CDC, Division of Global Migration and Quarantine regulations concerning entry or reentry of military and nonmilitary personnel into the United States or its commonwealths, territories, and possessions.

f. Other uniformed Service personnel. Members of other uniformed Services are authorized immunizations according to their occupation, official duties, travel plans, health status, or other relevant factors.

3–3. Certain civilian employees

a. Federal civilian employees.

(1) *General.* Federal civilian employees will receive country-specific immunizations without charge at military activities upon presentation of official orders or authorization. Area preventive medicine authorities are consulted for recommendations applicable to specific areas. People declining immunizations required for entry into foreign countries

are referred to the appropriate authority for counseling. Document counseling in the health record and note that omission of certain immunizations may have consequences under host country policies, which could include compulsory immunization, detention, quarantine, or denial of entry.

(2) *Civilian employees at occupational risk for vaccine-preventable disease.* Federal civilian employees who are at risk of exposure to an infectious disease associated with their occupation may receive appropriate immunizations, without charge, at military activities. Administer immunizations upon recommendation of the responsible occupational medicine authority.

(3) *Civilian health care employees.* Susceptible or occupationally exposed health care employees (including volunteers) who are at risk of exposure to an infectious disease (for example, influenza) associated with their occupation may receive appropriate immunizations, without charge, at military activities. This policy applies to all health care settings, regardless of age or sex of the health care employee. Employees, including volunteers, who have contact with or potential exposure to human blood or blood products (whether from patient care, laboratory, or other health care settings) are provided hepatitis B virus vaccine in accordance with the local bloodborne pathogen exposure-control plan. Refer to the Occupational Safety and Health Administration standards (29 CFR 1910.1030) for additional information. Immunizations or immune status may be a condition of employment.

(4) *Employees with potential occupational exposure to wastewater or sewage.* Employees at occupational risk of exposure to wastewater or sewage will receive tetanus-diphtheria toxoids (preferably with pertussis vaccine) per ACIP recommendations. Other vaccines are not routinely required based solely on occupational exposure for wastewater treatment system workers, including sewage generated by medical facilities.

(5) *Individuals immunized per categories above.* Individuals immunized per the civilian personnel categories above are authorized treatment and necessary medical care related to adverse events after immunization, consistent with applicable occupational health program requirements.

b. Civilian Expeditionary Workforce. Civilian employees and others in the Civilian Expeditionary Workforce may receive, without charge, appropriate immunizations at military activities. In accordance with DODD 1404.10, components should ensure emergency-essential and non-combat essential employees are aware of potential deployment immunizations as a condition of employment. Components should also ensure the employee completes and signs a record of notification with a signed DD Form 2365 (DOD Civilian Employee Overseas Emergency-Essential Position Agreement). Applicable vacancy announcements and position descriptions will note obligations to receive immunizations. Emergency-essential and non-combat essential employees have the same access as military personnel to treatment and necessary medical care related to adverse events after immunization, consistent with applicable occupational health program requirements.

c. Bargaining units. For Federal employees in a bargaining unit, local management must meet applicable labor relations obligations before implementing any changes to the bargaining unit employees' conditions of employment. Civilian personnel advisory centers provide guidance on these matters.

d. Biological warfare defense. Immunization of civilian employees and contracted workers for biological warfare defense are addressed in DODI 6205.4.

e. Emergency situations. In emergency situations, the provisions of DODD 6200.03 apply.

3–4. Contracted workers

a. Provide immunizations to contracted workers according to the terms of the contract and as stated in the contract agreement. If the contract does not provide for provision of immunizations by the government, contractors are responsible for providing appropriate immunizations to their employees For vaccines with limited distribution (for example, anthrax, smallpox), DOD or USCG may provide the immunizations, regardless of the terms of the contract. The contractor is responsible for work-related illnesses, injuries, or disabilities under worker-compensation programs, supplemented by existing Secretarial designee authority.

b. Contracted health care workers are eligible for immunizations required or offered to health care employees and are provided as stated in the contract agreement. Contracts will include specifications describing immunizations required of contracted health care workers.

c. Family members of contracted workers in foreign-duty settings under military sponsorship will receive country-specific immunizations without charge at military activities upon presentation of official orders or authorization. People declining immunizations required for entry into foreign countries are referred to the appropriate authority for counseling. Document counseling in the health record and note that omission of certain immunizations may subject them to adverse action according to host country policies, which could include compulsory immunization, detention, quarantine, or denial of entry.

3–5. Department of Defense, U.S. Coast Guard schools, childcare centers and youth programs

a. As a condition of employment, schoolteachers, childcare center workers, youth program workers, and volunteers are administered appropriate vaccines against communicable diseases in accordance with ACIP adult immunization schedule recommendations, unless already immune, based on seroimmunity, physician diagnosed illness, or documented proof of immunization.

b. Children attending DOD and USCG-sponsored primary and secondary schools, childcare centers, or similar facilities are required to be up to date on all age appropriate ACIP-recommended vaccines for children unless there is documentation of previous immunization, religious exemption, or medical contraindication. For foreign-national children outside the United States, observe host country recommendations or requirements.

3–6. Other populations

a. Department of Defense and U.S. Coast Guard beneficiaries.

(1) *Family members of military personnel.* Family members receive immunizations according to current ACIP recommendations. In addition, Family members may be subject to Service-specific requirements and recommendations for immunizations applicable to the country in which they will reside while accompanying military members under military sponsorship.

(2) Family members or sponsored individuals of other Federal civilian employees in foreign-duty settings under military sponsorship. These Family members will receive country-specific immunizations without charge at military activities upon presentation of official orders or authorization. People declining immunizations required for entry into foreign countries are referred to the appropriate authority for counseling. Document counseling in the health record and note that omission of certain immunizations may have consequences under host country policies, which could include compulsory immunization, detention, quarantine, or denial of entry.

b. Foreign nationals. Foreign nationals who come to the United States, its territories, commonwealths, or possessions under Armed Forces sponsorship receive immunizations required for entry into the United States and by local jurisdictions. When returning to their country of origin, foreign nationals receive immunizations required by international health regulations or their country of origin. These immunizations are administered without charge at military activities upon presentation of official orders or authorization.

c. Detainees. The installation or activity commander, upon the recommendation of the appropriate medical authority, will provide immunizations against diseases that may be a significant cause of death or illness among detainees. Such immunizations are voluntary and are administered without charge to the detainee. Annotate all immunizations and chemoprophylactic medications in the detainee's health record. Before immunization, inform detainees in their own language about the relative benefits and risks of the specific immunizations offered. Factors to consider in deciding which immunizations to offer detainees include their likely preexisting immunity, the anticipated length of detention, seasonal threat of infection, and other risk factors related to personal health status and living conditions. (Refer to DODI 2310.08E for additional guidance.)

d. Overseas commander authority. The overseas commander, commanding officer, or officer-in-charge, upon the recommendation of the appropriate medical authority, will provide immunizations against communicable diseases judged to be a potential hazard to the health of the command; such vaccines are administered without charge.

e. Other than U.S. Forces. Immunization of other than U.S. Forces for biological warfare defense are addressed in DODI 6205.4.

f. Emergency situations. In emergency situations, the provisions of DODD 6200.03 apply.

Chapter 4
Specific Immunization Requirements for Department of Defense and U.S. Coast Guard Personnel

(Also see appendix D for a chart on the required immunizations for military personnel.)

4–1. Civilian applicability

Certain civilian employees may be required to receive immunizations as a condition of their employment or participation in a particular assignment. In such cases, failure to voluntarily receive the immunizations may result in a personnel action being taken (see chap 3), but in no case will immunizations be involuntarily administered.

4–2. Adenovirus types 4 and 7

a. Military indication. To prevent adenovirus infection, an acute febrile respiratory disease caused by adenovirus serotypes 4 and 7. Direct contact and fecal oral transmission of the virus may result in a respiratory disease infection or outbreak of disease among an unvaccinated recruit population.

b. Basic trainees. Administer adenovirus vaccine to military enlisted basic trainees before or at the beginning of collective training at the same time the first live virus vaccines are administered. Routine administration in other populations is not generally recommended except when directed by preventive medicine guidance, based on disease incidence and severity.

4–3. Anthrax

a. Military indication. To prevent anthrax, an acute infectious disease caused by the spore forming bacterium

Bacillus anthracis. Direct exposure to anthrax spores may result in cutaneous, gastrointestinal, or inhalational infection. *Bacillus anthracis* has been identified as a potential biological warfare agent.

b. Military and civilian personnel. Administer anthrax vaccine to military personnel and applicable civilians according to DOD or USCG policy for the Anthrax Vaccine Immunization Program and Service-specific implementation plans. Immunize personnel based on geographical areas at higher risk for release of anthrax as a weapon or in occupational roles as designated by the Services, Chairman of the Joint Chiefs, or the Office of the Secretary of Defense.

c. Occupational risk. Administer anthrax vaccine to at-risk veterinary and laboratory workers and others at occupational risk of exposure.

4–4. Haemophilus influenzae serotype b, commonly called Hib

a. Military indication. To prevent invasive Haemophilus influenza disease and infection of many organ systems caused by the bacterium *Haemophilus influenzae* serotype b (Hib). The disease is transmitted via respiratory droplets. The most common types of invasive Hib disease are: meningitis, epiglottitis, pneumonia, arthritis, and cellulitis.

b. Military and civilian personnel. Administer Hib vaccine to those who are immunocompromised, have sickle cell disease, or do not have a spleen or a functioning spleen.

4–5. Hepatitis A

a. Military indication. To prevent hepatitis A, an acute infection of the liver that is acquired by consuming food or water contaminated with hepatitis A virus, particularly during deployment or travel to areas with poor food, water, and sewage sanitation. It can range in severity from a mild illness lasting a few weeks to a severe illness lasting several months. Hepatitis A infections occur worldwide.

b. Basic trainees and other accessions. Unless seroimmune, administer hepatitis A vaccine to trainees and accessions during initial entry training.

c. Military and civilian personnel. Unless seroimmune, or evidence of appropriate complete vaccination, administer hepatitis A vaccine to all military personnel, and civilian personnel when indicated.

d. Occupational risk. Hepatitis A vaccine is indicated per ACIP guidelines and locally designated food handlers.

4–6. Hepatitis B

a. Military indication. To prevent hepatitis B, an acute or potentially chronic infection of the liver that is acquired through percutaneous, sexual, and other mucosal exposure to blood and body fluids from people infected with hepatitis B virus. Chronic infections may result in cirrhosis or cancer of the liver. Hepatitis B infections occur worldwide, and some infected people maintain a chronic carrier state.

b. Basic trainees and other accessions. Unless seroimmune, administer hepatitis B vaccine to basic trainees and accessions during initial entry training.

c. Military and civilian personnel. Unless seroimmune, or evidence of appropriate complete vaccination, administer hepatitis B vaccine to all military personnel, and civilian personnel, when indicated.

d. Occupational risk. Administer hepatitis B vaccine to susceptible personnel who are at risk of potential exposure to bloodborne pathogens per the Occupational Safety and Health Administration standards (29 CFR 1910.1030). For military purposes, this includes occupational specialties involving health care workers, emergency medical technicians, mortuary affairs personnel, search and rescue specialists, correctional facility staff, and designated special operations forces.

e. Serologic testing. Conduct serologic testing of health care workers who have direct contact with patients and those who have potential occupational risk for exposure to bloodborne pathogens 1 to 2 months after completion of the hepatitis B vaccine series to determine serologic response according to CDC and ACIP recommendations.

4–7. Influenza

a. Military indication. To prevent influenza, an acute febrile respiratory viral infection that can cause epidemics within military populations, especially under conditions of crowding, such as initial entry training, aboard ships, extended air transport, or deployment settings. Influenza has the potential for widespread transmission through person-to-person contact and fomites.

b. Military personnel. Administer influenza vaccine(s) annually or as indicated to all active duty, Reserve, and National Guard personnel.

c. Occupational risk. Administer influenza vaccine(s) annually or as indicated to personnel who work or volunteer in DOD MTFs.

4–8. Japanese encephalitis

a. Military indication. To prevent Japanese encephalitis, a mosquito-borne viral disease, during deployments and travel to endemic areas in Eastern Asia and certain western Pacific Islands. Japanese encephalitis virus (JEV) can cause

an acute infection of the brain, spinal cord, and meninges with high rates of complications, chronic disability, and death.

b. Military and civilian personnel. Administer the JEV vaccine to military personnel and civilian personnel who have a substantial risk of exposure to the virus based on their geographic location.

c. Temporary flying restrictions. Impose temporary flying restrictions post-JEV immunization for aircrew personnel per Service-specific policy.

4–9. Measles, mumps, and rubella (MMR)

a. Military indication. To prevent MMR, primarily by boosting immunity acquired from childhood immunization. These three acute viral infections are spread by the respiratory route or person-to-person contact. In military trainee populations, each can cause disease outbreaks. Rubella usually causes a mild infection, but infection during the first trimester of pregnancy puts the fetus at high risk of congenital rubella syndrome and birth defects. Young adults may experience more severe complications from mumps infection. All three diseases occur worldwide, primarily among children.

b. Basic trainees and other accessions. Unless seroimmune to both measles and rubella, administer MMR vaccine to susceptible basic trainees and accessions within the first 2 weeks of training.

c. Military and civilian personnel. Presume immunity through infection for persons born in 1957 or earlier. Ensure personnel born after 1957 have received two lifetime doses of MMR vaccine or have positive serologic test results. Immunity against mumps is not necessary as a military requirement, but may be appropriate in exceptional clinical circumstances such as outbreaks.

d. Occupational risk. Ensure health care workers have received two documented doses of MMR vaccine or have positive serologic test results.

4–10. Meningococcal

a. Military indication. To prevent meningococcal disease or meningitis and other systemic infections caused by the bacteria *Neisseria meningitidis* serogroups A, C, W–135, and Y. No vaccine against serogroup B meningococcus, another common pathogen, is currently licensed in the United States. Basic trainees and other military populations living in crowded conditions are at an increased risk for meningococcal infection. Historically, outbreaks have occurred in training populations. Meningococcal vaccine may be indicated for deployment and travel to areas with highly endemic meningococcal disease.

b. Basic trainees and other accessions. Administer meningococcal vaccine to basic trainees, cadets, and midshipmen at Service academies within the first 2 weeks of training, if no evidence of vaccination within the last 5 years.

c. Military and civilian personnel. Administer meningococcal vaccine to personnel traveling to countries in which *N. meningitidis* is hyperendemic or epidemic and other countries as required by DOD and USCG policy or recommended by the CDC.

d. Alert personnel. Administer meningococcal vaccine to personnel who are designated to deploy within 10 days of notification.

e. Other personnel. Administer one dose of meningococcal vaccine to persons who do not have spleens or functional spleens.

4–11. Pertussis

Tetanus, diphtheria, and pertussis guidance is in paragraph 4–16.

4–12. Pneumococcal

a. Military indication. To prevent pneumococcal disease due to *Streptococcus pneumoniae* in personnel who fall into a high-risk category due to age or underlying health conditions (for example, persons who smoke, have asthma, or have no spleen) or who are in high-risk situations, such as certain training populations. *Streptococcus pneumoniae* may result in pneumonia, bacteremia, and meningitis.

b. Basic trainees and other accessions. Routine administration of vaccine is not generally practiced, but may be directed by preventive medicine guidance, based on disease incidence and severity.

c. Military personnel. Administer pneumococcal vaccine to military personnel who are in a high-risk category per ACIP recommendations. Administer a second dose to persons without spleens or severely immunocompromised five years after the initial dose.

4–13. Poliomyelitis

a. Military indication. To prevent poliomyelitis, a viral infection that affects the central nervous system resulting in paralytic symptoms, primarily by boosting immunity acquired from childhood immunization. Poliomyelitis is acquired by person-to-person transmission through the fecal-oral route. Military and civilian personnel deploying or traveling to areas with poor sanitation are at increased risk, although international immunization efforts have decreased poliomyelitis incidence worldwide. Only inactivated poliovirus vaccine (IPV) is available in the US.

b. Basic trainees and other accessions. Administer a single booster dose of IPV to basic trainees and accessions. Personnel who have not received the primary series must complete the series using IPV. Unless there is reason to suspect otherwise (for example, childhood spent in a developing country, childhood immunizations not administered), receipt of the primary series of IPV may be assumed.

c. Military personnel. Because of the high level of childhood immunization against this disease, do not screen immunization records with regard to poliovirus immunity after completion of initial entry training except in an outbreak setting or for individual clinical purposes.

4–14. Rabies

a. Military indication. To prevent rabies, a life threatening viral disease caused by exposure to the saliva of animals or humans infected with the rabies virus, which includes bites.

(1) *Pre-exposure prophylactic immunization.* A pre-exposure immunization series may be indicated for people with potential occupational risk of exposure to rabid animals, or for forces assigned to locations where access to definitive care likely exceeds 24 hours. Pre-exposure prophylaxis should not be considered sufficient for the prevention of rabies; however, it reduces the need for human rabies immune globulin-better known as HRIG-and reduces the number of shots required for post-exposure prophylaxis.

(2) *Post-exposure prophylaxis.* Consult with a preventive medicine physician and veterinarian for guidance and to report the animal exposure. Post-exposure treatment includes immediate wound care, and may include the post-exposure vaccine series, and human rabies immune globulin in an unvaccinated patient. Post-exposure prophylaxis is safe and effective.

b. Military personnel. Administer pre-exposure rabies vaccine series to special operations personnel, including designated special operations enablers and the occupational risk groups listed below, in accordance with Service policy.

c. Occupational risk. Administer pre-exposure rabies vaccine series to veterinary workers, animal handlers, certain laboratory workers, and personnel who have animal control duties and personnel assigned long-term to regions with endemic rabies. Give booster doses every 2 years or when antibody concentrations indicate.

4–15. Smallpox

a. Military indication. To prevent smallpox disease due to the deliberate release or spread of the smallpox virus. In 1980, the WHO declared the global eradication of naturally occurring smallpox. Nonetheless, stocks of variola virus, the causative agent of smallpox, could be used as a biological warfare agent.

b. Military and civilian personnel. Vaccinate designated military and civilian personnel according to DOD and other designed personnel in accordance with USCG policy and Service-specific implementation plans. These include military personnel and applicable civilians who are smallpox epidemic response team members, assigned to medical teams at hospitals and clinics, or assigned to designated forces that constitute mission-critical capabilities. Immunize personnel based on geographical areas at higher risk for release of smallpox as a weapon or in occupational roles as designated by the Services, Chairman of the Joint Chiefs, or the Office of the Secretary of Defense.

c. Training and education. Before administering smallpox vaccine to military or civilian personnel who are eligible to receive smallpox vaccine, provide education on the criteria for exemption from immunization, expected response at the vaccination site, vaccination-site care, risks of spreading vaccinia to close contacts, adverse events following immunizations (AEFI) such as myopericarditis, and other relevant topics per Service implementation plans.

d. Screening. Use the DOD-specific screening form posted at http://www.vaccines.mil to identify persons with personal or household contraindications to smallpox vaccination (for example heart conditions, immunosuppressed conditions, pregnancy, skin conditions such as eczema and atopic dermatitis). Screening will include assessing pregnancy status and recency of testing for human immunodeficiency virus infection. In the event of a smallpox outbreak, "permanent" exemptions may be rescinded according to individual risk of exposure to variola virus.

e. Vaccination. Internal MTF and command clinical quality management programs will have mechanisms to confirm that vaccinators demonstrate proper vaccination technique.

f. Post-vaccination site care. Take appropriate care to prevent the spread of vaccinia virus from a vaccinee's vaccination site. MTFs will monitor the vaccination sites of vaccinated health care workers (for example, operating site-care stations), promote effective bandaging, and encourage scrupulous hand washing.

g. Post-vaccination evaluation ("take" check). Assessment and documentation of response (a "take") to vaccination is required for health care workers and members of smallpox response teams who would travel into a smallpox outbreak area. Evaluate and record the vaccination response of individuals receiving smallpox vaccine in a DOD and USCG-approved electronic ITS.

4–16. Tetanus, diphtheria, and pertussis

a. Military indication. To prevent tetanus, diphtheria, and pertussis, primarily by boosting immunity acquired from childhood immunization.

(1) Tetanus is an acute disease of the nervous system caused by the serotoxin produced by *Clostridium tetani*. The *C. tetani* spores enter the body through breaks in the skin, and the bacterium then grows at the wound site. A tetanus

infection results in generalized rigidity and convulsive spasms of the skeletal muscles. The *C. tetani* spores occur in the environment worldwide.

(2) Diphtheria is an acute disease caused by a cytotoxin of the bacteria *Corynebacterium diphtheriae. C. diphtheriae* is transmitted person-to-person via respiratory droplets and direct contact. Diphtheria can lead to airway obstruction, and more severe complications may result from toxin absorption into organs and tissues. Diphtheria occurs worldwide.

(3) Pertussis is a highly communicable acute respiratory illness caused by the bacteria *Bordetella pertussis.* Pertussis is spread via direct contact with respiratory secretions. Pertussis occurs worldwide.

b. Basic trainees and other accessions. For those individuals lacking a reliable history of prior immunization, administer one dose of Tetanus-diphtheria and acellular pertussis (Tdap) vaccine according to ACIP guidelines. Unless there is reason to suspect otherwise (for example, childhood spent in a developing country, childhood immunizations not administered), receipt of the basic immunizing series may be assumed.

c. Military and civilian personnel. Administer booster doses of Tetanus-diphtheria (Td) to all personnel every 10 years following the completion of the primary three-dose series. A one-time dose of Tdap in place of a Td booster during adulthood is required, regardless of interval.

d. All personnel. Following ACIP wound-management guidelines for the treatment of contaminated wounds. Tdap is preferred to Td for adults vaccinated 5 years earlier who require a tetanus toxoid-containing vaccine as part of wound management and who have not previously received Tdap. For adults previously vaccinated with Tdap, Td should be used if a tetanus toxoid-containing vaccine is indicated for wound care.

4–17. Typhoid fever

a. Military indication. To prevent typhoid fever, a systemic bacterial disease acquired by consuming food or water contaminated with *Salmonella typhi*, particularly during deployment or travel to typhoid-endemic areas and other areas with poor sanitation.

b. Military and civilian personnel. Administer typhoid vaccine before overseas deployment to typhoid-endemic areas.

c. Alert personnel. Administer typhoid vaccine to alert personnel, per Service policy, who are prepared for deployment to typhoid-endemic areas or who have potential risks of exposure to contaminated local food and drink. Administer booster doses per immunization schedule. For Air Force, only units specifically identified by the MAJCOM surgeon require initial and subsequent immunization against typhoid fever.

4–18. Varicella

a. Military indication. To prevent varicella (chickenpox), a generally mild and self-limiting viral infection caused by the varicella zoster virus. Although varicella is a common childhood disease, adults may experience more severe illness and have higher complication and case-fatality rates. Adolescents and adults are at higher risk for severe disease complications such as secondary skin infections, neurologic disease, and multi-organ involvement. Varicella zoster virus is transmitted by respiratory secretions, direct contact, and aerosolization of the virus from skin lesions. Military members at higher risk for infection include basic trainees, cadets/midshipmen at Service academies, officer trainees, and special operations personnel, and others living in military environments conducive to person-to-person spread of respiratory diseases (for example, barracks, ships).

b. Basic trainees and other accessions. Administer varicella vaccine to susceptible trainees and other accessions within the first 2 weeks of initial entry training. Serologic screening of trainees is the preferred means of determining those susceptible to varicella infection and in need of immunization. Identify those people who do not have a personal history of varicella disease, documentation of two prior varicella immunizations, or documentation of immunity based on serologic testing as susceptible. Document positive results of serologic testing in a DOD-approved electronic ITS. Adults and adolescents require two doses of varicella vaccine given 4 to 8 weeks apart.

c. Health care workers. Administer varicella vaccine to susceptible health care workers. Determine susceptibility as noted above for trainees, birth before 1980 should not be considered evidence of immunity for health care workers. Routine post-immunization testing for antibodies to varicella is not recommended.

d. Other susceptible adults. Offer varicella vaccine to other susceptible persons, especially nonpregnant women of childbearing age and men living in households with young children.

4–19. Yellow fever

a. Military indication. To prevent yellow fever disease, a viral infection that may result in severe systemic disease and organ failure. Yellow fever infection is transmitted via the bite of an infected mosquito. Documented vaccination status must be verified to meet international health requirements during deployment or travel to yellow-fever-endemic areas. Areas of greatest risk are sub-Saharan Africa and tropical South America.

b. Military personnel. Administer yellow fever vaccine to all Marine Corps accessions and military personnel traveling to or transiting through yellow-fever-endemic areas.

c. Alert personnel. Administer yellow fever vaccine to alert personnel prepared for deployment to yellow-fever-endemic areas. Administer booster doses per immunization schedule. For Air Force, only units specifically identified

by the MAJCOM surgeon require initial and subsequent immunization against yellow fever. For Navy, administer to those assigned to units subject to deployment within 10 days of notification into land areas where yellow fever is endemic.

d. Civilian and other personnel. Administer yellow fever vaccine to personnel traveling to, or transiting through, endemic areas.

Chapter 5
Chemoprophylaxis

5–1. General

a. Chemoprophylaxis. This section does not relate to the treatment of diseases but provides a brief review of military relevant diseases and associated chemoprophylaxis guidelines. Chemoprophylaxis is defined here as the administration of medication before, during, or after possible exposure to an infectious agent, to prevent either infection or disease. Most agents used for chemoprophylaxis are not FDA-approved for this indication and thus may not be administered to units under a force health protection strategy or policy; rather, these agents must be prescribed to individuals and documented accordingly by an appropriate health care provider. Follow instructions from the relevant combatant command surgeon who will consult with the appropriate preventive medicine authority for the use of chemoprophylactic agents. Command medical officers will review indications for use and potential adverse effects of specific chemoprophylactic medications before use. These recommendations for drugs or agents are current as of the date of this publication. Consult current information and guidance for appropriate drugs and dosing regimens (for example the CDC, the ACIP, the National Center for Medical Intelligence (NCMI), and the American Public Health Association's "Control of Communicable Diseases Manual"). The following classes of chemoprophylaxis are not addressed in this publication:

(1) Chemical warfare-related chemoprophylaxis. Consult the current version of "Medical Management of Chemical Casualties," published by the U.S. Army Medical Research Institute of Chemical Defense.

(2) Medical therapy for tuberculosis infection. Consult publications from CDC, the American Thoracic Society, the Advisory Council for the Elimination of Tuberculosis, and similar authorities.

(3) Radiation-related chemoprophylaxis (for example, potassium iodide, granisetron, or Prussian blue).

(4) Other forms of prevention involving nonbiological medications (for example, calcium, aspirin, or vitamins).

(5) Immunotherapy.

b. Packaging. Dispense chemoprophylaxis agents to individuals in child-resistant containers, consistent with 15 USC 1471–1476 (The Poison Prevention Packaging Act), or unit-of-use packaging. Use appropriate packaging to keep the medication clean and dry.

c. Labeling. Dispense chemoprophylaxis agents to individuals in packages that contain the name of the product, directions for proper use, and the name of the person to whom the medication was dispensed.

5–2. Anthrax

a. Military indication. The use of antibiotics and immunoglobulin following a possible exposure to anthrax is locally-directed and is prescribed by preventive medicine based on risk. The use of antibiotics and immunoglobulin have been shown to increase survival when used after exposure to anthrax and before onset of symptoms (post-exposure prophylaxis or empiric treatment).

b. Chemoprophylaxis. Recommended drugs include ciprofloxacin and doxycylcine. Refer to Service-specific policies. Anthrax immunoglobulin is available through the CDC's Emergency Operation Center.

5–3. Group A streptococcus

a. Military indication. Outbreaks of group A streptococci can spread rapidly in groups in settings of close contact, such basic training and contingency operations.

b. Chemoprophylaxis. The primary drug used for prophylaxis is penicillin, specifically the long-acting injectable form, penicillin G benzathine. Oral penicillin VK and azithromycin have also been used effectively. Administer penicillin prophylactically, when required, to terminate disease transmission. Routine administration of penicillin for prophylaxis of basic trainees against group A streptococcal infection has been shown to be effective at some installations with historically high incidence of disease. This practice should be directed by local preventive medicine authority.

5–4. Influenza

a. Military indication. Influenza can be a significant cause of morbidity in a susceptible population and can degrade mission capability.

b. Chemoprophylaxis. Consider prophylactic use of antiviral therapy if available vaccine does not antigenically

match circulating strains or if an outbreak occurs early in the season before widespread immunization. For additional guidance, refer to CDC.

5–5. Leptospirosis

a. Military indication. Leptospirosis can cause morbidity in personnel exposed to contaminated water sources.

b. Chemoprophylaxis. Doxycycline is effective in preventing leptospirosis in exposed military personnel during periods of high risk of exposure. Consult an infectious diseases or preventive medicine authority for proper use and dosing.

5–6. Malaria

a. Military indication. Malaria has caused morbidity and mortality in military populations for centuries. It continues to be one of the most important disease threats to military and civilian personnel deployed to areas where the disease is endemic.

b. Chemoprophylaxis. The Services or the combatant command surgeon determine specific chemoprophylactic regimens, typically with guidance from the NCMI, for the area of operations based on degree and length of exposure and the prevalence of drug resistant strains of *plasmodia* in the area(s) of travel. Prescribe anti-malarials per package insert. Health care providers will screen individuals for contraindications to specific malaria chemoprophylaxis (for example G6PD deficiency and primaquine) and determine the appropriate malaria chemoprophylaxis. Health care providers must document malaria chemoprophylaxis prescriptions in the health record when anti-malarial medications are prescribed. Include the member's electronic medication profile (for example, Composite Health Care System II), whenever possible.

5–7. Meningococcal disease

a. Military indication. Meningococcal disease can result in morbidity and potential mortality in populations experiencing crowded conditions. Chemoprophylaxis has been shown to prevent disease when administered post-exposure to susceptible people.

b. Chemoprophylaxis. There are several drugs available for prophylaxis of close contacts of meningococcal disease cases. Consult an infectious diseases or preventive medicine authority for determination of individuals to offer prophylaxis and for assistance with drug selection and dosing.

5–8. Plague

a. Military indication. Plague has been identified as a potential biological warfare agent, especially if aerosolized to cause pneumonic plague. There is no licensed vaccine that is effective against pneumonic plague. Provide chemoprophylaxis to persons potentially exposed to cases of pneumonic plague.

b. Chemoprophylaxis. Consult an infectious diseases or preventive medicine authority for determination of individuals to offer prophylaxis and for assistance with drug selection and dosing.

5–9. Scrub typhus

a. Military indication. Spread by the bite of infective larval mites. Mite bites may be a source of morbidity in populations encountering field conditions.

b. Chemoprophylaxis. Doxycycline has been shown to be effective in preventing scrub typhus in exposed personnel. Consult an infectious diseases or preventive medicine authority for proper use and dosing.

5–10. Smallpox

a. Military indication. Various forms of vaccinial infections may develop following receipt of the smallpox vaccine. Chemoprophylaxis may be indicated to prevent morbidity in immunized Servicemembers or their contacts.

b. Chemoprophylaxis. VIG and vaccinia-specific antivirals are available through the DOD. Contact MILVAX to request and coordinate administration of these chemoprophylactic agents.

5–11. Traveler's diarrhea

a. Military indication. Diarrhea can cause morbidity in personnel exposed to contaminated food and water sources.

b. Chemoprophylaxis. Chemoprophylaxis for traveler's diarrhea is only recommended on rare occasions where diarrhea would compromise a mission. Prophylactic antibiotics may be considered for short-term travelers who are high-risk hosts (such as those who are immunosuppressed) or those taking critical trips during which even a short bout of diarrhea could significantly impact the purpose of the trip. Instead of prophylaxis travelers, should be prescribed appropriate medications and provided instructions for self-treatment of diarrhea. Consult an infectious diseases or preventive medicine authority for assistance.

Chapter 6
Biological Warfare Defense

6–1. Responsibilities

a. The combatant commanders, annually and as required, provide the Chairman of the Joint Chiefs of Staff with their assessment of the biological warfare threats to their theaters.

b. The President of the Defense Health Board, in consultation with the Secretaries of the Military Departments, annually and as required, identifies to the Assistant Secretary of Defense (Health Affairs) (ASD (HA)) vaccines available to protect against validated biological warfare threat agents and recommends appropriate immunization protocols and/or chemoprophylaxis.

6–2. Procedures

The DOD Immunization Program for Biological Warfare Defense is conducted as follows:

a. The combatant commanders, annually and as required, provide the Chairman of the Joint Chiefs of Staff with their assessment of the biological warfare threats to their theater.

b. The Chairman of the Joint Chiefs of Staff, in consultation with the combatant commanders; the chiefs of the Military Services; and the Director, Defense Intelligence Agency, annually validates and prioritizes the biological warfare threats to DOD personnel and forwards the threat list to the DOD Executive Agent through the ASD (HA).

c. Within 30 days of receiving the validated and prioritized biological warfare threat list from the Chairman of the Joint Chiefs of Staff, the DOD Executive Agent, in consultation with the Secretaries of the military departments and the President of the Defense Health Board, provides recommendations to the ASD (HA) on vaccines and immunization protocols necessary to enhance protection against validated biological warfare threat agents.

d. Within 30 days of receiving the coordinated recommendations of the DOD Executive Agent, the ASD (HA) directs the Secretaries of the military departments to begin immunization of the specified DOD and USCG personnel against specific biological warfare threat agents. The ASD (HA) will coordinate with and obtain approval from the Secretary or Deputy Secretary of Defense before issuing the appropriate direction.

e. The Secretaries of the military departments will program and budget for required vaccinations, including the costs of the biological warfare defense vaccines.

Chapter 7
Vaccines and Other Products in Investigational New Drug Status

7–1. Purpose

For infectious disease threats for which the only available vaccine or chemoprophylaxis product is in an IND status, the IND product must be administered in full accordance with FDA regulations at 21 CFR Parts 50 and 312, as well as 10 USC 1107, Executive Order 13139, and DODD 6200.2. DOD may use products that have not been approved or licensed for commercial marketing as force health protection measures in combat settings, other military operations, peacekeeping, or humanitarian missions. DOD will provide comparable access to IND products to military personnel, civilian personnel, contracted workers, and beneficiaries based on the health risk to the people involved.

7–2. General guidance on investigational new drug products

Commanders, through the appropriate chain, must request approval from the Secretary of Defense to use INDs for force health protection. If the member's use of an IND product is voluntary, the product must be administered with documented informed consent in accordance with a protocol approved by the FDA for IND product use. A vaccine, antibiotic, or other product in an IND status may be mandatory for military members, if the President of the United States has approved a waiver of the requirement for informed consent. Under 10 USC 1107, only the President has the authority to grant a waiver of the requirement that a military member provide prior consent to receive an IND or a drug unapproved for its applied use in connection with the member's participation in a particular military operation. The President must determine, in writing, that obtaining consent (1) is not feasible, (2) is contrary to the best interests of the member, or (3) is not in the interests of national security. The requirement for informed consent may not be waived for civilian personnel, contracted workers, and beneficiaries.

7–3. Health recordkeeping requirements for investigational new drug products

All IND vaccines or chemoprophylaxis products that are administered, whether with the member's informed consent or with an approved waiver of informed consent, must be recorded in the individual's permanent health record or DOD and USCG-approved electronic ITS. For vaccines, the documentation is the same as that required for other vaccines with an annotation "IND" with the vaccine name. This recordkeeping requirement is in addition to any recordkeeping

requirements of the FDA-approved IND protocol. The requirement for recordkeeping applies to IND vaccines, antibiotics, and other medications in IND status.

7–4. Information requirements for investigational new drug products

Any recipient of an IND vaccine or chemoprophylaxis product must receive the information (for example, briefing, individual counseling, information statements) required by the FDA-approved IND protocol. Full compliance with this requirement is extremely important whether the IND product is voluntary or mandatory.

7–5. Coordination

The Army, as the Executive Agent for the Immunization Program for Biological Warfare Defense, maintains a program office at the U.S. Army Medical Materiel Development Activity (USAMMDA) to execute oversight and coordination of the use of IND products for Force Health Protection.

Chapter 8
Vaccines and Other Products Used Under Emergency Use Authorization

8–1. General

Under 21 USC 564 (The Food, Drug, and Cosmetic Act), some drugs, vaccines, or devices that have not been approved or licensed by the FDA through the regular drug approval process (or not approved for an intended use) may be used as medical countermeasures to chemical, biological, radiological, and nuclear (CBRN) agents or threats, if the FDA grants an EUA. This EUA authority is an alternative to the otherwise applicable requirement to file an IND application and follow IND rules (see chap. 7) to use such unapproved drugs as CBRN medical countermeasures.

8–2. Criteria

In general, the FDA may grant an EUA for up to 12 months, with potential renewal, based on the following:

a. The Secretary of Defense or designee has determined that there is a military emergency or significant potential for a military emergency relating to a particular CBRN agent or threat.

b. The Secretary of DHHS declares an emergency based on the Secretary of Defense's determination.

c. The Secretary of DHHS determines—

(1) The vaccine or drug may be effective in diagnosing, treating, or preventing the disease or condition.

(2) The known and potential benefits of the vaccine or drug outweigh the known and potential risks.

(3) There is no adequate, approved, and available alternative medical countermeasure.

d. The duration of authorization corresponds to the duration of the emergency or significant potential for an emergency.

8–3. Refusal options

The FDA may decide that potential recipients of a drug under an EUA should have the option to refuse it. The President may waive this option for military personnel.

8–4. Health recordkeeping requirements for emergency use authorization products

All EUA vaccines or chemoprophylaxis products that are administered must be recorded in the individual's permanent health record and/or DOD-approved electronic ITS.

8–5. Information requirements for emergency use authorization products

Any recipient of an EUA vaccine or chemoprophylaxis product must receive the information (for example, briefing, individual counseling, information statements) required by the FDA-approved EUA. Full compliance with this requirement is critical.

8–6. Department of Defense requests for emergency use authorizations

Requests for possible EUAs for military purposes must be submitted to ASD (HA) for consideration.

8–7. Coordination

The Army, as the Executive Agent for the Immunization Program for Biological Warfare Defense, maintains a program office at the USAMMDA. This office oversees and coordinates EUA product use for force health protection.

Appendix A
References

Section I
Required Publications

Unless otherwise stated, all publications are available at: http://www.apd.army.mil/. Department of Defense regulations are available at: http://www.dtic.mil/.

DODI 6200.03
Public Health Emergency Management within the Department of Defense (Cited in paras 3–3*d*, 3–6*f*.)

DODI 6205.4
Immunization of Other Than U.S. Forces (OTUSF) for Biological Warfare Defense (Cited in paras 3–3*e*, 3–6*f*.)

Section II
Related Publications

A related publication is a source of additional information. The user does not have to read a related publication to understand this regulation. Unless otherwise stated, all publications are available at: http://www.apd.army.mil/. Department of Defense regulations are available at: http://www.dtic.mil/. The U.S. Code and the Code of Federal Regulations are available at: http://www.gpoaccess.gov/fdsys/.

AR 11–2
Managers' Internal Control Program

AR 25–30
The Army Publishing Program

AR 600–20
Army Command Policy

AFI 48–123
Medical Examination and Standards (Available at http://www.e-publishing.af.mil/.)

Control of Communicable Diseases Manual
Communicable disease control and the international health regulations (Available at http://www.apha.org/.)

COMDTINST M6000.1
Medical Manual

DODD 1241.01
Reserve Component Medical Care and Incapacitation Pay for Line of Duty Conditions

DODD 1404.10
DOD Civilian Expeditionary Workforce

DODI 6200.02
Application of Food and Drug Administration (FDA) Rules to Department of Defense Force Health Protection Programs

DODD 6205.02E
Policy and Program for Immunizations to Protect the Health of Service Members and Military Beneficiaries

DODD 6205.3
DOD Immunization Program for Biological Warfare Defense

DODI 1300.17
DOD Accommodation of Religious Practices Within the Military Services

DODI 1400.32
DOD Civilian Work Force Contingency and Emergency Planning Guidelines and Procedures

DODI 2310.08E
Medical Program Support for Detainee Operations

DODI 5010.40
Manager's Internal Control (MCIP) Program Procedures

Executive Order 13139
Improving Health Protection of Military Personnel Participating in Particular Military Operations (Available at http://www.archives.gov/federal-register/executive-orders/disposition.html/.)

NATO STANAG 2037
Vaccination of NATO Forces(Available at http://www.nato.int/docu/standard.htm/.)

NATO STANAG 2491
NBC/MED Policy for the Immunization of NATO Personnel Against Biological Warfare Agents(Available at http://www.nato.int/docu/standard.htm/.)

NATO STANAG 3474
Temporary Flying Restrictions Due to Exogenous Factors Affecting Aircrew Efficiency (Available at http://www.nato.int/docu/standard.htm/.)

10 USC 1107
Notice of use of an investigational new drug or a drug unapproved for its applied use

15 USC 1471
Definitions

15 USC 1472
Special packaging standards

15 USC 1473
Conventional packages, marketing

15 USC 1474
Regulations for special packing instructions

15 USC 1475
Repealed. Section 1205(c), Act of 13 August 1981, Public Law 97–35, Title XII, Volume 95, U.S. Statute at Large, p. 716.

15 USC 1476
Preemption of Federal standards

21 USC 360
Registration of producers of drugs or devices

42 USC 300aa
Public Health Service

42 USC 300aa–1 to 300aa–34
The National Childhood Vaccine Injury Act of 1986

42 USC 300aa–25
Recording and Reporting of Information

21 CFR 312
Investigational New Drug Application

29 CFR 1605
Guidelines on Discrimination Because of Religion

29 CFR 1910.1030.
Blood borne pathogens

Section III
Prescribed Forms
This section contains no entries.

Section IV
Referenced Forms
Except where otherwise indicated below, the following forms are available as follows: DA forms are available on the APD Web site, at http://www.apd.army.mil; DD forms are available from the OSD Web site, at http://www.dtic.mil/whs/directives/infomgt/forms/index.htm; standard forms (SFs) and optional forms (OFs) are available from the GSA Web site (http://www.gsa.gov).

DA Form 11–2
Internal Control Evaluation Certification

DA Form 2028
Recommended Changes to Publications and Blank Forms

DD Form 2365
DOD Civilian Employee Overseas Emergency-Essential Position Agreement

DD Form 2766
Adult Preventive and Chronic Care Flowsheet (Available through normal forms supply channel.)

DD Form 2766C
Adult Preventive and Chronic Care Flowsheet (Continuation Sheet) (Available through normal forms supply channel.)

FDA Form 3500
MedWatch: The FDA Safety Information and Adverse Event Reporting System (Available at http://www.fda.gov/Safety/MedWatch/default.htm).

Form VAERS–1
Vaccine Adverse Event Reporting System (Available at http://vaers.hhs.gov/esub/index)

CDC Form 731
International Certificate of Vaccination (Available through normal forms supply channel. Also available at http://bookstore/gpo.gov, or toll free at 1-866-512-1800.) (Marine Corps and Navy - S/ N 0108–LF–400–0706. Available from the Navy Supply System and may be requisitioned per NAVSUP P–2002D.)

SF 600
Medical Record - Chronological Record of Medical Care

SF 601
Health Record - Immunization Record

Appendix B
Standards for Military Immunization

B–1. Standard #1: immunization availability

a. Ensure immunizations are available when required to minimize disruption of deployment or training schedules.

b. Ensure immunizations are available at convenient times, without unnecessary barriers and are available on a walk-in basis, as staffing permits. As clinically appropriate, administer any vaccine doses required simultaneously to avoid missed immunization opportunities.

c. Ensure immunization services are responsive to the needs of beneficiaries.

d. Review the vaccination status of all beneficiaries at every health care visit to determine which vaccines are indicated.

e. Implement standing orders if written orders are unavailable. Standing orders must address vaccine dosage and administration, contraindications and precautions, and documentation procedures. Ensure standing orders are signed by the privileged physician who has medical oversight of the clinic.

B–2. Standard #2: vaccine information and vaccinee education

a. Educate beneficiaries about the benefits and risks of vaccination in a culturally appropriate manner and at an appropriate education level.

b. Prior to vaccination, provide all parents/guardians and vaccinees the most current Vaccine Information Sheets (VISs) for each vaccine as mandated by Federal law (42 USC 300aa-26). Allow sufficient time to discuss any concerns or questions as noted by the vaccinee. Ensure VISs are accessible and visible in the patient waiting area of the clinic or activity that provides immunizations.

c. Prior to each vaccination provide all potential vaccinees the opportunity to read the current DOD and/or FDA mandated vaccine information brochure. Additional education requirements may be required as outlined in vaccination policy.

d. Ensure immunization personnel are readily available to accurately answer patients' immunization questions and concerns about vaccines. Ensure personnel have ready access to immunization information resources.

B–3. Standard #3: vaccine storage and handling

a. Ensure staff members adhere to cold-chain management principles during administration, transportation, and storage. Ensure up-to-date, written cold-chain management protocols are accessible at all locations where vaccines are stored.

b. Implement temperature monitoring processes at any clinic or activity that administers immunizations. All vaccine storage devices should have a calibrated thermometer and alarm systems that are visually monitored at a minimum of twice a day.

c. The CDC's National Center for Immunization and Respiratory Diseases strongly recommends that providers draw vaccine only at the time of administration to ensure that the cold chain is maintained and that vaccine is not inappropriately exposed to light. Do not pre-draw doses; draw them when they are needed.

B–4. Standard #4: indications and contraindications

a. Screen each patient for allergies, health status, recent vaccinations, and previous vaccine adverse events before immunization. Provide each patient an opportunity to ask questions about potential contraindications. Refer patients for appropriate medical evaluation, as needed.

b. Screen each patient's immunization record to determine vaccine needs or requirements.

c. Ensure staff members document any contraindication to an immunization in the health record and ITS. Screen all women for pregnancy status.

B–5. Standard #5: immunization recordkeeping

a. Record immunizations accurately in a DOD and USCG-approved electronic ITS according to Service-specific policy at the time of immunization, or no later than 24 hours after administration of immunization. Transcribe all historical immunizations into the immunization tracking system.

b. Recommend any clinic or activity that administers immunizations has one or more mechanisms for notifying patients when the next dose of an immunization series is needed (a reminder system) or when doses are overdue (recall system). Reminder and recall systems may be automated or manual and may include mailed, emailed, or telephone messages.

c. Record all military personnel immunization information in an electronic ITS immunization record. All Services must record military immunization data into an electronic database that communicates with a centralized DOD registry.

B–6. Standard #6: immunization personnel training

a. Ensure all persons who administer vaccines, including immunization augmentees, are appropriately trained and work within their appropriate scope of practice as determined by Service policies.

b. Immunization training must meet a standard acceptable to the MTF commander, command surgeon, or other appropriate medical authority. Training will include vaccine storage and handling; vaccine characteristics; recommended vaccine schedules; patient screening; contraindications; vaccine administration techniques; and treatment and reporting of adverse events to include anaphylaxis, vaccine benefit and risk communication, and documentation and management.

c. Ensure personnel who administer vaccines complete a comprehensive immunization orientation and annual continuing education that addresses training standards and competency of vaccine related topics based on an individual's role in administering and/or handling vaccines. Individuals who routinely administer vaccines should complete at least 8 hours of training annually. Training resources include resident courses, self-paced online training programs, and video training (see table B–1).

Table B–1
Training standards

Medical standard or procedure	Physicians and medical directors	Immunizers	Chapter and appendix paragraph locations
Quality patient care and delivery of immunizations			
Properly trained in accordance with DOD, Service, USCG, and Centers for Disease Control and Prevention (CDC) guidelines and act within their scope of practice as determined by each Service.	B[1], A[2]	B, A	1–4*c*(1)
Understands standing order procedures for administering immunizations including dose, route, time indication, contraindications, and so forth.	B, A	B, A	2–1*b* and B–1
Demonstrates the ability and knowledge to screen individuals for contraindications, hypersensitivities, allergies, and so forth, before administering vaccines.	B	B, A	2–1*d* and B–4
Understands and adheres to immunization dosing and interval schedules.	B	B, A	2–1*e* and B–6
Understands how to properly document exemptions from further immunization in the ITS (DD Form 2766C), on the DD Form 2766 (Adult Preventive and Chronic Care Flowsheet), and/or in other relevant paper-based immunization records.	B	B, A	2–6, 2–7, and B–4
Patient information and education before immunization			
Understands the purpose of and legal requirements for making VISs available to vaccine recipients.	B	B, A	2–7*d*(2) and B–2
Understands how to document the date of the VIS in the ITS when documenting an immunization given.	B	B, A	2–7*d*(3) and B–2
Vaccine storage and handling			
Trained in cold-chain management principles and procedures.	B, A	B, A	2–3 and B–3
Demonstrates how to read a vaccine package insert for storage and handling requirements.	B	B, A	2–3 and B–3
Understands proper reporting procedures for vaccine storage and handling losses.	B, A	B, A	2–3*f* and B–3
Emergency care and adverse-event reporting			
Basic cardiopulmonary resuscitation and the administration of epinephrine.	B, R[3]	B, R	2–9*b* and B–6
Knows how to use the emergency equipment available for treating an anaphylactic reaction. Ensures medications in kit are not expired.	B	B, A	2–9*c* and B–6
Demonstrates the ability to initiate anaphylactic reaction treatments per protocol.	B	B, A	2–9*c* and B–6
Understands the procedure for documenting an adverse event after an immunization.	B	B, A	2–10*d* and B–7

Table B–1
Training standards—Continued

Knows how to submit a Vaccine Adverse Event Reporting System (VAERS) Form 1.	B	B, A	2–10*d* and B–7
Comprehends DOD's Clinical Guidelines for Managing Adverse Events after Immunization.	B, A	B	2–10 and B–7
Understands how to handle and administer specific vaccines			
Military and civilian personnel eligible to receive smallpox vaccine will be educated before immunization regarding criteria for exemption from immunization, expected response at the vaccination site, vaccination-site care, risks of spreading vaccinia to close contacts, and other relevant topics.	B, A	B, A	4–15
Immunization record keeping (documentation)			
Trained to accurately document immunizations, historical immunization data, and medical exception codes in ITS.	B	B, A	2–6*a* and *b,* 2–7, and B–5
Training			
Demonstrates understanding of and ability to follow this multi-Service publication and other pertinent references such as DOD, USCG, and CDC guidance in the performance of duties.	B, A	B, A	1–5

Notes:
[1] B=baseline or initial training
[2] A=annually
[3] R=as required

d. Ensure persons who administer vaccines have ready access to information resources regarding current recommendations for childhood, general adult, travel, and military-specific immunizations.

B–7. Standard #7: adverse events after immunization

a. Epinephrine (such as auto-injectable epinephrine) must be properly stored and readily available at all vaccination locations along with other supplies determined locally to manage adverse events (see para 2–9). Ensure all immunization personnel are trained to administer epinephrine.

b. Provide easy access to telephones or radios to persons who administer vaccines for summoning emergency medical personnel. Medical providers document adverse events in the health record at the time of the event or as soon as possible thereafter.

c. Report all clinically significant adverse events after vaccination to VAERS. Provide staff members with ready access to reporting options for the VAERS.

d. Develop a quality improvement process to assure adverse events are reported to VAERS promptly.

B–8. Standard #8: vaccine advocacy to protect the military Family

a. Develop a mechanism at the MTF level to determine the extent of influenza and pneumococcal immunization coverage among its high-risk patients. Develop a plan to optimize vaccination uptake and coverage.

b. Implement a plan to optimize immunization rates among cardiac, pulmonary, diabetic, asplenic, and other patient groups at elevated risk of complications from vaccine-preventable infectious diseases.

c. Conduct a quality improvement program to optimize the performance in immunizing children, adolescents, and adults against the preventable infections that most threaten them.

d. Ensure commanders use immunization databases to identify and resolve the vulnerabilities of their units.

e. All health care providers (not just those in any clinic or activity that administers immunizations) should routinely determine the immunization status of their patients, offer vaccines to those for whom they are indicated, and maintain complete immunization records.

Appendix C
Medical and Administrative Exemption Codes

This appendix gives details about medical and administrative exemption codes, as well as information on duration.

C–1. Medical exemption codes

Medical exemption codes appear in table C–1.

Table C–1
Medical exemption codes

Code	Meaning	Explanation of example	Duration
MD	Medical, declined	Declination of optional vaccines (not applicable to military required vaccinations).	Indefinite
MA	Medical, assumed	Prior immunization reasonably inferred from individual's past experiences (for example, basic military training), but documentation missing. Code used to avoid superfluous immunization. Code can be reversed upon further review.	Indefinite
MI	Medical, immune	Evidence of immunity (for example, by serologic antibody test); documented previous infection (for example, chickenpox infection); natural infection presumed (for example, measles, if born before 1957).	Indefinite
MP	Medical, permanent	HIV infection, prolonged or permanent immune suppression, upper age limit, other contraindication determined by physician. Can be reversed if the condition changes. For tuberculosis, positive tuberculosis test.	Indefinite
MR	Medical, reactive	Permanent restriction from receiving additional doses of a specific vaccine. Use only after severe reaction after vaccination (for example, anaphylaxis). Report such reactions to VAERS. Code can be reversed if an alternate form of prophylaxis is available. Do not code mild, transient reactions as MR. code events referred for medical consultation as MT.	Indefinite
MS	Medical, supply	Exempt due to lack of vaccine supply.	Up to 90 days
MT	Medical, temporary	Pregnancy, hospitalization, events referred for medical consultation, temporary immune suppression, convalescent leave, pending medical evaluation board, any temporary contraindication to immunization.	Up to 365 days

C–2. Administrative exemption codes

Administrative exemption codes appear in table C–2.

Table C–2
Administrative exemption codes

Code	Meaning	Explanation of example	Duration
AD	Administrative, deceased	Individual is deceased.	Indefinite
AL	Administrative, emergency leave	Individual is on emergency leave.	Up to 30 days
AM	Administrative, missing	Missing in action, prisoner of war.	Indefinite
AP	Administrative, PCS	Permanent change of station.	Up to 90 days
AR	Administrative, refusal	Personnel involved in actions under the Uniformed Code of Military Justice, religious waiver. (Indefinite and revocable. May be revoked at any time. See paragraph 2–6*b*(2.	Until resolution
AS	Administrative, separation	Pending discharge, separation (typically within 60 days), and retirement (typically within 180 days).	Until 180 days
AT	Administrative, temporary	Absent without leave, legal action pending (other than code AR).	Until 90 days
NR	Not required	Individuals who received immunization while eligible, subsequently changed occupational category and now serve as civilian employees or contract workers not otherwise required to be immunized.	Indefinite

Appendix D
Immunizations for Military Personnel

D–1. Text citations

Paragraphs 4–2 to 4–19 provide additional information on immunizations for military personnel.

D–2. Required immunizations

This table provides a listing of required immunizations for military personnel.

Table D–1
Immunizations for military personnel

Name of vaccine	Army	Navy	Air Force	Marine Corps	Coast Guard
Adenovirus[1]	Acc[2]	Acc	Acc	Acc	Acc
Anthrax	Risk	Risk	Risk	Risk	Risk
Haemophilus influenzae type b	Risk	Risk	Risk	Risk	Risk
Hepatitis A	Acc, Rou[3]	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou
Hepatitis B	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou
Influenza	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou
Japanese encephalitis	Risk[4]	Risk	Risk	Risk	Risk
Measles, mumps, rubella	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou
Meningococcal	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou
Pneumococcal	Risk	Risk	Risk	Risk	Risk
Poliovirus[5]	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou
Rabies	Risk	Risk	Risk	Risk	Risk
Smallpox (vaccinia)	Risk	Risk	Risk	Risk	Risk
Tetanus-diphtheria (preferably with pertussis vaccine)	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou
Typhoid fever	Risk	Risk	Risk	Risk	Risk
Varicella	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou	Acc, Rou
Yellow fever	Risk	Risk	Risk	Acc, Risk	Risk

Notes:
[1] Initial entry and basic training accessions only
[2] Acc=accessions
[3] Rou=adult routine
[4] Risk=special, risk-based, and occupational
[5] Refer to paragraph 4–13.

Appendix E
Internal Control Evaluation Process

E–1. Function
The function covered by this checklist is immunization and chemoprophylaxis.

E–2. Purpose
The purpose of this checklist is to assist in evaluating key management controls and is not intended to address all controls. The evaluation is focused at the clinic level, regardless of Service, to include both fixed facilities (MTFs, TDA units) and TOE field units. The checklist serves as a clinical quality improvement tool and is described at http://www.vaccines.mil/cqiip.

E–3. Instructions
Answers must be based on the actual testing of key management controls (for example, document analysis, direct observation, interviewing, sampling, or simulation). Answers that indicate deficiencies must be explained and corrective action indicated in supporting documentation. These key management controls must be formally evaluated at least once every 5 years. Certification that this evaluation has been conducted must be accomplished on DA Form 11–2–5 (Internal Control Evaluation Certification Statement).

E–4. Test questions
Test questions are available directly via a link at the Web site address in paragraph E–2, above.

E–5. Supersession
This evaluation replaces the evaluation for immunization and chemoprophylaxis previously published in AR 40–562, dated 29 September 2006.

Glossary

Section I
Abbreviations

ACIP
Advisory Committee on Immunization Practices

AFI
Air Force Instruction

AFJI
Air Force Joint Instruction

ASD (HA)
Assistant Secretary of Defense (Health Affairs)

CBRN
chemical, biological, radiological, and nuclear

CDC
Centers for Disease Control and Prevention

CFR
Code of Federal Regulations

CG–11
Coast Guard, Director, Health, Safety, and Work-Life

COMDTINST
Commandant Instructions

DCJI
disposable-cartridge jet injectors

DD
Department of Defense Form

DHHS
Department of Health and Human Services

DODD
Department of Defense Directive

DODI
Department of Defense Instruction

EUA
emergency use authorization

FDA
Food and Drug Administration

G6PD
glucose-6-phosphate dehydrogenase

Hib
Haemophilus influenzae type b

HQ
headquarters

HQDA
Headquarters, Department of the Army

IND
investigational new drug

IPV
inactivated poliovirus vaccine

ITS
immunization tracking systems

JTF CapMed
Joint Task Force - National Capital Region/Medical

JEV
Japanese-encephalitis vaccine

MAJCOM
major command (Air Force)

MILVAX
Military Vaccine Office

MMR
measles, mumps, rubella

MTF
medical treatment facility

NCVIA
National Childhood Vaccine Injury Act

NVIC
National Vaccine Injury Compensation (Program)

OTUSF
other than U.S. Forces

RC
reserve component

ROTC
Reserve Officers' Training Corps

SF
Standard Form

SOP
standard operating procedure

SSN
social security number

STANAG
standardized agreement

TB
tuberculosis

Td
Tetanus-diphtheria

Tdap
Tetanus-diphtheria and acellular pertussis (vaccine)

USAMMDA
U.S. Army Medical Materiel Development Activity

USC
United States Code

USCG
United States Coast Guard

VAERS
Vaccine Adverse Events Reporting System

VIS
vaccine information statement

WHO
World Health Organization

Section II
Terms
This section contains no entries.

Section III
Special Abbreviations and Terms

Accession
The attainment of rank or dignity.

Alert personnel
Specified forces maintained (alert force) in a special degree of readiness.

Antigen
A substance that, when introduced into the body, stimulates the production of an antibody.

Contraindication
A factor that renders the administration of a drug or the carrying out of a medical procedure inadvisable.

Hyperendemic
Equally endemic, at a high level, in all age groups of a population.

Neisseria meningitides
The bacteria that is the causative agent of cerebrospinal meningitis.

Plasmodia
A genus of apicomplexan protozoa, in the family Plasmodiidae parasitic, in the blood cells of animals and humans; the malarial parasite.

Primaquine
An ant malarial agent especially effective against Plasmodium vivax.

Seroimmunity
Immunity conferred by administration of an antiserum.

Serologic
The scientific study of blood serum and other bodily fluids.

Toxoid
A bacterial toxin (usually an exotoxin) whose toxicity has been weakened or suppressed either by chemical (formalin) or heat treatment, while other properties, typically immunogenicity, are maintained.

Urticaria
A skin condition characterized by intensely itching welts and caused by allergic reactions.

Variola virus
The causative agent of smallpox.

Exhibit 6

SECRETARY OF THE AIR FORCE
WASHINGTON

3 September 2021

MEMORANDUM FOR DEPARTMENT OF THE AIR FORCE COMMANDERS

SUBJECT: Mandatory Coronavirus Disease 2019 Vaccination of Department of the Air Force Military Members

On 24 August 2021, the Secretary of Defense issued a mandate for all members of the Armed Forces under Department of Defense authority on active duty or in the Ready Reserve, including the National Guard, to immediately begin full vaccination against COVID-19.

Effective immediately, commanders in the Department of the Air Force shall take all steps necessary to ensure all uniformed Airmen and Guardians receive the COVID-19 vaccine, which includes issuing unit-wide and individual orders to their military members. Commanders must take action systematically and as expeditiously as possible to ensure prompt and full vaccination of Service members. Unless exempted, Active Duty Airmen and Guardians will be fully vaccinated by 2 November 2021. Unless exempted, Ready Reserve, to include National Guard, Airmen and Guardians will be fully vaccinated by 2 December 2021. To aid in the process, there are additional resources available in the COVID-19 Commander's Toolkit, available at https://usaf.dps.mil/teams/COVID-19/SitePages/Home.aspx.

Only COVID-19 vaccines that receive full licensure from the Food and Drug Administration (FDA) will be utilized for mandatory vaccinations unless a military member volunteers to receive a vaccine that has obtained U.S. Food and Drug Administration Emergency Use Authorization or is included in the World Health Organization's Emergency Use Listing. Individuals with previous COVID-19 infection or positive serology are not considered fully vaccinated and are not exempt.

Pursuant to my authority under Article 22 of the Uniform Code of Military Justice and Rules for Courts-Martial 306, 401, and 601, I hereby withhold initial disposition authority from all commanders within the Department of the Air Force who do not possess at least special court-martial convening authority and who are not in the grade of O-6 with respect to any alleged offense that constitutes refusal or failure to obtain the COVID-19 vaccine. Commanders are advised to consult with their servicing staff judge advocate for further guidance.

Together, we will win this fight against COVID-19. *One Team, One Fight.*

Frank Kendall

2 Attachments:
1. Secretary of Defense Memorandum, "Mandatory Coronavirus Disease 2019 Vaccination of Department of Defense Service Members," 24 August 2021
2. Department of the Air Force COVID-19 Vaccination Implementation Guidance, 2 September 2021

cc:
AF/CC
SF/CSO

COVID-19 MANDATORY VACCINATION IMPLEMENTATION GUIDANCE FOR SERVICE MEMBERS

Deputy Director of Staff for COVID-19

3 September 2021

Chapter 1

INTRODUCTION

1.1. Purpose. This document provides Department of the Air Force implementation guidance pursuant to the 24 August 2021 Secretary of Defense memorandum and the subsequent 3 September 2021 Secretary of the Air Force memorandum. Accomplishment of mandatory COVID-19 vaccinations will be carried out as soon as possible after receiving this implementation guidance.

1.2. Background.

1.2.1. On 23 August 2021, the US Food and Drug Administration (FDA) approved the Pfizer-BioNTech mRNA COVID-19 vaccine which will be now be marketed as "COMIRNATY®" for prevention of COVID-19 disease in individuals 16 years of age and older. The vaccine also continues to be available under Emergency Use Authorization (EUA) for individuals 12 through 15 years of age and for the administration of a third dose in certain immunocompromised individuals.

1.2.1.1. The FDA approved COMIRNATY® and the FDA authorized Pfizer-BioNTech COVID-19 vaccine under emergency use authorization have the same formulation and can be used interchangeably.

1.2.1.2. Providers can use doses distributed under the EUA to administer the vaccination series as if the doses were the licensed vaccine according to the FDA. Other vaccines may be added to this list in the future.

1.2.2. All other vaccines authorized by the FDA under an EUA will remain voluntary until they receive full FDA approval.

1.2.3. Following the FDA news release, the Secretary of Defense announced that the COVID-19 vaccine would be a requirement for all members of the Armed Forces under DoD authority on active duty or in the Ready Reserve, including National Guard.

1.2.4. Service members voluntarily immunized with a COVID-19 vaccine under FDA EUA or World Health Organization (WHO) Emergency Use Listing (EUL) IAW applicable dose requirements prior to, or after, the establishment of this policy are considered fully vaccinated.

1.3. Key Messages. Education of all levels of the command structure is imperative to ensure the success of this program. The key messages for this vaccination effort are:

1.3.1. Your health and safety are our #1 concern.

1.3.2. The vaccine is safe and effective.

1.3.3. The threat from COVID-19 is real and deadly.

1.3.4. Vaccination offers a layer of protection, in addition to hand washing, use of cloth face masks, social distancing, tele-working, and other non-pharmaceutical interventions.

1.4. Applicability and Scope.

1.4.1. All individuals identified in section 1.2.3.

1.4.2. All other eligible personnel are strongly recommended to voluntarily receive either the approved COMIRNATY® or other FDA EUA or WHO EUL COVID-19 vaccines.

1.4.3. Members who are actively participating in COVID-19 clinical trials are exempt from mandatory vaccination against COVID-19 until the trial is complete.

Chapter 2

ROLES AND RESPONSIBILITIES

2.1. AF/DDS COVID-19.

2.1.1. As OPR for implementation of the vaccination mandate, develop and implement necessary DAF policy.

2.1.2. Provide program oversight.

2.1.3. Coordinate with other Services and agencies on policy implementation and execution as appropriate.

2.1.4. Review and coordinate requests from MAJCOMs and FLDCOMS for exceptions to policy.

2.2. AF/SG.

2.2.1. Coordinate with DHA Director.

2.2.2. Serve as the final appeal authority for all denials of requests for religious accommodations per DAFI 52-201.

2.3. MAJCOMs and FLDCOMs.

2.3.1 Designate a staff element as OPR for management of implementation of this guidance. (Designate any OCRs as deemed necessary.)

2.3.2. Consult with installations on vaccination issues which require command support.

2.3.3. Coordinate requests for exceptions to policy with installations and HAF/DDS COVID-19.

2.3.4. Adjudicate religious exemptions per DAFI 52-201.

2.4. Installation Commander.

2.4.1. Ensure compliance with this guidance by maintaining oversight and ownership of the installation's implementation plan for mandatory vaccination.

2.4.2. As needed, develop a base implementation plan consistent with DoD and DAF guidance. The Department of the Air Force plan may be used as the foundation for the installation's implementation plan.

2.4.3. As needed, designate a senior line officer as the installation OIC to oversee the implementation of this guidance and the vaccination mandate.

2.4.4. Direct the Medical Treatment Facility (MTF) Commander or Senior Officer in the Reserve Medical Unit to coordinate the medical administrative and clinical functions of COVID-19 vaccination pursuant to this guidance.

2.4.5. Ensure all installation personnel receive education on the ma as outlined in Chapter 3 of this plan.

2.4.6. Submit requests for exception to policy to MAJCOM and FLDCOM OPRs for coordination.

2.5. Public Affairs.

2.5.1. Prioritize community education and provide support to command teams.

2.5.2. Coordinate responses to media inquiries.

2.6. Legal.

2.6.1. Educate base personnel as needed on relevant legal issues.

2.6.2. Answer any inquiries regarding legal issues related to mandatory vaccination and this guidance (e.g., Freedom of Information Act requests and refusals to receive mandatory vaccinations) and provide guidance to commanders as needed/requested.

2.7. Chaplain.

2.7.1. Assist with vaccine exemptions based on religious accommodations IAW DAFI 52-201. The senior chaplain leads the RRT in providing recommendations to commanders on how to resolve religious matters. See Attachment 1, Religious Accommodation Requests.

2.8. Unit Commanders.

2.8.1. Ensure unit personnel are educated on the vaccine and the vaccination requirement IAW Chapter 3 of this plan. Helpful documents such as “DoD & MHS Talking Points – COVID-19 Updates (29 Jul 21)”, “COVID19 Vaccine FAQs_V1_3Aug 2021” and others are accessible from https://www.milsuite.mil/book/groups/daf-covid-19-vaccine-confidence-working-group-cvcwg.

2.8.2. Enforce compliance with the mandate from the Secretary of Defense and the Secretary of the Air Force by issuing an order for all unvaccinated members under the unit’s command to receive the COVID-19 vaccine.

2.8.3. For personnel subject to the vaccination mandate, manage cases of individual refusal to receive the vaccine IAW section 5.3 of this plan. Begin taking refusal management steps as soon as possible following notification by the MTF of vaccine refusal by a unit member.

2.9. Military Treatment Facility Commander or Local Equivalent.

2.9.1. Provide oversight for all medical administrative and clinical aspects of vaccination IAW DHA-IPM 20-004.

2.9.2. Assign medical provider(s), as needed, to support:

2.9.2.1. The installation's Religious Resolution Team (RRT) and medical counseling for personnel requesting religious waivers;

2.9.2.2. The medical evaluation of personnel requiring a medical exemptions; and

2.9.2.3. Notification of commanders if the initial refusal of the COVID-19 vaccine takes place in the MTF or Points of Dispensing (PODs). (See paragraph 5.3.2.)

2.9.3. Ensure appropriate medical personnel are educated on the clinical and policy aspects of the vaccine program (see Chapter 3). Be prepared to provide additional information to Commanders and individuals.

2.9.4. Ensure a process is in place for access to health care for individuals who may have an adverse reaction to the vaccine.

2.9.5. Ensure those receiving vaccination are offered education prior to vaccine administration.

2.9.6. Oversee management of adverse events IAW DHA-IPM 20-004.

2.9.7. Ensure providers are educated on evaluation for vaccine exemption requests. (See paragraph 3.4.)

2.10. Vaccine Site Coordinator.

2.10.1. Ensure education and training of vaccinators on current vaccination policy is accomplished IAW DHA-IPM 20-004 and any supplemental guidance from DHA-IHD.

2.10.2. Ensure the most current version of the FDA Fact Sheet is readily available/distributed at education venues and within the MTF until an Advisory Committee on Immunization Practices (ACIP)-approved Vaccine Information Statement (VIS) becomes available.

2.10.3. Continue to coordinate with the vaccine coordinators and logistics champions.

2.10.4. For deployers going to countries where yellow shot record is required, ensure COVID-19 vaccine is also documented in their yellow shot record.

2.11. Individuals Receiving Vaccination.

2.11.1. Receive education on the COVID-19 disease threat and information on the vaccine.

2.11.2. Read the FDA Fact Sheet.

2.11.3. Address any concerns with medical staff prior to receiving the vaccine.

2.11.4. Air Reserve Component (ARC) members who receive vaccination outside a military facility will provide documentation to their unit health monitor and reserve medical unit within 72 hours of vaccination.

Chapter 3

EDUCATION PLAN FOR VACCINATION

3.1. General. Education is the key to a successful COVID-19 vaccination program. Commanders at all levels are responsible for educating their personnel before vaccination. This educational program will inform personnel of the following:

3.1.1. The Food and Drug Administration (FDA) has licensed the Pfizer-BioNTech mRNA COVID-19 vaccine, now marketed as "COMIRNATY®," for prevention of COVID-19 disease as well as preventing COVID-19-related serious negative outcomes. (Note: IAW FDA guidance, COMIRNATY® has the same formulation and can be used interchangeably with the FDA-authorized Pfizer-BioNTech COVID-19 Vaccine. Providers can use doses distributed under the EUA to administer the vaccination series as if the doses were the licensed vaccine.)

3.1.2. Known and potential benefits and risks of COMIRNATY®.

3.1.3. Only an FDA-licensed vaccine may be mandated; however, Service members may be voluntarily immunized with a COVID-19 vaccine under FDA Emergency Use Authorization (EUA) or World Health Organization (WHO) Emergency Use Listing prior to or after the establishment of this policy and are considered fully vaccinated.

3.1.4. The FDA and Centers for Disease Control and Prevention (CDC) have monitoring systems in place to ensure that any safety concerns continue to be identified and evaluated in a timely manner.

3.2. Key Messages.

3.2.1. Your health and safety are our #1 concern.

3.2.2. The vaccine is safe and effective.

3.2.3. The threat from COVID-19 is real and deadly.

3.2.4. Vaccination offers a layer of protection, in addition to hand washing, use of cloth face masks, social distancing, tele-working, and other non-pharmaceutical interventions.

3.3. Education for Individuals. All unvaccinated personnel (as identified in section 1.2) must receive education on the COVID-19 vaccinations before receiving the vaccine. This applies to individuals initiating or continuing the vaccination series.

3.3.1. The primary mode of providing education to individuals is the FDA Fact Sheet that will be disseminated at the Immunizations Clinic and/or PODs at minimum. Prior to

receiving a fully FDA-approved COVID-19 vaccine or an EUA/EUL COVID-19 vaccine, individuals must have had the opportunity to review the product-specific information.

3.3.1.1. Upon arrival at the MTF to receive the COVID-19 vaccine, individuals will be offered a copy of the product specific Fact Sheet. Prior to administering the COVID-19 vaccine, the immunization technician will confirm the individual has understood the information within the FDA Fact Sheet. Any questions should be addressed prior to vaccination.

3.4. Education for Medical Personnel. Medical personnel are the primary source of information on the disease, the vaccine, and vaccine side effects. For those individuals who experience an adverse event associated with the vaccine, medical personnel will provide the appropriate treatment and referral, if necessary, for diagnosis and treatment of medical conditions.

3.4.1. Military Treatment Facility Commander or local equivalent will ensure that healthcare professionals and vaccinators involved in COVID-19 vaccination review and comply with implementation guidance.

3.4.2. Medical personnel involved with vaccination must understand healthcare-access guidance, procedures for reporting in the Vaccine Adverse Events Reporting System (VAERS) and reasons for medical exemption.

3.4.3. Understand the healthcare provider's roles and responsibilities with medical and administrative exemptions to include religious exemptions.

3.4.4. Personnel providing COVID-19 immunizations must acknowledge training IAW DHA-IPM 20-004.

3.4.5. The Chief of Medical Staff (SGH) will ensure education on the vaccine and the vaccination requirement is accomplished for: clinical supervisors of vaccinators, preventive medicine and public health staff, relevant healthcare providers (e.g., allergy-immunology, ambulatory care, flight medicine, emergency care), and any other provider designated by the Medical Commander. Education must also include the components listed in 3.1.

Chapter 4

MEDICAL ISSUES

4.1. Vaccine Administration.

4.1.1. Administer COVID-19 vaccine IAW DHA-IPM 20-004.

4.1.2. ASIMS will turn "yellow" for not fully vaccinated personnel on 3 September 2021. ASIMS will turn "red" for those not fully vaccinated personnel by the respective timelines.

4.1.3. An order to receive the COVID-19 vaccine is not related to the colors in ASIMS. The colors are for MTF tracking purposes only.

4.1.4. For individuals recently diagnosed with COVID-19, treated with monoclonal antibodies, or treated with convalescent plasma, administer COVID-19 immunization in accordance with recommendations from the CDC, recommendations from the CDC's Advisory Committee on Immunization Practices (ACIP), and FDA guidelines.

4.2. Pregnancy and Nursing Considerations. The COVID-19 vaccine is recommended during pregnancy.

4.2.1. Pregnant Service members (unless under medical exemption) are recommended to receive COVID-19 vaccination consistent with guidance from the CDC, American College of Obstetricians and Gynecologists (ACOG), and the Society for Maternal-Fetal Medicine (SMFM); however, a pregnant Service member with concerns about vaccination during pregnancy may pursue a temporary medical exemption following vaccine counseling from her healthcare provider, as per paragraph 2-6.a.(1)(a) of AFI 48-110.

4.2.2. As needed, consult medical providers to weigh the benefit/risk of getting COMIRNATY® during pregnancy.

4.2.3. Nursing mothers (unless under a medical exemption) are mandated to receive COMIRNATY®.

4.2.4. Individuals seeking information related to vaccination during pregnancy or while nursing are encouraged to access the following website: https://www.acog.org/womens-health/faqs/coronavirus-covid-19-pregnancy-and-breastfeeding.

4.3. Pre-vaccination Screening. Medically screen patients prior to administering the COVID-19 vaccine to ensure there are no contraindications for receiving the vaccine.

4.4. Adverse Reactions.

4.4.1 General Information. Medical personnel must be prepared to manage perceived or actual adverse events after vaccination: how to minimize them, respond to them, and report

them IAW AFI 48-110. Treat each concern with care; some symptoms following COVID-19 vaccination may or may not be caused by the vaccination, but all deserve individual attention.

4.4.2 Immunization Technician's Role. Immunization technicians will have the most current version of the FDA Fact Sheet and other sources of information available in the clinic, which provide details on potential side effects. If a patient returns to the clinic after receiving a vaccination and indicates that they had an adverse reaction, the immunization technician can, again, provide these information sources to the patient. If the adverse reaction is anything more than a mild, local reaction, they should be referred to a provider. In every case, the patient should be given the option of seeing a provider.

4.4.3 Any serious adverse event temporally associated with receipt of a dose of a fully FDA-approved COVID-19 vaccine or an EUA/EUL COVID-19 vaccine should be immediately evaluated by a privileged healthcare provider. Adverse event management should be thoroughly documented in medical records.

4.4.4. Adverse reactions from DoD-directed immunizations are Line of Duty (LOD) conditions.

4.4.5. Adverse event reporting follow the procedures IAW DHA-IPM 20-004.

4.5. Medical Exemptions.

4.5.1. Granting medical exemptions is a medical function that must be performed by a privileged military health care provider IAW AFI 48-110. Medical exemptions may be based on pre-existing conditions or result from vaccine adverse reactions and should be consistent with the CDC Interim Clinical Considerations for Use of COVID-19 Vaccines: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html#vaccinated-part-clinical-trail. See the Medical Exemption Process Attachment for more detail.

4.5.1.1. For the COVID-19 vaccines, IAW CDC guidance, contraindications include: 1) severe allergic reaction (anaphylaxis) after previous dose or to a component of the specific COVID-19 vaccine; 2) immediate allergic reaction of any severity to a previous dose or known (diagnosed) allergy to a component of the specific COVID-19 vaccine; and 3) development of pericarditis or myocarditis after the first dose.

4.5.1.2. Previous infections or positive serology do not exempt Service members from full vaccination requirements. (At this time, DoD, consistent with CDC recommendations, has not determined that a serological test is sufficient to meet the immunization requirements.)

4.5.1.3. Only "MT" or "Medical, Temporary" medical exemption code should used in ASIMS. A temporary medical exemption for up to 365 days allows future evaluation against other fully approved/biologics license application vaccines.

4.5.2. Granting of medical exemptions may require a duty status change or deployment limitation for the individual. Any change in duty status/deployment eligibility/assignment limitation due to a medical exemption must be processed IAW applicable AFIs.

4.5.2.1. Use of medical exemption codes in ASIMS must be IAW AFI 48-110, Table C-1.

4.6. COVID-19 Vaccine Tracking and Documentation.

4.6.1. The Public Health Office or the Base Operational Medicine Clinic (BOMC) will assist commanders and their designees with ASIMS access.

4.6.2. COVID-19 vaccination documentation will ensure clinical decision making is captured.

4.6.2.1 Vaccination sites using MHS GENESIS will continue to use this EHR platform for vaccination documentation.

4.6.2.2 Vaccination sites using AHLTA will use either ASIMS or AHLTA. Do not double document. Data entered into ASIMS or AHLTA will flow to the other.

4.6.2.3 ASIMS can be used as an alternate in locations (Guard/Reserve) who do not have access to AHLTA/MHS GENESIS but do have ASIMS/ Health Artifact and Image Management Solution (HAIMS) capabilities.

4.6.3. ASIMS will serve as the tracking mechanism for immunizations of Airmen and Guardians.

4.6.4 For deployers going to countries where yellow shot record is required, document COVID-19 vaccine in their yellow shot record.

4.7. Medical Logistics/Vaccine Distribution. The US Army Medical Materiel Agency (USAMMA) is responsible for coordinating the distribution of COVID-19 vaccine within DoD.

4.7.1. Base level medical logistics personnel can order the COVID-19 vaccine from USAMMA.

4.7.2. Ensure proper COMIRNATY® storage requirements are met.

4.7.3. Monitor for any relevant shelf-life extensions.

4.8. Aircrew Management.

4.8.1. Adverse reactions are rare for all vaccines. Benefits of administration of vaccine for this population far outweigh the risks. After receiving COVID-19 vaccine, all flyers, controllers, and special warfare airmen (DD Form 2992 holders) will maintain access to medical care on the ground and not perform aviation-related duties (e.g., flying, controlling, or jumping) for a period of 48 hours after each dose IAW Department of the Air Force Memorandum, "HAF SII 20-02: DNIF Guidance for COVID Vaccines," December 21, 2020. No formal grounding is required for uncomplicated immunizations.

Chapter 5

ADMINISTRATIVE ISSUES

5.1. Exemptions.

5.1.1. Guidance for religious accommodations is found in DAFI 52-201. The MAJCOM, FLDCOM, DRU or FOA commander is the approval and denial authority for religious exemptions. AF/SG is the appellate authority for any religious vaccine exemption requests.

5.1.2. Administrative and medical exemptions are handled and coded IAW AFI 48-110.

5.1.2.1. The only administrative exemption is for members on approved terminal leave.

5.1.2.1.1. Official documentation from the Squadron Commander including the administrative code and duration (specific date, temporary, indefinite) of exemption will be presented to the Immunization Clinic. Validated administrative exemptions will then be entered into ASIMS by the Immunization Clinic staff.

5.1.2.2. Medical Exemptions may be authorized under AFI 48-110. See paragraph 4.5.1. for procedures.

5.2. Healthcare Access Guidelines. At the time of immunization, all vaccine recipients will be provided information on potential adverse events.

5.2.1. Whenever an individual presents to an MTF expressing a belief that the condition for which the treatment is sought is related to an immunization received in a DoD clinic, they are authorized initial or emergency care to evaluate and treat an actual or perceived adverse reaction. Care may also be provided by a civilian medical facility in the following circumstances: an individual believes the situation to be an emergency and the civilian hospital is the nearest facility or an individual is on leave status, TDY or in a non-duty status (ARC personnel) and there are no MTFs within 50 miles. Pre-approval may still be required depending on the specific circumstances when not an emergent situation. Refer to AFI 48-110 for additional guidance.

5.2.1.1. ARC Personnel. If a member suffers an adverse reaction from a DoD-directed immunization while in an approved duty status, it is an LOD condition.

5.3. Refusal Management.

5.3.1. Military Members. A commander ordering a military member to take the COVID-19 vaccine constitutes a lawful order. However, the member's commander may exercise his or her discretion in handling refusal cases. When issuing an order to a military member to take the COVID-19 vaccine, if an individual indicates he or she is going to refuse the COVID-19 vaccination or has initially refused the vaccination the following approach should be used:

5.3.1.1. Find out why the individual is reluctant.

5.3.1.2. Provide the member with appropriate education.

5.3.1.3. Combinations of concerns may require education by a number of people; for example:

5.3.1.3.1. Concerns with vaccine safety, efficacy, or health risks should be sent to the supporting medical organization (if not previously accomplished). Medical education should be tailored to the specific concerns of the individual (efficacy, reproduction, allergic reactions, etc.) and should be accomplished by a health care provider knowledgeable about the COVID-19 vaccine and who is able to address the specific medical concerns of the individual. The medical counseling will be documented in the individual's medical record.

5.3.1.3.2. If the member is still reluctant after additional education, send the member to the Area Defense Counsel for an explanation of the potential consequences of his/her refusal.

5.3.1.4. The commander should ensure the order, and accompanying counseling on appropriate resources, is documented in writing.

5.3.1.5. If the member refuses to follow the order to vaccinate, consult with the servicing Staff Judge Advocate's office for appropriate action.

5.3.1.6. Notify the Immunization Clinic of the decision so the proper administrative code can be entered in ASIMS.

5.3.2. Management of Vaccine Refusal in the Immunization Clinic.

5.3.2.1. If an individual subject to the vaccination requirement, as identified in paragraph 1.2.3 of this plan, refuses a fully FDA-approved COVID-19 vaccine, the technician should notify the Immunization Clinic NCOIC/OIC before that individual leaves the clinic. The NCOIC/OIC (or technician if they are not available) should verify again that the individual has been offered the FDA Fact Sheet and the opportunity to ask questions. Notify the SGH. (Note: IAW FDA guidance, COMIRNATY® has the same formulation and can be used interchangeably with the FDA-authorized Pfizer-BioNTech COVID-19 Vaccine. Providers can use doses distributed under the EUA to administer the vaccination series as if the doses were the licensed vaccine.)

5.3.2.2. SGH will ensure appropriate commanders are aware of refusals.

5.3.2.3. Vaccine refusal should be handled with the appropriate regard to the individual's privacy.

ATTACHMENT 1 – RELIGIOUS ACCOMMODATION REQUESTS

Post-Accession Immunization Exemption Requests		
STEPS		**NOTES**
1	**Member** requests exemption of immunization requirements via letter addressed to the appropriate approval authority (MAJCOM/FLDCOM) for immunizations)	Include, at a minimum, the name, grade, DoD Identification number, faith group, unit, and specialty code of the Airman or Guardian; the nature of the accommodation requested; the religious basis for the request; a comment on the sincerity of the request; and the substantial burden on the member's expression of religion. (DAFI 52-201, par. 5.3) • Example at DAFI 52-201, Attachment 6. • Decision authority is member's MAJCOM/FLDCOM, DRU or FOA commander (DAFI 52-201, par. 6.6.1) • Member has a *temporary exemption* from immunization while request is processing (DAFI 52-201, par. 2.12)
2	Unit **commander** counsels the requestor after receiving the request	CC should counsel member that noncompliance with immunization requirements may adversely affect readiness for deployment, assignment, international travel, or result in other administrative consequences (DAFI 52-201, par. 6.6.1.1) CC's counseling must be documented in a memorandum and included with the religious accommodation request package.
3	Military **medical provider** counsels the requestor	Counseling must be documented in a memorandum and included with the request package (DAFI 52-201, par. 6.6.1.) Military provider must ensure member is making an informed decision and should address, at minimum, specific info about the disease concerned, specific vaccine info (including product constituents, benefits, risks), and potential risks of infection for unimmunized individuals (AFI 48-110, para 2-6b.(3)(a)2.)
4	Military **Chaplain** interviews the requestor	Chaplain must complete Interview Checklist (Attachment 5) and draft written memo (DAFI 52-201, par. 5.4)
5	Submit package to the Religious Resolution Team (**RRT**) for review.	At Installation level, the RRT will include the commander (or designee), Senior Installation Chaplain (or equivalent), public affairs officer, and staff judge advocate, and a medical provider (DAFI 52-201, par. 3.8.1.1) Wing/Delta Chaplain, as lead for RRT, shall write the memo to the decision authority detailing the RRT recommendation and any dissenting views of others (DAFI 52-201, par. 5.6.3)
6	**Staff judge advocate** will draft a written legal review.	The review will also state whether the request and enclosures are complete within the provisions of the DAFI 52-201.

7	**Each commander** shall endorse the request with recommendation for approval or disapproval and forward through the chain of command to the decision authority.	Endorsements must address (DAFI 52-201, par. 6.6.1.5): • If there is a compelling government interest and any effect the accommodation will have on readiness, unit cohesion, good order and discipline, health, or safety, and impact on the duties of the member • whether **less restrictive means** can be used to meet the government's compelling government interest • **30 business days** for CONUS requests (**60 business days** for OCONUS requests and requests from Reserve Component members not on active duty) from the date of submission to unit to final action by MAJCOM/FLDCOM commander and notification to the member (DAFI 52-201, Table 2.1) NOTE: Although AFI 48-110 says the AF only grants temporary immunization exemptions, the newer DAFI 52-201 states that approvals will remain in effect during follow-on duties, assignments, or locations, and for the duration of a Service member's military career. However, there may be a change in circumstances that requires the accommodation to be reevaluated in the future (e.g., deployment, new duties, or other material change in circumstances). (DAFI 52-201, par. 5.7.2) • DAFI 52-201, par. 5.7.3. New requests for the same accommodation are not necessary upon new assignment, transfer of duty stations, temporary duty, or other significant changes in circumstances, including deployment unless noted on the approval memorandum.DAFI 52-201, par. 5.7.4. Approved accommodations will continue unless the member's commander determines a compelling government interest exists requiring a temporary or permanent withdrawal of the approval. (T-1).
8	**MAJCOM/FLDCOM, DRU, or FOA commander determines whether approval, or partial / complete denial is appropriate**	If denial - he/she will indicate so on the memorandum, indicate the reasoning for disapproval and forward it to the servicing FSS (DAFI 52-201, par. 6.6.1.6).
9	**Servicing FSS ensures a copy of the final decision is included in the member's automated personnel records.**	DAFI 52-201, par. 6.6.1.6
10	**Member's commander should notify the member of the final decision.**	DAFI 52-201, par. 6.6.1.6

11	**Member may appeal decision to AF/SG**	Member shall address a memorandum to the appeal authority with a copy given to the previous disapproval authority and provide the memorandum to the unit commander for processing (DAFI 52-201, par. 5.8.2) AF/SG is ultimate appeal authority for immunization exemptions (DAFI 52-201, Table 6.1) 30 business days to resolve appeal (DAFI 52-201, par. 2.10)

Checklist for Required Package Items	
	Member's request letter *(DAFI 52-201, par. 5.3 and 6.6.1)*
	Unit CC's Written Counseling w/ requestor *(DAFI 52-201, par. 6.6.1.1)*
	Chaplain's Interview Memo w/ requestor *(DAFI 52-201, par. 5.4 and 4.2.7)*
	Military Medical Provider Counseling Memo w/ requestor *(DAFI 52-201, par. 6.6.1.2 and AFI 48-110,*
	par. 2-6b.(3)(a)2.)
	SJA Legal Review (DAFI 52-201, par. 5.6.2)
	RRT's Recommendation from Wing Chaplain to Unit CC (DAFI 52-201, par. 5.6.1 and 6.6.1.3)
	Chain of Command Recommendations (DAFI 52-201, par. 6.6.1.5). NOTE: there may be a change in circumstances that requires the accommodation to be reevaluated in the future (e.g., deployment, new duties, or other material change in circumstances). (DAFI 52-201, par. 5.7.2). We recommend CC endorsements consider whether to include any recommended circumstances that would require reevaluation (such as overseas PCS or deployments).

ATTACHMENT 2 - MEDICAL EXEMPTION REQUESTS

Immunization Medical Exemption Requests		
STEPS		**NOTES**
1	**Member** requests medical exemption of COVID-19 immunization requirements	- Member notifies commander of possible contraindication to vaccine
2	Unit **commander** ensures member is evaluated by military medical provider	
3	Military **medical provider** evaluates member	- Provider evaluates potential contraindication based on the health of vaccine candidate and the nature of the vaccine under consideration; counsels member on vaccine compliance
4	**Medical provider makes determination**	- Provider documents exemption in ASIMS and electronic health record
5	**Commander** reviews ASIMS	- Commander has awareness of member's readiness status

Exhibit 7

SECRETARY OF THE AIR FORCE
WASHINGTON

07 DEC 2021

MEMORANDUM FOR ALMAJCOM-FLDCOM-FOA-DRU/CC
DISTRIBUTION C

SUBJECT: Supplemental Coronavirus Disease 2019 Vaccination Policy

This memorandum establishes specific policy and provides guidance applicable to regular Air Force and Space Force members, Air Force Reserve and Air National Guard members. This memo includes supplemental guidance concerning those who requested separation or retirement prior to 2 November 2021, those whose requests for medical, religious or administrative exemption from the COVID-19 vaccine are denied, and those who refuse to take the COVID-19 vaccine. Compliance with this memorandum is mandatory.

As the Secretary of the Air Force, it is my responsibility to promote the health, safety and military readiness of all Air Force and Space Force personnel, regardless of duty status, to include Air National Guard performing any duty or training under both Title 10 and Title 32 of the United States Code. COVID-19 poses a direct risk to the health, safety, and readiness of the force. Vaccination against COVID-19 is an essential military readiness requirement for all components of the Air Force and Space Force to ensure we maintain a healthy force that is mission ready.

Commanders will take appropriate administrative and disciplinary actions consistent with federal law and Department of the Air Force (DAF) policy in addressing service members who refuse to obey a lawful order to receive the COVID-19 vaccine and do not have a pending separation or retirement, or medical, religious or administrative exemption. Refusal to comply with the vaccination mandate without an exemption will result in the member being subject to initiation of administrative discharge proceedings. Service characterization will be governed by the applicable Department of the Air Force Instructions.

Pending Separation or Retirement - unvaccinated regular Airmen and Guardians who submitted a request to retire or separate prior to 2 November 2021, with a retirement or separation date on or before 1 April 2022, may be granted an administrative exemption from the COVID-19 vaccination requirement until their retirement or separation date.

Medical, Religious or Administrative Exemption - unvaccinated regular Airmen or Guardians with a request for medical, religious, or administrative exemption will be temporarily exempt from the COVID-19 vaccination requirement while their exemption request is under review. Service members who receive a denial of their medical, religious, or administrative exemption request have five (5) calendar days from that denial to do one of the following: 1) Begin a COVID-19 vaccination regimen. If the service member indicates his or her intent is to begin the vaccination regimen, commanders may use their discretion to adjust the timeline based on local COVID-19 vaccination supplies; 2) Submit an appeal to the Final Appeal Authority or

request a second opinion (medical). If a final appeal or exemption is denied, the service member will have five (5) calendar days from notice of denial to begin the COVID-19 vaccination regimen; 3) If able, based upon the absence of or a limited Military Service Obligation (MSO), and consistent with opportunities afforded service members prior to 2 November 2021, request to separate or retire on or before 1 April 2022, or no later than the first day of the fifth month following initial or final appeal denial.

Regular service members who continue to refuse to obey a lawful order to receive the COVID-19 vaccine after their exemption request or final appeal has been denied or retirement/separation has not been approved will be subject to initiation of administrative discharge. Discharge characterization will be governed by the applicable Department of the Air Force Instructions. Service members separated due to refusal of the COVID-19 vaccine will not be eligible for involuntary separation pay and will be subject to recoupment of any unearned special or incentive pays.

Commanders will ensure all unvaccinated service members comply with COVID-19 screening and testing requirements and applicable safety standards. Leaders should continue to counsel all unvaccinated individuals on the health benefits of receiving the COVID-19 vaccine.

Unique guidance associated with the Air Force Reserve is provided at Attachment 1. Unique guidance associated with the Air National Guard is provided at Attachment 2.

This Memorandum becomes void one-year after date of issuance.

Frank Kendall
Secretary of the Air Force

Attachments
1. Supplementary Guidance for Members of the Air Force Reserve
2. Supplementary Guidance for Members of the Air National Guard

Attachment 1

Supplementary Guidance for Members of the Air Force Reserve

1. This supplementary addendum establishes specific policy and provides guidance applicable to Air Force Reserve (AFR) members, pursuant to Secretary of Defense and Secretary of the Air Force guidance as well as AFRC/CD's *AFRC Vaccine Guidance* memo, dated 24 September 2021. Compliance with this guidance is mandatory.

2. Effective 2 December 2021, all AFR members were required to fall into one of the following categories to comply with the vaccination mandate:

    a. Completed a vaccination regimen.
    b. Have requested or received a medical exemption.
    c. Have requested or received a Religious Accommodation Request (RAR).
    d. Have requested or received an administrative exemption.

3. Unvaccinated members who request a medical exemption or RAR will be temporarily exempt from the COVID-19 vaccination requirement while their exemption request is under review. For those members who have declined to be vaccinated, or have not otherwise complied with the guidance above, they are potentially in violation of the Uniform Code of Military Justice (UCMJ) by refusing to obey a lawful order. Commanders should use their discretion as appropriate when initiating disciplinary action.

4. Traditional Reserve (TR) and Individual Mobilization Augmentee (IMA) members who fail to be vaccinated and have not submitted an exemption or accommodation will be placed in a no pay/no points status and involuntarily reassigned to the Individual Ready Reserve (IRR). Active Guard and Reserve (AGR) members who fail to be vaccinated and have not submitted an exemption or accommodation will have their AGR tour curtailed and involuntarily reassigned to the IRR.

5. Members whose medical exemption or RAR is denied have five (5) calendar days from receipt of their denial to do one of the following:

    a. Begin a COVID-19 vaccination regimen.
    b. Request a second opinion (medical) or submit an appeal to the final RAR appeal authority (AF/SG). If a final appeal is denied, the member will have five (5) calendar days from notice of denial to begin the COVID-19 vaccination regimen.
    c. If eligible to retire:
        i. IMAs and TRs may request to retire with a retirement date on or before 1 June 2022 and will be placed in a no pay/no points status not later than 60 calendar days post RAR/appeal notification.

ii. AGR members may be able to retire if they begin terminal leave status NLT 60 calendar days from RAR/appeal notification.

6. Immediately following notification of final adjudication, AFR members must comply with the vaccination requirement. Any refusal to receive the COVID-19 vaccine, absent an approved exemption, may be punishable under the UCMJ. Continued refusal will result in involuntary reassignment to the IRR.

7. Members will be subject to recoupment for any unearned special, incentive pays or certain training.

8. Where required, AFR Airmen will complete all out-processing requirements, to include the Transition Assistance Program or Permanent Change of Station actions.

Attachment 2

Supplementary Guidance for Members of the Air National Guard

1. This supplementary addendum establishes specific policy and provides guidance applicable to Air National Guard (ANG) members pursuant to Secretary of Defense and Secretary of the Air Force guidance. Compliance with this guidance is mandatory.

2. IAW 32 U.S.C. 328, the Secretary of the Air Force hereby withdraws consent for members not fully vaccinated to be placed on or to continue on previously issued Title 32 Active Guard and Reserve (AGR) orders.

3. By 31 December 2021, ANG members, regardless of status, will be classified in the following categories:

    a. Completed or have started a vaccination regimen.
    b. Have requested or received a medical exemption.
    c. Have requested or received a Religious Accommodation Request (RAR).
    d. Have requested or received an administrative exemption.
    e. Declined to be vaccinated.

4. Unvaccinated members who request a medical exemption or RAR will be temporarily exempt from the COVID-19 vaccination requirement while their exemption request is under review.

5. Excluding members with pending or approved medical, religious, or administrative exemption requests, ANG members that have not initiated a vaccination regimen by 31 December 2021 may not participate in drills, training, or other duty conducted under Title 10 or Title 32 U.S.C., and those with a remaining Military Service Obligation will be involuntarily assigned to the Individual Ready Reserve (IRR) in accordance with 10 U.S.C. §651 and DoDI 1235.13.

6. Members whose medical exemption or RAR is denied have five (5) calendar days from receipt of their denial to do one of the following:

    a. Begin a COVID-19 vaccination regimen.
    b. Request a second opinion (medical) or submit an appeal to the final RAR appeal authority (AF/SG). If a final appeal is denied, the member will have five (5) calendar days from notice of denial to begin the COVID-19 vaccination regimen.
    c. If eligible to retire:
        i. Title 32 Drill Status Guardsmen, to include Dual Status Technicians, may request to retire with a retirement date on or before 1 April 2022.
        ii. Active Guard and Reserve (AGR) members may be able to retire if they begin terminal leave status NLT 60 calendar days from the RAR/appeal notification.

7. Immediately following notification of final adjudication, ANG members must comply with the vaccination requirement. Those with a remaining Military Service Obligation who continue to refuse vaccination, will be involuntarily assigned to the IRR.

8. Members will be subject to recoupment for any unearned special, incentive pays or certain training.

9. Where required, ANG members will complete all out-processing requirements, to include the Transition Assistance Program or Permanent Change of Station actions.

Exhibit 8

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLORADO

DANIEL ROBERT and **HOLLI MULVIHILL** Plaintiffs, v. **LLOYD AUSTIN**, in his official capacity as Secretary of Defense; **XAVIER BECERRA**, in his official capacity as Secretary of Health and Human Services; and **JANET WOODCOCK**, in her official capacity as Acting Commissioner of the U.S. Food and Drug Administration, Defendants.	Case No. 1:21-cv-02228-RM-STV

DECLARATION OF PETER MARKS, M.D., Ph.D.

I, Peter Marks, declare as follows:

1. I am the Director of the Center for Biologics Evaluation and Research ("CBER"), United States Food and Drug Administration ("FDA"), a position I have held since 2016. In this role, I direct the development and implementation of programs and policies for assuring the safety, purity, and potency of biological products, including vaccines, allergenic products, blood and blood products, and cellular, tissue, and gene therapies.

2. I joined FDA in 2012 as the Deputy Director for CBER, after practicing medicine, and working in industry and academia for several years. I received my graduate degree in cell and molecular biology and my medical degree at New York University, am board certified in internal medicine, hematology and medical oncology, and am a Fellow of the American College of Physicians.

3. In my capacity as Director of CBER, I am fully familiar with the instant matter and the facts stated herein. This declaration is based on my personal knowledge, my background, training, and experience and my review and consideration of information available to me in my official capacity, including information furnished by FDA personnel in the course of their official duties. My conclusions have been reached in accordance therewith.

4. Vaccines are biological products that are regulated under the Public Health Service Act ("PHSA"), 42 U.S.C. § 262(i)(1), as well as "drugs" subject to regulation under the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 321(g)(1)(B). Vaccines are approved for marketing through applications known as Biologics License Applications ("BLA"); a vaccine that is the subject of an approved BLA need not also obtain approval of a new drug application ("NDA") under 21 U.S.C. § 355. 42 U.S.C. § 262(a), (j).

5. Under the PHSA, FDA approves a BLA on the basis of a demonstration that: (1) the vaccine is "safe, pure, and potent"[1]; (2) the facility in which the vaccine is produced meets standards designed to assure that the vaccine continues to be safe, pure, and potent; and (3) the applicant consents to inspection of the manufacturing facility. 42 U.S.C. § 262(a)(2)(C). FDA may, but is not required to, consult with its standing advisory committee with scientific expertise in biological products, the Vaccines and Related Biological Products Advisory Committee, as part of the approval process. *See* 21 C.F.R. § 14.171(a). FDA has also issued several guidances and other public documents on biologics and vaccine development. *See generally* Biologics License Applications (BLA) Process, https://www.fda.gov/vaccines-blood-

[1] The standard for licensure of a biological product as potent under 42 U.S.C. § 262 has long been interpreted by FDA to include effectiveness. *See* 21 C.F.R. § 600.3(s); FDA Guidance, Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products at 4 (May 1998), available at https://www.fda.gov/media/71655/download.

biologics/development-approval-process-cber/biologics-license-applications-bla-process-cber; Guidance, Compliance & Regulatory Information (Biologics), https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics; Vaccine and Related Biological Product Guidances, https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/vaccine-and-related-biological-product-guidances; Vaccine Development 101, https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/vaccine-development-101.

6. On August 23, 2021, FDA approved a BLA for a COVID-19 vaccine known as Comirnaty, for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. *See* Comirnaty Approval Letter (August 23, 2021), attached as Exhibit A. Comirnaty is a mRNA vaccine. It contains a piece of the SARS-CoV-2 virus's genetic material that instructs cells in the body to make the virus's distinctive "spike" protein. After a person is vaccinated, their body produces copies of the spike protein, which does not cause disease, and triggers the immune system to learn to react defensively, producing an immune response against SARS-CoV-2. After delivering instructions, the mRNA is rapidly broken down. It does not enter the nucleus of the cell and does not affect DNA.

7. Prior to approval, beginning in December 2020, the same formulation of the vaccine, known as Pfizer-BioNTech Covid-19 vaccine, was available under an emergency use authorization ("EUA"). *See* https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19. FDA has discretion to issue an EUA for an FDA-regulated product if: (1) the Secretary of the Department of Health and Human Services has declared a public health emergency involving a biological or

other agent that can cause a serious or life-threatening disease or condition; (2) it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing that disease or condition, and the known and potential benefits of the product outweigh the known and potential risks of the product; and (3) there is no "adequate, approved, and available" alternative to the product. 21 U.S.C. § 360bbb-3(c).[2]

8. Even after FDA approved Comirnaty, FDA authorized continued use of the Pfizer-BioNTech Covid-19 vaccine under an EUA for indications that included the approved use. FDA determined that there is not sufficient approved vaccine available for distribution to the 16 years and older population in its entirety at the time of FDA's reissuance of the EUA. *See* Letter to Pfizer, Inc. reissuing EUA authorization for Covid-19 vaccine, p. 8, n.15 (November 19, 2021), attached as Exhibit B. FDA also determined that there are no products that are approved to prevent COVID-19 in additional populations covered by the EUA, as the vaccine remains available under the EUA for uses that have not been approved, specifically for individuals ages 5 through 15 years old; for a third dose in certain populations; and for a "booster" dose in certain circumstances.

9. The licensed vaccine has the same formulation as the originally authorized Pfizer-BioNTech vaccine. The products are legally distinct with certain differences that do not impact safety or effectiveness. Exhibit B at 10.

10. On October 29, 2021, FDA authorized a new formulation of the Pfizer-BioNTech vaccine for use in children 5 to 11 years of age when diluted to a lower strength. *Id.* at 2-3 n.12.

[2] Distribution of a product pursuant to an EUA is not a "clinical trial" subject to the requirements for clinical trials conducted under an investigational new drug ("IND") application. 21 U.S.C. §§ 360bbb-3(k); 355(i). Clinical trials must be conducted in accordance with an approved IND and involve only enrolled study participants. Only clinical trial participants enrolled in a clinical study conducted according to an approved IND receive the study drug.

FDA also authorized the new formulation, without dilution, for individuals 12 years of age and older. *Id.* The new formulation contains the same mRNA and lipids, and the same quantity of these ingredients, per 0.3 mL dose. *Id.* at 10. The two formulations differ only with respect to certain inactive ingredients and have been shown to be analytically comparable. *Id.* Therefore, FDA determined that "for individuals 12 years of age and older, COMIRNATY (COVID-19 Vaccine, mRNA) and the[] two formulations of the Pfizer-BioNTech COVID-19 Vaccine, when prepared according to their respective instructions for use, can be used interchangeably without presenting any safety or effectiveness concerns." *Id.* at 11. FDA provided this information in the Letter of Authorization to make clear that pharmacies and other healthcare practitioners could provide the vaccination series to recipients using Pfizer-BioNTech, Comirnaty, or both (*e.g.*, first dose of Pfizer-BioNTech followed by second dose of Comirnaty, or vice versa), since the products have an identical formulation and are made by the same manufacturer under current good manufacturing practice requirements. FDA included this clarification in the authorization letter to avoid the unnecessary operational complications that may have resulted if pharmacies or other healthcare practitioners had believed that the authorization did not include use in individuals who had received Pfizer-BioNTech for the first dose and Comirnaty for the second dose, or vice versa. Nevertheless, for individuals 12 years of age and older, only the original formulation is available at this time in the United States. *See* https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/comirnaty-and-pfizer-biontech-covid-19-vaccine. As a result, all currently available Pfizer-BioNTech vaccine in the United States for use in individuals 12 years of age and older has the same formulation as the approved Comirnaty vaccine.

11. The determination that FDA made for Comirnaty and Pfizer-BioNTech Covid-19

vaccine should not be confused with the statutory interchangeability determination that FDA may make when reviewing a BLA for a biological product manufactured by one company and comparing it with a biological product manufactured by a different company. Under 42 U.S.C. § 262(k)(4), FDA may determine that a biological product is "interchangeable" with a "reference product." "Reference product" is defined at 42 U.S.C. § 262(i)(4) as a "single biological product licensed under [42 U.S.C. § 262(a)] against which a biological product is evaluated in an application submitted under [42 U.S.C. § 262(k)]." The statutory interchangeability determination requires a licensed reference product and a subsequent applicant seeking licensure, which is not present here. The PHSA interchangeability provision also contains obligations related to exclusivity and exchange of patent information for interchangeable products, which would not make sense for two products produced by a single company. *See* 42 U.S.C. § 242(k)(6), (*l*).

12. While FDA determined Comirnaty and Pfizer-BioNTech Covid-19 vaccine are medically interchangeable, there are legal distinctions between BLA-approved and EUA-authorized products. For example, products approved under BLAs are required to have the labeling that was approved as part of the BLA, whereas products authorized under the EUA would have the EUA labeling, and there may also be differences in manufacturing sites for BLA and EUA vaccine. Both the EUA and BLA processes have required the sponsor to identify specific facilities that will manufacture the vaccine. *See* Summary Basis for Regulatory Action – Comirnaty, pp. 12-13 (August 23, 2021), available at https://www.fda.gov/media/151733/download.

13. Vaccine manufactured at sites listed in the BLA also undergoes lot release, which is designed to ensure conformity with standards applicable to the product. 21 C.F.R. § 610.1; *see*

also https://www.fda.gov/vaccines-blood-biologics/biologics-post-market-activities/lot-release#lotrelease. Vaccine manufactured at sites that are not listed in the BLA is not subject to the lot release requirement.[3] Manufacturing of the BLA and EUA vaccine must adhere to FDA's current good manufacturing practice regulations, which are designed to ensure that the products meet specified standards of safety, purity, and potency. *See* 21 C.F.R. Part 211 (CGMP regulations for drugs), § 211.1(b) (applicability of CGMP regulations to drugs that are also biological products); Exhibit B at 15.

14. In conjunction with the approval of Comirnaty, FDA asked the applicant to identify available lots of vaccine that were manufactured at facilities listed in the BLA that had undergone lot release. For these lots and other lots produced at facilities listed in the BLA, at this time, FDA is exercising its enforcement discretion with respect to certain labeling requirements, in that FDA is not taking enforcement with respect to vials that bear the EUA label.[4] FDA considers these lots to be manufactured in compliance with the BLA and they are not subject to the EUA requirements when used for the approved indication. Thus, the conditions in the Letter of Authorization for the EUA—including the condition requiring vaccination providers to provide recipients with the Fact Sheet for Recipients, which advises recipients that "under the EUA, it is your choice to receive or not receive the vaccine"—do not apply when these lots or

[3] Although not subject to lot release, as a condition of the EUA, Pfizer submits to the EUA file Certificates of Analysis for each drug product lot at least 48 hours prior to vaccine distribution; these Certificates include the established specifications and specific results for each quality control test performed on the final drug product lot. Additionally, also as a condition of the EUA, Pfizer submits quarterly manufacturing reports to the EUA file that include specified information about each lot of vaccine manufactured. *See* Exhibit B at 15.

[4] Each vial contains six doses of vaccine and a dose is withdrawn from the vial immediately before injection into a recipient, who would not ordinarily be handling the vial or viewing its label. Fact Sheet for Healthcare Providers Administering Vaccine, pp. 6-12 (Oct. 29, 2021), available at https://www.fda.gov/media/153713/download.

other BLA-compliant lots are used for the approved indication. FDA worked with the Applicant to develop a Dear Health Care Provider letter and website to identify those lots. Summary Basis for Regulatory Action – Comirnaty ("SBRA"), p. 27 (Nov. 8, 2021), attached as Exhibit C. Also, for operational efficiency, to account for the fact that recipients may receive either the BLA or EUA vaccine, after licensure of Comirnaty, vaccine has been distributed with unified Fact Sheets, one for providers and one for recipients, that provide information regarding the EUA product, as well as information about the licensed product. *See* Fact Sheet for Recipients and Caregivers 12 Years of Age and Older (Oct. 29, 2021), available at https://www.fda.gov/media/153716/download.

15. FDA has programs to expedite the development of drugs that are being studied to treat life-threatening or severely debilitating diseases. 21 U.S.C. § 356. These programs, one of which is "Fast Track" designation, are designed to help ensure that therapies for serious conditions are approved and available for patients as soon as it can be concluded that the therapies' benefits outweigh their risks. *See* Guidance for Industry, Expedited Programs for Serious Conditions – Drugs and Biologics (May 2014), available at https://www.fda.gov/media/86377/download. Fast Track designation was granted for Comirnaty on July 7, 2020. *See* Exhibit C, SBRA at 5. As explained on FDA's website, "Once a drug receives *Fast Track* designation, early and frequent communication between the FDA and a drug company is encouraged throughout the entire drug development and review process. The frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients." https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/fast-track.

16. In addition to granting Comirnaty "Fast Track" designation, FDA took other steps to speed development and review of COVID-19 vaccines in response to the urgent public health threat posed by SARS-CoV-2, without sacrificing the stringent statutory requirements for approval. Vaccines typically undergo three phases of clinical trial. *See* https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/vaccine-development-101. Phase 1 generally involves 20 to 100 healthy volunteers and focuses on safety. *Id.* Phases 2 and 3 studies typically enroll more subjects and are designed to gather more safety information on common short-term side effects and risks, examine the relationship between the dose administered and the immune response, and generate critical efficacy data. *Id.* In the case of the COVID-19 vaccines, those phases overlapped to speed the development process; no phases were skipped. *See* 21 C.F.R. § 312.21 ("Although in general the phases are conducted sequentially, they may overlap."). Also, because COVID-19 continues to be widespread, the vaccine clinical trials have been conducted more quickly than if the disease were less common.

17. The Comirnaty BLA was approved based on six months of safety and efficacy data from two ongoing clinical trials, C4591001 and BNT162-01, as well as safety information from the millions of vaccine doses administered under the EUA. C4591001 is a randomized, placebo-controlled, combined Phase 1, 2, and 3 study that has enrolled more than 43,000 participants. *See* Exhibit C, SBRA at 15. Initially, during Phases 2 and 3, study participants, as well as study investigators/personnel collecting and evaluating safety and efficacy information were blinded to the participants' treatment assignment (observer-blinded).[5] The study population for Phase 2/3

[5] "Blind" means that one or more parties of the clinical trial are kept unaware of the treatment assignment. Study participants, investigators, and health care providers may all be blinded to the treatment a participant is receiving, for example, whether a study participant is receiving the

includes participants at higher risk for acquiring COVID-19 and at higher risk of severe COVID-19, such as participants working in the healthcare field, participants with autoimmune disease, and participants with chronic but stable medical conditions such as hypertension, asthma, diabetes, and infection with HIV, hepatitis B or hepatitis C. *Id.* at 16.

18. In accordance with C4591001's study protocol (the plan that describes the objectives, design, methodology, statistical considerations, and organization of a clinical trial, *see* Glossary of Clinical Trial Terms, *available at* https://www.fda.gov/media/108378/download#:~:text=A%20document%20that%20describes%20the,in%20other%20protocol%20referenced%20documents), participants ages 16 and older in C4591001 have been progressively "unblinded" since the December 2020 issuance of the EUA for the Pfizer-BioNTech Covid-19 vaccine and offered the vaccine if they were randomized to the placebo group. Exhibit C, SBRA at 17. The study was unblinded in stages, either when participants were eligible according to local recommendations for vaccination or after conclusion of their six-month post–Dose 2 study visit (whichever was earlier). *Id.* Despite the unblinding, the data collected during the clinical trial still allowed FDA to evaluate the safety and effectiveness of the vaccine, considering the data collected during the blinded stage and the other information submitted supporting safety and effectiveness. Although C4591001 is ongoing and

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study drug or a placebo. Glossary of Clinical Trial Terms, *available at* https://www.fda.gov/media/108378/download#:~:text=A%20document%20that%20describes%20the,in%20other%20protocol%20referenced%20documents). Blinding may be done to prevent skewing of the data by the placebo effect, by risk-seeking behavior, by unconscious bias or by other factors. Blinding may impose a significant burden on the volunteer trial participants, and medical ethicists generally agree that researchers are sometimes ethically bound to unblind a study and permit placebo recipients to receive an effective treatment at some point. The knowledge that treatment will be made available at some point to placebo recipients if it proves to be effective also encourages participation in clinical trials. Overall, the decision regarding when to "unblind" a clinical trial involves a delicate balance of competing priorities.

safety will be evaluated for the duration of the study for blinded and unblinded participants, because most adverse events linked to vaccination occur within two months of vaccination (*see* Table VI. National Vaccine Injury Compensation Program. Rockville, MD: Health Resources and Services Administration, 2017, https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/vaccine-injury-table.pdf), FDA determined that a BLA for a COVID-19 vaccine could be supported by six months of safety data.[6] *See* FDA Guidance, Development and Licensure of Vaccines to Prevent COVID-19, at 15 (June 2020), attached as Exhibit D. Because the applicant submitted sufficient safety and efficacy data, the ongoing nature of the phase 3 clinical trial was not a basis for declining to license Comirnaty. The estimated completion date for C4591001 is May 2023, *see* https://www.clinicaltrials.gov/ct2/show/NCT04368728?term=C4591001&draw=2&rank=4).

19. BNT162-01 an ongoing Phase 1/2, open-label, dose-finding study with 24 participants, designed to evaluate the safety and immunogenicity of several candidate vaccines, including the dose that was approved by FDA on August 23, 2021. *See* Exhibit C, SBRA at 15. Safety data from the study was included in the BLA for Comirnaty and supported selection of the final vaccine candidate and dose level. *Id*. at 21. Although FDA did not refer the BLA to its

[6] Indeed, requesting six-months of follow-up safety data is not unique to Covid-19 vaccines. *See* Guidance for Industry Clinical Data Needed to Support the Licensure of Pandemic Influenza Vaccines, at 5,7, 10 (May 2007), available at https://www.fda.gov/files/vaccines, blood & biologics/published/Guidance-for-Industry--Clinical-Data-Needed-to-Support-the-Licensure-of-Pandemic-Influenza-Vaccines.pdf (generally recommending six-months of safety data to support influenza vaccines). FDA explained the rationale for requesting at least six-months of safety data to support licensure of Comirnaty in its response to a Citizen Petition submitted by the Informed Consent Action Network ("ICAN"), raising concerns similar to those raised by Plaintiffs. *See* Response to ICAN Citizen Petition, Docket FDA-2021-P-0529, at 9-10 (August 23, 2021), available at https://www.regulations.gov/document/FDA-2021-P-0529-1077.

advisory committee, the agency considered the committee's feedback from prior meetings considering the EUA for the Pfizer-BioNTech Covid-19 vaccine. *Id.* at 26-27.

20. In addition to reviewing clinical data, before approving the Comirnaty BLA, FDA assessed, among other things, its chemistry, manufacturing, and controls ("CMC"); nonclinical and clinical pharmacology and nonclinical toxicology data; safety and pharmacovigilance data; labeling; and manufacturing facilities. *See* 21 C.F.R. § 601.2 (requirements for contents of BLA application). Along with the Summary Basis for Regulatory Action for Comirnaty, also available on FDA's website for the Comirnaty BLA review are three Statistical Reviews; an assessment of Real World Evidence; two Pharmacovigilance Plan Reviews; two CMC Reviews, Clinical Review; CBER Sentinel Program Sufficiency Review; Bioresearch Monitoring Review; Benefit-Risk Assessment Review; Analytical Method Review; and Toxicology Review. *See* https://www.fda.gov/vaccines-blood-biologics/comirnaty (click on Approval History, Letters, Reviews, and Related Document – COMIRNATY).

21. FDA approved Comirnaty based on data from the two clinical studies that demonstrated that the overall efficacy rate in the 16 and older subject population was 91.1% for the prevention of COVID-19 infection and between 95% and 100% for the avoidance of severe infection. Exhibit C, SBRA at 19-20. FDA also considered the safety data from the two clinical studies, in addition to safety information from EUA use. *Id.* at 22-25. In sum, based on its review of the clinical, pre-clinical, and product-related data submitted in the Comirnaty BLA, FDA determined that the product had a favorable benefit/risk balance, and was safe, pure, and potent. The agency approved the license for Comirnaty on August 23, 2021. *Id.* at 27-28; Exhibit A, FDA Approval Letter (Aug. 23, 2021).

22. Comirnaty is subject to specified post market requirements and commitments. *See* 21 U.S.C. §§ 355(o)(2)(B)(ii) and 356b. Those requirements and commitments are: (1) Study C4591009, entitled "A Non-Interventional Post-Approval Safety Study of the Pfizer-BioNTech COVID-19 mRNA Vaccine in the United States," to evaluate the occurrence of myocarditis and pericarditis following administration of COMIRNATY; (2) Study C4591021, entitled "Post Conditional Approval Active Surveillance Study Among Individuals in Europe Receiving the Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine," to evaluate the occurrence of myocarditis and pericarditis following administration of COMIRNATY; (3) Study C4591021 sub-study to describe the natural history of myocarditis and pericarditis following administration of COMIRNATY; (4) Study C4591036, a prospective cohort study with at least 5 years of follow-up for potential long-term sequelae of myocarditis after vaccination; (5) Study C4591007 sub-study to prospectively assess the incidence of subclinical myocarditis following administration of the second dose of COMIRNATY in a subset of participants 5 through 15 years of age; (6) Study C4591031 sub-study to prospectively assess the incidence of subclinical myocarditis following administration of a third dose of COMIRNATY in a subset of participants 16 to 30 years of age; (7) Study C4591022, entitled "Pfizer-BioNTech COVID-19 Vaccine Exposure during Pregnancy: A Non-Interventional Post-Approval Safety Study of Pregnancy and Infant Outcomes in the Organization of Teratology Information Specialists (OTIS)/MotherToBaby Pregnancy Registry"; (8) Study C4591007 sub-study to evaluate the immunogenicity and safety of lower dose levels of COMIRNATY in individuals 12 through < 30 years of age; (9) Study C4591012, entitled "Post-emergency Use Authorization Active Safety Surveillance Study Among Individuals in the Veteran's Affairs Health System Receiving Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine"; (10) Study C4591014, entitled

"Pfizer-BioNTech COVID-19 BNT162b2 Vaccine Effectiveness Study - Kaiser Permanente Southern California"; (11) Deferred pediatric study C4591001 to evaluate the safety and effectiveness of COMIRNATY in children 12 years through 15 years of age; (12) Deferred pediatric study C4591007 to evaluate the safety and effectiveness of COMIRNATY in children 6 months to < 12 years of age; and (13) Deferred pediatric study C4591023 to evaluate the safety and effectiveness of COMIRNATY in infants < 6 months of age. Exhibit C, SBRA at 29-30.

23. FDA also collects adverse event reports from the general population receiving the vaccine via the Vaccine Adverse Event Reporting System (VAERS). VAERS is a national passive surveillance vaccine safety database that receives unconfirmed reports of possible adverse events following the use of a vaccine licensed or authorized in the United States. VAERS reports provide a very important tool in monitoring vaccine safety, but these reports alone cannot be used to determine if a vaccine caused or contributed to an adverse event or illness. *See* VAERS Data Disclaimer, https://vaers.hhs.gov/data.html. There are particular scientific limitations in comparing VAERS reports for COVID-19 vaccines with reports for previously approved vaccines for other conditions. For example, under the EUAs for the authorized COVID-19 vaccines, unlike for previously approved vaccines, vaccination providers are required to report to VAERS serious adverse events following vaccination with the COVID-19 vaccines "irrespective of attribution to vaccination" and regardless of how long after vaccination the adverse event occurs. In addition, CDC deployed the smartphone-based active-surveillance "v-safe" system only for the COVID-19 vaccines. V-safe has solicited adverse event reports directly from patients, which are then included in VAERS, but this system has only been deployed for COVID-19 vaccines and not for other vaccines. Finally, another potential factor that limits comparisons between VAERS reports for COVID-19 vaccines and reports for

other vaccines is the concept of "stimulated reporting." Because of extensive media coverage and awareness of the public health emergency – and of the authorized COVID-19 vaccines and their reported side effects – vaccine recipients, health care providers, and others are more likely to report adverse events for these vaccines than for other vaccines that have been widely available for longer periods of time. Although VAERS is not designed to assess causality, FDA and CDC actively monitor VAERS reports and engage in additional studies or investigations if VAERS monitoring suggests that a vaccine might be causing a health problem. *See* Children's Health Defense Petition Response, Docket FDA-2021-P-0460, at 17-28 (Aug. 23, 2021), attached as Exhibit E.

24. On the same day that FDA approved the license for Comirnaty, the agency responded to a Citizen Petition submitted by the Coalition Advocating for Adequately Licensed Medicines (CAALM) on July 23, 2021. CAALM Petition, Docket FDA-2021-P-0786, attached as Exhibit F. Among other things, the petition requested that FDA require "substantial evidence of clinical effectiveness that outweighs harms in special populations such as: infants, children, and adolescents; those with past SARS-CoV-2 infection; immunocompromised; pregnant women; nursing women; frail older adults; and individuals with cancer, autoimmune disorders, and hematological conditions" before licensing a Covid-19 vaccine, and that there should be information about "what kind of efficacy" exists for these populations, referring to "reduction in risk of symptomatic COVID-19 vs. reduction in risk of hospitalization or death." *Id.* at 2. Some of the populations identified by petitioners participated in the clinical trials and additional information will be obtained from post-marketing studies. For example, approximately 3% of the clinical trial participants had evidence of prior COVID-19 infection (*see* Clinical Review Memo at 35, referenced in paragraph 20, above). Additionally, although pregnant individuals

were excluded from participation in the trial and the applicant has committed to study the vaccine in this population segment as described in paragraph 22 above, participants in both the treatment and placebo arms of the trial became pregnant during the trial, and pregnancy outcomes of spontaneous abortion, miscarriages and elective abortions was similar between the vaccine and the placebo group. *Id.* at 84. In response to CAALM's Citizen Petition, FDA concluded that petitioners had not provided sufficient scientific justification for requiring effectiveness data from clinical trials specific to each population group and specifically designed to evaluate disease endpoints of varying severity, and petitioner's argument was not consistent with "scientifically valid methods of assessing safety and effectiveness," such as immunobridging or extrapolation across population groups. CAALM Petition Response, Docket FDA-2021-P-0786, at 7-8, attached as Exhibit G.

25. FDA also considered and responded to petitioner's claims that people previously affected with COVID-19 "are likely to have immunity to subsequent infections for as long or longer than immunity conferred by vaccine" and "may also be at heightened risk for adverse effects" from the vaccine, finding there was scientific uncertainty about the duration of immunity from natural infection and that petitioners had not provided sufficient scientific support for the latter claim. CAALM Petition Response at 8-9, n.31. In reaching that conclusion, FDA evaluated each study put forward by petitioners and carefully explained why the studies did not support petitioner's arguments. *Id.; see also* Response to ICAN Citizen Petition at 13-15. To the contrary, while there is scientific uncertainty about the duration of protection provided by previous natural infection, evidence is emerging that people get better protection by being fully vaccinated compared with having had COVID-19 natural infection. *See* CDC, COVID-19 Frequently Asked Questions, last updated August 2021, https://www.cdc.gov/coronavirus/2019-

ncov/vaccines/faq.html; Boyton, R. and D Altmann, 2021, Risk of SARS-CoV-2 reinfection after natural infection, Lancet, 397(10280):1161-1163, https://doi.org/10.1016/S0140-6736(21)00662-0. In addition, FDA and CDC medical officers conduct on-going active surveillance of serious adverse event reports for COVID-19 vaccines, including examination of narrative and other fields of adverse event reports that allow participants to input relevant information, which could include information about past COVID-19 infection. The reviewers conducting these surveillance efforts have not identified patterns of adverse events associated with receiving a COVID-19 vaccine after prior COVID-19 infection. *See* CAALM Petition Response at 8-9, n.31. In summary, FDA has not observed a heightened risk of adverse events for people who receive a COVID-19 vaccine after natural infection, either in the Comirnaty clinical study population (which included participants with evidence of prior COVID-19 infection) or in adverse event reports from the general population.

26. Safety surveillance reports received by FDA and CDC identified the risk of myocarditis and pericarditis following administration of Comirnaty. Comirnaty Summary Basis for Regulatory Action at 23 (Nov. 8, 2021). Reporting rates for medical chart-confirmed myocarditis/pericarditis in VAERS have been higher among males under 40 years of age than among females and older males and have been highest in males 12-17 years of age (65 cases per million doses administered as per CDC communication on August 20, 2021), particularly following the second dose, and onset of symptoms within 7 days following vaccination. *Id.* Although some cases of vaccine-associated myocarditis/pericarditis required intensive care support, available data from short-term follow up suggest that the large majority of individuals have had resolution of symptoms with conservative management. *Id.* Because vaccine-associated myocarditis/pericarditis is the most clinically significant identified risk, FDA

developed a quantitative model to compare the excess risk of myocarditis/pericarditis to the expected benefits of preventing COVID-19 and associated hospitalizations, ICU admissions, and deaths. *Id.* at 24. The model used an estimate of risk of myocarditis/pericarditis far higher than the rates estimated from reports to VAERS and assessed the benefit over a range of COVID-19 prevalence scenarios. *Id.* For males and females 18 years of age and older, even before accounting for morbidity prevented from non-hospitalized COVID-19, the model predicts that the benefits of prevented COVID-19 hospitalizations, ICU admissions and deaths would clearly outweigh the predicted excess risk of vaccine-associated myocarditis/pericarditis under all conditions examined. *Id.*[7] FDA further adopted measures to mitigate the risk of myocarditis/pericarditis, including through labeling statements, continued safety surveillance, postmarketing studies (as described in Paragraph 22), and prescriber information and public health messaging. *Id.* Myocarditis remains a manageable adverse event with risks that are far outweighed by the benefits of preventing COVID-19, including the resultant risks of death, hospitalization, and myocarditis induced by COVID-19.

27. In approving the BLA for Comirnaty, FDA applied its scientific expertise to evaluate the data contained in the application and determined that Comirnaty's benefits outweigh its risks and that it is safe, pure, potent, and effective for its proposed use. In response to the urgent public health emergency presented by COVID-19, FDA worked expeditiously to provide

[7] The same was true for females 16-17 years of age. *Id.* For males 16-17 years of age, the model predicts that the benefits of prevented COVID-19 hospitalizations, ICU admissions and deaths would clearly outweigh the predicted excess risk of vaccine-associated myocarditis/pericarditis under the "most likely" scenario, but that predicted excess cases of vaccine-associated myocarditis/pericarditis would exceed COVID-19 hospitalizations and deaths under the "worst case" scenario. *Id.* However, this predicted numerical imbalance does not account for the greater severity and length of hospitalization, on average, for COVID-19 compared with vaccine-associated myocarditis/pericarditis. *Id.* It also does not account for the risks of non-hospitalized COVID-19, or the societal benefits of vaccination. *Id.*

guidance to entities seeking to develop vaccines for this disease, and to review the BLA for Comirnaty once it was submitted to the agency to ensure it fully met the statutory standards for approval, to further the objective of protecting the public health.

28. An injunction affecting the licensure of Comirnaty would cause irreparable harm. Safe and effective vaccines are currently the most powerful tool we have against the pandemic and have been estimated to have already saved hundreds of thousands of lives. An injunction based on the Court's evaluation of the vaccine would call into question the data supporting FDA's determination that Comirnaty is safe and effective. The consequence could be to undermine the vaccine development process, if vaccine developers see that courts are willing to disregard FDA's rigorous review process and remove products from the market on the basis of mere allegations. In addition, another serious consequence could be to undermine the government's efforts to encourage vaccination in all eligible populations by exacerbating vaccine hesitancy. One of the most significant barriers to widespread vaccination is vaccine hesitancy and vaccine misinformation. It would also create considerable public and administrative confusion as to the effect of the injunction because the identical formulation has been authorized pursuant to an EUA. Even a more limited injunction, somehow limited to these plaintiffs, would generate extraordinary doubt and confusion.

I declare under penalty of perjury that the foregoing is true and correct to the best of my information, knowledge, and belief.

Dated: November 22, 2021

Peter Marks, M.D., Ph.D.
Director, Center for Biologics Evaluation
and Research
United States Food and Drug Administration

Marks Decl. Exhibit A

U.S. FOOD & DRUG ADMINISTRATION

Our STN: BL 125742/0 **BLA APPROVAL**

BioNTech Manufacturing GmbH August 23, 2021
Attention: Amit Patel
Pfizer Inc.
235 East 42nd Street
New York, NY 10017

Dear Mr. Patel:

Please refer to your Biologics License Application (BLA) submitted and received on May 18, 2021, under section 351(a) of the Public Health Service Act (PHS Act) for COVID-19 Vaccine, mRNA.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2229 to BioNTech Manufacturing GmbH, Mainz, Germany, under the provisions of section 351(a) of the PHS Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product, COVID-19 Vaccine, mRNA, which is indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT04368728 and NCT04380701.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture COVID-19 Vaccine, mRNA drug substance at Wyeth BioPharma Division of Wyeth Pharmaceuticals LLC, 1 Burtt Road, Andover, Massachusetts. The final formulated product will be manufactured, filled, labeled and packaged at Pfizer Manufacturing Belgium NV, Rijksweg 12, Puurs, Belgium and at Pharmacia & Upjohn Company LLC, 7000 Portage Road, Kalamazoo, Michigan. The diluent, 0.9% Sodium Chloride Injection, USP, will be manufactured at Hospira, Inc., (b) (4) and at Fresenius Kabi USA, LLC, (b) (4) .

You may label your product with the proprietary name, COMIRNATY, and market it in 2.0 mL glass vials, in packages of 25 and 195 vials.
We did not refer your application to the Vaccines and Related Biological Products Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

DATING PERIOD

The dating period for COVID-19 Vaccine, mRNA shall be 9 months from the date of manufacture when stored between -90ºC to -60ºC (-130ºF to -76ºF). The date of manufacture shall be no later than the date of final sterile filtration of the formulated drug product (at Pharmacia & Upjohn Company LLC in Kalamazoo, Michigan, the date of manufacture is defined as the date of sterile filtration for the final drug product; at Pfizer Manufacturing Belgium NV in Puurs, Belgium, it is defined as the date of the (b) (4) Following the final sterile filtration, (b) (4) , no reprocessing/reworking is allowed without prior approval from the Agency. The dating period for your drug substance shall be (b) (4) when stored at (b) (4) We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of your drug substance and drug product under 21 CFR 601.12.

FDA LOT RELEASE

Please submit final container samples of the product in final containers together with protocols showing results of all applicable tests. You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to the Director, Office of Compliance and Biologics Quality, electronically through the eBPDR web application or at the address below. Links for the instructions on completing the electronic form (eBPDR) may be found on CBER's web site at https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviations:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center

10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of COVID-19 Vaccine, mRNA, or in the manufacturing facilities.

LABELING

We hereby approve the draft content of labeling including Package Insert, submitted under amendment 74, dated August 21, 2021, and the draft carton and container labels submitted under amendment 63, dated August 19, 2021.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert submitted on August 21, 2021. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELS

Please electronically submit final printed carton and container labels identical to the carton and container labels submitted on August 19, 2021, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-certain-human-pharmaceutical-product-applications.

All final labeling should be submitted as Product Correspondence to this BLA STN BL 125742 at the time of use and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

ADVERSE EVENT REPORTING

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80), and you must submit distribution reports at monthly intervals as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format —Postmarketing Safety Reports for Vaccines* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports-vaccines. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm.

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric studies for ages younger than 16 years for this application because this product is ready for approval for use in individuals 16 years of age and older, and the pediatric studies for younger ages have not been completed.

Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) are required postmarketing studies. The status of these postmarketing studies must be reported according to 21 CFR 601.28 and section 505B(a)(4)(C) of the FDCA. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

Label your annual report as an "**Annual Status Report of Postmarketing Study Requirement/Commitments**" and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements under section 506B of the FDCA are released or fulfilled. These required studies are listed below:

1. Deferred pediatric Study C4591001 to evaluate the safety and effectiveness of COMIRNATY in children 12 years through 15 years of age.

   Final Protocol Submission: October 7, 2020

   Study Completion: May 31, 2023

   Final Report Submission: October 31, 2023

2. Deferred pediatric Study C4591007 to evaluate the safety and effectiveness of COMIRNATY in infants and children 6 months to <12 years of age.

   Final Protocol Submission: February 8, 2021

   Study Completion: November 30, 2023

   Final Report Submission: May 31, 2024

3. Deferred pediatric Study C4591023 to evaluate the safety and effectiveness of COMIRNATY in infants <6 months of age.

   Final Protocol Submission: January 31, 2022

   Study Completion: July 31, 2024

   Final Report Submission: October 31, 2024

Submit the protocols to your IND 19736, with a cross-reference letter to this BLA STN BL 125742 explaining that these protocols were submitted to the IND. Please refer to the PMR sequential number for each study/clinical trial and the submission number as shown in this letter.
Submit final study reports to this BLA STN BL 125742. In order for your PREA PMRs to be considered fulfilled, you must submit and receive approval of an efficacy or a labeling

supplement. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated as:

- **Required Pediatric Assessment(s)**

We note that you have fulfilled the pediatric study requirement for ages 16 through 17 years for this application.

POSTMARKETING REQUIREMENTS UNDER SECTION 505(o)

Section 505(o) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)).

We have determined that an analysis of spontaneous postmarketing adverse events reported under section 505(k)(1) of the FDCA will not be sufficient to assess known serious risks of myocarditis and pericarditis and identify an unexpected serious risk of subclinical myocarditis.

Furthermore, the pharmacovigilance system that FDA is required to maintain under section 505(k)(3) of the FDCA is not sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, we have determined that you are required to conduct the following studies:

4. Study C4591009, entitled “A Non-Interventional Post-Approval Safety Study of the Pfizer-BioNTech COVID-19 mRNA Vaccine in the United States,” to evaluate the occurrence of myocarditis and pericarditis following administration of COMIRNATY.

   We acknowledge the timetable you submitted on August 21, 2021, which states that you will conduct this study according to the following schedule:

   Final Protocol Submission: August 31, 2021

   Monitoring Report Submission: October 31, 2022

   Interim Report Submission: October 31, 2023

   Study Completion: June 30, 2025

   Final Report Submission: October 31, 2025

5. Study C4591021, entitled “Post Conditional Approval Active Surveillance Study Among Individuals in Europe Receiving the Pfizer-BioNTech Coronavirus

Disease 2019 (COVID-19) Vaccine," to evaluate the occurrence of myocarditis and pericarditis following administration of COMIRNATY.

We acknowledge the timetable you submitted on August 21, 2021, which states that you will conduct this study according to the following schedule:

Final Protocol Submission: August 11, 2021

Progress Report Submission: September 30, 2021

Interim Report 1 Submission: March 31, 2022

Interim Report 2 Submission: September 30, 2022

Interim Report 3 Submission: March 31, 2023

Interim Report 4 Submission: September 30, 2023

Interim Report 5 Submission: March 31, 2024

Study Completion: March 31, 2024

Final Report Submission: September 30, 2024

6. Study C4591021 substudy to describe the natural history of myocarditis and pericarditis following administration of COMIRNATY.

   We acknowledge the timetable you submitted on August 21, 2021, which states that you will conduct this study according to the following schedule:

   Final Protocol Submission: January 31, 2022

   Study Completion: March 31, 2024

   Final Report Submission: September 30, 2024

7. Study C4591036, a prospective cohort study with at least 5 years of follow-up for potential long-term sequelae of myocarditis after vaccination (in collaboration with Pediatric Heart Network).

   We acknowledge the timetable you submitted on August 21, 2021, which states that you will conduct this study according to the following schedule:

   Final Protocol Submission: November 30, 2021

   Study Completion: December 31, 2026

Final Report Submission: May 31, 2027

8. Study C4591007 substudy to prospectively assess the incidence of subclinical myocarditis following administration of the second dose of COMIRNATY in a subset of participants 5 through 15 years of age.

   We acknowledge the timetable you submitted on August 21, 2021, which states that you will conduct this assessment according to the following schedule:

   Final Protocol Submission: September 30, 2021

   Study Completion: November 30, 2023

   Final Report Submission: May 31, 2024

9. Study C4591031 substudy to prospectively assess the incidence of subclinical myocarditis following administration of a third dose of COMIRNATY in a subset of participants 16 to 30 years of age.

   We acknowledge the timetable you submitted on August 21, 2021, which states that you will conduct this study according to the following schedule:

   Final Protocol Submission: November 30, 2021

   Study Completion: June 30, 2022

   Final Report Submission: December 31, 2022

Please submit the protocols to your IND 19736, with a cross-reference letter to this BLA STN BL 125742 explaining that these protocols were submitted to the IND. Please refer to the PMR sequential number for each study/clinical trial and the submission number as shown in this letter.

Please submit final study reports to the BLA. If the information in the final study report supports a change in the label, the final study report must be submitted as a supplement to this BLA STN BL 125742. For administrative purposes, all submissions related to these postmarketing studies required under section 505(o) must be submitted to this BLA and be clearly designated as:

- **Required Postmarketing Correspondence under Section 505(o)**
- **Required Postmarketing Final Report under Section 505(o)**
- **Supplement contains Required Postmarketing Final Report under Section 505(o)**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise

undertaken to investigate a safety issue. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

You must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing requirement;
- the original milestone schedule for the requirement;
- the revised milestone schedule for the requirement, if appropriate;
- the current status of the requirement (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status for the study or clinical trial. The explanation should include how the study is progressing in reference to the original projected schedule, including, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

We will consider the submission of your annual report under section 506B of the FDCA and 21 CFR 601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in section 505(o) and 21 CFR 601.70. We remind you that to comply with section 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to periodically report on the status of studies or clinical trials required under section 505(o) may be a violation of FDCA section 505(o)(3)(E)(ii) and could result in regulatory action.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We acknowledge your written commitments as described in your letter of August 21, 2021 as outlined below:

10. Study C4591022, entitled “Pfizer-BioNTech COVID-19 Vaccine Exposure during Pregnancy: A Non-Interventional Post-Approval Safety Study of Pregnancy and Infant Outcomes in the Organization of Teratology Information Specialists (OTIS)/MotherToBaby Pregnancy Registry.”

    Final Protocol Submission: July 1, 2021

Study Completion: June 30, 2025

Final Report Submission: December 31, 2025

11. Study C4591007 substudy to evaluate the immunogenicity and safety of lower dose levels of COMIRNATY in individuals 12 through <30 years of age.

    Final Protocol Submission: September 30, 2021

    Study Completion: November 30, 2023

    Final Report Submission: May 31, 2024

12. Study C4591012, entitled "Post-emergency Use Authorization Active Safety Surveillance Study Among Individuals in the Veteran's Affairs Health System Receiving Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine."

    Final Protocol Submission: January 29, 2021

    Study Completion: June 30, 2023

    Final Report Submission: December 31, 2023

13. Study C4591014, entitled "Pfizer-BioNTech COVID-19 BNT162b2 Vaccine Effectiveness Study - Kaiser Permanente Southern California."

    Final Protocol Submission: March 22, 2021

    Study Completion: December 31, 2022

    Final Report Submission: June 30, 2023

Please submit clinical protocols to your IND 19736, and a cross-reference letter to this BLA STN BL 125742 explaining that these protocols were submitted to the IND. Please refer to the PMC sequential number for each study/clinical trial and the submission number as shown in this letter.

If the information in the final study report supports a change in the label, the final study report must be submitted as a supplement. Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Correspondence Study Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment – Final Study Report**

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing commitment;
- the original schedule for the commitment;
- the status of the commitment (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

POST APPROVAL FEEDBACK MEETING

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application.

Sincerely,

Mary A. Malarkey
Director
Office of Compliance
and Biologics Quality
Center for Biologics
Evaluation and Research

Marion F. Gruber, PhD
Director
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research

Marks Decl. Exhibit B

November 19, 2021

Pfizer Inc.
Attention: Mr. Amit Patel
235 East 42nd St
New York, NY 10017

Dear Mr. Patel:

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act or the Act), the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes Coronavirus Disease 2019 (COVID-19).[1] On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Act (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.[2]

On December 11, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for emergency use of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 for individuals 16 years of age and older pursuant to Section 564 of the Act. FDA reissued the letter of authorization on: December 23, 2020,[3] February 25, 2021,[4] May

[1] U.S. Department of Health and Human Services, Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the FD&C Act, 21 U.S.C. § 360bbb-3, February 4, 2020.

[2] U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*, 85 FR 18250 (April 1, 2020).

[3] In the December 23, 2020 revision, FDA removed reference to the number of doses per vial after dilution from the letter of authorization, clarified the instructions for vaccination providers reporting to VAERS, and made other technical corrections. FDA also revised the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) to clarify the number of doses of vaccine per vial after dilution and the instructions for reporting to VAERS. In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and the Fact Sheet for Recipients and Caregivers were revised to include additional information on safety monitoring and to clarify information about the availability of other COVID-19 vaccines.

[4] In the February 25, 2021 revision, FDA allowed flexibility on the date of submission of monthly periodic safety reports and revised the requirements for reporting of vaccine administration errors by Pfizer Inc. The Fact Sheet for Health Care Providers Administering Vaccine (Vaccination Providers) was revised to provide an update to the storage and transportation temperature for frozen vials, direct the provider to the correct CDC website for information on monitoring vaccine recipients for the occurrence of immediate adverse reactions, to include data from a developmental toxicity study, and add adverse reactions that have been identified during post authorization use. The Fact Sheet for Recipients and Caregivers was revised to add adverse reactions that have been identified during post authorization use.

10, 2021,[5] June 25, 2021,[6] and August 12, 2021.[7] On August 23, 2021, FDA approved COMIRNATY (COVID-19 Vaccine, mRNA)[8] and reissued the letter in its entirety for both Pfizer-BioNTech COVID-19 Vaccine and certain uses of COMIRNATY (COVID-19 Vaccine, mRNA).[9] Subsequently, FDA reissued the letter of authorization on September 22, 2021,[10] October 20, 2021,[11] and October 29, 2021.[12]

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[5] In the May 10, 2021 revision, FDA authorized Pfizer-BioNTech Vaccine for the prevention of COVID-19 in individuals 12 through 15 years of age, as well as for individuals 16 years of age and older. In addition, FDA revised the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) to include the following Warning: "Syncope (fainting) may occur in association with administration of injectable vaccines, in particular in adolescents. Procedures should be in place to avoid injury from fainting." In addition, the Fact Sheet for Recipients and Caregivers was revised to instruct vaccine recipients or their caregivers to tell the vaccination provider about fainting in association with a previous injection.

[6] In the June 25, 2021 revision, FDA clarified terms and conditions that relate to export of Pfizer-BioNTech COVID-19 Vaccine from the United States. In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) was revised to include a Warning about myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine. The Fact Sheet for Recipients and Caregivers was updated to include information about myocarditis and pericarditis following administration of the Pfizer-BioNTech COVID-19 Vaccine.

[7] In the August 12, 2021 revision, FDA authorized a third dose of the Pfizer-BioNTech COVID-19 Vaccine administered at least 28 days following the two dose regimen of this vaccine in individuals 12 years of age or older who have undergone solid organ transplantation, or individuals 12 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

[8] COMIRNATY (COVID-19 Vaccine, mRNA) was approved for active immunization to prevent COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older.

[9] In the August 23, 2021 revision, FDA clarified that, subsequent to the FDA approval of COMIRNATY (COVID-19 Vaccine, mRNA) for the prevention of COVID-19 for individuals 16 years of age and older, this EUA would remain in place for the Pfizer-BioNTech COVID-19 Vaccine for the previously-authorized indication and uses. It also authorized COMIRNATY (COVID-19 Vaccine, mRNA) under this EUA for certain uses that are not included in the approved biologics license application (BLA). In addition, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) was revised to provide updates on expiration dating of the authorized Pfizer-BioNTech COVID-19 Vaccine and updated language regarding warnings and precautions related to myocarditis and pericarditis. The Fact Sheet for Recipients and Caregivers was updated as the Vaccine Information Fact Sheet for Recipients and Caregivers, which comprises the Fact Sheet for the authorized Pfizer-BioNTech COVID-19 Vaccine and information about the FDA-licensed vaccine, COMIRNATY (COVID-19 Vaccine, mRNA).

[10] In the September 22, 2021 revision, FDA authorized the administration of a single booster dose of COMIRNATY (COVID-19 Vaccine, mRNA) or Pfizer-BioNTech COVID-19 Vaccine at least 6 months after completing the primary series of this vaccine in individuals: 65 years of age and older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.

[11] In the October 20, 2021 revision, FDA clarified eligibility for the booster dose of COMIRNATY (COVID-19 Vaccine, mRNA) or Pfizer-BioNTech COVID-19 Vaccine and authorized the administration of a single booster dose of Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (COVID-19 Vaccine, mRNA) as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

[12] In the October 29, 2021 revision, FDA authorized: 1) the use of Pfizer-BioNTech COVID-19 Vaccine for children 5 through 11 years of age; and 2) a manufacturing change to include an additional formulation of the Pfizer-

On November 19, 2021, having concluded that revising this EUA is appropriate to protect the public health or safety under Section 564(g)(2) of the Act, FDA is again reissuing the October 29, 2021 letter of authorization in its entirety with revisions incorporated to amend the EUA for COMIRNATY (COVID-19 Vaccine, mRNA) and Pfizer-BioNTech COVID-19 Vaccine to authorize use of the vaccine as a single booster dose in individuals 18 years of age or older, at least 6 months after completing the primary series of this vaccine (i.e., as a homologous booster dose), and to authorize use of the vaccine as a single booster dose following completion of primary vaccination with another authorized COVID-19 vaccine (i.e., as a heterologous booster dose) in individuals 18 years of age or older. The dosing interval for the heterologous booster dose is the same as that authorized for a booster dose of the vaccine used for primary vaccination. The authorized uses, as well as the two formulations that have three presentations, are described in the Scope of Authorization section of this letter (Section II).

For the December 11, 2020 authorization for individuals 16 years of age and older, FDA reviewed safety and effectiveness data from an ongoing Phase 1/2/3 trial in approximately 44,000 participants randomized 1:1 to receive Pfizer-BioNTech COVID-19 Vaccine or saline control. The trial enrolled participants 12 years of age and older. FDA's review at that time considered the safety and effectiveness data as they relate to the request for emergency use authorization in individuals 16 years of age and older. FDA's review of the available safety data from 37,586 of the participants 16 years of age and older, who were followed for a median of two months after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. FDA's analysis of the available efficacy data from 36,523 participants 12 years of age and older without evidence of SARS-CoV-2 infection prior to 7 days after dose 2 confirmed that the vaccine was 95% effective (95% credible interval 90.3, 97.6) in preventing COVID-19 occurring at least 7 days after the second dose (with 8 COVID-19 cases in the vaccine group compared to 162 COVID-19 cases in the placebo group). Based on these data, and review of manufacturing information regarding product quality and consistency, FDA concluded that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 16 years of age and older. Finally, on December 10, 2020, the Vaccines and Related Biological Products Advisory Committee voted in agreement with this conclusion.

For the May 10, 2021 authorization for individuals 12 through 15 years of age, FDA reviewed safety and effectiveness data from the above-referenced, ongoing Phase 1/2/3 trial that enrolled approximately 46,000 participants, including 2,260 participants 12 through 15 years of age.

BioNTech COVID-19 Vaccine that uses tromethamine (Tris) buffer instead of phosphate buffered saline (PBS) used in the originally authorized Pfizer-BioNTech COVID-19 Vaccine. The formulation of the Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer was authorized in two presentations: 1) Multiple dose vials, with gray caps and labels with a gray border, formulated to provide, without need for dilution, doses (each 0.3 mL dose containing 30 µg nucleoside-modified messenger RNA (modRNA)) for individuals 12 years of age and older; and 2) Multiple dose vials, with orange caps and labels with an orange border, formulated to provide, after dilution, doses (each 0.2 mL dose containing 10 µg modRNA) for individuals 5 through 11 years of age. The formulation that uses Tris buffer is the only formulation that is authorized for use in individuals 5 through 11 years of age.

Trial participants were randomized 1:1 to receive Pfizer-BioNTech COVID-19 Vaccine or saline control. FDA's review of the available safety data from 2,260 participants 12 through 15 years of age, who were followed for a median of 2 months after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. FDA's analysis of SARS-CoV-2 50% neutralizing antibody titers 1 month after the second dose of Pfizer-BioNTech COVID-19 Vaccine in a subset of participants who had no serological or virological evidence of past SARS-CoV-2 infection confirm that the geometric mean antibody titer in participants 12 through 15 years of age was non-inferior to the geometric mean antibody titer in participants 16 through 25 years of age. FDA's analysis of available descriptive efficacy data from 1,983 participants 12 through 15 years of age without evidence of SARS-CoV-2 infection prior to 7 days after dose 2 confirm that the vaccine was 100% effective (95% confidence interval 75.3, 100.0) in preventing COVID-19 occurring at least 7 days after the second dose (with no COVID-19 cases in the vaccine group compared to 16 COVID-19 cases in the placebo group). Based on these data, FDA concluded that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in individuals 12 through 15 years of age. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 12 through 15 years of age.

For the August 12, 2021 authorization of a third primary series dose in individuals 12 years of age or older who have undergone solid organ transplantation, or individuals 12 years of age or older who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise, FDA reviewed safety and effectiveness data reported in two manuscripts on solid organ transplant recipients. The first study was a single arm study conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) a median of 97±8 months earlier. A third dose of the Pfizer-BioNTech COVID-19 Vaccine was administered to 99 of these individuals approximately 2 months after they had received a second dose. Levels of total SARS-CoV-2 binding antibodies meeting the pre-specified criteria for success occurred four weeks after the third dose in 26/59 (44.0%) of those who were initially considered to be seronegative and received a third dose of the Pfizer-BioNTech COVID-19 Vaccine; 67/99 (68%) of the entire group receiving a third vaccination were subsequently considered to have levels of antibodies indicative of a significant response. In those who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported. A supportive secondary study describes a double-blind, randomized-controlled study conducted in 120 individuals who had undergone various solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) a median of 3.57 years earlier (range 1.99-6.75 years). A third dose of a similar messenger RNA vaccine (the Moderna COVID-19 vaccine) was administered to 60 individuals approximately 2 months after they had received a second dose (i.e., doses at 0, 1 and 3 months); saline placebo was given to 60 individuals for comparison. The primary outcome was anti-RBD antibody at 4 months greater than 100 U/mL. This titer was selected based on NHP challenge studies as well as a large clinical cohort study to indicate this antibody titer was protective. Secondary outcomes were based on a virus neutralization assay and polyfunctional T cell responses. Baseline characteristics were comparable between the two study arms as were pre-intervention anti-RBD titer and neutralizing antibodies. Levels of total SARS-CoV-2 binding

antibodies indicative of a significant response occurred four weeks after the third dose in 33/60 (55.0%) of the Moderna COVID-19 vaccinated group and 10/57 (17.5%) of the placebo individuals. In the 60 individuals who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 adverse events were reported. Despite the moderate enhancement in antibody titers, the totality of data (i.e., supportive paper by Hall et al. demonstrated efficacy of the product in the elderly and persons with co-morbidities) supports the conclusion that a third dose of the Pfizer-BioNTech COVID-19 Vaccine may be effective in this population, and that the known and potential benefits of a third dose of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine for immunocompromised individuals at least 12 years of age who have received two doses of the Pfizer-BioNTech COVID-19 Vaccine and who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

For the September 22, 2021 authorization of a single booster dose administered at least 6 months after completing the primary series in individuals: 65 years of age and older; 18 through 64 years of age at high risk of severe COVID-19; and 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19, FDA reviewed safety and effectiveness data from the above-referenced, ongoing Phase 1/2/3 trial in which 329 participants 18 through 75 years of age received a booster dose of the Pfizer-BioNTech COVID-19 Vaccine approximately 6 months (range 4.8 to 8.8 months) after completion of the primary series. FDA's review of the available safety data from 329 participants 18 through 75 years of age, who had been followed for a median of 2.6 months after receiving the booster dose, did not identify specific safety concerns that would preclude issuance of an EUA. The effectiveness of the booster dose of the Pfizer-BioNTech COVID-19 Vaccine is based on an assessment of 50% neutralizing antibody titers (NT50) against SARS-CoV-2 (USA_WA1/2020). FDA's analysis of SARS-CoV-2 NT50 one month after the booster dose compared to 1 month after the primary series in study participants 18 through 55 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after the booster dose confirmed noninferiority for both geometric mean ratio and difference in seroresponse rates. Based on the totality of the scientific evidence available, including data from the above-referenced clinical trial, FDA concluded that a booster dose the Pfizer-BioNTech COVID-19 Vaccine may be effective, and that the known and potential benefits of a single booster dose at least 6 months after completing the primary series outweigh the known and potential risks for individuals 65 years of age and older; individuals 18 through 64 years of age at high risk of severe COVID-19; and individuals 18 through 64 years of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19.

For the October 20, 2021 authorization of a single booster dose as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine, FDA reviewed data from an ongoing Phase1/2 clinical trial in participants 19-85 years of age. In this trial, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose

series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series (N=151) at least 12 weeks prior to enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: Moderna COVID-19 Vaccine, Janssen COVID-19 Vaccine, or Pfizer-BioNTech COVID-19 Vaccine. Adverse events were assessed through 28 days after the booster dose. An overall review of adverse reactions reported following the Pfizer-BioNTech COVID-19 Vaccine heterologous booster dose did not identify any new safety concerns, as compared with adverse reactions reported following Pfizer-BioNTech COVID-19 Vaccine primary series doses or homologous booster dose. Neutralizing antibody titers, as measured by a pseudovirus neutralization assay using a lentivirus expressing the SARS-CoV-2 Spike protein with D614G mutation, were assessed on Day 1 prior to administration of the booster dose and on Day 15 after the booster dose. A booster response to the Pfizer-BioNTech COVID-19 Vaccine was demonstrated regardless of primary vaccination. Based on the on the totality of the scientific evidence available, including data from the above-referenced clinical trial, FDA concluded that a heterologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine may be effective, and that the known and potential benefits of a heterologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine following completion of primary vaccination with another authorized COVID-19 vaccine outweigh the known and potential risks.

For the October 29, 2021 authorization for the Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer for individuals 5 through 11 years of age, FDA reviewed safety and effectiveness data from an ongoing Phase 1/2/3 trial that has enrolled 4,695 participants 5 through 11 years of age, of whom 3,109 participants received Pfizer-BioNTech COVID-19 Vaccine (containing 10 µg modRNA) formulated using PBS buffer and approximately 1,538 participants received saline control in Phase 2/3. FDA's review of the available safety data from 3,109 participants 5 through 11 years of age who received Pfizer-BioNTech COVID-19 Vaccine (containing 10 µg modRNA), including 1,444 who were followed for at least 2 months after receiving the second dose, did not identify specific safety concerns that would preclude issuance of an EUA. SARS-CoV-2 50% neutralizing antibody titers 1 month after the second dose were compared between a subset of participants 5 through 11 years of age who received Pfizer-BioNTech COVID-19 Vaccine (containing 10 µg modRNA) and a subset of participants 16 through 25 years of age who received Pfizer-BioNTech COVID-19 Vaccine (containing 30 µg modRNA) in the above-referenced ongoing Phase 1/2/3 trial that enrolled approximately 46,000 participants. Immunobridging analyses included a subset of participants from each study who had no serological or virological evidence of past SARS-CoV-2 infection. FDA's analyses confirm that immunobridging criteria were met for both geometric mean antibody titers and seroresponse rates. FDA's analysis of available descriptive efficacy data from 1,968 participants 5 through 11 years of age without evidence of SARS-CoV-2 infection prior to 7 days after dose 2 confirm that the vaccine was 90.7% effective (95% confidence interval 67.7, 98.3) in preventing COVID-19 occurring at least 7 days after the second dose (with 3 COVID-19 cases in the vaccine group compared to 16 COVID-19 cases in the placebo group). Based on these data, FDA concluded that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in individuals 5 through 11 years of age. Additionally, FDA determined it is reasonable to conclude, based on the totality of the scientific evidence available, that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine outweigh the known and potential risks of the vaccine, for the prevention of COVID-19 in individuals 5 through 11 years of age. Finally, on

October 26, 2021, the Vaccines and Related Biological Products Advisory Committee voted in agreement with this conclusion.

For the October 29, 2021 authorization of the manufacturing change to include an additional formulation of the Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer instead of PBS buffer used in the originally authorized Pfizer-BioNTech COVID-19 Vaccine, FDA reviewed data on analytical comparability, which uses laboratory testing to demonstrate that a change in product formulation is not expected to impact safety or effectiveness. In the case of Pfizer-BioNTech COVID-19 Vaccine, multiple different release parameters were evaluated, ranging from product appearance to size of the lipid-nanoparticle to the integrity of the modRNA in the product. Release and characterization tests include tests for purity, composition, and critical attributes of mRNA associated with the activity of the vaccine. In this case, analytical comparability to the current PBS formulation of the Pfizer-BioNTech COVID-19 Vaccine was demonstrated for the Tris formulation of the Pfizer-BioNTech COVID-19 Vaccine through a combination of release and characterization testing.

For the November 19, 2021 authorization expanding the eligible population for the homologous and heterologous booster doses to individuals 18 years of age and older, FDA reviewed data provided by the sponsor and other data available to FDA, including real world evidence. Data previously reviewed to support the September 22, 2021 authorization of a homologous booster dose, together with new real-world data indicating increasing COVID-19 cases in the United States, including among vaccinated individuals, and suggesting a decreased risk of myocarditis following mRNA COVID-19 vaccine booster doses compared with second primary series doses, support expansion of the population eligible for a Pfizer-BioNTech COVID-19 vaccine homologous booster dose to include all individuals 18 years of age and older who completed the primary series at least 6 months previously. Data previously reviewed to support the October 20, 2021 authorization of a heterologous booster dose, together with data and information to support authorization of the EUA amendment to expand the eligible population for a homologous booster dose of the Moderna COVID-19 Vaccine, support a revision to the Pfizer-BioNTech COVID-19 Vaccine EUA such that the eligible population for a heterologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine is all adults 18 years of age and older who completed primary vaccination with another authorized COVID-19 vaccine. Based on the totality of the scientific evidence available, FDA concludes that a homologous or heterologous booster dose of the Pfizer-BioNTech COVID-19 Vaccine may be effective, and that the known and potential benefits of the booster dose of the Pfizer-BioNTech Vaccine following completion of primary vaccination with Pfizer-BioNTech COVID-19 Vaccine or another authorized COVID-19 vaccine, outweigh the known and potential risks in individuals 18 years of age and older.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of Pfizer-BioNTech COVID-19 Vaccine[13] for the prevention of COVID-19, as described in the Scope of Authorization section of this letter (Section II) and subject to the terms of this authorization. Additionally, as specified in

[13] Reference to the Pfizer-BioNTech COVID-19 Vaccine hereinafter refers to both the PBS and Tris formulations, unless specifically delineated otherwise.

subsection III.BB., I am authorizing use of COMIRNATY (COVID-19 Vaccine, mRNA) under this EUA as described in the Scope of Authorization section of this letter (Section II).

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of Pfizer-BioNTech COVID-19 Vaccine[14] for the prevention of COVID-19 when administered as described in the Scope of Authorization (Section II) meets the criteria for issuance of an authorization under Section 564(c) of the Act, because:

A. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;

B. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19, and that, when used under the conditions described in this authorization, the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine when used to prevent COVID-19 outweigh its known and potential risks; and

C. There is no adequate, approved, and available alternative[15] Pfizer-BioNTech COVID-19 Vaccine to prevent COVID-19.[16]

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- Pfizer Inc. will supply Pfizer-BioNTech COVID-19 Vaccine either directly or through authorized distributor(s),[17] to emergency response stakeholders[18] as directed by the U.S.

[14] In this section (Section I), references to Pfizer-BioNTech COVID-19 Vaccine also apply to COMIRNATY (COVID-19 Vaccine, mRNA).

[15] Although COMIRNATY (COVID-19 Vaccine, mRNA) is approved to prevent COVID-19 in individuals 16 years of age and older, there is not sufficient approved vaccine available for distribution to this population in its entirety at the time of reissuance of this EUA. Additionally, there are no COVID-19 vaccines that are approved to provide: COVID-19 vaccination in individuals 5 through 15 years of age; a third primary series dose to certain immunocompromised populations described in this EUA; a homologous booster dose to the authorized population described in this EUA; or a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine.

[16] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

[17] "Authorized Distributor(s)" are identified by Pfizer Inc. or, if applicable, by a U.S. government entity, such as the Centers for Disease Control and Prevention (CDC) and/or other designee, as an entity or entities allowed to distribute authorized Pfizer-BioNTech COVID-19 Vaccine.

[18] For purposes of this letter, "emergency response stakeholder" refers to a public health agency and its delegates that have legal responsibility and authority for responding to an incident, based on political or geographical boundary lines (e.g., city, county, tribal, territorial, State, or Federal), or functional (e.g., law enforcement or public health range) or sphere of authority to administer, deliver, or distribute vaccine in an emergency situation. In some cases (e.g., depending on a state or local jurisdiction's COVID-19 vaccination response organization and plans),

government, including the Centers for Disease Control and Prevention (CDC) and/or other designee, for use consistent with the terms and conditions of this EUA; and
- Pfizer-BioNTech COVID-19 Vaccine may be administered by a vaccination provider[19] without an individual prescription for each vaccine recipient.

For use in individuals 12 years of age and older

- The Pfizer-BioNTech COVID-19 Vaccine formulations that use Tris and PBS buffers (each 0.3 mL dose containing 30 µg modRNA), as described in more detail under *Product Description* below, covered by this authorization will be administered by vaccination providers and used only to prevent COVID-19 in individuals 12 years of age and older with a two-dose primary regimen (3 weeks apart) and to provide:
  - a third primary series dose at least 28 days following the second dose to individuals 12 years of age or older who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise;
  - a single booster dose at least 6 months after completion of a primary series of the vaccine to individuals 18 years of age or older; and
  - a single booster dose as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine, in individuals 18 years of age and older, where the dosing interval for the heterologous booster dose is the same as that authorized for a booster dose of the vaccine used for primary vaccination.

For use in individuals 5 through 11 years of age

- The Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer (each 0.2 mL dose containing 10 µg modRNA), as described in more detail under *Product Description* below, covered by this authorization will be administered by vaccination providers and

there might be overlapping roles and responsibilities among "emergency response stakeholders" and "vaccination providers" (e.g., if a local health department is administering COVID-19 vaccines; if a pharmacy is acting in an official capacity under the authority of the state health department to administer COVID-19 vaccines). In such cases, it is expected that the conditions of authorization that apply to emergency response stakeholders and vaccination providers will all be met.

[19] For purposes of this letter, "vaccination provider" refers to the facility, organization, or healthcare provider licensed or otherwise authorized by the emergency response stakeholder (e.g., non-physician healthcare professionals, such as nurses and pharmacists pursuant to state law under a standing order issued by the state health officer) to administer or provide vaccination services in accordance with the applicable emergency response stakeholder's official COVID-19 vaccination and emergency response plan(s) and who is enrolled in the CDC COVID-19 Vaccination Program. If the vaccine is exported from the United States, a "vaccination provider" is a provider that is authorized to administer this vaccine in accordance with the laws of the country in which it is administered. For purposes of this letter, "healthcare provider" also refers to a person authorized by the U.S. Department of Health and Human Services (e.g., under the PREP Act Declaration for Medical Countermeasures against COVID-19) to administer FDA-authorized COVID-19 vaccine (e.g., qualified pharmacy technicians and State-authorized pharmacy interns acting under the supervision of a qualified pharmacist). See, e.g., HHS. *Fourth Amendment to the Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID-19 and Republication of the Declaration*. 85 FR 79190 (December 9, 2020).

used only to prevent COVID-19 in individuals 5 through 11 years of age with a two-dose primary regimen (3 weeks apart).

For use in individuals who are 11 years old at the time of the first dose, and turn 12 years old before the second dose:

- Notwithstanding the age limitations for use of the different formulations and presentations described above, individuals who will turn from 11 years to 12 years of age between their first and second dose in the primary regimen may receive, for either dose, either: (1) the Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer (each 0.2 mL dose containing 10 µg modRNA) covered by this authorization; or (2) the Pfizer-BioNTech COVID-19 Vaccine and COMIRNATY formulations provided in one of the presentations for individuals 12 years of age and older (each 0.3 mL dose containing 30 µg modRNA) covered by this authorization.
- The vaccine will be administered by vaccination providers and used only to prevent COVID-19 with a two-dose primary regimen (3 weeks apart).

This authorization also covers the use of the licensed COMIRNATY (COVID-19 Vaccine, mRNA) product when used to provide: (1) a two-dose primary regimen (0.3 mL each, 3 weeks apart) for individuals 12 through 15 years of age; (2) a third primary series dose at least 28 days following the second dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise; (3) a single booster dose (0.3 mL) at least 6 months after completion of the primary series to individuals 18 years of age and older; and (4) a single booster dose (0.3 mL) as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine in individuals 18 years of age and older, where the dosing interval for the heterologous booster dose is the same as that authorized for a booster dose of the vaccine used for primary vaccination.

The Pfizer-BioNTech COVID-19 Vaccine that uses PBS buffer and COMIRNATY (COVID-19 Vaccine, mRNA) have the same formulation. The products are legally distinct with certain differences that do not impact safety or effectiveness. Accordingly, under this EUA, the Pfizer-BioNTech COVID-19 Vaccine that uses PBS buffer and COMIRNATY (COVID-19 Vaccine, mRNA) can be used interchangeably as described above, without presenting any safety or effectiveness concerns.

As described below under *Product Description*, the Pfizer-BioNTech COVID-19 Vaccine formulations that use Tris and PBS buffers, which are covered by this authorization for use in individuals 12 years of age and older, contain the same modRNA and lipids, and the same quantity of these ingredients, per 0.3 mL dose. The two formulations differ with respect to certain inactive ingredients only and have been shown to be analytically comparable.[20]

[20] Analytical comparability assessments use laboratory testing to demonstrate that a change in product formulation does not impact a product's safety or effectiveness. For the Pfizer-BioNTech COVID-19 Vaccine, multiple different release parameters were evaluated to assess the comparability of the modified formulation (the formulation with the Tris buffer) to the originally-authorized formulation (the formulation with the PBS buffer). These release parameters ranged from product appearance to size of the lipid-nanoparticle to the integrity of the modRNA in the

Accordingly, under this EUA, for individuals 12 years of age and older, COMIRNATY (COVID-19 Vaccine, mRNA) and these two formulations of the Pfizer-BioNTech COVID-19 Vaccine, when prepared according to their respective instructions for use, can be used interchangeably without presenting any safety or effectiveness concerns.

Therefore, for individuals 12 years of age and older, COMIRNATY (COVID-19 Vaccine, mRNA) is authorized to complete the primary regimen or provide a booster dose for individuals who received their initial primary dose(s) with the Pfizer-BioNTech COVID-19 Vaccine (whether the PBS formulation or Tris formulation), and the Pfizer-BioNTech COVID-19 Vaccine (whether the PBS formulation or Tris formulation) is authorized to complete the primary regimen or provide a booster for individuals who received their initial primary dose(s) with COMIRNATY (COVID-19 Vaccine, mRNA).

Product Description[21]

The Pfizer-BioNTech COVID-19 Vaccine, supplied in two formulations, is provided in three different vials:

For use in individuals 12 years of age and older

- The Pfizer-BioNTech COVID-19 Vaccine that uses PBS buffer is available in multiple dose vials with purple caps. It is formulated to provide, after dilution, 0.3 mL doses (each containing 30 μg modRNA) and can be used for all authorized indications in individuals 12 years of age and older.
- The Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer, and is available in multiple dose vials with gray caps and labels with gray borders, is formulated to provide, after dilution, 0.3 mL doses (each containing 30 μg modRNA) and can be used for all authorized indications in individuals 12 years of age and older.

For use in individuals 5 through 11 years of age

- The Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer, and is available in multiple dose vials with orange caps and labels with orange borders, is formulated to provide, after dilution, 0.2 mL doses (each containing 10 μg modRNA) and can be used for administration to individuals 5 through 11 years of age.

For use in individuals 12 years of age and older

The Pfizer-BioNTech COVID-19 Vaccine that uses PBS buffer (supplied in multiple dose vials with purple caps) is supplied as a frozen suspension; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. The Pfizer-

product. Release and characterization tests include tests for purity, composition, and critical attributes of mRNA associated with the activity of the vaccine. The combination of release testing and characterization testing demonstrated that the modified formulation is analytically comparable to the original formulation.

[21] For COMIRNATY (COVID-19 Vaccine, mRNA) product description, please see the COMIRNATY (COVID-19 Vaccine, mRNA) prescribing information, found here: *https://www.fda.gov/media/151707/download.*

BioNTech COVID-19 Vaccine does not contain a preservative. Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine contains 30 µg of modRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2. Each dose of the Pfizer-BioNTech COVID-19 Vaccine also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylee glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection) contributes an additional 2.16 mg sodium chloride per dose.

The Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer and that is supplied in multiple dose vials with gray caps is supplied as a frozen suspension and should not be diluted. The Pfizer-BioNTech COVID-19 Vaccine does not contain a preservative. Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine contains 30 µg of a modRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2. Each dose of the Pfizer-BioNTech COVID-19 Vaccine also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.19 mg cholesterol), 0.06 mg tromethamine, 0.4 mg tromethamine hydrochloride, and 31 mg sucrose.

For use in individuals 5 through 11 years of age

The Pfizer-BioNTech COVID-19 Vaccine that uses Tris buffer and that is supplied in multiple dose vials with orange caps is supplied as a frozen suspension; each vial must be diluted with 1.3 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each dose of the Pfizer-BioNTech COVID-19 Vaccine contains 10 µg of a modRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2. Each dose of the Pfizer-BioNTech COVID-19 Vaccine also includes the following ingredients: lipids (0.14 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.02 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.03 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.06 mg cholesterol), 10.3 mg sucrose, 0.02 mg tromethamine, and 0.13 mg tromethamine hydrochloride. The diluent (0.9% Sodium Chloride Injection, USP) contributes 0.9 mg sodium chloride per dose.

The manufacture of the authorized Pfizer-BioNTech COVID-19 Vaccine is limited to those facilities identified and agreed upon in Pfizer's request for authorization.

The Pfizer-BioNTech COVID-19 Vaccine vial label and carton labels are clearly marked for "Emergency Use Authorization." The Pfizer-BioNTech COVID-19 Vaccine is authorized to be distributed, stored, further redistributed, and administered by emergency response stakeholders when packaged in the authorized manufacturer packaging (i.e., vials and cartons), despite the fact that the vial and carton labels may not contain information that otherwise would be required under the FD&C Act.

Pfizer-BioNTech COVID-19 Vaccine is authorized for emergency use with the following product-specific information required to be made available to vaccination providers and recipients, respectively (referred to as "authorized labeling"):

- Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers): Emergency Use Authorization (EUA) of Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) - For 12 Years of Age and Older Dilute Before Use
- Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers): Emergency Use Authorization (EUA) of Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) - For 12 Years of Age and Older Do Not Dilute
- Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers): Emergency Use Authorization (EUA) of Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) - For 5 Through 11 Years of Age Dilute Prior To Use
- Vaccine Information Fact Sheet for Recipients and Caregivers About COMIRNATY (COVID-19 Vaccine, mRNA) and Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease (COVID-19) For Use in Individuals 12 Years of Age and Older
- Vaccine Information Fact Sheet for Recipients and Caregivers About the Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease (COVID-19) for Use in Individuals 5 Through 11 Years of Age

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine,[22] when used to prevent COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh its known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19 when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that Pfizer-BioNTech COVID-19 Vaccine (as described in this Scope of Authorization (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of Pfizer-BioNTech COVID-19 Vaccine under this EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section III). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), Pfizer-BioNTech COVID-19 Vaccine is authorized to prevent COVID-19 as described in

[22] The conclusions supporting authorization stated in this section (Section II) also apply to COMIRNATY (COVID-19 Vaccine, mRNA).

the Scope of Authorization (Section II) under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:

Pfizer Inc. and Authorized Distributor(s)

A. Pfizer Inc. and authorized distributor(s) will ensure that the authorized Pfizer-BioNTech COVID-19 Vaccine is distributed, as directed by the U.S. government, including CDC and/or other designee, and the authorized labeling (i.e., Fact Sheets) will be made available to vaccination providers, recipients, and caregivers consistent with the terms of this letter.

B. Pfizer Inc. and authorized distributor(s) will ensure that appropriate storage and cold chain is maintained until delivered to emergency response stakeholders' receipt sites.

C. Pfizer Inc. will ensure that the terms of this EUA are made available to all relevant stakeholders (e.g., emergency response stakeholders, authorized distributors, and vaccination providers) involved in distributing or receiving authorized Pfizer-BioNTech COVID-19 Vaccine. Pfizer Inc. will provide to all relevant stakeholders a copy of this letter of authorization and communicate any subsequent amendments that might be made to this letter of authorization and its authorized labeling.

D. Pfizer Inc. may develop and disseminate instructional and educational materials (e.g., video regarding vaccine handling, storage/cold-chain management, preparation, disposal) that are consistent with the authorized emergency use of the vaccine as described in the letter of authorization and authorized labeling, without FDA's review and concurrence, when necessary to meet public health needs during an emergency. Any instructional and educational materials that are inconsistent with the authorized labeling are prohibited.

E. Pfizer Inc. may request changes to this authorization, including to the authorized Fact Sheets for the vaccine. Any request for changes to this EUA must be submitted to Office of Vaccines Research and Review (OVRR)/Center for Biologics Evaluation and Research (CBER). Such changes require appropriate authorization prior to implementation.[23]

[23] The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), or (7), review and concurrence is required from the Preparedness and Response Team (PREP)/Office of the Center Director (OD)/CBER and the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS).

F. Pfizer Inc. will report to Vaccine Adverse Event Reporting System (VAERS):
- Serious adverse events (irrespective of attribution to vaccination);
- Cases of Multisystem Inflammatory Syndrome in children and adults; and
- Cases of COVID-19 that result in hospitalization or death, that are reported to Pfizer Inc.

These reports should be submitted to VAERS as soon as possible but no later than 15 calendar days from initial receipt of the information by Pfizer Inc.

G. Pfizer Inc. must submit to Investigational New Drug application (IND) number 19736 periodic safety reports at monthly intervals in accordance with a due date agreed upon with the Office of Biostatistics and Epidemiology (OBE)/CBER beginning after the first full calendar month after authorization. Each periodic safety report is required to contain descriptive information which includes:
- A narrative summary and analysis of adverse events submitted during the reporting interval, including interval and cumulative counts by age groups, special populations (e.g., pregnant women), and adverse events of special interest;
- A narrative summary and analysis of vaccine administration errors, whether or not associated with an adverse event, that were identified since the last reporting interval;
- Newly identified safety concerns in the interval; and
- Actions taken since the last report because of adverse experiences (for example, changes made to Healthcare Providers Administering Vaccine (Vaccination Providers) Fact Sheet, changes made to studies or studies initiated).

H. No changes will be implemented to the description of the product, manufacturing process, facilities, or equipment without notification to and concurrence by FDA.

I. All manufacturing facilities will comply with Current Good Manufacturing Practice requirements.

J. Pfizer Inc. will submit to the EUA file Certificates of Analysis (CoA) for each drug product lot at least 48 hours prior to vaccine distribution. The CoA will include the established specifications and specific results for each quality control test performed on the final drug product lot.

K. Pfizer Inc. will submit to the EUA file quarterly manufacturing reports, starting in July 2021, that include a listing of all Drug Substance and Drug Product lots produced after issuance of this authorization. This report must include lot number, manufacturing site, date of manufacture, and lot disposition, including those lots that were quarantined for investigation or those lots that were rejected. Information on the reasons for lot quarantine or rejection must be included in the report.

L. Pfizer Inc. and authorized distributor(s) will maintain records regarding release of Pfizer-BioNTech COVID-19 Vaccine for distribution (i.e., lot numbers, quantity, release date).

M. Pfizer Inc. and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.

N. Pfizer Inc. will conduct post-authorization observational studies to evaluate the association between Pfizer-BioNTech COVID-19 Vaccine and a pre-specified list of adverse events of special interest, including myocarditis and pericarditis, along with deaths and hospitalizations, and severe COVID-19. The study population should include individuals administered the authorized Pfizer-BioNTech COVID-19 Vaccine under this EUA in the general U.S. population (5 years of age and older), individuals who receive a booster dose, populations of interest such as healthcare workers, pregnant women, immunocompromised individuals, subpopulations with specific comorbidities. The studies should be conducted in large scale databases with an active comparator. Pfizer Inc. will provide protocols and status update reports to the IND 19736 with agreed-upon study designs and milestone dates.

Emergency Response Stakeholders

O. Emergency response stakeholders will identify vaccination sites to receive authorized Pfizer-BioNTech COVID-19 Vaccine and ensure its distribution and administration, consistent with the terms of this letter and CDC's COVID-19 Vaccination Program.

P. Emergency response stakeholders will ensure that vaccination providers within their jurisdictions are aware of this letter of authorization, and the terms herein and any subsequent amendments that might be made to the letter of authorization, instruct them about the means through which they are to obtain and administer the vaccine under the EUA, and ensure that the authorized labeling [i.e., Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and Vaccine Information Fact Sheet for Recipients and Caregivers] is made available to vaccination providers through appropriate means (e.g., e-mail, website).

Q. Emergency response stakeholders receiving authorized Pfizer-BioNTech COVID-19 Vaccine will ensure that appropriate storage and cold chain is maintained.

Vaccination Providers

R. Vaccination providers will administer the vaccine in accordance with the authorization and will participate and comply with the terms and training required by CDC's COVID-19 Vaccination Program.

S. Vaccination providers will provide the Vaccine Information Fact Sheet for Recipients and Caregivers to each individual receiving vaccination and provide the necessary information for receiving their second dose and/or third dose.

T. Vaccination providers administering the vaccine must report the following information associated with the administration of the vaccine of which they become

aware to VAERS in accordance with the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers):

- Vaccine administration errors whether or not associated with an adverse event
- Serious adverse events (irrespective of attribution to vaccination)
- Cases of Multisystem Inflammatory Syndrome in children and adults
- Cases of COVID-19 that result in hospitalization or death

Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. The VAERS reports should include the words "Pfizer-BioNTech COVID-19 Vaccine EUA" in the description section of the report. More information is available at vaers.hhs.gov or by calling 1-800-822-7967. To the extent feasible, report to Pfizer Inc. by contacting 1-800-438-1985 or by providing a copy of the VAERS form to Pfizer Inc.; Fax: 1-866-635-8337.

U. Vaccination providers will conduct any follow-up requested by the U.S government, including CDC, FDA, or other designee, regarding adverse events to the extent feasible given the emergency circumstances.

V. Vaccination providers will monitor and comply with CDC and/or emergency response stakeholder vaccine management requirements (e.g., requirements concerning obtaining, tracking, and handling vaccine) and with requirements concerning reporting of vaccine administration data to CDC.

W. Vaccination providers will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to CDC, and FDA for inspection upon request.

Conditions Related to Printed Matter, Advertising, and Promotion

X. All descriptive printed matter, advertising, and promotional material, relating to the use of the Pfizer-BioNTech COVID-19 Vaccine shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in Section 502(a) and (n) of the FD&C Act and FDA implementing regulations.

Y. All descriptive printed matter, advertising, and promotional material relating to the use of the Pfizer-BioNTech COVID-19 Vaccine clearly and conspicuously shall state that:

- This product has not been approved or licensed by FDA, but has been authorized for emergency use by FDA, under an EUA to prevent Coronavirus Disease 2019 (COVID-19) for use either in individuals 12 years of age and older, or in individuals 5 through 11 years of age, as appropriate; and
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of the medical product under Section 564(b)(1) of the FD&C Act unless the declaration is terminated or authorization revoked sooner.

Condition Related to Export

Z. If the Pfizer-BioNTech COVID-19 Vaccine is exported from the United States, conditions C, D, and O through Y do not apply, but export is permitted only if 1) the regulatory authorities of the country in which the vaccine will be used are fully informed that this vaccine is subject to an EUA and is not approved or licensed by FDA and 2) the intended use of the vaccine will comply in all respects with the laws of the country in which the product will be used. The requirement in this letter that the authorized labeling (i.e., Fact Sheets) be made available to vaccination providers, recipients, and caregivers in condition A will not apply if the authorized labeling (i.e., Fact Sheets) are made available to the regulatory authorities of the country in which the vaccine will be used.

Conditions With Respect to Use of Licensed Product

AA. COMIRNATY (COVID-19 Vaccine, mRNA) is licensed for individuals 16 years of age and older. There remains, however, a significant amount of Pfizer-BioNTech COVID-19 Vaccine that was manufactured and labeled in accordance with this emergency use authorization. The authorization remains in place with respect to the Pfizer-BioNTech COVID-19 Vaccine for this population.

BB. This authorization also covers the use of the licensed COMIRNATY (COVID-19 Vaccine, mRNA) product when used to provide: (1) a two-dose primary regimen for individuals 12 through 15 years of age;[24] (2) a third primary series dose to individuals 12 years of age or older who have undergone solid organ transplantation or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise; (3) a single booster dose at least 6 months after completing the primary series to individuals 18 years of age or older; and (4) a heterologous booster dose in individuals 18 years of age and older who have completed primary vaccination with a different authorized COVID-19 vaccine as described in the Scope of Authorization (Section II) under this EUA. Conditions A through W in this letter apply when COMIRNATY (COVID-19 Vaccine, mRNA) is provided for the uses described in this subsection III.BB., except that product manufactured and labeled in accordance with the approved BLA is deemed to satisfy the manufacturing, labeling, and distribution requirements of this authorization.

IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

[24] As noted above, this includes the first dose of a two-dose primary regimen for individuals who are 11 years old and will turn 12 years of age between their first and second dose in the primary regimen.

Sincerely,

--/S/--

Jacqueline A. O'Shaughnessy, Ph.D.
Acting Chief Scientist
Food and Drug Administration

Enclosures

Marks Decl. Exhibit C

Summary Basis for Regulatory Action

Date:	11/8/2021
From:	Ramachandra Naik, PhD, Review Committee Chair, DVRPA/OVRR
BLA STN:	125742/0
Applicant:	BioNTech Manufacturing GmbH (in partnership with Pfizer, Inc.)
Submission Receipt Date:	May 18, 2021
PDUFA Action Due Date:	January 16, 2022
Proper Name:	COVID-19 Vaccine, mRNA
Proprietary Name:	COMIRNATY
Indication:	Active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older

Recommended Action: The Review Committee recommends approval of this product.

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Director, Office of Vaccines Research and Review

_____

Director, Office of Compliance and Biologics Quality

Discipline Reviews	Reviewer / Consultant - Office/Division
CMC • CMC Product (OVRR) • Facilities Review (OCBQ/DMPQ) • Facilities Inspection (OCBQ/DMPQ and OVRR/DVP) • Lot Release, QC, Test Methods, Product Quality (OCBQ/DBSQC)	Xiao Wang, PhD, OVRR/DVP Anissa Cheung, MSc, OVRR/DVP Kathleen Jones, PhD, OCBQ/DMPQ Laura Fontan, PhD, OCBQ/DMPQ Gregory Price, PhD, OCBQ/DMPQ CDR Donald Ertel, MS, OCBQ/DMPQ Nicole Li, MS, OCBQ/DMPQ Christian Lynch, OCBQ/DMPQ Alifiya Ghadiali, OCBQ/DMPQ Zhongren Wu, PhD, OCBQ/DMPQ Ekaterina Allen, PhD, OCBQ/DMPQ Hsiaoling Wang, PhD, OCBQ/DBSQC Emnet Yitbarek, PhD, OCBQ/DBSQC Karla Garcia, MS, OCBQ/DBSQC Anil Choudhary, PhD, MBA, OCBQ/DBSQC Esmeralda Alvarado Facundo, PhD, OCBQ/DBSQC Marie Anderson, PhD, OCBQ/DBSQC Cheryl Hulme, OCBQ/DMPQ
Clinical • Clinical (OVRR) • Postmarketing Safety, Epidemiological Review (OBE/DE) • Real World Evidence • Benefit-Risk Assessment • BIMO	Susan Wollersheim, MD, OVRR/DVRPA CAPT Ann T. Schwartz, MD, OVRR/DVRPA Lucia Lee, MD, OVRR/DVRPA Deborah Thompson, MD, MSPH, OBE/DE Yun Lu, PhD, OBE Hong Yang, PhD, OBE Osman Yogurtcu, PhD, OBE Patrick Funk, PhD, OBE Haecin Chun, MT (ASCP) SSB, MS, OCBQ/DIS
Statistical • Clinical Data (OBE/DB) • Nonclinical Data	Lei Huang, PhD, OBE/DB Ye Yang, PhD, OBE/DB Xinyu Tang, PhD, OBE/DB
Nonclinical/Pharmacology/Toxicology • Toxicology (OVRR) • Developmental Toxicology (OVRR)	Nabil Al-Humadi, PhD, OVRR/DVRPA
Labeling • Promotional (OCBQ/APLB) • Carton and Container Labels • Labeling Review	CAPT Oluchi Elekwachi, PharmD, MPH, OCBQ/APLB Daphne Stewart, OVRR/DVRPA Laura Gottschalk, PhD, OVRR/DVRPA
• Consults (CDISC, Datasets) • Documentation Review	Brenda Baldwin, PhD, OVRR/DVRPA CAPT Michael Smith, PhD, OVRR/DVRPA
Advisory Committee Summary	No Advisory Committee meeting held

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1. Introduction

BioNTech Manufacturing GmbH (in partnership with Pfizer Inc.) submitted a Biologics License Application (BLA) STN BL 125742 for licensure of COVID-19 Vaccine, mRNA. The proprietary name of the vaccine is COMIRNATY. COMIRNATY is a vaccine indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. The vaccine is administered intramuscularly (IM) as a series of two 30 µg doses (0.3 mL each) 3 weeks apart.

COMIRNATY (also referred to as BNT162b2 in this document) contains a nucleoside-modified messenger RNA (mRNA) encoding the viral spike glycoprotein (S) of SARS-CoV-2 that is formulated in lipids including ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 1,2-distearoyl-sn-glycero-3-phosphocholine, and cholesterol.

COMIRNATY is supplied as a concentrated multi-dose liquid formulation (0.45 mL volume) stored frozen at -90°C to -60°C in a 2 mL Type 1 glass vial. A sterile diluent, 0.9% Sodium Chloride Injection, USP, is supplied separately in 2 mL glass vials manufactured by Fresenius Kabi LLC and in 10 mL vials manufactured by Hospira, Inc. The diluent is stored at 20°C to 25°C and will be shipped in parallel with shipments of COMIRNATY, with arrivals synchronized so that the diluent is delivered before the vaccine is delivered. Healthcare providers may also use other sources of sterile 0.9% Sodium Chloride Injection, USP as a diluent for COMIRNATY, if necessary.

The COMIRNATY Multiple Dose Vial is thawed in a refrigerator (2°C to 8°C) for 2 to 3 hours or at room temperature (up to 25°C) for 30 minutes. The vial must be warmed to room temperature for dilution. Once at room temperature, the COMIRNATY Multiple Dose Vial is diluted with 1.8 mL of the diluent. After dilution, each vial of COMIRNATY contain six doses of 0.3 mL of vaccine. Each 0.3 mL dose of COMIRNATY contains 30 µg of mRNA encoding the spike glycoprotein of SARS-CoV-2 and the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 2.52 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. After dilution, the vials are stored at 2°C to 25°C and must be used within 6 hours from the time of dilution. COMIRNATY is preservative-free.

The expiry dating period for COMIRNATY Multiple Dose Vial is 9 months from the date of manufacture when stored at -90°C to -60°C. The date of manufacture shall be no later than the date of final sterile filtration of the formulated drug product (at Pharmacia & Upjohn Company LLC in Kalamazoo, Michigan, the date of manufacture is defined as the date of sterile filtration for the final drug product; at Pfizer-Manufacturing Belgium NV in Puurs, Belgium, it is defined as the date of the (b) (4) .

2. Background

SARS-CoV-2 is a novel, zoonotic coronavirus that emerged in late 2019 and was identified in patients with pneumonia of unknown cause. The virus was named SARS-CoV-2 because of its similarity to the coronavirus responsible for severe acute respiratory syndrome (SARS-CoV, a lineage B betacoronavirus). SARS-CoV-2 is an enveloped, positive-sense, single-stranded RNA virus sharing more than 70% of its sequence with SARS-CoV, and ~50% with the coronavirus responsible for Middle Eastern respiratory syndrome (MERS-CoV). SARS-CoV-2 is the causative agent of COVID-19, an infectious disease with respiratory and systemic manifestations. Disease symptoms vary, with many persons presenting with asymptomatic or mild disease and some progressing to severe respiratory tract disease including pneumonia and acute respiratory distress syndrome (ARDS), leading to multiorgan failure and death.

The SARS-CoV-2 pandemic continues to present a challenge to global health and, as of August 2021, has caused approximately 208 million cases of COVID-19, including 4.3 million deaths worldwide. In the United States (U.S.), more than 37 million cases have

been reported to the Centers for Disease Control and Prevention (CDC), of which 90% have occurred in individuals 16 years of age or older. While the pandemic has caused morbidity and mortality on an individual level, the continuing spread of SARS-CoV-2 and emerging variants has caused significant challenges and disruptions in worldwide healthcare systems, economies, and many aspects of human activity (travel, employment, education).

In the U.S., there are no licensed vaccines or anti-viral drugs for the prevention of COVID-19. In December 2020, the FDA issued emergency use authorizations (EUAs) for two mRNA vaccines which encode the SARS-CoV-2 spike glycoprotein: Pfizer-BioNTech COVID-19 Vaccine (manufactured by Pfizer, Inc. in partnership with BioNTech manufacturing GmbH) for use in individuals 16 years of age and older, and Moderna COVID-19 Vaccine (manufactured by ModernaTX, Inc.) for use in individuals 18 years of age and older. In February 2021, the FDA issued an EUA for a replication-incompetent adenovirus type 26 (Ad26)-vectored vaccine encoding a stabilized variant of the SARS-CoV-2 spike glycoprotein, manufactured by Janssen Biotech, Inc. (Janssen COVID-19 Vaccine) for use in individuals 18 years of age and older. In May 2021, the FDA expanded the emergency use authorization for the Pfizer-BioNTech COVID-19 Vaccine to include adolescents 12 through 15 years of age. On October 22, 2020, FDA approved remdesivir for use in adult and pediatric patients 12 years of age and older and weighing at least 40 kilograms (about 88 pounds) for the treatment of COVID-19 requiring hospitalization. Several other therapies are currently available under emergency use.

Table 1. Regulatory History

Regulatory Events / Milestones	Date
1. Pre-IND meeting (Written Responses)	April 6, 2020 (Part 1) April 10, 2020 (Part 2)
2. IND submission	April 22, 2020
3. Fast Track designation granted	July 7, 2020
4. Submission of EUA request for individuals ≥16 years of age	November 20, 2020
5. Issuance of EUA for individuals ≥16 years	December 11, 2020
6. Submission of EUA request for individuals 12-15 years of age	April 9, 2021
7. Issuance of EUA for individuals 12-15 years of age	May 10, 2021
8. Pre-BLA meeting (Written Responses)	Clinical: March 9, 2021 CMC: March 31, 2021
9. BLA STN 125742/0 received	May 18, 2021
10. BLA filed	July 15, 2021
11. Mid-Cycle communication	The Applicant canceled
12. Late-Cycle meeting	The Applicant canceled
13. Action Due Date	January 16, 2022

3. Chemistry, Manufacturing and Controls (CMC)

a. Product Quality

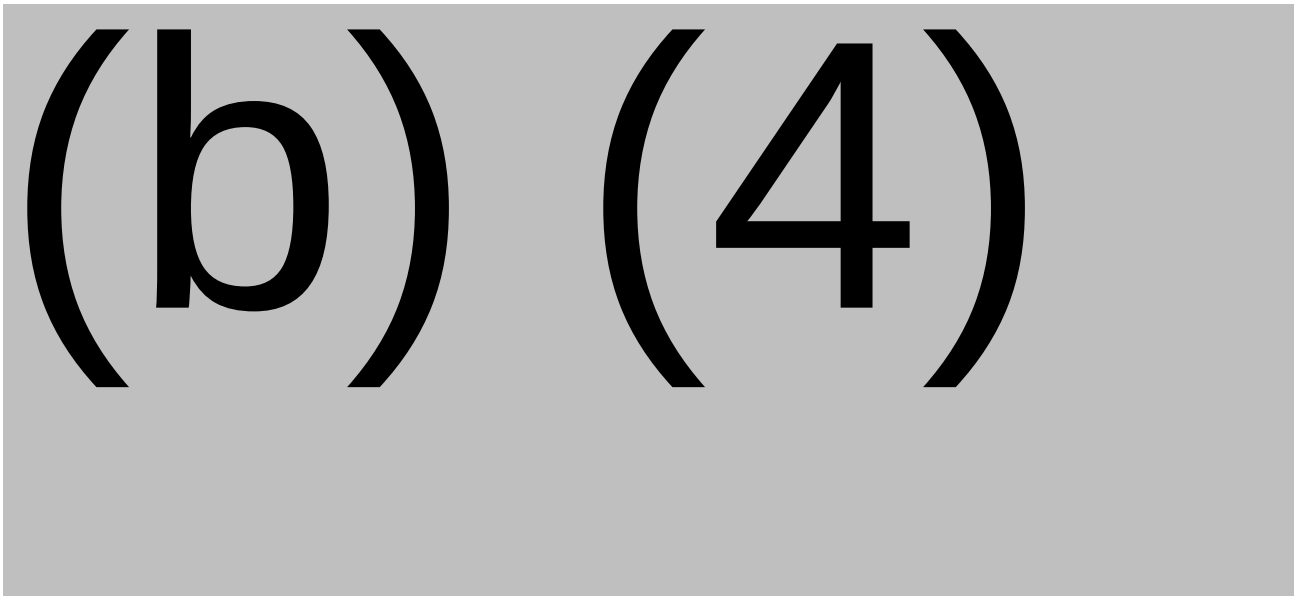
COMIRNATY Manufacturing Overview

COMIRNATY contains a nucleoside-modified messenger RNA (mRNA) encoding the viral spike glycoprotein (S) of SARS-CoV-2 that is formulated in lipids including ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2- hexyldecanoate), 2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide, 1,2-distearoyl-sn-glycero-3-phosphocholine, and cholesterol. COMIRNATY is supplied as a frozen suspension to be diluted with a diluent, 0.9% Sodium Chloride Injection, USP, that is supplied separately or can be acquired elsewhere, if necessary. Manufacture of the mRNA drug substance will take place in Andover, MA, USA. The final formulated drug product will be manufactured, filled, finished, labeled and packaged in Puurs, Belgium or in Kalamazoo, MI, USA. The 0.9% Sodium Chloride Injection, USP diluent will be manufactured by Fresenius-Kabi USA, LLC ((b) (4)) and Hospira, Inc. ((b) (4)).

The mRNA in COMIRNATY is a single-stranded, 5'-capped mRNA encoding the full-length SARS-CoV-2 spike glycoprotein derived from the Wuhan-Hu-1 isolate (GenBank MN908947.3 and GenBank QHD43416.1). The antigen-coding RNA sequence is codon-optimized and contains two proline mutations ((b) (4) 87P), which ensures an antigenically optimal trimerized pre-fusion confirmation (S-2P). The RNA also contains common structural elements, including 5'-cap, 5'-UTR, 3'-UTR, and poly(A) tail, all of which are designed for mediating high RNA stability and translation efficiency. During RNA transcription, (b) (4) is replaced with the (b) (4) . This nucleoside substitution has been demonstrated to enhance translation of *in vitro* transcribed mRNA while reducing its reactogenicity.

Drug Substance (DS)

The manufacture of mRNA DS is divided into (b) (4) major manufacturing process stages:



Drug Product (DP)

The manufacturing process of the DP is divided into the following critical steps:

- **Preparation of the DS:** (b) (4)
- **Formation of LNP:** In this step, (b) (4)
- **Formulation of the bulk DP:** The bulk DP is formulated by (b) (4)
- **Filling:** The bulk DP is sterile filtered and aseptically filled into 2 mL Type I borosilicate glass vials manufactured by (b) (4) .
- **Labeling and storage:** The filled vials are visually inspected, labeled, and frozen at -90°C to -60°C.

Composition

The composition of the formulation of COMIRNATY and the function of the ingredients are provided in Table 2.

Table 2. Composition of COMIRNATY Multiple Dose Vial

Ingredients	Amount per vial	Function
SARS-CoV-2 spike glycoprotein mRNA (UNII: 5085ZFP6SJ)	225 µg	Active Ingredient
ALC-0315 [4-hydroxybutyl)azanediyl)bis (hexane-6,1-diyl)bis(2-hexyldecanoate) (UNII: AVX8DX713V)	3.23 mg	Lipid component
ALC-0159 [2-(polyethylene glycol 2000)-N,N-ditetradecylacetamide] (UNII: PJH39UMU6H)	0.4 mg	Lipid component
DSPC [1,2-distearoyl-sn-glycero-3-phosphocholine] (UNII: 043IPI2M0K)	0.7 mg	Lipid component
Cholesterol (UNII: 97C5T2UQ7J)	1.4 mg	Lipid component
Potassium chloride (UNII: 660YQ98I10)	0.07 mg	Excipient
Monobasic potassium phosphate (UNII: 4J9FJ0HL51)	0.07 mg	Excipient
Sodium Chloride	2.7 mg	Excipient

Ingredients	Amount per vial	Function
(UNII: 451W47IQ8X)		
Dibasic sodium phosphate dihydrate (UNII: GR686LBA74)	0.49 mg	Excipient
Sucrose (UNII: C151H8M554)	46.0 mg	Excipient
Water for Injection (UNII: 059QF0KO0R)	q.s.	Excipient

UNII: Unique Ingredient Identifier
q.s. = quantum satis (as much as may suffice)

Stability of COMIRNATY in Multiple Dose Vial

For the long-term storage condition study, parameters monitored are Appearance, (b) (4) by (b) (4), LNP (b) (4), RNA content and (b) (4) Assay, Lipid (ALC-0315, ALC-0159, DSPC, and Cholesterol) Content by (b) (4), Container closure integrity test by (b) (4), Endotoxin content by (b) (4), and Sterility.

The stability data provided in the submission support a dating period of 9 months from the date of manufacture when stored at -90°C to -60°C for the COMIRNATY DP filled in 2 mL Type I borosilicate glass vials. Stability data on emergency use and process performance qualification lots also support storage at -20°C ± 5°C for up to 2 weeks as well as short term storage at 5°C ± 3°C for up to one month (within the 9-month expiry dating period).

The Diluent for COMIRNATY

The contents of the vaccine vial are diluted with sterile 0.9% Sodium Chloride Injection, USP. Vials of sterile 0.9% Sodium Chloride Injection, USP are provided but shipped separately. The provided diluent or another sterile 0.9% Sodium Chloride Injection, USP should be used as the diluent.

The provided 0.9% Sodium Chloride Injection, USP diluent will be supplied either as cartons of 10 mL single-use vials manufactured by Hospira, Inc (NDC 0409-4888-10), or 2 mL single-use vials manufactured by Fresenius Kabi USA, LLC (NDC 63323-186-02). The composition of the saline diluent and the function of the ingredients are provided in Table 3.

Table 3. Composition of the Diluent

Ingredients	Quantity (per 0.3 mL dose)	Function
SODIUM CHLORIDE (UNII: 451W47IQ8X)	2.16 mg	Excipient
Water for Injection (UNII: 059QF0KO0R)	0.3 mL	Excipient

UNII: Unique Ingredient Identifier

COMIRNATY

Product Composition

COMIRNATY Multiple Dose Vial is supplied as a frozen suspension that is diluted at the time of use with 1.8 mL of saline diluent. A single dose of COMIRNATY contains 30 ug mRNA in a volume of 0.3 mL, and it does not contain preservative. [*See section 10.b regarding exception to the 21 CFR 610.15(a) requirement for a preservative.*]

Stability of COMIRNATY

The Applicant conducted in-use stability studies to support the maximum temperature and time period that COMIRNATY can retain its physicochemical properties. Based on the data generated, COMIRNATY retains its quality attributes for up to 6 hours when stored between 2°C to 25°C (35°F to 77°F).

The carton labels and the Package Insert (PI) state that after dilution, vials should be stored between 2°C to 25°C (35°F to 77°F) and used within 6 hours from the time of dilution. During storage, exposure to room light should be minimized, and direct exposure to sunlight and ultraviolet light should be avoided. Any vaccine remaining in vials must be discarded after 6 hours and cannot be refrozen.

Assays used in clinical studies

Diagnostic Assays Used to Support Clinical Efficacy Endpoints

Two clinical diagnostic assays (Cepheid Xpert Xpress RT-PCR assay for the detection of SARS-CoV-2 in clinical specimens and Roche Elecsys Anti-SARS-CoV-2 assay for the evaluation of serostatus to SARS-CoV-2) were used to assess clinical endpoints. Both assays have received FDA authorization under EUA.

The Cepheid Xpert Xpress RT-PCR assay is a rapid, automated *in vitro* diagnostic test for the qualitative detection of the N and E gene sequences from nasopharyngeal, nasal, or mid-turbinate swab and/or nasal wash/aspirate specimens collected from patients suspected of having COVID-19. This assay is used to assess viral infection of the participants before vaccination and to confirm COVID-19 cases during study follow-up.

The Roche Elecsys Anti-SARS-CoV-2 assay is a rapid, automated *in vitro* diagnostic test for detecting the presence of antibodies to nucleocapsid (N) protein of SARS-CoV-2 (antigen not present in COMIRNATY) in serum or plasma samples. This is a qualitative assay marketed as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, which would indicate a recent or prior infection. This assay is used to assess serostatus of the participants before vaccination.

Data were submitted to support the suitability of both the Cepheid Xpert Xpress assay and the Roche Elecsys Anti-SARS-CoV-2 assay for their intended uses in Phase 2/3 clinical studies when performed at Pfizer's testing facility (Pfizer Vaccine Research and Development; Pearl River, NY).

Immunogenicity Assays Used for Exploratory Immunogenicity Endpoints

Two immunogenicity assays (SARS-CoV-2 mNeonGreen (mNG) virus microneutralization assay and (b) (4) direct Luminex assay (dLIA) for IgG

quantification) were used for evaluating the immune responses from clinical trial samples.

The SARS-CoV-2 mNG microneutralization assay measures neutralizing antibodies (50% inhibition titers) against SARS-CoV-2 using Vero cell monolayers in a 96-well plate format. The SARS-CoV-2 mNG virus is derived from the USA_WA1/2020 strain that had been rescued by reverse genetics and engineered to express a fluorescent reporter gene (mNeonGreen) upon productive infection of cells. The validation protocol (that includes evaluation of dilutional linearity, precision, limits of quantification, and limit of detection) and the results of the validation study, executed at Pfizer Hackensack Meridian Health Center (Nutley, New Jersey), were submitted to support the suitability of the assay for testing of clinical trial immunogenicity samples.

The (b) (4) S1 IgG dLIA measures IgG antibody levels to the subunit 1 (S1) of the SARS-CoV-2 spike protein in human serum samples. Qualification data provided in the submission support the (b) (4) dLIA for quantification of human IgG antibodies that bind to the S1 protein of SARS-CoV-2 and confirm that the assay is suitable for its intended use.

b. Testing Specifications

Specifications and Methods

The tests and specifications applied for routine release of COMIRNATY are shown in Table 4.

Table 4. Control of COMIRNATY: Tests and Specifications

Quality Attribute	Analytical Procedure	Acceptance Criteria
Appearance	Appearance (Visual)	White to off-white suspension
Appearance (Visible Particulates)	Appearance (Particles) (b) (4)	May contain white to off-white opaque, amorphous particles
(b) (4)	(b) (4)	(b) (4)
(b) (4)	(b) (4)	(b) (4)
(b) (4)	(b) (4)	(b) (4)
LNP (b) (4)	(b) (4)	(b) (4)
LNP (b) (4)	(b) (4)	(b) (4)
RNA (b) (4)	(b) (4) assay	(b) (4)
RNA content	(b) (4) assay	(b) (4)
ALC-0315 content	(b) (4)	(b) (4)
ALC-0159 content	(b) (4)	(b) (4)
DSPC content	(b) (4)	(b) (4)
Cholesterol content	(b) (4)	(b) (4)
Vial content (volume)	Container content	Not less than (b) (4)
Lipid identities	(b) (4)	(b) (4) (ALC-0315, ALC-0159, Cholesterol, DSPC)

Quality Attribute	Analytical Procedure	Acceptance Criteria
Identity of encoded RNA	(b) (4)	Identity confirmed
(b) (4)	(b) (4)	(b) (4)
RNA (b) (4)	(b) (4)	(b) (4)
Bacterial Endotoxin	Endotoxin ((b) (4)) (b) (4)	(b) (4)
Sterility	Sterility ((b) (4))	No Growth Detected
Container Closure Integrity	(b) (4)	Pass

Abbreviations: LNP = Lipid nanoparticles; (b) (4)

The analytical methods and their validations and/or qualifications for the COMIRNATY DS and DP were found to be adequate for their intended use.

c. CBER Lot Release

The lot release protocol template was submitted to CBER for review and found to be acceptable after revisions. A lot release testing plan was developed by CBER and will be used for routine lot release.

d. Facilities Review / Inspection

Facility information and data provided in the BLA were reviewed by CBER and found to be sufficient and acceptable. The facilities involved in the manufacture of COMIRNATY are listed in Table 5 below. The activities performed and inspectional histories are also noted in Table 5 and are further described in the paragraphs that follow.

Table 5. Facilities involved in the manufacture of COMIRNATY

Name/address	FEI Number	DUNS number	Inspection/ waiver	Results/ Justification
Pfizer Inc. 875 Chesterfield Parkway West Chesterfield, MO 63017 (b) (4) Manufacture *Drug Substance* Release and stability testing *Drug Product* Release and stability testing	1940118	004954111	Waiver	ORA Surveillance August 19-20, 2019 NAI
Wyeth BioPharma Division of Wyeth Pharmaceuticals LLC 1 Burtt Road Andover, MA 01810 *Drug Substance* Manufacture, release and stability testing *Drug Product* Release and stability testing	1222181	174350868	Pre-License Inspection	CBER Pre-license inspection July 19-23, 2021 VAI
Pharmacia & Upjohn Company LLC 7000 Portage Road Kalamazoo, MI 49001 *Drug Product* LNP production, bulk drug product formulation, fill and finish, primary packaging, secondary packaging, release and stability testing	1810189	618054084	Waiver	ORA/OBPO Surveillance May 11-20, 2021 VAI
Pfizer Manufacturing Belgium NV Rijksweg 12 Puurs, 2870 Belgium *Drug Product* LNP production, bulk drug product formulation, fill and finish, primary packaging, secondary packaging, release and stability testing	1000654629	370156507	Pre-license inspection	CBER Pre-license inspection June 24-July 2, 2021 NAI

Name/address	FEI Number	DUNS number	Inspection/ waiver	Results/ Justification
Pfizer Ireland Pharmaceuticals Grange Castle Business Park Clondalkin, Dublin 22 Ireland *Drug Product* Release and stability testing	3004145594	985586408	Waiver	ORA Surveillance November 4-12, 2019 VAI
(b) (4) *Drug Product* Release testing (sterility)	(b) (4)	(b) (4)	Waiver	CDER Pre-approval inspection (b) (4) VAI
(b) (4) *Drug Product* Release testing (sterility)	(b) (4)	(b) (4)	Waiver	ORA Surveillance (b) (4) VAI

ORA conducted a surveillance inspection of Pfizer Inc., Chesterfield, MO, from August 19 – 20, 2019. No Form FDA 483 was issued, and the inspection was classified as No Action Indicated (NAI).

CBER conducted a pre-license inspection (PLI) of Wyeth BioPharma Division of Wyeth Pharmaceuticals LLC from July 19 – 23, 2021. All inspectional issues were resolved, and the inspection was classified as Voluntary Action Indicated (VAI).

ORA conducted a surveillance inspection of Pharmacia & Upjohn Company LLC from May 11 – 20, 2021. All inspectional issues were resolved, and the inspection was classified as VAI.

CBER conducted a PLI of Pfizer Manufacturing Belgium NV from June 24 - July 2, 2021. No Form FDA 483 was issued, and the inspection was classified as NAI.

ORA conducted a surveillance inspection of Pfizer Ireland Pharmaceuticals from November 4 – 12, 2019. All inspectional issues were resolved, and the inspection was classified as VAI.

CDER conducted a pre-approval inspection of (b) (4) from (b) (4). All inspectional issues were resolved, and the inspection was classified as VAI.

ORA conducted a surveillance inspection of (b) (4) from (b) (4). All inspectional issues were resolved, and the inspection was classified as VAI.

e. Container/Closure System

The COMIRNATY drug product is filled and stored at -90°C to -60°C in a 2 mL glass vial sealed with a bromobutyl rubber stopper and an aluminum seal with flip-off plastic cap. The glass vials are supplied by (b) (4) The stopper and caps are supplied by (b) (4), respectively.

Pfizer performed container closure integrity testing (CCIT) on the filled 2 mL glass vials using a (b) (4) test method. All acceptance criteria were met.

f. Environmental Assessment

The BLA included a request for categorical exclusion from an Environmental Assessment under 21 CFR 25.31. The FDA concluded that this request is justified, and no extraordinary circumstances exist that would require an environmental assessment.

4. Nonclinical Pharmacology/Toxicology

Nonclinical Toxicology

For the nonclinical safety evaluation, COMIRNATY was evaluated in two repeat dose toxicity studies in Wistar Han rats and a Combined Fertility and Developmental Study (Including Teratogenicity and Postnatal Investigations) in Wistar Han rats.

The repeat dose toxicity evaluations were conducted on COMIRNATY and a similar vaccine termed BNT162b2 (V8). COMIRNATY and BNT162b2 (V8) have identical amino acid sequences of the encoded antigens but COMIRNATY includes the presence of optimized codons to improve antigen expression. The IM route of exposure was selected as it is the route of clinical administration. Generation of an immune response to COMIRNATY was confirmed in rats in both repeat-dose toxicity studies. In both repeat-dose toxicity studies, administration of COMIRNATY by IM injection to male and female rats once every week for a total of 3 doses was tolerated without evidence of systemic toxicity. Edema and erythema at the injection sites, transient elevation in body temperature, elevations in white blood cells and acute phase reactants and decreased albumin:globulin ratios were observed. Injection site reactions were common in all vaccine-administered animals and were greater after boost immunizations.

For the Combined Fertility and Developmental Study, COMIRNATY was administered to female rats twice before the start of mating and twice during gestation at the human clinical dose (30 µg RNA/dosing day). There were some effects (change in body weight and food consumption and effects localized to the injection site) observed in rats in these studies following administration of COMIRNATY that were not considered adverse and a relationship to COMIRNATY was not established. There were no effects on mating performance, fertility, or any ovarian or uterine parameters nor on embryo-fetal or postnatal survival, growth, or development in the offspring. An immune response was observed in female rats following administration of each vaccine candidate and these responses were also detectable in the offspring (fetuses and pups).

Nonclinical Pharmacology and Pharmacokinetics

COMIRNATY was evaluated in nonclinical pharmacology studies using animal models of mice, rats and nonhuman primates (NHP). The data from these studies indicate: (1) strong antigen-binding IgG and high titer neutralizing antibodies in mice, rat and rhesus macaques; (2) Th1-biased CD4+ T-cell response and IFNγ+, CD8+ T-cell response to BNT162b2 in both mouse and NHP studies; and (3) protection of rhesus macaques from an infectious SARS-CoV-2 challenge, with reduced detection of viral RNA in the BNT162b2-immunized animals as compared with the control-immunized macaques.

Nonclinical pharmacokinetics (PK) evaluation included (1) biodistribution of COMIRNATY using (b) (4) expressing RNA as a surrogate reporter in (b) (4) mice and in rats, and (2) the biodistribution and metabolism of the two novel lipids (ALC-0315 and ALC-0159) contained in COMIRNATY in *in vitro* studies and in a PK study in rats following administration of (b) (4) expressing RNA encapsulated in LNPs made with radiolabeled lipid markers. The study results indicate that following IM injection, the RNA encapsulated in LNP mainly localizes to the site of injection and, to a lesser extent, distributes to the liver. The metabolism of ALC-0315 and ALC-0159 was evaluated *in vitro* using blood, liver microsomes, S9 fractions, and hepatocytes from mice, rats, monkeys and humans and in *vivo* by examining the plasma, urine, feces, and liver samples from the PK study in rats. Approximately 50% of ALC-0159 is excreted unchanged in feces, while metabolism appears to play a role in the elimination of ALC-0315.

5. Clinical Pharmacology

Pharmacodynamic data, comprised of humoral immune responses to COMIRNATY, were obtained in the clinical studies. The data demonstrated that COMIRNATY induces a humoral immune response against the SARS-CoV-2 spike protein. The exact immunologic mechanism that confers protection against SARS-CoV-2 is unknown.

6. Clinical/Statistical

a. Clinical Program

Overview

The Applicant included data from two clinical studies in the BLA. The clinical studies which will be discussed in this SBRA are shown in Table 6.

Table 6. Overview of Clinical Studies

Study ID	**C4591001**	**BNT162-01**
NCT ID	04368728	04380701
Phase	1/2/3	1/2
Countries	Argentina, Brazil, Germany, South Africa, Turkey, U.S.	Germany
Enrollment	Phase 1: 30 participants Phase 2/3: 43,847 participants	24
Age	16 - 85 YOA	18 - 85 YOA
Purpose	Evaluate VE for prevention of COVID-19 (pivotal clinical endpoint study)	Evaluate safety and immunogenicity

Study ID	C4591001	BNT162-01
Control	Saline Placebo	None
Groups	Phase 2/3: 2 groups, randomized 1:1 to receive COMIRNATY or Placebo IM	1 group, randomized received COMIRNATY IM
Schedule	D0, D21	D0, D21
Total follow-up	6 Months (follow-up ongoing)	6 Months (follow-up ongoing)

YOA: years of age; VE: vaccine efficacy; IM: intramuscular; D: day

Study C4591001

Study C4591001 is an ongoing, randomized, placebo-controlled, observer-blind Phase 1/2/3 study being conducted in the U.S., Argentina, Brazil, Germany, South Africa and Turkey. Initially the study was designed as a Phase 1/2 study in healthy adults in the U.S. for vaccine candidate and dosage selection, as well as evaluation of immunogenicity and preliminary efficacy. The protocol was expanded to include a Phase 2/3 portion of the study to evaluate clinical disease efficacy endpoint in individuals 12 years of age and older in the U.S. and additional sites outside of the U.S.

The Phase 1 portion of the study was designed to identify a preferred vaccine candidate, vaccine dose, and administration schedule for further development based on the vaccine's safety, tolerability, and immunogenicity. To this end, two age groups were evaluated in separate cohorts, younger adults 18 through 55 years of age (N=45) and older adults 65 through 85 years of age (N=45). The study population included healthy men and women and excluded participants at high risk of SARS-CoV-2 infection or with serological evidence of prior or current SARS-CoV-2 infection. Two different vaccine candidates were evaluated, and younger participants received increasing dose levels (10, 20 and 30 µg) with progression to higher dose levels in a stepwise manner. Evaluation of increasing doses in the older age group (65 through 85 years) was based on recommendations from an internal review committee that reviewed safety and immunogenicity data derived from adults 18 through 55 years of age. For each vaccine candidate and dose, participants were randomized 4:1, such that 12 participants received the vaccine candidate and 3 participants received placebo. Review of the safety and immunogenicity from the Phase 1 portion of Study C4591001, in combination with data from Study BNT162-01, supported the final vaccine candidate, dose and dosing regimen (BNT162b2 administered at 30 µg, given 3 weeks apart) to proceed to the Phase 2/3 portion of Study C4591001.

In Phase 2/3, participants were enrolled with stratification by age (younger adults: 18 through 55 years of age; older adults: over 55 years of age) with the goal for the older age strata to consist of 40% of the entire study population. Adolescents were added to the protocol, based on review of safety data in younger adults enrolled in the ongoing study; thus, the age strata were revised as follows: 16 through 55 years of age, and 56 years of age and older. The study population for Phase 2/3 includes participants at higher risk for acquiring COVID-19 and at higher risk of severe COVID-19, such as participants working in the healthcare field, participants with autoimmune disease, and participants with chronic but stable medical conditions such as hypertension, asthma, diabetes, and infection with HIV, hepatitis B or hepatitis C. Participants were randomized 1:1 to receive 2 doses of either COMIRNATY or placebo, 3 weeks apart. The Phase 2 portion of the study evaluated reactogenicity and immunogenicity of the vaccine in 360

participants in the early stage of Phase 2/3, and these participants also contribute to the overall efficacy and safety data in the Phase 3 portion.

The ongoing Phase 3 portion of the study is evaluating the safety and efficacy of COMIRNATY for the prevention of COVID-19 occurring at least 7 days after the second dose of vaccine. Efficacy is being assessed throughout a participant's blinded follow-up in the study through surveillance for potential cases of COVID-19. If, at any time, a participant develops acute respiratory illness, an illness visit occurs. Assessments for illness visits include a nasal (mid-turbinate) swab, which is tested at a central laboratory using a reverse transcription-polymerase chain reaction (RT-PCR) test (i.e., Cepheid; FDA- authorized under EUA), or other sufficiently validated nucleic acid amplification-based test (NAAT), to detect SARS-CoV-2. The central laboratory NAAT result is used for the case definition, unless it was not possible to test the sample at the central laboratory. In that case, the following NAAT results are acceptable: Cepheid Xpert Xpress SARS-CoV-2, Roche cobas SARS-CoV-2 real-time RT-PCR test (EUA200009/A001), and Abbott Molecular/RealTime SARS-CoV-2 assay (EUA200023/A001).

The study design included a planned interim analysis of the first primary efficacy endpoint (the efficacy of BNT162b2 against confirmed COVID-19 occurring from 7 days after Dose 2 in participants without evidence of SARS-CoV-2 infection before vaccination) at pre-specified numbers of COVID-19 cases (at least 62, 92, and 120 cases). All primary and secondary efficacy endpoints were analyzed in the final efficacy analysis after at least 164 COVID-19 cases were accrued. Participants are expected to participate for a maximum of approximately 26 months.

Per protocol, since December 14, 2020, following issuance of the emergency use authorization for the Pfizer-BioNTech COVID-19 Vaccine, study participants 16 years of age and older have been progressively unblinded to their treatment assignment (when eligible per local recommendations) and offered BNT162b2 vaccination if they were randomized to placebo.

The study was unblinded in stages as all ongoing participants were either individually unblinded (when eligible per local recommendations) or the subject had concluded their 6-month post–Dose 2 study visit. Participants 16 years of age and older who participated in the Phase 2/3 study were given the opportunity to receive COMIRNATY no later than the 6-month timepoint after the second study vaccination. Participants who originally received placebo but received COMIRNATY were moved to a new visit schedule to receive both doses of COMIRNATY, 3 weeks apart.

The primary safety and efficacy endpoints were:

1. Primary safety endpoint (descriptive): Solicited local adverse reactions (injection site pain, redness, swelling), solicited systemic adverse events (AE) (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain), unsolicited AEs, serious adverse events (SAEs).

2. First primary efficacy endpoint: COVID-19 incidence per 1000 person-years of follow-up based on laboratory-confirmed NAAT in participants with no serological or virological evidence (up to 7 days after Dose 2) of past SARS-CoV-2 infection.

3. Second primary efficacy endpoint: COVID-19 incidence per 1000 person-years of follow-up based on laboratory-confirmed NAAT in participants with and without serological or virological evidence (up to 7 days after Dose 2) of past SARS-CoV-2 infection.

The pertinent secondary endpoint was:

1. Severe COVID-19 incidence per 1000 person-years of follow-up.

Study C4591001 results

The population in the protocol-specified, event-driven final primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020 and followed for the development of COVID-19 through November 14, 2020. For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0% (95% credible interval: 90.0, 97.9), which met the pre-specified success criterion. The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group. This protocol-specified, event-driven final primary efficacy analysis was the basis for issuance of the emergency use authorization for the Pfizer-BioNTech COVID-19 Vaccine on December 11, 2020.

Therefore, the primary study objective of VE against COVID-19 was met as the point estimate was above 50% and the lower bound of the 95% CI of the point estimate of VE was above 30%.

The population for the updated vaccine efficacy analysis per protocol included participants 16 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 during blinded placebo-controlled follow-up through March 13, 2021, representing up to ~6 months of follow-up after Dose 2. Overall, 60.8% of participants in the COMIRNATY group and 58.7% of participants in the placebo group had ≥4 months of follow-up time after Dose 2 in the blinded placebo-controlled follow-up period. The overall VE against COVID-19 in participants without evidence of prior SARS-CoV-2 infection was 91.1% (95% CI: 88.8 to 93.1). The overall VE against COVID-19 in participants with or without evidence of prior SARS-CoV-2 infection was 90.9% (95% CI: 88.5 to 92.8).

Subgroup analyses of vaccine efficacy (although limited by small numbers of cases in some subgroups) did not suggest meaningful differences in efficacy across genders, ethnic groups, geographies, or for participants with obesity or medical comorbidities associated with high risk of severe COVID-19.

The updated vaccine efficacy information is presented in Tables 7a and 7b.

Table 7a: First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection - Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period *

Subgroup	COMIRNATY N[a]=19,993 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=20,118 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
All participants	77 6.092 (19,711)	833 5.857 (19,741)	91.1 (88.8, 93.1)
16 through 64 years	70 4.859 (15,519)	709 4.654 (15,515)	90.5 (87.9, 92.7)
65 years and older	7 1.233 (4192)	124 1.202 (4226)	94.5 (88.3, 97.8)

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Table 7b: First COVID-19 occurrence from 7 days after Dose 2 in participants with or without* evidence of prior SARS-CoV-2 infection - Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up Period *

Subgroup	COMIRNATY N[a]=21,047 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21,210 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
All participants	81 6.340 (20,533)	854 6.110 (20,595)	90.9 (88.5, 92.8)
16 through 64 years	74 5.073 (16,218)	726 4.879 (16,269)	90.2 (87.5, 92.4)
65 years and older	7 1.267 (4315)	128 1.232 (4326)	94.7 (88.7, 97.9)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = Number of participants in the specified group.
b. n1 = Number of participants meeting the endpoint definition.
c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint.
e. Two-sided confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Efficacy Against Severe COVID-19

Vaccine efficacy against severe COVID-19 for participants with or without prior SARS-CoV-2 infection is shown in Tables 8a and 8b. The VE against severe COVID-19 in participants with or without evidence of prior SARS-CoV-2 infection was 95.3% (95% CI: 71.0 to 99.9) using the protocol definition of severe COVID-19 and 100.0% (95% CI: 87.6 to 100.0) based on the CDC definition of severe COVID-19.

Table 8a: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Protocol† Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	Placebo Cases n1[a] Surveillance Time[b] (n2[c])	Vaccine Efficacy % (95% CI[d])
7 days after Dose 2[d]	1 6.353 (20,540)	21 6.237 (20,629)	95.3 (70.9, 99.9)

Table 8b: Vaccine Efficacy – First Severe COVID-19 Occurrence in Participants 16 Years of Age and Older With or Without* Prior SARS-CoV-2 Infection Based on Centers for Disease Control and Prevention (CDC)‡ Definition From 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population During the Placebo-Controlled Follow-up

	COMIRNATY Cases n1[a] Surveillance Time[b] (n2[c])	Placebo Cases n1[a] Surveillance Time[b] (n2[c])	Vaccine Efficacy % (95% CI[d])
7 days after Dose 2[d]	0 6.345 (20,513)	31 6.225 (20,593)	100 (87.6, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Severe illness from COVID-19 is defined in the protocol as confirmed COVID-19 and presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, saturation of oxygen ≤93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen <300 mm Hg);
- Respiratory failure [defined as needing highflow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)];
- Evidence of shock (systolic blood pressure <90 mm Hg, diastolic blood pressure <60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an Intensive Care Unit;
- Death.

‡ Severe illness from COVID-19 as defined by CDC is confirmed COVID-19 and presence of at least 1 of the following:

- Hospitalization;
- Admission to the Intensive Care Unit;
- Intubation or mechanical ventilation;
- Death.

a. n1 = Number of participants meeting the endpoint definition.
b. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
c. n2 = Number of participants at risk for the endpoint.

d. Two-side confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time

Study BNT162-01

Study BNT162-01 is an ongoing Phase 1/2, open-label, dose-finding study to evaluate the safety and immunogenicity of several candidate vaccines, including BNT162b2 (1, 3, 10, 20, and 30 μg), conducted in Germany in healthy and immunocompromised adults. Only safety and immunogenicity data in individuals 16 years of age and older, the population for the intended use and who received the final vaccine formulation (30 μg BNT162b2) are used to support this application. The 30 μg dosage of BNT162b2 was administered to 12 adults 18 to 55 years of age and 12 adults 56 to 85 years of age.

The primary objective was to evaluate the safety of the BNT162 candidate vaccines. Secondary and exploratory objectives were to describe humoral and cellular immune responses following vaccination, measured at baseline and various time points after vaccination, specifically 7 days post Dose 2. Adverse event monitoring was the same as the safety monitoring in study C4591001.

The study started April 23, 2020. The BLA contains safety data (reactogenicity and AE analyses) up to 1 month after Dose 2 (data cutoff date: October 23, 2020), neutralizing antibody data up to ~2 months after Dose 2 (data cutoff date: October 23, 2020), and T-cell data up to ~6 months after Dose 2 (data cutoff date: March 2, 2021).

Study BNT162-01 Results

Disposition of 30 μg BNT162b2 group:

- Safety: Of a total of 24 participants, 12 participants 18 to 55 years of age and 12 participants 56 to 85 years of age completed the visit at 1- month post-Dose 2.
- Immunogenicity: Of the 12 participants, serum neutralizing antibody and T-cell responses were available for 10 and 12 participants, respectively.

Safety: The safety profiles for adult participants 18-55 and 56-85 years of age receiving 30 μg BNT162b2 in this study were similar to age-matched participants in study C4591001.

Immunogenicity: Dose-dependent increases were noted 42 days after Dose 2, compared to SARS-CoV-2 neutralizing GMTs at baseline (pre-Dose 1), and most pronounced at the 30 μg dose level. The Th1 polarization of the T-helper response was indicated by IFNγ and IL-2 production, and only minimal IL-4 production upon antigen-specific (SARS-CoV-2 S protein peptide pools) re-stimulation.

Review of the safety and immunogenicity from Phase 1 part of Study C4591001, in combination with data from Study BNT162-01, supported selection of the final vaccine candidate and dose level (BNT162b2 at 30 μg, given as two doses 3 weeks apart) to proceed into Phase 2/3 part of Study C4591001.

Lot Consistency

Consistency of process performance qualification (PPQ) batches manufactured at both Pfizer Puurs and Pfizer Kalamazoo was demonstrated by verifying process parameters and in-process testing results as well as DP release testing. Data obtained from the analytical comparability assessments on the PPQ batches manufactured at both sites

provide evidence of reproducible and consistent manufacture of COMIRNATY DP of acceptable product quality across all supply nodes.

b. Bioresearch Monitoring (BIMO) – Clinical/Statistical/Pharmacovigilance

BIMO inspection assignments were issued for a total of nine (9) clinical study sites that participated in the conduct of study Protocol C4591001. Three (3) of these inspection assignments focused on clinical study sites that enrolled the pediatric population and six (6) of the study sites enrolled the adult population. The inspections did not reveal findings that impact the BLA.

c. Pediatrics

The Applicant's Pediatric Plan was presented to the FDA Pediatric Review Committee (PeRC) on August 3, 2021. The committee agreed with the Applicant's request for a deferral for studies in participants 0 to <16 years of age because the biological product is ready for approval for use in individuals 16 years of age and older before pediatric studies in participants 0 to <16 years of age are completed (Section 505B(a)(3)(A)(i) of PREA).

The PREA-required studies specified in the approval letter and agreed upon with the Applicant are as follows:

1. Study C4591001 to evaluate the safety and effectiveness of COMIRNATY in children 12 years through 15 years of age

2. Study C4591007 to evaluate the safety and effectiveness of COMIRNATY in children 6 months to <12 years of age

3. Study C4591023 to evaluate the safety and effectiveness of COMIRNATY in infants <6 months of age

7. Safety and Pharmacovigilance

The most commonly reported (≥10%) solicited adverse reactions in COMIRNATY recipients 16 through 55 years of age following any dose were pain at the injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), fever (17.8%), and injection site swelling (10.6%). The most commonly reported (≥10%) solicited adverse reactions in COMIRNATY recipients 56 years of age and older following any dose were pain at the injection site (78.2%), fatigue (56.9%), headache, (45.9%), muscle pain (32.5%), chills (24.8%), joint pain (21.5%), injection site swelling (11.8%), fever (11.5%), and injection site redness (10.4%).

Among participants 16 through 55 years of age who had received at least 1 dose of COMIRNATY (N=12,995) or placebo (N=13,026), serious adverse events from Dose 1 up to the participant unblinding date in ongoing follow-up were reported by 103 (0.8%) COMIRNATY recipients and 117 (0.9%) placebo recipients. In a similar analysis in participants 56 years of age and older (COMIRNATY=8,931, placebo=8,895), serious adverse events were reported by 165 (1.8%) COMIRNATY recipients and 151 (1.7%) placebo recipients who received at least 1 dose of COMIRNATY or placebo, respectively. In these analyses, 58.2% of study participants had at least 4 months of

follow-up after Dose 2. There were no notable patterns between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COMIRNATY.

From Dose 1 through the March 13, 2021 data cutoff date, there were a total of 38 deaths, 21 in the COMIRNATY group and 17 in the placebo group. None of the deaths were considered related to vaccination.

Since the issuance of the EUA (December 11, 2020), post-authorization safety data has been reported from individuals 16 years of age and older following any dose of COMIRNATY. Because these reactions are reported from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. Below are presented adverse reactions categorized as important identified risks in the pharmacovigilance plan that have occurred during the conduct of the clinical trial and have been reported following the issuance of the EUA.

Myocarditis/Pericarditis

During the time from Dose 1 to unblinding in Study C4591001, one report of pericarditis was identified in the COMIRNATY group, occurring in a male participant ≥55 years of age, with no medical history, 28 days after Dose 2; the event was assessed by the investigator as not related to the study intervention and was ongoing at the time of the data cutoff. One report of myocarditis was identified in a male participant <55 years of age in the placebo group, occurring 5 days after his second placebo dose.

Post-EUA safety surveillance reports received by FDA and CDC identified serious risks for myocarditis and pericarditis following administration of COMIRNATY. Reporting rates for medical chart-confirmed myocarditis/pericarditis in VAERS have been higher among males under 40 years of age than among females and older males and have been highest in males 12-17 years of age (65 cases per million doses administered as per CDC communication on August 20, 2021), particularly following the second dose, and onset of symptoms within 7 days following vaccination. Although some cases of vaccine-associated myocarditis/pericarditis required intensive care support, available data from short-term follow up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae and outcomes in affected individuals. A mechanism of action by which the vaccine could cause myocarditis and pericarditis has not been established.

These safety findings of increased risk for myocarditis/pericarditis led to warning in section 5.2 Warning and Precautions of the PI.

Myocarditis and pericarditis are considered important identified risks in the pharmacovigilance plan included in the BLA. Of note, the Applicant will be required to conduct postmarketing requirement (PMR) safety studies under Section 505(o) of the Federal Food, Drug, and Cosmetic Act (FDCA) to assess the known serious risks of myocarditis and pericarditis as well as an unexpected serious risk for subclinical myocarditis (see Section 11c Recommendation for Postmarketing Activities, for study details).

Moreover, since vaccine-associated myocarditis/pericarditis is the most clinically significant identified risk, FDA undertook a quantitative benefit-risk assessment to model the excess risk of myocarditis/pericarditis vs. the expected benefits of preventing COVID-19 and associated hospitalizations, ICU admissions, and deaths. For estimation of risk, the model took a conservative approach by relying on non-chart-confirmed cases from a US healthcare claims database (OPTUM) that could provide a control group and greater confidence in denominators for vaccine exposures. Thus, the estimates of excess risk in this model are higher than the rates estimated from reports to VAERS (an uncontrolled passive surveillance system), with an estimated excess risk approaching 200 cases per million vaccinated males 16-17 years of age (the age/sex-stratified group with the highest risk). For estimation of benefit, the model output was highly dependent on the assumed COVID-19 incidence, as well as assumptions about vaccine efficacy and duration of protection. The assessment therefore considered a range of scenarios including but not limited to a “most likely” scenario associated with recent Delta variant surge and diminished vaccine effectiveness (70% overall, 80% against COVID-19 hospitalization) compared to that observed in the clinical trial. The “worst-case” scenario with low COVID-19 incidence reflecting the July 2021 nadir and the same somewhat diminished vaccine effectiveness as in the “most likely” scenario.

For males and females 18 years of age and older and for females 16-17 years of age, even before accounting for morbidity prevented from non-hospitalized COVID-19, the model predicts that the benefits of prevented COVID-19 hospitalizations, ICU admissions and deaths would clearly outweigh the predicted excess risk of vaccine-associated myocarditis/pericarditis under all conditions examined. For males 16-17 years of age, the model predicts that the benefits of prevented COVID-19 hospitalizations, ICU admissions and deaths would clearly outweigh the predicted excess risk of vaccine-associated myocarditis/pericarditis under the “most likely” scenario, but that predicted excess cases of vaccine-associated myocarditis/pericarditis would exceed COVID-19 hospitalizations and deaths under the “worst case” scenario. However, this predicted numerical imbalance does not account for the greater severity and length of hospitalization, on average, for COVID-19 compared with vaccine-associated myocarditis/pericarditis. Additionally, the “worst case” scenario model predicts prevention of >13,000 cases of non-hospitalized COVID-19 per million vaccinated males 16-17 years of age, which would include prevention of clinically significant morbidity and/or long-term sequelae associated with some of these cases. Finally, the model does not account for indirect societal/public health benefits of vaccination. Considering these additional factors, FDA concluded that even under the “worst case” scenario the benefits of vaccination sufficiently outweigh risks to support approval of the vaccine in males 16-17 years of age.

Mitigation of the observed risks and associated uncertainties will be accomplished through labeling (including warning statements) and through continued safety surveillance and postmarketing studies to further assess and understand these risks, including an immunogenicity and safety study of lower dose levels of COMIRNATY in individuals 12 through <30 years of age. The Applicant will be required to conduct postmarketing requirement (PMR) safety studies under Section 505(o) of the Federal Food, Drug, and Cosmetic Act (FDCA) to assess the known serious risks of myocarditis and pericarditis and an unexpected serious risk for subclinical myocarditis (see section 11c for study details).

Anaphylaxis
The risk of anaphylaxis was recognized early in the post-authorization time period and it is included as an important identified risk in the PVP. The estimated crude reporting rate for anaphylaxis is 6.0 cases per million doses. Therefore, the incidence of anaphylaxis after receipt of COMIRNATY is comparable with those reported after receipt of other vaccines.

There were no reports of anaphylaxis associated with COMIRNATY in clinical study participants through the cutoff date of March 13, 2021.

A contraindication for individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of COMIRNATY is included in section 4 of the PI. Additionally, a warning statement is included in section 5.1 of the PI instructing that "appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of COMIRNATY"

Pharmacovigilance Plan (PVP)
The Applicant's proposed pharmacovigilance plan (version 1.1) includes the following important risks and missing information:

- Important identified risks: Anaphylaxis; Myocarditis and Pericarditis
- Important potential risk: Vaccine-Associated Enhanced Disease (VAED), including Vaccine-Associated Enhanced Respiratory Disease (VAERD)
- Missing information: Use in pregnancy and lactation; Vaccine effectiveness; Use in pediatric individuals <12 years of age

In addition to routine pharmacovigilance, the Applicant will conduct the postmarketing studies listed in Section 11c Recommendation for Postmarketing Activities.

Adverse event reporting under 21 CFR 600.80 and the postmarketing studies in Section 11c are adequate to monitor the postmarketing safety for COMIRNATY.

8. Labeling

The proprietary name, COMIRNATY, was reviewed by CBER's Advertising and Promotional Labeling Branch (APLB) on July 2, 2021, and found to be acceptable. CBER communicated this decision to the Applicant on July 6, 2021. The APLB found the PI and package/container labels to be acceptable from a promotional and comprehension perspective. The Review Committee negotiated revisions to the PI, including modifying the proposed proper name from "COVID-19 mRNA vaccine (nucleoside-modified)" to "COVID-19 Vaccine, mRNA" and including a warning for an increased risk of myocarditis and pericarditis following administration of COMIRNATY. All labeling issues regarding the PI and the carton and container labels were acceptably resolved after exchange of information and discussions with the Applicant.

9. Advisory Committee Meetings

Vaccines and Related Biological Products Committee (VRBPAC) meetings were convened on October 22, 2020 to discuss, in general, development for EUA and licensure of vaccines to prevent COVID-19 and on December 10, 2020, to discuss BioNTech Manufacturing GmbH/Pfizer's EUA request for the Pfizer-BioNTech COVID-19 Vaccine.

On October 22, 2020, the VRBPAC was presented with the following items for discussion (no vote):

1. Please discuss FDA's approach to safety and effectiveness data as outlined in the respective guidance documents.

2. Please discuss considerations for continuation of blinded Phase 3 clinical trials if an EUA has been issued for an investigational COVID-19 vaccine.

3. Please discuss studies following licensure and/or issuance of an EUA for COVID-19 vaccines to
    a. Further evaluate safety, effectiveness and immune markers of protection
    b. Evaluate the safety and effectiveness in specific populations

In general, the VRBPAC endorsed FDA's approach and recommendations on the safety and effectiveness data necessary to support a BLA and EUA for COVID-19 vaccines as outlined in the respective guidance documents. VRBPAC members recommended for the median follow-up of 2 month to be the minimum follow-up period and suggested longer follow-up periods to evaluate, both safety and efficacy, if feasible. The VRBPAC endorsed the importance of additional studies to further evaluate safety and effectiveness of the vaccine after EUA issuance and/or licensure and underscored the need to evaluate the safety and effectiveness of COVID-19 vaccines in specific populations.

On December 10, 2020, VRBPAC discussed Pfizer- BioNTech Manufacturing GmbH's EUA request for their vaccine to prevent COVID-19 in individuals 16 years of age and older. The committee discussed the safety and efficacy data derived from the clinical disease endpoint efficacy study C4591001.

The VRPBAC voted on one question:

1. Based on the totality of scientific evidence available, do the benefits of the Pfizer-BioNTech COVID-19 Vaccine outweigh its risks for use in individuals 16 years of age and older?

    The results of the vote were as follows:
    Yes = 17 No = 4 Abstain = 1

The VRBPAC was presented with the following items for discussion (no vote):

1. Pfizer has proposed a plan for continuation of blinded, placebo-controlled follow-up in ongoing trials if the vaccine were made available under EUA. Please discuss

Pfizer's plan, including how loss of blinded, placebo-controlled follow-up in ongoing trials should be addressed.

2. Please discuss any gaps in plans described today and in the briefing documents for further evaluation of vaccine safety and effectiveness in populations who receive the Pfizer-BioNTech COVID-19 Vaccine under an EUA.

The committee discussed potential implications of loss of blinded, placebo-controlled follow-up in ongoing trials including how this may impact availability of safety data to support a BLA. The VRBPAC commented on the need to further assess vaccine effect on asymptomatic infection and viral shedding, and further evaluation of safety and effectiveness in subpopulations such as HIV-infected individuals, individuals with prior exposure to SARS-CoV-2.

FDA did not refer this application to the VRBPAC because our review of the information submitted to this BLA did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

10. Other Relevant Regulatory Issues

a. Identification of BLA Lots

Upon CBER's request inquiring about what BLA-compliant EUA-labeled lots may be available for use upon licensure of COMIRNATY, the Applicant submitted information listing which lots they considered to be manufactured according to the BLA. To address the issue of these lots not bearing the vial label associated with BLA approval, CBER worked with the Applicant to develop a Dear HCP letter to be included with lots considered by CBER to be BLA-compliant. This letter explained that some lots labeled for EUA use were also considered BLA-compliant and refers HCP to a website for additional information. CBER requested and the Applicant agreed that only EUA-labeled lots that had also undergone CBER lot release according to the BLA would be considered BLA-compliant and listed at the website included in the Dear HCP letter.

b. Exception to the 21 CFR 610.15(a) Requirement for a Preservative

Under 21 CFR 610.15(a), a vaccine product in multiple-dose containers must (absent certain exceptions) contain a preservative. The Applicant submitted a request for exception to this requirement and provided a justification for the multi-dose presentation of COMIRNATY not containing a preservative. CBER considered the Applicant's request for an exception to the 21 CFR 610.15(a) for COMIRNATY as a multiple dose preservative-free presentation acceptable.

11. Recommendations and Benefit/Risk Assessment

a. Recommended Regulatory Action

Based on the review of the clinical, pre-clinical, and product-related data submitted in the original BLA, the Review Committee recommends approval of COMIRNATY for the labeled indication and usage.

b. Benefit/Risk Assessment

Considering the data submitted to support the safety and effectiveness of COMIRNATY that have been presented and discussed in this document, as well as the seriousness of COVID-19, the Review Committee is in agreement that the risk/benefit balance for COMIRNATY is favorable and supports approval for use in individuals 16 years of age and older.

c. Recommendation for Postmarketing Activities

BioNTech Manufacturing GmbH has committed to conduct the following postmarketing activities, which will be included in the approval letter.

POSTMARKETING REQUIREMENTS UNDER SECTION 505(o)

1. Study C4591009, entitled "A Non-Interventional Post-Approval Safety Study of the Pfizer-BioNTech COVID-19 mRNA Vaccine in the United States," to evaluate the occurrence of myocarditis and pericarditis following administration of COMIRNATY

   Final Protocol Submission: August 31, 2021
   Monitoring Report Submission: October 31, 2022
   Interim Report Submission: October 31, 2023
   Study Completion: June 30, 2025
   Final Report Submission: October 31, 2025

2. Study C4591021, entitled "Post Conditional Approval Active Surveillance Study Among Individuals in Europe Receiving the Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine," to evaluate the occurrence of myocarditis and pericarditis following administration of COMIRNATY

   Final Protocol Submission: August 11, 2021
   Progress Report Submission: September 30, 2021
   Interim Report 1 Submission: March 31, 2022
   Interim Report 2 Submission: September 30, 2022
   Interim Report 3 Submission: March 31, 2023
   Interim Report 4 Submission: September 30, 2023
   Interim Report 5 Submission: March 31, 2024
   Study Completion: March 31, 2024
   Final Report Submission: September 30, 2024

3. Study C4591021 substudy to describe the natural history of myocarditis and pericarditis following administration of COMIRNATY

   Final Protocol Submission: January 31, 2022
   Study Completion: March 31, 2024
   Final Report Submission: September 30, 2024

4. Study C4591036, a prospective cohort study with at least 5 years of follow-up for potential long-term sequelae of myocarditis after vaccination (in collaboration with Pediatric Heart Network)

Final Protocol Submission: November 30, 2021
Study Completion: December 31, 2026
Final Report Submission: May 31, 2027

5. Study C4591007 substudy to prospectively assess the incidence of subclinical myocarditis following administration of the second dose of COMIRNATY in a subset of participants 5 through 15 years of age

   Final Protocol Submission: September 30, 2021
   Study Completion: November 30, 2023
   Final Report Submission: May 31, 2024

6. Study C4591031 substudy to prospectively assess the incidence of subclinical myocarditis following administration of a third dose of COMIRNATY in a subset of participants 16 to 30 years of age

   Final Protocol Submission: November 30, 2021
   Study Completion: June 30, 2022
   Final Report Submission: December 31, 2022

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

7. Study C4591022, entitled “Pfizer-BioNTech COVID-19 Vaccine Exposure during Pregnancy: A Non-Interventional Post-Approval Safety Study of Pregnancy and Infant Outcomes in the Organization of Teratology Information Specialists (OTIS)/MotherToBaby Pregnancy Registry”

   Final Protocol Submission: July 1, 2021
   Study Completion: June 1, 2025
   Final Report Submission: December 1, 2025

8. Study C4591007 substudy to evaluate the immunogenicity and safety of lower dose levels of COMIRNATY in individuals 12 through <30 years of age

   Final Protocol Submission: September 30, 2021
   Study Completion: November 30, 2023
   Final Report Submission: May 31, 2024

9. Study C4591012, entitled “Post-emergency Use Authorization Active Safety Surveillance Study Among Individuals in the Veteran’s Affairs Health System Receiving Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) Vaccine”

   Final Protocol Submission: January 29, 2021
   Study Completion: June 30, 2023
   Final Report Submission: December 31, 2023

10. Study C4591014, entitled “Pfizer-BioNTech COVID-19 BNT162b2 Vaccine Effectiveness Study - Kaiser Permanente Southern California”

Final Protocol Submission: March 22, 2021
Study Completion: December 31, 2022
Final Report Submission: June 30, 2023

PEDIATRIC REQUIREMENTS

11. Deferred pediatric study C4591001 to evaluate the safety and effectiveness of COMIRNATY in children 12 years through 15 years of age

    Final Protocol Submission: October 7, 2020
    Study Completion: May 31, 2023
    Final Report Submission: October 31, 2023

12. Deferred pediatric study C4591007 to evaluate the safety and effectiveness of COMIRNATY in children 6 months to <12 years of age

    Final Protocol Submission: February 8, 2021
    Study Completion: November 30, 2023
    Final Report Submission: May 31, 2024

13. Deferred pediatric study C4591023 to evaluate the safety and effectiveness of COMIRNATY in infants <6 months of age

    Final Protocol Submission: January 31, 2022
    Study Completion: July 31, 2024
    Final Report Submission: October 31, 2024

Marks Decl. Exhibit D

Contains Nonbinding Recommendations

Development and Licensure of Vaccines to Prevent COVID-19

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
June 2020

Preface

Public Comment

This guidance is being issued to address the coronavirus disease 2019 (COVID-19) public health emergency. This guidance is being implemented without prior public comment because the Food and Drug Administration (FDA or Agency) has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 371(h)(1)(C)) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to https://www.regulations.gov. All comments should be identified with the docket FDA-2020-D-1137 and complete title of the guidance in the request.

Additional Copies

Additional copies are available from the FDA webpage titled "COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders," *available at* https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders, the FDA webpage titled "Search for FDA Guidance Documents," *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents, and the FDA webpage titled "Biologics Guidances," *available at* https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances. You may also send an email request to ocod@fda.hhs.gov to receive an additional copy of the guidance. Please include the docket number FDA-2020-D-1137 and complete title of the guidance in the request.

Questions

For questions about this document, contact the Office of Communication, Outreach, and Development (OCOD) by email at ocod@fda.hhs.gov or at 800-835-4709 or 240-402-8010.

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Development and Licensure of Vaccines to Prevent COVID-19

Guidance for Industry

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

FDA plays a critical role in protecting the United States from threats such as emerging infectious diseases, including the Coronavirus Disease 2019 (COVID-19) pandemic which has been caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). FDA is committed to providing timely guidance to support response efforts to this pandemic.

FDA is issuing this guidance to assist sponsors in the clinical development and licensure of vaccines for the prevention of COVID-19.

This guidance is intended to remain in effect for the duration of the public health emergency related to COVID-19 declared by the Secretary of Health and Human Services (HHS) on January 31, 2020, effective January 27, 2020, including any renewals made by the HHS Secretary in accordance with section 319(a)(2) of the Public Health Service Act (PHS Act) (42 U.S.C. 247d(a)(2)). The recommendations described in the guidance are expected to assist the Agency and sponsors in the clinical development and licensure of vaccines for the prevention of COVID-19 and reflect the Agency's current thinking on this issue.

Given this public health emergency, and as discussed in the Notice in the *Federal Register* of March 25, 2020, titled "Process for Making Available Guidance Documents Related to Coronavirus Disease 2019" (85 FR 16949), *available at* https://www.govinfo.gov/content/pkg/FR-2020-03-25/pdf/2020-06222.pdf, this guidance is being implemented without prior public comment because FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), (21 U.S.C. 371(h)(1)(C)), and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices. However, FDA expects that the recommendations set forth in this revised guidance will continue to apply outside the context of the current public health emergency.

Therefore, within 60 days following the termination of the public health emergency, FDA intends to revise and replace this guidance with an updated guidance that incorporates any appropriate changes based on comments received on this guidance and the Agency's experience with implementation.

In general, FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. BACKGROUND

There is currently an outbreak of respiratory disease caused by a novel coronavirus. The virus has been named "SARS-CoV-2" and the disease it causes has been named "COVID-19." On January 31, 2020, the Secretary of HHS issued a declaration of a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS.[1] In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.[2]

The SARS-CoV-2 pandemic presents an extraordinary challenge to global health. There are currently no FDA-licensed vaccines to prevent COVID-19. Commercial vaccine manufacturers and other entities are developing COVID-19 vaccine candidates using different technologies including RNA, DNA, protein, and viral vectored vaccines.

This guidance describes FDA's current recommendations regarding the data needed to facilitate clinical development and licensure of vaccines to prevent COVID-19. There are currently no accepted surrogate endpoints that are reasonably likely to predict clinical benefit of a COVID-19 vaccine. Thus, at this time, the goal of development programs should be to pursue traditional approval via direct evidence of vaccine safety and efficacy in protecting humans from SARS-CoV-2 infection and/or clinical disease.

This guidance provides an overview of key considerations to satisfy regulatory requirements set forth in the investigational new drug application (IND) regulations in 21 CFR Part 312 and licensing regulations in 21 CFR Part 601 for chemistry, manufacturing, and controls (CMC), and nonclinical and clinical data through development and licensure, and for post-licensure safety evaluation of COVID-19 preventive vaccines.[3] FDA is committed to supporting all scientifically sound approaches to attenuating the clinical impact of COVID-19. Sponsors engaged in the development of vaccines to prevent COVID-19 should also see the guidance for industry and investigators, *COVID-19 Public Health Emergency: General Considerations for Pre-IND Meeting Requests for COVID-19 Related Drugs and Biological Products* (Ref. 1).

[1] Secretary of Health and Human Services Alex M. Azar, Determination that a Public Health Emergency Exists. (Jan. 31, 2020, renewed April 21, 2020), *available at* https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx.
[2] Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak (Mar. 13, 2020), *available at* https://www.whitehouse.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/.
[3] Novel devices used to administer COVID-19 vaccines raise additional issues which are not addressed in this guidance.

There are many COVID-19 vaccines currently in development and FDA recognizes that the considerations presented here do not represent all the considerations necessary to satisfy statutory and regulatory requirements applicable to the licensure of vaccines intended to prevent COVID-19. The nature of a particular vaccine and its intended use may impact specific data needs. We encourage sponsors to contact the Center for Biologics Evaluation and Research (CBER) Office of Vaccines Research and Review (OVRR) with specific questions.

III. CHEMISTRY, MANUFACTURING, AND CONTROLS – KEY CONSIDERATIONS

A. General Considerations

- COVID-19 vaccines licensed in the United States must meet the statutory and regulatory requirements for vaccine development and approval, including for quality, development, manufacture, and control (section 351(a) of the Public Health Service Act (PHS Act), (42 U.S.C. 262)). The vaccine product must be adequately characterized and its manufacture in compliance with applicable standards including current good manufacturing practice (cGMP) (section 501(a)(2)(B) of the FD&C Act (21 U.S.C. 351(a)(2)(B)) and 21 CFR Parts 210, 211, and 610). It is critical that vaccine production processes for each vaccine are well defined and appropriately controlled to ensure consistency in manufacturing.

- COVID-19 vaccine development may be accelerated based on knowledge gained from similar products manufactured with the same well-characterized platform technology, to the extent legally and scientifically permissible. Similarly, with appropriate justification, some aspects of manufacture and control may be based on the vaccine platform, and in some instances, reduce the need for product-specific data. FDA recommends that vaccine manufacturers engage in early communications with OVRR to discuss the type and extent of chemistry, manufacturing, and control information needed for development and licensure of their COVID-19 vaccine.

B. Manufacture of Drug Substance and Drug Product

- Data should be provided to show that all source material used in manufacturing is adequately controlled, including, for example, history and qualification of cell banks, history and qualification of virus banks, and identification of all animal derived materials used for cell culture and virus growth.

- Complete details of the manufacturing process must be provided in a Biologics License Application (BLA) to support licensure of a COVID-19 vaccine (21 CFR 601.2). Accordingly, sponsors should submit data and information identifying critical process parameters, critical quality attributes, batch records, defined hold times, and the in-process testing scheme. Specifications should be established for

each critical parameter. Validation data from the manufacture of platform-related products may provide useful supportive information, particularly in the identification of critical parameters.

- In-process control tests must be established that allow quality to be monitored for each lot for all stages of production (section 501(a)(2)(B) of the FD&C Act (21 U.S.C. 351(a)(2)(B)) and, as applicable, 21 CFR 211.110(a)).

- Data to support the consistency of the manufacturing process should be provided, including process validation protocols and study reports, data from engineering lots, and drug substance process performance qualification.

- The manufacturing process must be adequately validated (section 501(a)(2)(B) of the FD&C Act (21 U.S.C. 351(a)(2)(B)) and, as applicable, 21 CFR 211.100(a) and 211.110). Validation would typically include a sufficient number of commercial-scale batches that can be manufactured routinely, meeting predetermined in-process controls, critical process parameters, and lot release specifications. Typically, data on the manufacture of at least three commercial-scale batches are sufficient to support the validation of the manufacturing process (Ref. 2).

- A quality control system should be in place for all stages of manufacturing, including a well-defined testing program to ensure in process/intermediate product quality and product quality throughout the formulation and filling process. This system should also include a well-defined testing program to ensure drug substance quality profile and drug product quality for release. Data on the qualification/validation for all quality indicating assays should be submitted to the BLA to support licensure.

- All quality-control release tests, including key tests for vaccine purity, identity and potency, should be validated and shown to be suitable for the intended purpose. Release specifications are product specific and will be discussed with the sponsor as part of the review of a BLA.

- If adequately justified, final validation of formulation and filling operations may be completed after product approval if the impact on product quality is not compromised. It is important that any data that will be submitted after product approval be agreed upon prior to licensure and be submitted as a postmarketing commitment using the appropriate submission category.

- For vaccine licensure, the stability and expiry date of the vaccine in its final container, when maintained at the recommended storage temperature, should be demonstrated using final containers from at least three final lots made from different vaccine bulks.

- Storage conditions, including container closure integrity, must be fully validated (21 CFR 211.166).

- The vaccine must have been shown to maintain its potency for a period equal to that from the date of release to the expiry date (21 CFR 601.2 and 610.10). Post marketing commitments to provide full shelf life data may be acceptable with appropriate justification.

- A product specific stability program should be established to verify that licensed product maintains quality over the defined shelf life.

C. Facilities and Inspections

- Facilities must be of suitable size and construction to facilitate operations and should be adequately designed to prevent contamination, cross-contamination and mix-ups (section 501(a)(2)(B) of the FD&C Act (21 U.S.C. 351(a)(2)(B)) and, as applicable,21 CFR 211.42(a)). All utilities (including plumbing and sanitation) must be validated, and HVAC systems must provide adequate control over air pressure, micro-organisms, dust, humidity, and temperature, and sufficient protection or containment as needed (section 501(a)(2)(B) of the FD&C Act (21 U.S.C. 351(a)(2)(B)) and, as applicable, 21 CFR 211.46(c)) (Ref. 3). Facility and equipment cleaning and maintenance processes must be developed and validated (section 501(a)(2)(B) of the FD&C Act (21 U.S.C. 351(a)(2)(B)) and, as applicable, 21 CFR 211.56(c) and 211.67(b)).

- Manufacturing equipment should be qualified and sterile filtration and sterilization processes validated. Aseptic processes should be adequately validated using media simulations and personnel should be trained and qualified for their intended duties.

- A quality control unit must be established and must have the responsibility for oversight of manufacturing, and review and release of components, containers and closures, labeling, in-process material, and final products (section 501(a)(2)(B) of the FD&C Act (21 U.S.C. 351(a)(2)(B)) and, as applicable, 21 CFR 211.22). The quality control unit must have the responsibility for approving validation protocols, reports, investigate deviations, and institute corrective and preventive actions.

- FDA recommends that vaccine manufacturers engage in early communication with CBER's Office of Compliance and Biologics Quality, Division of Manufacturing and Product Quality to discuss facility preparation and inspection timing.

- Pre-license inspections of manufacturing sites are considered part of the review of a BLA and are generally conducted following the acceptance of a BLA filing (21 CFR 601.20). During the COVID-19 public health emergency, FDA is utilizing all available tools and sources of information to support regulatory decisions on applications that include sites impacted by FDA's ability to inspect due to COVID-19. During this interim period, we are using additional tools, where available, to determine the need for an on-site inspection and to support the

application assessment, such as reviewing a firm's previous compliance history, and requesting records in advance of or in lieu of on-site inspections or voluntarily from facilities and sites.

IV. NONCLINICAL DATA – KEY CONSIDERATIONS

A. General Considerations

- The purpose of nonclinical studies of a COVID-19 vaccine candidate is to define its immunogenicity and safety characteristics through *in vitro* and *in vivo* testing. Nonclinical studies in animal models[4] help identify potential vaccine related safety risks and guide the selection of dose, dosing regimen, and route of administration to be used in clinical studies. The extent of nonclinical data required to support proceeding to first in human (FIH) clinical trials depends on the vaccine construct, the supportive data available for the construct and data from closely related vaccines.

- Data from studies in animal models administered certain vaccine constructs against other coronaviruses (SARS-CoV and MERS-CoV) have raised concerns of a theoretical risk for COVID-19 vaccine-associated enhanced respiratory disease (ERD). In these studies, animal models were administered vaccine constructs against other coronaviruses and subsequently challenged with the respective wild-type virus. These studies have shown evidence of immunopathologic lung reactions characteristic of a Th-2 type hypersensitivity similar to ERD described in infants and animals that were administered formalin-inactivated respiratory syncytial virus (RSV) vaccine and that were subsequently challenged with RSV virus due to natural exposure or in the laboratory, respectively (Refs. 4-9). Vaccine candidates should be assessed in light of these studies as described in section D, below.

- FDA recommends that vaccine manufacturers engage in early communications with FDA to discuss the type and extent of nonclinical testing required for the particular COVID-19 vaccine candidate to support proceeding to FIH clinical trials and further clinical development.

B. Toxicity Studies (Refs. 10-14)

- For a COVID-19 vaccine candidate consisting of a novel product type and for which no prior nonclinical and clinical data are available, nonclinical safety studies will be required prior to proceeding to FIH clinical trials 21 CFR 312.23(a)(8).

[4] The preclinical program for any investigational product should be individualized with respect to scope, complexity, and overall design. We support the principles of the "3Rs," to reduce, refine, and replace animal use in testing when feasible. Proposals, with justification for any potential alternative approaches (e.g., in vitro or in silico testing), should be submitted during early communication meetings with FDA (see section VI of this document). We will consider if such an alternative method could be used in place of an animal test method.

- In some cases, it may not be necessary to perform nonclinical safety studies prior to FIH clinical trials because adequate information to characterize product safety may be available from other sources. For example, if the COVID-19 vaccine candidate is made using a platform technology utilized to manufacture a licensed vaccine or other previously studied investigational vaccines and is sufficiently characterized, it may be possible to use toxicology data (e.g., data from repeat dose toxicity studies, biodistribution studies) and clinical data accrued with other products using the same platform to support FIH clinical trials for that COVID-19 vaccine candidate. Vaccine manufacturers should summarize the findings and provide a rationale if considering using these data in lieu of performing nonclinical safety studies.

- When needed to support proceeding to FIH clinical trials, nonclinical safety assessments including toxicity and local tolerance studies must be conducted under conditions consistent with regulations prescribing good laboratory practices for conducting nonclincial laboratory studies (GLP) (21 CFR Part 58). Such studies should be completed and analysed prior to initiation of FIH clinical trials. When toxicology studies do not adequately characterize risk, additional safety testing should be conducted as appropriate.

- Data from toxicity studies may be submitted as unaudited final draft toxicicologic reports to accelerate proceeding to FIH clincial trials with COVID-19 vaccine candidates. The final, fully quality-assured reports should be available to FDA within 120 days of the start of the FIH clinical trial.

- Use of COVID-19 preventive vaccines in pregnancy and in women of childbearing potential will be an important consideration for vaccination programs. Therefore, FDA recommends that prior to enrolling pregnant women and women of childbearing potential who are not actively avoiding pregnancy in clinical trials, sponsors conduct developmental and reproductive toxicity (DART) studies with their respective COVID-19 vaccine candidate. Alternatively, sponsors may submit available data from DART studies with a similar product using comparable platform technology if, after consultation with the agency, the agency agrees those data are scientifically sufficient.

- Biodistribution studies in an animal species should be considered if the vaccine construct is novel in nature and there are no existing biodistribution data from the platform technology. These studies should be conducted if there is a likelihood of altered infectivity and tissue tropism or if a novel route of administration and formulation is to be used.

C. Characterization of the Immune Response in Animal Models

- Immunogenicity studies in animal models responsive to the selected COVID-19 vaccine antigen should be conducted to evaluate the immunologic properties of the COVID-19 vaccine candidate and to support FIH clinical trials. The aspects of

immunogenicity to be measured should be appropriate for the vaccine construct and its intended mechanism of action.

- Studies should include an evaluation of humoral, cellular, and functional immune responses, as appropriate to each of the included COVID-19 antigens. Use of antigen-specific enyzme linked immunosorbent assays (ELISA) should be considered to characterize the humoral response. Evaluation of cellular reponses should include the examination of CD8+ and CD4+ T cell responses using sensitive and specific assays. The functional activity of immune responses should be evaluated *in vitro* in neutralization assays using either wild-type virus or pseudovirion virus. The assays used for immunogencity evaluation should be demonstrated to be suitable for their intended purpose.

D. Studies to Address the Potential for Vaccine-associated Enhanced Respiratory Disease

- Current knowledge and understanding of the potential risk of COVID-19 vaccine associated ERD is limited, as is understanding of the value of available animal models in predicting the likelihood of such occurrence in humans. Nevertheless, studies in animal models (e.g., rodents and non-human primates) are considered important to address the potential for vaccine-associated ERD.

- Post-vaccination animal challenge studies and the characterization of the type of the nonclinical and clinical immune response induced by the particular COVID-19 vaccine candidate can be used to evaluate the likelihood of the vaccine to induce vaccine-associated ERD in humans.

- To support proceeding to FIH clinical trials, sponsors should conduct studies characterizing the vaccine-induced immune response in animal models evaluating immune markers of potential ERD outcomes. These should include assessments of functional immune responses (e.g., neutralizing antibody) versus total antibody responses and Th1/Th2 balance in animals vaccinated with clinically relevant doses of the COVID-19 vaccine candidate.

- COVID-19 vaccine candidates with immunogenicity data demonstrating high neutralizing antibody titers and Th1-type T cell polarization may be allowed to proceed to FIH trials without first completing postvaccination challenge studies in appropriate animal models, provided adequate risk mitigation strategies are put in place in the FIH trials. In these situations, postvaccination challenge studies are expected to be conducted in parallel with FIH trials to ensure the potential for vaccine-associated ERD is addressed prior to enrolling large numbers of human subjects into Phase 2 and 3 clinical trials. For COVID-19 vaccine candidates for which other data raise increased concerns about ERD, postvaccination animal challenge data and/or animal immunopathology studies are critical to assess protection and/or ERD *prior* to advancing to FIH clinical trials.

- The totality of data for a specific COVID-19 vaccine candidate, including data from postvaccination challenge studies in small animal models and from FIH clinical trials characterizing the type of immune responses induced by the vaccine will be considered in determining whether Phase 3 studies can proceed in the absence of postvaccination challenge data to address risk of ERD.

V. CLINICAL TRIALS – KEY CONSIDERATIONS

A. General Considerations

- Understanding of SARS-CoV-2 immunology, and specifically vaccine immune responses that might predict protection against COVID-19, is currently limited and evolving. Thus, while evaluation of immunogenicity is an important component of COVID-19 vaccine development, at this time, the goal of development programs should be to pursue traditional approval via direct evidence of vaccine efficacy in protecting humans from SARS-CoV-2 infection and/or disease.

- Clinical development programs for COVID-19 vaccines might be expedited by adaptive and/or seamless clinical trial designs (described below) that allow for selection between vaccine candidates and dosing regimens and for more rapid progression through the usual phases of clinical development.

- Regardless of whether clinical development programs proceed in discrete phases with separate studies or via a more seamless approach, an adequate body of data, including data to inform the risk of vaccine-associated ERD, will be needed as clinical development progresses to support the safety of vaccinating the proposed study populations and number of participants and, for later stage development, to ensure that the study design is adequate to meet its objectives.

- FDA can provide early advice, and potentially concurrence in principle, on plans for expedited/seamless clinical development. However, sponsors should plan to submit summaries of data available at each development milestone for FDA review and concurrence prior to advancing to the next phase of development.

- Conducting clinical trials in the setting of a public health emergency presents operational challenges. FDA has issued guidance to provide general considerations to assist sponsors in assuring the safety of trial participants, maintaining compliance with good clinical practice (GCP), and minimizing risks to trial integrity for the duration of the COVID-19 public health emergency. It should be noted that not all of the recommendations in that guidance may be applicable to vaccine development, given some of the different considerations for these products (Ref. 15).

B. Trial Populations

- Once acceptable pre-clinical data are available, FIH and other early phase studies (which typically expose 10–100 participants to each vaccine candidate being evaluated) should first enroll healthy adult participants who are at low risk of severe COVID-19. Exclusion of participants at higher risk of severe COVID-19 from early phase studies is necessary to mitigate potential risk of vaccine-associated ERD until additional data to inform that potential risk becomes available through ongoing product development.

    - As the understanding of COVID-19 pathogenesis continues to evolve, exclusion criteria should reflect the current understanding of risk factors for more severe COVID-19, such as those described by the Centers for Disease Control and Prevention (Ref. 16).

    - Older adult participants (e.g., over 55 years of age) may be enrolled in FIH and other early phase studies so long as they do not have medical comorbidities associated with an increased risk of severe COVID-19. Some preliminary safety data in younger adults (e.g., 7 days after a single vaccination) should be available prior to enrolling older adult participants, especially for vaccine platforms without prior clinical experience.

    - If possible, early clinical studies should also exclude participants at high risk of SARS-CoV-2 exposure (e.g., healthcare workers).

- Sponsors should collect and evaluate at least preliminary clinical safety and immunogenicity data for each dose level and age group (e.g., younger versus older adults) to support progression of clinical development to include larger numbers (e.g., hundreds) of participants and participants at higher risk of severe COVID-19.

    - Preliminary immunogenicity data from early phase development should include assessments of neutralizing vs. total antibody responses and Th1 vs. Th2 polarization.

    - Additional data to further inform potential risk of vaccine-associated ERD and to support progression of clinical development, if available, may include preliminary evaluation of COVID-19 disease outcomes from earlier clinical development and results of non-clinical studies evaluating protection and/or histopathological markers of vaccine-associated ERD following SARS-CoV-2 challenge.

- To generate sufficient data to meet the BLA approval standard, late phase clinical trials to demonstrate vaccine efficacy with formal hypothesis testing will likely need to enroll many thousands of participants, including many with medical comorbidities for trials seeking to assess protection against severe COVID-19.

    - Initiation of late phase trials should be preceded by adequate characterization of safety and immunogenicity (e.g., in a few hundred participants for each

vaccine candidate, dose level, and age group to be evaluated) to support general safety, potential for vaccine efficacy, and low risk of vaccine-associated ERD.

- Results of non-clinical studies evaluating protection and/or histopathological markers of vaccine-associated ERD following SARS-CoV-2 challenge and COVID-19 disease outcomes from earlier clinical development are other potentially important sources of information to support clinical trials with thousands of participants.

- Although establishing vaccine safety and efficacy in SARS-CoV-2 naïve individuals is critical, vaccine safety and COVID-19 outcomes in individuals with prior SARS-CoV-2 infection, which might have been asymptomatic, is also important to examine because pre-vaccination screening for prior infection is unlikely to occur in practice with the deployment of licensed COVID-19 vaccines. Therefore, COVID-19 vaccine trials need not screen for or exclude participants with history or laboratory evidence of prior SARS-CoV-2 infection. However, individuals with acute COVID-19 (or other acute infectious illness) should be excluded from COVID-19 vaccine trials.

- FDA encourages the inclusion of diverse populations in all phases of vaccine clinical development. This inclusion helps to ensure that vaccines are safe and effective for everyone in the indicated populations.

  - FDA strongly encourages the enrollment of populations most affected by COVID-19, specifically racial and ethnic minorities.

  - Evaluation of vaccine safety and efficacy in late phase clinical development in adults should include adequate representation of elderly individuals and individuals with medical comorbidities.

  - FDA encourages vaccine developers to consider early in their development programs data that might support inclusion of pregnant women and women of childbearing potential who are not actively avoiding pregnancy in pre-licensure clinical trials (Ref. 17).

  - It is important for developers of COVID-19 vaccines to plan for pediatric assessments of safety and effectiveness, given the nature of the COVID-19 public health emergency, and to help ensure compliance with the Pediatric Research Equity Act (PREA) (section 505B of the FD&C Act (21 U.S.C. 355c)) (Ref. 18). The epidemiology and pathogenesis of COVID-19, and the safety and effectiveness of COVID-19 vaccines, may be different in children compared with adults. In order to ensure compliance with 21 CFR Part 50 Subpart D (Additional safeguards for children in clinical investigations), considerations on the prospect of direct benefit and acceptable risk to support initiation of pediatric studies, and the appropriate design and endpoints for pediatric studies, should be discussed in the context of specific vaccine development programs.

C. Trial Design

- Early phase trials often aim to down-select among multiple vaccine candidates and/or dosing regimens via randomization of participants to different treatment groups. While including a placebo control and blinding are not required for early phase studies, doing so may assist in interpretation of preliminary safety data.

- Later phase trials, including efficacy trials, should be randomized, double-blinded, and placebo controlled.

    - An individually randomized controlled trial with 1:1 randomization between vaccine and placebo groups is usually the most efficient study design for demonstrating vaccine efficacy. Other types of randomization, such as cluster randomization, may be acceptable but require careful consideration of potential biases that are usually avoided with individual randomization.

    - An efficacy trial that evaluates multiple vaccine candidates against a single placebo group may be an acceptable approach to further increase efficiency, provided that the trial is adequately designed with appropriate statistical methods to evaluate efficacy.

    - If the availability of a COVID-19 vaccine proven to be safe and effective precludes ethical inclusion of a placebo control group, that vaccine could serve as the control treatment in a study designed to evaluate efficacy with non-inferiority hypothesis testing.

- Protocols for adaptive trials should include pre-specified criteria for adding or removing vaccine candidates or dosing regimens, and protocols for seamless trials should include pre-specified criteria (e.g., safety and immunogenicity data) for advancing from one phase of the study to the next.

- Follow-up of study participants for COVID-19 outcomes (in particular, for severe COVID-19 disease manifestations) should continue as long as feasible, ideally at least one to two years, to assess duration of protection and potential for vaccine-associated ERD as immune responses to the vaccine wane.

- Efficacy trials should include contingency plans for continued follow up and analysis of safety and effectiveness outcomes in the event that a safe and effective vaccine becomes available (e.g., as demonstrated in a planned interim analysis or as demonstrated in another clinical trial). In that case, discussion with the agency may be necessary to address ethical arguments to break the blind and offer vaccine to placebo recipients.

- In cases where statistical equivalency testing of vaccine immune responses in humans is required to support manufacturing consistency (clinical lot-to-lot consistency trial), this testing can be incorporated into the design of an efficacy trial and does not need to be conducted in a separate study.

D. Efficacy Considerations

- Either laboratory-confirmed COVID-19 or laboratory-confirmed SARS-CoV-2 infection is an acceptable primary endpoint for a COVID-19 vaccine efficacy trial.

  - Acute cases of COVID-19 should be virologically confirmed (e.g., by RT-PCR).

  - SARS-CoV-2 infection, including asymptomatic infection, can be monitored for and confirmed either by virologic methods or by serologic methods evaluating antibodies to SARS-CoV-2 antigens not included in the vaccine.

- Standardization of efficacy endpoints across clinical trials may facilitate comparative evaluation of vaccines for deployment programs, provided that such comparisons are not confounded by differences in trial design or study populations. To this end, FDA recommends that either the primary endpoint or a secondary endpoint (with or without formal hypothesis testing) be defined as virologically confirmed SARS-CoV-2 infection with one or more of the following symptoms:

  - Fever or chills
  - Cough
  - Shortness of breath or difficulty breathing
  - Fatigue
  - Muscle or body aches
  - Headache
  - New loss of taste or smell
  - Sore throat
  - Congestion or runny nose
  - Nausea or vomiting
  - Diarrhea

- As it is possible that a COVID-19 vaccine might be much more effective in preventing severe versus mild COVID-19, sponsors should consider powering efficacy trials for formal hypothesis testing on a severe COVID-19 endpoint. Regardless, severe COVID-19 should be evaluated as a secondary endpoint (with or without formal hypothesis testing) if not evaluated as a primary endpoint. FDA recommends that severe COVID-19 be defined as virologically confirmed SARS-CoV-2 infection with any of the following:

  - Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥ 30 per minute, heart rate ≥ 125 per minute, $SpO2 \leq 93\%$ on room air at sea level or $PaO2/FiO2 < 300$ mm Hg)
  - Respiratory failure (defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation or ECMO)
  - Evidence of shock (SBP < 90 mm Hg, DBP < 60 mm Hg, or requiring vasopressors)
  - Significant acute renal, hepatic, or neurologic dysfunction

- Admission to an ICU
- Death

- SARS-CoV-2 infection (whether or not symptomatic) should be evaluated as a secondary or exploratory endpoint, if not evaluated as a primary endpoint.

- The above diagnostic criteria may need to be modified in certain populations; for example, in pediatric patients and those with respiratory comorbidities. Sponsors should discuss their proposed case definitions with the Agency prior to initiating enrollment.

E. Statistical Considerations

- To ensure that a widely deployed COVID-19 vaccine is effective, the primary efficacy endpoint point estimate for a placebo-controlled efficacy trial should be at least 50%, and the statistical success criterion should be that the lower bound of the appropriately alpha-adjusted confidence interval around the primary efficacy endpoint point estimate is >30%.

  - The same statistical success criterion should be used for any interim analysis designed for early detection of efficacy.

  - A lower bound ≤30% but >0% may be acceptable as a statistical success criterion for a secondary efficacy endpoint, provided that secondary endpoint hypothesis testing is dependent on success on the primary endpoint.

- For non-inferiority comparison to a COVID-19 vaccine already proven to be effective, the statistical success criterion should be that the lower bound of the appropriately alpha-adjusted confidence interval around the primary relative efficacy point estimate is >-10%.

- For each vaccine candidate, appropriate statistical methods should be used to control type 1 error for hypothesis testing on multiple endpoints and/or interim efficacy analyses.

- Late phase studies should include interim analyses to assess risk of vaccine-associated ERD (see section F) and futility.

- Study sample sizes and timing of interim analyses should be based on the statistical success criteria for primary and secondary (if applicable) efficacy analyses and realistic, data-driven estimates of vaccine efficacy and incidence of COVID-19 (or SARS-CoV-2 infection) for the populations and locales in which the trial will be conducted.

F. Safety Considerations

- The general safety evaluation of COVID-19 vaccines, including the size of the safety database to support vaccine licensure, should be no different than for other preventive vaccines for infectious diseases. Safety assessments throughout clinical development should include:

  - Solicited local and systemic adverse events for at least 7 days after each study vaccination in an adequate number of study participants to characterize reactogenicity (including at least a subset of participants in late phase efficacy trials).

  - Unsolicited adverse events in all study participants for at least 21–28 days after each study vaccination.

  - Serious and other medically attended adverse events in all study participants for at least 6 months after completion of all study vaccinations. Longer safety monitoring may be warranted for certain vaccine platforms (e.g., those that include novel adjuvants).

  - All pregnancies in study participants for which the date of conception is prior to vaccination or within 30 days after vaccination should be followed for pregnancy outcomes, including pregnancy loss, stillbirth, and congenital anomalies.

- The pre-licensure safety database for preventive vaccines for infectious diseases typically consists of at least 3,000 study participants vaccinated with the dosing regimen intended for licensure. FDA anticipates that adequately powered efficacy trials for COVID-19 vaccines will be of sufficient size to provide an acceptable safety database for each of younger adult and elderly populations, provided that no significant safety concerns arise during clinical development that would warrant further pre-licensure evaluation.

- COVID-19 vaccine trials should periodically monitor for unfavorable imbalances between vaccine and control groups in COVID-19 disease outcomes, in particular for cases of severe COVID-19 that may be a signal for vaccine-associated ERD.

  - Studies should include pre-specified criteria for halting based on signals of potential vaccine-associated ERD.

  - FDA recommends use of an independent data safety monitoring board (DSMB) (Ref. 18) for vaccine-associated ERD and other safety signal monitoring, especially during later stage development.

VI. POST-LICENSURE SAFETY EVALUATION – KEY CONSIDERATIONS

A. General Considerations

- As with all licensed vaccines, there can be limitations in the safety database accrued from the pre-licensure clinical studies of a COVID-19 vaccine. For example:
    - The number of subjects receiving a COVID-19 vaccine in pre-licensure clinical studies may not be adequate to detect some adverse reactions that may occur infrequently.
    - Pre-licensure safety data in some subpopulations likely to receive a COVID-19 vaccine (e.g., pregnant individuals, or individuals with medical comorbidities) may be limited at the time of licensure.
    - For some COVID-19 vaccines, the safety follow-up period to monitor for possible vaccine-associated ERD and other adverse reactions may not have been completed for all subjects enrolled in pre-licensure clinical studies before the vaccine is licensed.

- For COVID-19 vaccines, it is likely that during the early postmarketing period, a large population might be vaccinated in a relatively short timeframe. Thus, FDA recommends early planning of pharmacovigilance activities before licensure.

- To facilitate accurate recording and identification of vaccines in health records, manufacturers should consider establishment of individual Current Procedural Terminology (CPT) codes and the use of bar codes to label the immediate container.

B. Pharmacovigilance Activities for COVID-19 Vaccines

- Routine pharmacovigilance for licensed biological products includes expedited reporting of serious and unexpected adverse events as well as periodic safety reports in accordance with 21 CFR 600.80 (Postmarketing reporting of adverse experiences).

- FDA recommends that at the time of a BLA submission for a COVID-19 vaccine, applicants submit a Pharmacovigilance Plan (PVP) as described in the FDA Guidance for Industry; E2E Pharmacovigilance Planning (Ref. 20). The contents of a PVP for a COVID-19 vaccine will depend on its safety profile and will be based on data, which includes the pre-licensure clinical safety database, preclinical data, and available safety information for related vaccines, among other considerations.

- The PVP should include actions designed to address all important identified risks, important potential risks or important missing information. Pharmacoepidemiologic studies or other actions to evaluate notable potential risks, such as vaccine-associated ERD, should be considered. FDA may recommend one or more of the following as components of a PVP for a COVID-19 vaccine:

- Submission of reports of specific adverse events of interest in an expedited manner beyond routine required reporting;
- Submission of adverse event report summaries at more frequent intervals than specified for routine required reporting;
- Ongoing and/or extended safety follow-up (under an IND) for vaccine-associated ERD of subjects enrolled in pre-licensure clinical studies;
- A pharmacoepidemiologic study to further evaluate (an) important identified or potential risk(s) from the clinical development program, such as vaccine-associated ERD or other uncommon or delayed-onset adverse events of special interest;
- A pregnancy exposure registry that actively collects information on vaccination during pregnancy and associated pregnancy and infant outcomes (Ref. 21).

C. Required Postmarketing Safety Studies

- Section 505(o)(3) of the FD&C Act (21 U.S.C. 355(o)(3)) authorizes FDA to require certain postmarketing studies or clinical trials for prescription drugs approved under section 505(b) of the FD&C Act (21 U.S.C. 355(b)) and biological products approved under section 351 of the PHS Act (42 U.S.C. 262) (Ref. 22). Under section 505(o)(3), FDA can require such studies or trials at the time of approval to assess a known serious risk related to the use of the drug, to assess signals of serious risk related to the use of the drug, or to identify an unexpected serious risk when available data indicate the potential for a serious risk. Under section 505(o)(3), FDA can also require such studies or trials after approval if FDA becomes aware of new safety information, which is defined at section 505-1(b)(3) of the FD&C Act (21 U.S.C. 355-1(b)(3)).

- For COVID-19 vaccines, FDA may require postmarketing studies or trials to assess known or potential serious risks when such studies or trials are warranted.

VII. DIAGNOSTIC AND SEROLOGICAL ASSAYS – KEY CONSIDERATIONS

- Diagnostic assays used to support the pivotal efficacy analysis (e.g., RT-PCR) should be sensitive and accurate for the purpose of confirming infection and should be validated before use.

- Assays used for immunogenicity evaluation should be suitable for their intended purpose of assessing relevant immune responses to vaccination and be validated before use in pivotal clinical trials.

VIII. ADDITIONAL CONSIDERATIONS

A. Additional Considerations in Demonstrating Vaccine Effectiveness

- Given the current state of knowledge about COVID-19, the most direct approach to demonstrate effectiveness for a COVID-19 vaccine candidate is based on clinical endpoint efficacy trials showing protection against disease (see section V. D. above).

- Once additional understanding of SARS-CoV-2 immunology, and specifically vaccine immune responses that might be reasonably likely to predict protection against COVID-19, is acquired, accelerated approval of a COVID-19 vaccine pursuant to section 506 of the FD&C Act (21 U.S.C. 356) and 21 CFR 601.40 may be considered if an applicant provides sufficient data and information to meet the applicable legal requirements. For a COVID-19 vaccine, it may be possible to approve a product under these provisions based on adequate and well-controlled clinical trials establishing an effect of the product on a surrogate endpoint (e.g., immune response) that is reasonably likely to predict clinical benefit.

- A potential surrogate endpoint likely would depend on the characteristics of the vaccine, such as antigen structure, mode of delivery, and antigen processing and presentation in the individual vaccinated. For example, an immune marker established for an adenovirus-based vaccine cannot be presumed applicable to a VSV-based vaccine, given that the two vaccines present antigen in different ways and engender different types of protective immune responses.

- Since SARS-CoV-2 represents a novel pathogen, a surrogate endpoint reasonably likely to predict protection from COVID-19 should ideally be derived from human efficacy studies examining clinical disease endpoints. If the surrogate endpoint is derived from other data sources, sponsors should consult the FDA to reach agreement on the use of the surrogate endpoint.

- An adequate dataset evaluating the safety of the vaccine in humans would need to be provided for consideration of licensure.

- For drugs granted accelerated approval, postmarketing confirmatory trials have been required to verify and describe the predicted effect on clinical benefit. These studies should usually be underway at the time of the accelerated approval, 21 CFR Part 601, Subpart E, and must be completed with due diligence (section 506(c)(3)(A) of the FD&C Act (21 U.S.C. 356(c)(3)(A)) and 21 CFR 601.41).

- If it is no longer possible to demonstrate vaccine effectiveness by way of conducting clinical disease endpoint efficacy studies, the use of a controlled human infection model to obtain evidence to support vaccine efficacy may be considered. However, many issues, including logistical, human subject protection, ethical, and scientific issues, would need to be satisfactorily addressed. At this

time no controlled human infection models for SARS-CoV-2 have been established or characterized.

B. Emergency Use Authorization

- An Emergency Use Authorization (EUA) may be issued only after several statutory requirements are met (section 564 of the FD&C Act (21 U.S.C. 360bbb-2)) (Ref. 23). Among these requirements is a determination by FDA that the known and potential benefits of a product, when used to diagnose, prevent, or treat serious or life-threatening diseases, outweigh the known and potential risks of the product.

- Issuance of an EUA (Ref. 23) may be appropriate for a COVID-19 vaccine provided the standard for issuing an EUA is met. Issuance of an EUA for a COVID-19 vaccine prior to the completion of large randomized clinical efficacy trials could reduce the ability to demonstrate effectiveness of the investigational vaccine in a clinical disease endpoint efficacy trial to support licensure, and such clinical disease endpoint efficacy trials may be needed to investigate the potential for vaccine-associated ERD. Thus, for a vaccine for which there is adequate manufacturing information, issuance of an EUA may be appropriate once studies have demonstrated the safety and effectiveness of the vaccine but before the manufacturer has submitted and/or FDA has completed its formal review of the biologics license application.

- In the case of investigational vaccines being developed for the prevention of COVID-19, any assessment regarding an EUA would be made on a case by case basis considering the target population, the characteristics of the product, the preclinical and human clinical study data on the product, and the totality of the available scientific evidence relevant to the product.

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* When finalized, this guidance will represent FDA's current thinking on this topic.

Marks Decl. Exhibit E

August 23, 2021

Meryl Nass, M.D.
Robert F. Kennedy, Jr.
Children's Health Defense
1227 North Peachtree Parkway
Suite 202
Peachtree City, GA 30269

Re: Citizen Petition (Docket Number FDA-2021-P-0460)

Dear Dr. Nass and Mr. Kennedy,

This letter responds to the citizen petition dated May 16, 2021 that you submitted to the Food and Drug Administration (FDA, the Agency, we) on behalf of Children's Health Defense (Petitioner) relating to: clinical trials, Emergency Use Authorization, licensure, and advertising and promotion of vaccines to prevent Coronavirus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (the Petition).

In the Petition, Petitioner requests that FDA:

1. "revoke all EUAs and refrain from approving any future EUA, NDA, or BLA for any COVID vaccine for all demographic groups";
2. "immediately refrain from allowing minors to participate in COVID vaccine trials, refrain from amending EUAs to include children, and immediately revoke all EUAs that permit vaccination of children under 16 for the Pfizer vaccine and under 18 for other COVID vaccines";
3. "immediately revoke tacit approval that pregnant women may receive any EUA or licensed COVID vaccines and immediately issue public guidance to that effect";
4. "immediately amend [FDA's] existing guidance for the use of the chloroquine drugs, ivermectin, and any other drugs demonstrated to be safe and effective against COVID…and immediately issue notifications to all stakeholders";
5. "issue guidance to the Secretary of the Defense [sic] and the President not to grant an unprecedented Presidential waiver of prior consent regarding COVID vaccines for Servicemembers [sic]";
6. "issue guidance…to affirm that all citizens have the option to accept or refuse administration of investigational COVID vaccines without adverse work, educational or other non-health related consequences"; and

7. "[p]ending revocation of COVID vaccine EUAs, FDA should issue guidance that all marketing and promotion of COVID vaccines must refrain from labeling them 'safe and effective.'"

Petition at 1-2.

In this letter, we discuss the safety of licensed and authorized vaccines. We then turn to the requests contained in the Petition. We consider each of your requests in light of the legal standards for FDA action, and provide our conclusions based on the facts, the science, and the law.

This letter responds to the Petition in full. FDA has carefully reviewed the Petition and other relevant information available to the Agency. Based on our review of these materials and for the reasons described below, we conclude that the Petition does not contain facts demonstrating any reasonable grounds for the requested action. In accordance with 21 CFR § 10.30(e)(3), and for the reasons stated below, FDA is denying the Petition.

Here is an outline of our response:

I. Background

There is currently a pandemic of respiratory disease, COVID-19, caused by a novel coronavirus, SARS-CoV-2. The COVID-19 pandemic presents an extraordinary challenge to global health. On January 31, 2020, the Department of Health and Human Services (HHS) issued a declaration

of a public health emergency related to COVID-19.[1]On February 4, 2020, pursuant to section 564 of the FD&C Act (21 U.S.C. § 360bbb-3), the Secretary of HHS determined that there is a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad, and that involves the virus that causes COVID-19.[2] On the basis of such determination, on March 27, 2020, the Secretary then declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic ("COVID-19 EUA Declaration"), pursuant to section 564(b)(1) of the FD&C Act.[3] In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.[4]

Commercial vaccine manufacturers and other entities are developing COVID-19 vaccine candidates, and clinical studies of these vaccines are underway and/or have been completed. Between December 11, 2020 and February 27, 2021, FDA issued emergency use authorizations for three vaccines to prevent COVID-19, including vaccines sponsored by Pfizer Inc. (Pfizer); ModernaTX, Inc. (Moderna); and Janssen Biotech, Inc. (Janssen), a pharmaceutical company of Johnson & Johnson. FDA received a Biologics License Application (BLA) for the COVID-19 vaccine, BNT162b2, intended to prevent COVID-19 in individuals 16 years of age and older. As announced by FDA on August 23, 2021, the Agency is issuing a biologics license for this COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty) to BioNTech Manufacturing GmbH.[5]

II. Vaccines That Are FDA-Licensed or Receive an Emergency Use Authorization Meet Relevant Statutory Requirements

a. Vaccines that are FDA-Licensed are Safe

i. Vaccines that are FDA-Licensed Are Shown to Be Safe at the Time of Licensure

FDA has a stringent regulatory process for licensing vaccines.[6,7] The Public Health Service Act (PHS Act) authorizes FDA to license biological products, including vaccines, if they have

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[1] Secretary of Health and Human Services Alex M. Azar, Determination that a Public Health Emergency Exists. (Originally issued on Jan. 31, 2020, and subsequently renewed), https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx

[2] HHS, Determination of Public Health Emergency, 85 FR 7316, February 7, 2020, https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.

[3] HHS, Emergency Use Authorization Declaration, 85 FR 18250, April 1, 2020, https://www.federalregister.gov/documents/2020/04/01/2020-06905/emergency-use-authorization-declaration.

[4] Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak, issued March 13, 2020, https://trumpwhitehouse.archives.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/ .

[5] BioNTech Manufacturing GmbH is the biologics license holder for this vaccine, which is manufactured by Pfizer Inc. for BioNTech Manufacturing GmbH (hereinafter "BioNTech"). The basis for FDA's licensure decision is set forth in FDA's Summary Basis for Regulatory Action (SBRA) for the BioNTech application. This memorandum will be posted on fda.gov. We incorporate by reference the SBRA for the BLA.

[6] CDC, Ensuring the Safety of Vaccines in the United States, February 2013, https://www.cdc.gov/vaccines/hcp/patient-ed/conversations/downloads/vacsafe-ensuring-bw-office.pdf.

[7] FDA, Vaccine Safety Questions and Answers, last updated March 2018, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/vaccine-safety-questions-and-answers.

been demonstrated to be "safe, pure, and potent."[8] Prior to approval by FDA, vaccines are extensively tested in non-clinical studies and in humans. FDA's regulations describe some of the extensive data and information that each sponsor of a vaccine must submit to FDA in order to demonstrate the product's safety before FDA will consider licensing the vaccine. FDA requires that the sponsor's biologics license application (BLA) include, among other things, data derived from nonclinical and clinical studies showing the product's safety, purity, and potency; a full description of manufacturing methods for the product; data establishing the product's stability through the dating period; and a representative sample of the product and summaries of results of tests performed on the lot(s) represented by the sample.[9]

As is evident from the language of the PHS Act and FDA's regulations, the licensure process for a vaccine requires the sponsor to establish, through carefully controlled laboratory and clinical studies, as well as through other data, that the product is safe and effective for its approved indication(s) and use. FDA's multidisciplinary review teams then rigorously evaluate the sponsor's laboratory and clinical data, as well as other information, to help assess whether the safety, purity, and potency of a vaccine has been demonstrated.[10] Only when FDA's standards are met is a vaccine licensed.

FDA regulations explicitly state that "[a]pproval of a biologics license application or issuance of a biologics license shall constitute a determination that the establishment(s) and the product meet applicable requirements to ensure the continued safety, purity, and potency of such products."[11] Therefore, the manufacturers of vaccines that have been licensed in the U.S. have necessarily demonstrated the safety of the vaccines within the meaning of the applicable statutory and regulatory provisions before the vaccines were licensed and allowed to be marketed.

For more information on FDA's thorough process for evaluating the safety of vaccines, see Appendix I of this letter, *Aspects of Vaccine Development and Process for Licensure*.

ii. Vaccine Safety Continues to Be Monitored Post-Licensure

FDA's oversight of vaccine safety continues after licensure of the product. Once the licensed vaccine is on the market, post-marketing surveillance of vaccine safety is conducted in order to detect any rare, serious, or unexpected adverse events, as well as to monitor vaccine lots. FDA employs multiple surveillance systems and databases to continue to evaluate the safety of these vaccines. In certain cases, FDA may require the manufacturer to conduct post-marketing studies to further assess known or potential serious risks.

b. An Emergency Use Authorization for a COVID-19 Preventative Vaccine Is Issued Only If the Relevant Statutory Standards Are Met

Congress established the Emergency Use Authorization (EUA) pathway to ensure that, during public health emergencies, potentially lifesaving medical products could be made available before being approved. The EUA process allows the Secretary of HHS, in appropriate circumstances, to declare that EUAs are justified for products to respond to certain types of

[8] 42 U.S.C. § 262(a)(2)(C)(i)(I).
[9] 21 CFR § 601.2(a).
[10] FDA, Vaccines, last updated January 2021, https://www.fda.gov/vaccines-blood-biologics/vaccines.
[11] 21 CFR § 601.2(d) (emphasis added).

threats. When such a declaration is made, FDA may issue an EUA, which is different from the regulatory process for vaccine licensure.

Section 564 of the Food Drug & Cosmetic Act (FD&C Act) (21 U.S.C. § 360bbb-3) authorizes FDA to, under certain circumstances, issue an EUA to allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by chemical, biological, radiological, or nuclear threat agents when there are no adequate, approved, and available alternatives.

On February 4, 2020, pursuant to section 564(b)(1)(C) of the FD&C Act (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of HHS determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States (U.S.) citizens living abroad, and that involves the virus that causes COVID-19.[12] On the basis of such determination, on March 27, 2020, the Secretary then declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to section 564(b)(1) of the FD&C Act (21 U.S.C. § 360bbb-3(b)(1)).[13]

Based on this declaration and determination, under section 564(c) of the FD&C Act (21 U.S.C. § 360bbb-3(c)), FDA may issue an EUA during the COVID-19 pandemic after FDA concludes that the following statutory requirements are met:

- The agent referred to in the March 27, 2020 EUA declaration by the Secretary (SARS-CoV-2) can cause a serious or life-threatening disease or condition.

- Based on the totality of scientific evidence available, including data from adequate and well-controlled trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing such serious or life-threatening disease or condition that can be caused by SARS-CoV-2.

- The known and potential benefits of the product, when used to diagnose, prevent, or treat the identified serious or life-threatening disease or condition, outweigh the known and potential risks of the product.

- There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the disease or condition.

Although EUAs are governed under a different statutory framework than BLAs, FDA has made clear that issuance of an EUA for a COVID-19 vaccine would require that the vaccine demonstrated clear and compelling safety and efficacy in a large, well-designed Phase 3 clinical trial. In the guidance document *Emergency Use Authorization for Vaccines to Prevent COVID-19* (October 2020 Guidance), FDA has provided recommendations that describe key information

[12] HHS, Determination of Public Health Emergency, 85 FR 7316, February 7, 2020, https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.
[13] HHS, Emergency Use Authorization Declaration, 85 FR 18250, April 1, 2020, https://www.federalregister.gov/documents/2020/04/01/2020-06905/emergency-use-authorization-declaration.

that would support issuance of an EUA for a vaccine to prevent COVID-19.[14] In the October 2020 Guidance, FDA explained that, in the case of such investigational vaccines, any assessment regarding an EUA will be made on a case-by-case basis considering the target population, the characteristics of the product, the preclinical and human clinical study data on the product, and the totality of the available scientific evidence relevant to the product.[15] FDA has also stated, in this guidance, that for a COVID-19 vaccine for which there is adequate manufacturing information to ensure its quality and consistency, issuance of an EUA would require a determination by FDA that the vaccine's benefits outweigh its risks based on data from at least one well-designed Phase 3 clinical trial that demonstrates the vaccine's safety and efficacy in a clear and compelling manner.[16]

A Phase 3 trial of a vaccine is generally a large clinical trial in which a large number of people are assigned to receive the investigational vaccine or a control. In general, in Phase 3 trials that are designed to show whether a vaccine is effective, neither people receiving the vaccine nor those assessing the outcome know who received the vaccine or the comparator.

In a Phase 3 study of a COVID-19 vaccine, the efficacy of the investigational vaccine to prevent disease will be assessed by comparing the number of cases of disease in each study group. For Phase 3 trials, FDA has recommended to manufacturers in guidance that the vaccine should be at least 50% more effective than the comparator, and that the outcome be reliable enough so that it is not likely to have happened by chance.[17] During the entire study, subjects will be monitored for safety events. If the evidence from the clinical trial meets the pre-specified criteria for success for efficacy and the safety profile is acceptable, the results from the trial can potentially be submitted to FDA in support of an EUA request.

Investigational COVID-19 vaccines continue to be studied in Phase 2 or Phase 3 trials. Following clinical trials, manufacturers analyze data prior to submitting to FDA a BLA to request approval from FDA to market the vaccine. A BLA for a new vaccine includes information and data regarding the safety, effectiveness, chemistry, manufacturing and controls, and other details regarding the product. During the current public health emergency, manufacturers may, with the requisite data and taking into consideration input from FDA, choose to submit a request for an EUA.

Importantly, FDA has made clear that any vaccine that meets FDA's standards for effectiveness is also expected to meet the Agency's safety standards. FDA has stated that the duration of safety follow-up for a vaccine authorized under an EUA may be shorter than with a BLA (which the Agency expects will ultimately be submitted by manufacturers of vaccines that are authorized under an EUA). Specifically, FDA's guidance to manufacturers recommends that data from Phase 3 studies to support an EUA include a median follow-up duration of at least 2 months after completion of the full vaccination regimen.[18] Furthermore, robust safety monitoring is conducted after a vaccine is made available. The monitoring systems include the

[14] Emergency Use Authorization for Vaccines to Prevent COVID-19; Guidance for Industry, October 2020 (October 2020 Guidance), https://www.fda.gov/media/142749/download.
[15] Id. at 3.
[16] Id. at 4.
[17] Development and Licensure of Vaccines to Prevent COVID-19; Guidance for Industry, June 2020, https://www.fda.gov/media/139638/download.
[18] October 2020 Guidance at 10-11.

Vaccine Adverse Event Reporting System (VAERS), FDA's Biologics Effectiveness and Safety (BEST) System, and the Centers for Disease Control and Prevention's (CDC) Vaccine Safety Datalink. In addition, FDA has a partnership with the Centers for Medicare & Medicaid Services (CMS) to study vaccine safety. Other tools to monitor vaccine safety are under development. Collectively, these programs will help detect any new, unusual and rare side effects after vaccination that might not have been observed during clinical trials, as well as monitor for increases in any known side effects.

It is FDA's expectation that, following submission of an EUA request and issuance of an EUA, a sponsor would continue to evaluate the vaccine and would also work towards submission of a BLA as soon as possible.

III. Discussion

The Petition makes a request regarding clinical trials of COVID-19 vaccines that include or propose to include children. FDA's investigational new drug process applies to the development of new drugs and biological products, including vaccines.[19]

a. Investigational New Drugs

Before a vaccine is licensed (approved) by FDA for use by the public, FDA requires that it undergo a rigorous and extensive development program to determine the vaccine's safety and effectiveness. This development program encompasses preclinical research (laboratory research, animal studies[20]) and clinical studies. At the preclinical stage, the sponsor focuses on collecting the data and information necessary to establish that the product will not expose humans to unreasonable risks when used in limited, early-stage clinical studies. Clinical studies, in humans, are conducted under well-defined conditions and with careful safety monitoring through all the phases of the investigational new drug process. FDA's regulations governing the conduct of clinical investigations are set out at 21 CFR Part 312.

Before conducting a clinical investigation in the U.S. in which a new drug or biological product is administered to humans, a sponsor must submit an investigational new drug application (IND) to FDA.[21] The IND describes the proposed clinical study in detail and, among other things, helps protect the safety and rights of human subjects.[22] In addition to other information, an IND must contain information on clinical protocols and clinical investigators. Detailed protocols for proposed clinical studies permit FDA to assess whether the initial-phase trials will expose subjects to unnecessary risks. Information on the qualifications of clinical investigators (professionals, generally physicians, who oversee the administration of the experimental drug) permits FDA to assess whether they are qualified to fulfill their clinical trial duties. The IND

[19] See 21 CFR § 312.2 (explaining that the IND regulations apply to clinical investigations of both drugs and biologics).

[20] We support the principles of the "3Rs," to reduce, refine, and replace animal use in testing when feasible. We encourage sponsors to consult with us if they wish to use a non-animal testing method they believe is suitable, adequate, validated, and feasible. We will consider if such an alternative method could be assessed for equivalency to an animal test method.

[21] See 21 CFR § 312.20(a).

[22] For additional information regarding the IND review process and general responsibilities of sponsor-investigators related to clinical investigations see Investigational New Drug Applications Prepared and Submitted by Sponsor-Investigators; Draft Guidance for Industry, May 2015, https://www.fda.gov/media/92604/download.

includes commitments to obtain informed consent from the research subjects, to obtain review of the study by an institutional review board (IRB),[23] and to adhere to the investigational new drug regulations.

Once the IND is submitted, the sponsor must wait 30 calendar days before initiating any clinical trials, unless FDA informs the sponsor that the trial may begin earlier. During this time, FDA reviews the IND. FDA's primary objectives in reviewing an IND are, in all phases of the investigation, to assure the safety and rights of subjects, and, in Phase 2 and Phase 3, to help assure that the quality of the scientific evaluation of drugs is adequate to permit an evaluation of the drug's effectiveness and safety.[24]

FDA's regulations provide that, once an IND is in effect, the sponsor may conduct a clinical investigation of the product, with the investigation generally being divided into three phases. With respect to vaccines, the initial human studies, referred to as Phase 1 studies, are generally safety and immunogenicity studies performed in a small number of closely monitored subjects. Phase 2 studies may include up to several hundred individuals and are designed to provide information regarding the incidence of common short-term side effects such as redness and swelling at the injection site or fever and to further describe the immune response to the investigational vaccine. If an investigational new vaccine progresses past Phase 1 and Phase 2 studies, it may progress to Phase 3 studies. For Phase 3 studies, the sample size is often determined by the number of subjects required to establish the effectiveness of the new vaccine, which may be in the thousands or tens of thousands of subjects. Phase 3 studies provide the critical documentation of effectiveness and important additional safety data required for licensing.

Additionally, FDA regulations require that an IRB must review clinical investigations involving children as subjects covered by 21 CFR 50, subpart D and only approve those clinical investigations involving children as subjects that satisfy the criteria in 21 CFR 50, subpart D, Additional Safeguards for Children in Clinical Investigations. As explained in the preamble to the final rule, "[t]hese safeguards are intended to ensure that the rights and welfare of children who participate in clinical investigations are adequately protected."[25]

At any stage of development, if data raise significant concerns about either safety or effectiveness, FDA may request additional information or studies; FDA may also halt ongoing clinical studies. The FD&C Act provides a specific mechanism, called a "clinical hold," for prohibiting sponsors of clinical investigations from conducting the investigation (section

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[23] The IRB is a panel of scientists and non-scientists in hospitals and research institutions that oversees clinical research. IRBs approve clinical study protocols, which describe the type of people who may participate in the clinical study; the schedule of tests and procedures; the medications and dosages to be studied; the length of the study; the study's objectives; and other details. IRBs make sure that the study is acceptable, that participants have given consent and are fully informed of the risks, and that researchers take appropriate steps to protect patients from harm. See The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective web page, last updated November 2017, https://www.fda.gov/drugs/drug-information-consumers/fdas-drug-review-process-ensuring-drugs-are-safe-and-effective.

[24] 21 CFR § 312.22(a).

[25] Preamble to final rule, "Additional Safeguards for Children in Clinical Investigations of Food and Drug Administration-Regulated Products" (78 FR 12937 at 12938, February 26, 2013), https://www.federalregister.gov/documents/2013/02/26/2013-04387/additional-safeguards-for-children-in-clinical-investigations-of-food-and-drug.

505(i)(3) of the FD&C Act; 21 U.S.C. § 355(i)(3)), and FDA's IND regulations in 21 CFR § 312.42 identify the circumstances that may justify a clinical hold. Generally, a clinical hold is an order issued by FDA to the sponsor of an IND to delay a proposed clinical investigation or to suspend an ongoing investigation.[26]

b. The Citizen Petition

i. Petitioner's Request to Revoke all Emergency Use Authorizations for COVID-19 Vaccines and Refrain from Issuing any Future EUA or Approving any Future NDA, or BLA for any COVID-19 Vaccine for all Demographic Groups because the Current Risks of Serious Adverse Events or Deaths Outweigh the Benefits, and Because Existing, Approved Drugs Provide Highly Effective Prophylaxis and Treatment against COVID-19, Mooting the EUAs

Petitioner makes several requests regarding COVID-19 vaccines in the Petition and, in support of these requests, argues that (1) the rates of serious adverse events or deaths outweigh the benefits of these vaccines and (2) approved drugs provide highly effective prophylaxis/treatment against COVID, thereby "mooting" the EUAs. We interpret this as an argument that the authorizations of COVID-19 vaccines to date did not meet the relevant legal standard. Below, we address each of Petitioner's requests and the information provided by Petitioner in support of these requests.

1. Petitioner's Request to Revoke all Emergency Use Authorizations for COVID-19 Vaccines

In this section, we address Petitioner's request that FDA "revoke all EUAs . . . for any COVID vaccine for all demographic groups because the current risks of serious adverse events or deaths outweigh the benefits, and because existing, approved drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs." Petition at 1.

a. EUAs for COVID-19 Vaccines

As noted above in Section II above, FDA may issue an EUA during the COVID-19 public health emergency after FDA concludes that the statutory requirements provided in section 564 of the FD&C Act are met. In an attempt to prevent the spread of disease and to control the pandemic, numerous COVID-19 vaccine candidates have been developed. COVID-19 vaccines that have been developed or are currently in development are based on various platforms and include mRNA, DNA, viral vectored, subunit, inactivated, and live-attenuated vaccines. Most COVID-19 candidate vaccines express the spike protein or parts of the spike protein, i.e., the receptor binding domain, as the immunogenic determinant.

To date, FDA has issued EUAs for three COVID-19 vaccines ("the Authorized COVID-19 Vaccines"), as described in the Scope of Authorization for these COVID-19 vaccines, pursuant

[26] 21 CFR § 312.42(a).

to section 564 of the FD&C Act. Additionally, FDA has expanded the authorized age range for one COVID-19 vaccine.

- On December 11, 2020, FDA issued an EUA for emergency use of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 in individuals 16 years of age and older.
    - On May 10, 2021, FDA authorized the emergency use of Pfizer-BioNTech COVID-19 Vaccine to include individuals 12 through 15 years of age.
- On December 18, 2020, FDA issued an EUA for emergency use of Moderna COVID-19 Vaccine for the prevention of COVID-19 in individuals 18 years of age and older.
- On February 27, 2021, FDA issued an EUA for emergency use of Janssen COVID-19 Vaccine for the prevention of COVID-19 in individuals 18 years of age and older.

The Agency issued these EUAs after a thorough evaluation of scientific data regarding the safety, effectiveness, and manufacturing information (which helps ensure product quality and consistency) of these COVID-19 vaccines and after reaching a determination that these vaccines meet the statutory requirements under section 564 of the FD&C Act. This letter incorporates by reference the EUA Review Memoranda for the Authorized COVID-19 Vaccines,[27] which discuss this determination, and the data upon which it was based, in detail as well as the Summary Basis of Regulatory Action for the BioNTech COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty).[28]

Petitioner argues that the authorizations for these vaccines should be revoked, and that future COVID vaccines should not be authorized or licensed, because (1) "the current risks of serious adverse events or deaths outweigh the benefits," and (2) "existing, approved drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs." We address each of Petitioner's arguments, and data submitted in the Petition in support of these arguments, below.

FDA disagrees with Petitioner's position that the Authorized COVID-19 Vaccines did not meet the statutory standard at the time of authorization, and finds no basis in the information submitted in the Petition, or in any postmarket data regarding these vaccines, to support a revocation of any of these authorizations. FDA is not aware of any information indicating that the known and potential benefits of the Authorized COVID-19 Vaccines are outweighed by their known and potential risks, nor has Petitioner provided any such information in the Petition. The

[27] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum (Dec. 11, 2020), https://www.fda.gov/media/144416/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age (May 10, 2021), https://www.fda.gov/media/148542/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of an Additional Dose in Certain Immunocompromised Individuals (August 12, 2021) https://www.fda.gov/media/151613/download; FDA, Moderna COVID-19 Vaccine EUA Decision Memorandum (Dec. 18, 2020), https://www.fda.gov/media/144673/download; FDA, Moderna COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of an Additional Dose in Certain Immunocompromised Individuals (August 12, 2021) https://www.fda.gov/media/151611/download; FDA, Janssen COVID-19 Vaccine EUA Decision Memorandum (Feb. 27, 2021), https://www.fda.gov/media/146338/download.

[28] This letter incorporates by reference FDA's Summary Basis for Regulatory Action (SBRA) for the BioNTech BLA. This memorandum will be posted on www.fda.gov.

known and potential benefits of the Authorized COVID-19 Vaccines continue to outweigh their known and potential risks, given the risk of COVID-19 and related, potentially severe, complications. Furthermore**,** as explained below, there is no adequate, approved, and available alternative to the Authorized COVID-19 Vaccines for preventing COVID-19. Accordingly, this request is denied.

b. Standard for Revocation of EUAs is not Met for the Authorized COVID-19 Vaccines

Section 564(g)(2) of the FD&C Act provides the standard for revocation of an EUA. Under this statutory authority, FDA may revise or revoke an EUA if:

> (A) the circumstances described under [section 564(b)(1) of the FD&C Act] no longer exist;
> (B) the criteria under [section 564(c) of the FD&C Act] for issuance of such authorization are no longer met; or
> (C) other circumstances make such revision or revocation appropriate to protect the public health or safety.

FDA's guidance entitled *Emergency Use Authorization of Medical Products and Related Authorities* ("EUA Guidance"),[29] notes that once an EUA is issued for a product, in general, that EUA will remain in effect for the duration of the EUA declaration under which it was issued, "unless the EUA is revoked because the criteria for issuance . . . are no longer met or revocation is appropriate to protect public health or safety (section 564(f),(g) [of the FD&C Act])."[30] Regarding the circumstances that would make a revision or revocation appropriate to protect the public health or safety, FDA explains in the EUA guidance that

> Such circumstances may include significant adverse inspectional findings (e.g., when an inspection of the manufacturing site and processes has raised significant questions regarding the purity, potency, or safety of the EUA product that materially affect the risk/benefit assessment upon which the EUA was based); reports of adverse events (number or severity) linked to, or suspected of being caused by, the EUA product; product failure; product ineffectiveness (such as newly emerging data that may contribute to revision of the FDA's initial conclusion that the product "may be effective" against a particular CBRN agent); a request from the sponsor to revoke the EUA; a material change in the risk/benefit assessment based on evolving understanding of the disease or condition and/or availability of authorized MCMs; or as provided in section 564(b)(2), a change in the approval status of the product may make an EUA unnecessary.

[29] Emergency Use Authorization of Medical Products and Related Authorities; Guidance for Industry and Other Stakeholders, January 2017 (EUA Guidance), https://www.fda.gov/media/97321/download.
[30] Id. at 28.

EUA guidance at 29.

Thus, in addressing Petitioner's request for FDA to revoke the Authorized COVID-19 Vaccines, we assess whether any of the statutory conditions under which FDA may revoke an EUA are met, namely: (1) whether the circumstances justifying their issuance under section 564(b)(1) of the FD&C Act no longer exist, (2) whether the criteria for their issuance under section 564(c) of the FD&C Act are no longer met, and (3) whether other circumstances make a revision or revocation appropriate to protect the public health or safety.

i. Circumstances Continue to Justify the Issuance of the EUAs for the Authorized COVID-19 Vaccines

As explained above in section II.b., on February 4, 2020, pursuant to section 564(b)(1)(C) of the FD&C Act (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of HHS determined that there is a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad, and that involves the virus that causes COVID-19.[31] On the basis of such determination, on March 27, 2020, the Secretary then declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic ("COVID-19 EUA Declaration"), pursuant to section 564(b)(1) of the FD&C Act (21 U.S.C. § 360bbb-3(b)(1)).[32]

Based on this declaration and determination, under section 564(c) of the FD&C Act (21 U.S.C. § 360bbb-3(c)), FDA may issue an EUA during the COVID-19 pandemic after FDA concludes that the statutory requirements provided in section 564(c) are met. Section 564(b)(2) sets forth the statutory standard for termination of an EUA declaration. An EUA declaration remains in place until the earlier of: (1) a determination by the HHS Secretary that the circumstances that precipitated the declaration have ceased (after consultation as appropriate with the Secretary of Defense) or (2) a change in the approval status of the product such that the authorized use(s) of the product are no longer unapproved. Neither of those statutory criteria is satisfied with respect to the Authorized COVID-19 Vaccines.

Thus, the circumstances described under section 564(b)(1) of the FD&C Act continue to exist. FDA therefore is not revoking the EUAs for the Authorized COVID-19 Vaccines under the authority in section 564(g)(2)(A) of the FD&C Act.

ii. The Criteria for The Issuance of the Authorized COVID-19 Vaccines Continue to Be Met

This section describes in detail why the criteria under section 564(c) of the FD&C Act continue to be met with respect to the Authorized COVID-19 Vaccines and why, therefore, FDA is not revoking the EUAs for the Authorized COVID-19 Vaccines under the authority in section 564(g)(2)(B) of the FD&C Act.

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[31] HHS, Determination of Public Health Emergency, 85 FR 7316, February 7, 2020, https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.
[32] HHS, Emergency Use Authorization Declaration, 85 FR 18250, April 1, 2020, https://www.federalregister.gov/documents/2020/04/01/2020-06905/emergency-use-authorization-declaration.

1. Serious or life-threatening disease or condition.

Section 564(c)(1) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude "the agent(s) referred to in [the HHS Secretary's EUA declaration] can cause a serious or life-threatening disease or condition." FDA has concluded that SARS-CoV-2, which is the subject of the EUA declaration, meets this standard.

The SARS-CoV-2 pandemic continues to present an extraordinary challenge to global health and, as of August 3, 2021, has caused more than 199 million cases of COVID-19 and claimed the lives of more than 4.2 million people worldwide.[33] In the United States, more than 34 million cases and over 611,000 deaths have been reported to the CDC.[34] On January 31, 2020, the U.S. Secretary of Health and Human Services (HHS) declared a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS, and the U.S. President declared a national emergency in response to COVID-19 on March 13, 2020.
FDA is not aware of science indicating that there is any change in the ability of the SARS-CoV-2 virus to cause a serious or life-threatening disease or condition, namely COVID-19, nor has Petitioner provided any information about such a change. Therefore, the criterion under section 564(c)(1) continues to be met with respect to the Authorized COVID-19 Vaccines.

2. Evidence of Effectiveness

Section 564(c)(2)(A) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude "based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled trials, if available, it is reasonable to believe that the product may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition that can be caused by SARS-CoV-2."

FDA issued EUAs for the Authorized COVID-19 Vaccines after determining that, among other things, these products were demonstrated in clinical trials to prevent symptomatic and severe COVID-19 in vaccinated clinical trial subjects.[35] FDA is not aware of any data that changes this conclusion, nor has Petitioner provided any such data in the Petition. This section addresses Petitioner's arguments regarding the effectiveness of the Authorized COVID-19 vaccines and explains why the information submitted by Petitioner does not change FDA's analysis regarding the effectiveness of these vaccines.

After FDA approves a vaccine or authorizes a vaccine for emergency use, the vaccine continues to be studied to determine how well it works under real-world conditions. FDA, CDC, and other federal partners have been assessing, and will continue to assess, COVID-19 vaccine

[33] Johns Hopkins University School of Medicine, Coronavirus Resource Center, https://coronavirus.jhu.edu/map.html.
[34] CDC, COVID Data Tracker, https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases.
[35] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum (Dec. 11, 2020), at 23, https://www.fda.gov/media/144416/download; FDA, Moderna COVID-19 Vaccine EUA Decision Memorandum (Dec. 18, 2020), at 24, https://www.fda.gov/media/144673/download; FDA, Janssen COVID-19 Vaccine EUA Decision Memorandum (Feb. 27, 2021), at 25, https://www.fda.gov/media/146338/download.

effectiveness under real-world conditions. Such evaluations will help us understand if vaccines are performing as expected outside the more controlled setting of a clinical trial.

Petitioner raises concerns regarding the post-market effectiveness of the Authorized COVID-19 Vaccines (Petition at 6). Petitioner points to CDC-reported "breakthrough cases" to suggest that the Authorized COVID-19 Vaccines are not effective and argues that the EUAs for the Authorized COVID-19 Vaccines should therefore be revoked because the current risks of these vaccines outweigh their benefits. This perspective fails to recognize several important points regarding the concept of breakthrough cases and regarding the CDC publication cited in the Petition.

First, we note that the Letters of Authorization for the Authorized COVID-19 Vaccines require EUA-holders to report to VAERS "cases of COVID-19 that result in hospitalization or death, that are reported to [the EUA holder]."[36] Thus, the possibility that individuals who received one of the Authorized COVID-19 Vaccines could develop breakthrough COVID-19 cases was recognized by FDA when the Agency evaluated the EUA requests for these vaccines and determined that their known and potential benefits outweigh their known and potential and risks.

Second, the Authorized COVID-19 Vaccines are indicated to prevent *symptomatic* COVID-19,[37] not to prevent SARS-CoV-2 infection. Over 353 million doses of COVID-19 vaccines have been administered in the United States[38] and FDA's ongoing post authorization monitoring informs us that the known and potential benefits continue to outweigh the known and potential risks. Additionally, CDC's post-authorization data regarding the Authorized COVID-19 Vaccines continues to support FDA's conclusion that these vaccines prevent *symptomatic* COVID-19.[39]

Third, a vaccine does not need to be 100% effective in preventing the target disease in order to meet the licensure or EUA standard. It is expected that some vaccinated individuals will contract the target disease despite having been vaccinated against it. No FDA licensed or authorized vaccine is 100% effective, but scientific data has nevertheless demonstrated that vaccinations have been a very effective approach to protecting the public's health in the United States.[40]

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[36] Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors, Pfizer-BioNTech COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine, https://www.fda.gov/media/144413/download; Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors, Moderna COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine, https://www.fda.gov/media/144637/download; Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors, Janssen COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine, https://www.fda.gov/media/146304/download.

[37] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum (Dec. 11, 2020), at 23, https://www.fda.gov/media/144416/download; FDA, Moderna COVID-19 Vaccine EUA Decision Memorandum (Dec. 18, 2020), at 24, https://www.fda.gov/media/144673/download; FDA, Janssen COVID-19 Vaccine EUA Decision Memorandum (Feb. 27, 2021), at 25, https://www.fda.gov/media/146338/download.

[38] CDC, COVID Data Tracker Weekly Review, Interpretive Summary for August 13, 2021, https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html

[39] CDC, COVID-19 Vaccine Effectiveness Research, https://www.cdc.gov/vaccines/covid-19/effectiveness-research/protocols.html.

[40] Vaccine Safety Questions and Answers, last updated March 2018, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/vaccine-safety-questions-and-answers.

Similarly, a COVID-19 vaccine need not be 100% effective in preventing symptomatic COVID-19, or even close to 100% effective in doing so, in order to have a significant effect in altering the course of the COVID-19 pandemic. As FDA noted in its June 2020 Guidance for Industry, Development and Licensure of Vaccines to Prevent COVID-19, ("The Vaccine Development and Licensure Guidance") "[t]o ensure that a widely deployed COVID-19 vaccine is effective, the primary efficacy endpoint point estimate for a placebo-controlled efficacy trial should be at least 50%, and the statistical success criterion should be that the lower bound of the appropriately alpha-adjusted confidence interval around the primary efficacy endpoint point estimate is >30%."[41] This statistical consideration provided in the Vaccine Development and Licensure Guidance reflects FDA's assessment that a vaccine with at least 50 percent efficacy would have a significant impact on disease, both at the individual and societal level.

Finally, we note that Petitioner refers to "CDC-reported" breakthrough cases in support of its argument that there are effectiveness concerns with the Authorized COVID-19 Vaccines but fails to acknowledge that CDC reported a set of breakthrough cases that includes a large proportion of *asymptomatic* individuals who tested positive for SARS-CoV-2. Petitioner thus applies a narrower definition of the term "breakthrough case" to a set of cases than CDC has in its COVID-19 Vaccine Breakthrough Case Investigation.[42] Petitioner refers to breakthrough cases in which vaccinated individuals "fall ill and potentially transmit the virus" (Petition at 6) and states that "CDC reported over 9,000 'breakthrough cases' and 132 COVID-caused deaths among vaccinated people." Petition at 6.

CDC's objective in the COVID-19 Vaccine Breakthrough Case Investigation is to[43] ensure the COVID-19 vaccines are working as expected and to "identify patterns or trends" in:

- Patients' characteristics, such as age or underlying medical conditions
- The specific vaccine that patients received
- Whether a specific SARS-CoV-2 variant caused the infections"[44]

The objective of this investigation is not simply to count symptomatic COVID-19 cases. Currently, COVID-19 cases are increasing again in nearly all states. The highest rate of COVID-19 case spread is in areas with low vaccination rates.[45]

Petitioner's submitted data regarding CDC-reported "breakthrough cases" therefore does not present new data or information that the Agency has not previously considered regarding the effectiveness of the Authorized COVID-19 Vaccines. Available data regarding effectiveness of

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[41] Development and Licensure of Vaccines to Prevent COVID-19, Guidance for Industry, June 2020, at 14, https://www.fda.gov/media/139638/download.

[42] CDC, COVID-19 Vaccine Breakthrough Case Investigations and Reporting, https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html.

[43] CDC, COVID-19 Vaccine Breakthrough Case Investigations and Reporting, https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html.

[44] CDC, COVID-19 Vaccine Breakthrough Case Investigations and Reporting, https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html.

[45] "As of July 22 [2021], 35% of U.S. counties are experiencing high levels of community transmission. COVID-19 cases are on the rise in nearly 90% of U.S. jurisdictions, and we are seeing outbreaks in parts of the country that have low vaccination coverage." CDC, COVID Data Tracker Weekly Review, Interpretive Summary for July 23, 2021, available at https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html.

the Authorized COVID-19 Vaccines continues to support the conclusion that these vaccines may be effective in preventing COVID-19. FDA is not aware of any data that changes this conclusion, nor has Petitioner provided any such data in the Petition. Therefore, the criterion under section 564(c)(2)(A) continues to be met with respect to the Authorized COVID-19 Vaccines.

3. Benefit-Risk Analysis

Section 564(c)(2)(B) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude "the known and potential benefits of the product, when used to diagnose, prevent, or treat [the identified serious or life-threatening disease or condition], outweigh the known and potential risks of the product . . . ." Petitioner argues that the current risks of serious adverse events or deaths associated with the Authorized COVID-19 Vaccines outweigh the benefits of COVID-19 vaccines. This section addresses Petitioner's arguments regarding the safety of COVID-19 vaccines and explains why the information submitted by Petitioner does not change FDA's analysis regarding the benefits and risks of the Authorized COVID-19 Vaccines.

FDA issued EUAs for the Authorized COVID-19 Vaccines after reaching a determination regarding each of these vaccines that, among other things, the known and potential benefits of the vaccine, when used to prevent COVID-19, outweigh its known and potential risks.[46] FDA is not aware of any data that changes this determination, nor has Petitioner provided any such data in the Petition. The known and potential benefits of the Authorized COVID-19 Vaccines, when used to prevent COVID-19, continue to outweigh their known and potential risks, given the risk of COVID-19 and related, potentially severe, complications.

Petitioner raises numerous concerns regarding safety of the Authorized COVID-19 Vaccines (Petition at 2-6) and asserts that the EUAs for the Authorized COVID-19 Vaccines should be revoked due in part to these safety concerns. For reasons explained below, FDA disagrees with Petitioner's assertions regarding the safety of the Authorized COVID-19 Vaccines.

As an initial matter, we note that the Petition discusses several assertions made by CDC and requests that have been directed to CDC. For requests intended for CDC, you should contact CDC directly.

a. Petitioner's Claims Regarding VAERS Data

[46] For an extensive discussion of FDA's analysis of the clinical trial data regarding the risks and benefits of each of the authorized COVID-19 Vaccines, *see* FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum (Dec. 11, 2020), at 49, https://www.fda.gov/media/144416/download; FDA, Moderna COVID-19 Vaccine EUA Decision Memorandum (Dec. 18, 2020), at 55, https://www.fda.gov/media/144673/download; FDA, Janssen COVID-19 Vaccine EUA Decision Memorandum (Feb. 27, 2021), at 59, https://www.fda.gov/media/146338/download. *See also*, FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age (May 10, 2021), at 38, https://www.fda.gov/media/148542/download.

In arguing that the Authorized COVID-19 Vaccines should be revoked due, in part, to safety concerns, Petitioners assert that "Vaccine Adverse Event Reporting System (VAERS) data reveal unprecedented levels of deaths and other adverse events since the FDA issued Emergency Use Authorizations (EUAs) for three COVID vaccines. As of May 10, 2021, VAERS reported 4,434 deaths of people who received at least one COVID vaccination." As an initial matter, we note that VAERS is a national passive surveillance vaccine safety database that receives unconfirmed reports of possible adverse events following the use of a vaccine licensed or authorized in the United States. VAERS is not designed to assess whether a reported adverse event was caused by a vaccine. This section explains vaccine safety surveillance, including VAERS, in greater detail below.

Regarding the number of VAERS reports submitted for the Authorized COVID-19 Vaccines, this figure can be attributed to multiple factors. First, we note that a large number of COVID-19 vaccine doses have been administered in the United States and that certain adverse event reporting by vaccination providers is *required* for the Authorized COVID-19 Vaccines. As of August 13, 2021, over 353,000,000 doses of the Authorized COVID-19 Vaccines have been administered.[47] We note that the crude number of VAERS reports of death is extremely small compared to the to the large number of people who have been vaccinated. The VAERS reporting rate for deaths (which is the number of VAERS death reports received out of the number of individuals vaccinated) for the Authorized COVID-19 Vaccines is actually very low (6,490 reports of death out of 346 million doses administered (0.0019%) as of August 2, 2021).[48] Petitioner's assertion fails to account for this fact.

For licensed vaccines, healthcare providers are legally required under 42 USC 300aa-25 to report to VAERS two categories of adverse events: "[a]ny adverse event listed in the VAERS Table of Reportable Events Following Vaccination that occurs *within the specified time period after vaccination* [and] [a]n adverse event listed by the vaccine manufacturer as a contraindication to further doses of the vaccine"[49] Vaccine manufacturers are also required to report to VAERS all adverse events that come to their attention.[50]
Under the EUAs for the Authorized COVID-19 Vaccines, however, vaccination providers are required to report to VAERS serious adverse events following vaccination with the Authorized COVID-19 Vaccines, "irrespective of attribution to vaccination" and without a specified time period after vaccination.[51] Another contributing factor is the v-safe system,[52] which is a new CDC smartphone-based active-surveillance system in which participants who have been

[47] CDC, COVID Data Tracker, COVID-19 Vaccinations in the United States, https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-total-admin-rate-total.
[48] CDC, Selected Adverse Events Reported after COVID-19 Vaccination, https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html.
[49] VAERS, Frequently Asked Questions, https://vaers.hhs.gov/faq.html (emphasis added).
[50] 21 CFR 600.80. See also VAERS, Frequently Asked Questions, https://vaers.hhs.gov/faq.html.
[51] Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors, Pfizer-BioNTech COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine, https://www.fda.gov/media/144413/download; Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors, Moderna COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine, https://www.fda.gov/media/144637/download; Section 8, Requirements and Instructions for Reporting Adverse Events and Vaccine Administration Errors, Janssen COVID-19 Fact Sheet for Healthcare Providers Administering Vaccine, https://www.fda.gov/media/146304/download.
[52] CDC, v-safe Overview, https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe.html.

vaccinated may voluntarily enroll. This system was developed for the COVID-19 vaccination program. V-safe sends text messages and web surveys to participants who can report side effects following receipt of a COVID-19 vaccine. If a participant indicates through the v-safe surveys that he or she required medical care at any time, CDC calls the participant to complete a report through VAERS. This system is unique to COVID-19 vaccines and may be contributing to the number of VAERS reports submitted for the Authorized COVID-19 Vaccines.
Finally, another potential factor is the concept of "stimulated reporting."[53] Because of extensive media coverage and awareness of the public health emergency – and of the Authorized COVID-19 Vaccines and their reported side effects –vaccine recipients, health care providers, and others are more likely to report adverse events for the Authorized COVID-19 Vaccines than for other vaccines that have been widely available for longer periods of time. Additionally, one of the articles submitted by Petitioner in support of their argument actually provides support for this explanation for the number of VAERS reports submitted for the Authorized COVID-19 Vaccines. The article notes "[t]he relatively rapid increase in numbers of reports to VAERS following the introduction and initial uptake of a new vaccine, an expected occurrence, has been *misinterpreted as actual increases in incidence of adverse events and vaccine related risk*."[54] Petitioner's argument regarding VAERS data for the Authorized COVID-19 Vaccines is unavailing because it fails to account for the factors outlined above.

In addressing Petitioner's assertion regarding VAERS claims, this section addresses the extensive vaccine safety surveillance efforts, in addition to VAERS, that are in place for the Authorized COVID-19 Vaccines.[55] FDA is monitoring the safety of the Authorized COVID-19 Vaccines through both passive and active safety surveillance systems. FDA is doing so in collaboration with the Centers for Disease Control and Prevention (CDC), the Centers for Medicare and Medicaid Services (CMS), the Department of Veterans Affairs (VA), and other academic and large non-government healthcare data systems.

In addition, FDA participates actively in ongoing international pharmacovigilance efforts, including those organized by the International Coalition of Medicines Regulatory Authorities

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[53] We note that an article submitted by Petitioner in support of their arguments regarding VAERS acknowledges this concept: "Like all spontaneous public health reporting systems, VAERS has limitations. VAERS is subject to reporting bias, including underreporting of adverse events – especially common, mild ones– and stimulated reporting, which is elevated reporting that might occur in response to intense media attention and increased public awareness, such as during the 2009 H1N1 pandemic influenza vaccination program" Shimabukuro et al., Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS), Vaccine (Nov. 4, 2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/. See also "The number of reports and reporting rate following 2009-H1N1 vaccination were higher than following 2009–2010 seasonal influenza vaccines for all age groups. These findings, however, should be interpreted in light of the publicity around the 2009-H1N1 vaccine and efforts to increase reporting to VAERS. Heightened public awareness and stimulated reporting likely enhanced reporting to VAERS. Furthermore, although 2009-H1N1 was licensed similarly to seasonal influenza vaccines, it was likely perceived as a 'new' vaccine by the public and susceptible to the known tendency (i.e., the Weber effect) for adverse events to be reported more frequently following newly licensed products." Vellozzi, et al., Adverse events following influenza A (H1N1) 2009 monovalent vaccines reported to the Vaccine Adverse Event Reporting System, United States, October 1, 2009–January 31, 2010, Vaccine (Oct. 21, 2010), https://www.sciencedirect.com/science/article/pii/S0264410X10013319.

[54] Shimabukuro et al., Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS), Vaccine (Nov. 4, 2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/ (emphasis added).

[55] FDA, COVID-19 Vaccine Safety Surveillance, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/covid-19-vaccine-safety-surveillance.

(ICMRA) and the World Health Organization (WHO). These efforts are in addition to the pharmacovigilance efforts being undertaken by the individual manufacturers for authorized vaccines. A coordinated and overlapping approach using state-of the art technologies has been implemented. As part of our efforts to be transparent about our COVID-19 vaccine safety monitoring activities, FDA is posting summaries of the key safety monitoring findings on the FDA website. [56]

i. Vaccine Safety Surveillance

Passive Surveillance

VAERS is a national passive surveillance vaccine safety database that receives unconfirmed reports of possible adverse events following the use of a vaccine licensed or authorized in the United States. Passive surveillance is defined as unsolicited reports of adverse events that are sent to a central database or health authority. In the United States, these are received and entered into VAERS, which is co-managed by FDA and CDC. In the current pandemic, these reports are being used to monitor the occurrence of both known and unknown adverse events, as providers of COVID-19 vaccines are required to report serious adverse events to VAERS.
As part of FDA and CDC's multi-system approach to post-licensure and post-authorization vaccine safety monitoring, VAERS is designed to rapidly detect unusual or unexpected patterns of adverse events, also known as "safety signals." VAERS reports generally cannot be used to determine if a vaccine caused or contributed to an adverse event or illness. If the VAERS data suggest a possible link between an adverse event and vaccination, the relationship may be further studied in a controlled fashion.[57]

Anyone can make a report to VAERS, including vaccine manufacturers, private practitioners, state and local public health clinics, vaccine recipients, and their parents or caregivers. Surveillance programs like VAERS perform a critical function by generating signals of potential problems that may warrant further investigation.

VAERS is not designed to assess causality. It is often difficult to determine with certainty if a vaccine caused an adverse event reported to VAERS. Many events that occur after vaccination can happen by chance alone. Some adverse events are so rare that their association with a vaccine is difficult to evaluate. In addition, we often receive reports where there is no clear clinical diagnosis. FDA draws upon multiple sources of data and medical and scientific expertise to assess the potential strength of association between a vaccine, including COVID-19 vaccines, and a possible adverse event.

If VAERS monitoring suggests that a vaccine might be causing a health problem, additional scientifically rigorous studies or investigations can be performed by FDA and CDC. Monitoring and analysis of VAERS reports typically includes daily in-depth medical review of all serious reports, statistical data mining techniques, and epidemiological analysis. We look for patterns and similarities in the onset timing and clinical description. We review published literature to

[56] FDA, COVID-19 Vaccine Safety Surveillance, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/covid-19-vaccine-safety-surveillance
[57] FDA, VAERS Overview, https://www.fda.gov/vaccines-blood-biologics/vaccine-adverse-events/vaers-overview.

understand possible biologic hypotheses that could plausibly link the reported adverse event to the vaccine. We review the pre-licensure or pre-authorization data and any other post-marketing studies that have been conducted. We also consider "background rate," meaning the rate at which a type of adverse event occurs in the unvaccinated general population. When necessary, we discuss the potential adverse event with our federal and international safety surveillance partners. We also carefully evaluate unusual or unexpected reports, as well as reports of "positive re-challenges" (adverse events that occur in the same patient after each dose received). When there is sufficient evidence for a potential safety concern, we may proceed to conduct large studies, and we may coordinate with our federal, academic, and private partners to further assess the potential risk after vaccination. In addition, when potential safety issues arise, they are often presented to various U.S. government advisory committees, including the Vaccines and Related Biological Products Advisory Committee, the Advisory Committee on Immunization Practices (ACIP), and the Advisory Committee on Childhood Vaccines, and are often discussed with experts from other countries and from the World Health Organization. Federal agencies that assist in population-based vaccines safety studies include the CDC, Centers for Medicaid and Medicare (CMS), the Department of Defense (DoD), and the Indian Health Services (IHS). In addition, we generally communicate and work with international regulatory authorities and international partners to conduct studies in vaccine safety.

Active Surveillance

Active surveillance involves proactively obtaining and rapidly analyzing information related to millions of individuals and recorded in large healthcare data systems to verify safety signals identified through passive surveillance or to detect additional safety signals that may not have been reported as adverse events to passive surveillance systems. FDA is conducting active surveillance using the Sentinel BEST (Biologics Effectiveness and Safety) System and the CMS system, and is also collaborating with other federal and non-federal partners.

BEST

To elaborate further, the BEST system,[58] which is part of the Sentinel initiative,[59] comprises large-scale claims data, electronic health records (EHR), and linked claims-EHR databases with a data lag of approximately three months. The system makes use of multiple data sources and enables rapid queries to detect or evaluate adverse events as well as studies to answer specific safety questions for vaccines. The linked claims-EHR database makes it possible to study the safety of vaccines in sub-populations with pre-existing conditions or in pregnant women. The major partners for BEST currently are Acumen, IBM Federal HealthCare, IQVIA, and Columbia University and many affiliated partners such as MedStar Health, BlueCross BlueShield of

[58] CBER Biologics Effectiveness and Safety (BEST) System, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-biologics-effectiveness-and-safety-best-system.
[59] FDA's Sentinel Initiative, https://www.fda.gov/safety/fdas-sentinel-initiative.

America, the Observational Health Data Sciences and Informatics (OHDSI), OneFlorida, University of California and several others.[60]

Using BEST, CBER plans to monitor about 15 adverse events[61] that have been seen with the deployment of previous vaccines but have yet to be associated with a safety concern for an authorized COVID-19 vaccine at this time. CBER further plans to use the BEST system to conduct more in-depth analyses should a safety concern be identified from sources such as VAERS.

CMS

FDA has worked over the past several years with CMS to develop capabilities for routine and time-sensitive assessments of the safety of vaccines for people 65 years of age and older using the Medicare Claims database.[62] Because it was already in place, this system was immediately put into use for COVID-19 vaccine surveillance to monitor for adverse events.[63]

During the current pandemic, FDA, CMS, and CDC have already used the Medicare data to publish a study showing that frailty, comorbidities, and race/ethnicity were strong risk factors of COVID-19 hospitalization and death among the U.S. elderly.[64]

VSD

In addition, the Vaccine Safety Datalink (VSD) is a collaborative project between CDC's Immunization Safety Office and nine health care organizations. As noted on the CDC's

[60] To confirm the utility of the BEST system for situations such as COVID-19 vaccine surveillance, a test case was conducted. This study aimed to replicate a previous study by the CDC's Vaccine Safety Datalink (VSD) (Klein et al. Pediatrics 2010) that examined the databases and analytic capabilities of the new system. The objective of this study was to test the new system's ability to reproduce the increased risk of febrile seizures in children receiving the first dose of measles-mumps-rubella-varicella (MMRV) vaccine, compared to that of MMR and varicella vaccines separately but on the same day. The results of the study met the objectives and demonstrated the ability of the BEST Initiative data network to run a complex study protocol at multiple sites using a distributed data network and the Observational Medical Outcomes Partnership Common Data Model (organizing disparate data sources into the same database design using a common format).

[61] Background Rates of Adverse Events of Special Interest for COVID-19 Vaccine Safety Monitoring, Draft Protocol (December 31, 2020), https://www.bestinitiative.org/wp-content/uploads/2021/01/C19-Vaccine-Safety-AESI-Background-Rate-Protocol-2020.pdf.

[62] CMS, Standard Analytical Files (Medicare Claims) – LDS, https://www.cms.gov/Research-Statistics-Data-and-Systems/Files-for-Order/LimitedDataSets/StandardAnalyticalFiles.

[63] As one example of the capabilities of this system, FDA, CMS, and CDC evaluated the risk of Guillain-Barré syndrome (GBS) following influenza vaccination after CDC's Vaccine Safety Datalink, identified safety signals suggesting an increased risk of GBS following high-dose influenza vaccinations and Shingrix vaccinations during the 2018-2019 influenza season. CBER, CDC, and CMS formed working groups in February 2019 to refine these safety signals in the CMS data.

[64] Hector S Izurieta, David J Graham, Yixin Jiao, Mao Hu, Yun Lu, Yue Wu, Yoganand Chillarige, Michael Wernecke, Mikhail Menis, Douglas Pratt, Jeffrey Kelman, Richard Forshee, Natural History of Coronavirus Disease 2019: Risk Factors for Hospitalizations and Deaths Among >26 Million US Medicare Beneficiaries, The Journal of Infectious Diseases, Volume 223, Issue 6, 15 March 2021, Pages 945–956, https://doi.org/10.1093/infdis/jiaa767 https://academic.oup.com/jid/article/223/6/945/6039057.

webpage, the VSD started in 1990 and continues today in order to monitor safety of vaccines and conduct studies about rare and serious adverse events following immunization.

The VSD uses electronic health data from each participating site. This includes information on vaccines: the kind of vaccine given to each patient, date of vaccination, and other vaccinations given on the same day. The VSD also uses information on medical illnesses that have been diagnosed at doctors' offices, urgent care visits, emergency department visits, and hospital stays. The VSD conducts vaccine safety studies based on questions or concerns raised from the medical literature and reports to the Vaccine Adverse Event Reporting System (VAERS). When there are new vaccines that have been recommended for use in the United States or if there are changes in how a vaccine is recommended, the VSD will monitor the safety of these vaccines.

The VSD has a long history of monitoring and evaluating the safety of vaccines. Since 1990, investigators from the VSD have published many studies to address vaccine safety concerns.[65]

In summary, in collaboration and coordination with several different partners, FDA has assembled passive surveillance systems - including VAERS - and active surveillance systems that can detect and refine safety findings with the Authorized COVID-19 Vaccines in a relatively rapid manner. These systems can also potentially be leveraged to assess safety in specific subpopulations and to assess vaccine effectiveness.

ii. Articles Submitted in Petition Regarding Vaccine Surveillance

We note at the outset that Petitioner raises concerns regarding the methodology by which CDC calculated rates of anaphylactic adverse events post-vaccination. Such concerns are best directed to CDC and are outside the scope of FDA's Petition response.

Regarding Petitioner's contention that a low percentage of adverse events have been reported to VAERS and that therefore "the safety of COVID vaccines is considerably worse than it currently appears" (Petition at 4), as explained in detail above in this section, VAERS is only one part of a multi-tiered vaccine safety surveillance system, so the information derived from VAERS reports does not represent the full extent of vaccine safety information being monitored by FDA and its federal partners.

Specifically, Petitioner cites to three studies in support of the argument that "[g]iven that only 1 to 13% of adverse reactions have been reported to the FDA and CDC via the VAERS passive reporting system, according to Lazarus et al., the high number of adverse events and deaths following COVID vaccines is alarming." Petition at 5. The articles cited by Petitioner in support of this contention do not support Petitioner's position that, due to underreporting of adverse events, the rate of reported adverse events associated with COVID-19 vaccination is low in comparison to the actual rate of adverse events. As discussed above in this section, there are several factors unique to the surveillance of the Authorized COVID-19 Vaccines that have

[65] *See, e.g.*, CDC, White Paper on the Safety of the Childhood Immunization Schedule, Vaccine Safety Datalink, available at https://www.cdc.gov/vaccinesafety/pdf/WhitePaperSafety_WEB.pdf.

contributed to the number of VAERS reports submitted for these vaccines. Petitioner's argument that adverse events associated with the Authorized COVID-19 Vaccines are underreported because of the figures presented in the articles cited fail to account for any of those factors that are unique to the Authorized COVID-19 Vaccines.

Petitioner cites to a publication from the Agency for Healthcare Research and Quality (Lazarus et al.) in support of the argument that deaths and adverse events associated with the Authorized COVID-19 Vaccines are underreported because "only 1 to 13% of adverse reactions have been reported to the FDA and CDC via the VAERS passive reporting system" (Petition at 5), and therefore the actual rate of COVID-19 Vaccine adverse events is significantly higher than reported.[66] As an initial matter, we note that the language cited from the Lazarus article is referring to adverse event reporting for drugs and vaccines, not just vaccine adverse events reported to VAERS.[67] Furthermore, as explained in detail above, several factors have contributed to the number of VAERS reports submitted for the Authorized COVID-19 Vaccines. The issues raised in this article regarding underreporting of drug adverse event reporting are not directly relevant to the claims Petitioner makes regarding adverse event reporting for the Authorized COVID-19 Vaccines. The article was published in 2010 and does not consider the numerous factors outlined above regarding reporting of adverse events following COVID-19 vaccination.

Petitioner cites to a journal article in the publication *Vaccine*[68] regarding VAERS safety monitoring in support of their argument that adverse event reports for the Authorized COVID-19 Vaccines are underreported. This article generally discusses the limitations of VAERS and passive surveillance, which are well-understood by the FDA and which are discussed in this letter. Additionally, this article notes "[p]erhaps the two most common misconceptions about VAERS are that temporally associated reports represent true adverse reactions caused by vaccination, and that VAERS reports equate to rates of adverse events or indicate risk of adverse events associated with vaccination."[69] This statement from the article demonstrates the flaws underlying Petitioner's claims that the Authorized COVID-19 Vaccines are unsafe due to the number of serious adverse events reported to VAERS following administration of these vaccines. Additionally, the article notes "[t]he relatively rapid increase in numbers of reports to VAERS following the introduction and initial uptake of a new vaccine, an expected occurrence, has been misinterpreted as actual increases in incidence of adverse events and vaccine related risk."[70] Thus, the article cited by Petitioner directly contradicts Petitioner's claims regarding the safety of the Authorized COVID-19 Vaccines based on the number of VAERS adverse event reports associated with these vaccines.

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[66] Lazarus et al., Electronic Support for Public Health-Vaccine Adverse Event Reporting System, Agency for Healthcare Research and Quality, HHS (Sept. 30, 2010), https://digital.ahrq.gov/ahrq-funded-projects/electronic-support-public-health-vaccine-adverse-event-reporting-system.
[67] Id. at 6.
[68] Shimabukuro et al., Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS), Vaccine (Nov. 4, 2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/.
[69] Id. at 9.
[70] Id.

Finally, Petitioner also cites to a journal article in the American Journal of Public Health.[71] This article does not raise issues that have not already been addressed in this letter's discussion of safety surveillance. For instance, the article notes that passive surveillance has several limitations, specifically, passive surveillance may involve underreporting of adverse events, and passive surveillance data is not adequate to determine causation. Additionally, this article notes that passive surveillance can provide valuable information, "[n]evertheless, if reporting is reasonably consistent, it may be possible to detect changes in trends of known common adverse events."[72]

Therefore, the articles submitted by Petitioner do not present data or information regarding the Authorized COVID-19 Vaccines that change the Agency's analysis regarding the benefits and risks of the Authorized COVID-19 Vaccines.

Petitioner further asserts that extensive safety information regarding vaccines is inaccessible to the public ("the VAERS database is the only safety database to which the public has access. The government withholds extensive safety information from the public despite having at least ten additional data sources and expert consultants to analyze these data . . . ." Petition at 2.). This contention represents a misunderstanding by Petitioner of the sources of data analyzed by FDA and its federal partners, and of the types of information available to the public.
As noted above, Petitioner's questions regarding databases operated by other federal partners, such as DOD, CMS, CDC, VA, should be directed to those federal entities. Regarding FDA's BEST system, Petitioner erroneously claims that the public does not have access to the information on this system. As noted above, the BEST system,[73] which is part of the Sentinel initiative,[74] comprises large-scale claims data, electronic health records (EHR), and linked claims-EHR databases with a data lag of approximately three months. The system makes use of multiple data sources and enables rapid queries to detect or evaluate adverse events as well as studies to answer specific safety questions for vaccines. The system is not intended to be a source of raw EHR data. Instead, as explained on FDA's webpage describing the BEST system, the purpose of the BEST system is to: (1) build data, analytics, infrastructure for an active, large-scale, efficient surveillance system for biologic products; and (2) develop innovative methods to utilize electronic health records (EHR) effectively and establish automated adverse events reporting, utilizing natural language processing and artificial intelligence.[75] BEST does not have access to the raw, identifiable data. BEST data partners analyze the raw data per publicly posted protocols and send the results in aggregated form to BEST for review. The information is summarized in either final reports, manuscripts or public presentations. BEST publicly posts study protocols of surveillance activities on the BEST site with open public comments regarding the protocols, final reports and manuscripts as well as communication on CBER safety site and public meetings, e.g., VRBPAC, where appropriate. These protocols delineate the scientific approach to analyzing the raw data, where in the raw form is of limited utility to the public, to

[71] S. Rosenthal and R. Chen, The reporting sensitivities of two passive surveillance systems for vaccine adverse events, American Journal of Public Health (Dec. 1995), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1615747/.
[72] Id.
[73] CBER Biologics Effectiveness and Safety (BEST) System, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-biologics-effectiveness-and-safety-best-system.
[74] FDA's Sentinel Initiative, https://www.fda.gov/safety/fdas-sentinel-initiative.
[75] CBER Biologics Effectiveness and Safety (BEST) System, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-biologics-effectiveness-and-safety-best-system.

generate information on vaccine safety. The final reports and manuscripts summarize the information and conclusions inferred from well-conducted surveillance studies.

iii. FDA Has Responded to Safety Signals Related to the Authorized COVID-19 Vaccines by Extensively Reviewing Data, Updating the Authorized Labeling, and Communicating to the Public

Petitioner further asserts that "FDA and CDC have not responded to these data by issuing any warnings or restricting the use of these vaccines." Petition at 2. This assertion is inaccurate. As explained in detail above, FDA and its federal partners, including CDC, have closely monitored post-market safety data regarding the Authorized COVID-19 Vaccines. FDA has worked to identify and investigate serious adverse events occurring in people after receiving the Authorized COVID-19 Vaccines, and to communicate these risks to the public and revise the authorized labeling to reflect these risks in a timely fashion.[76] The surveillance systems that are in place to monitor the safety of COVID-19 vaccines authorized for emergency use are working, as demonstrated by FDA's and CDC's work to identify and investigate these serious adverse events in a timely manner.

Adverse events reported to VAERS following administration of one of the authorized COVID-19 vaccines are reviewed to assess possible safety concerns. Such review of VAERS data regarding the authorized COVID-19 vaccines has been conducted since these vaccines were authorized. Such review has prompted the Agency to take action with respect to the currently authorized COVID-19 vaccines:

- On April 13, 2021, FDA and CDC recommended a pause in the use of the Janssen COVID-19 vaccine following six VAERS reports in the U.S. of thrombosis with thrombocytopenia.[77] The FDA and CDC thoroughly reviewed VAERS and other post-authorization information and data related to the Janssen COVID-19 vaccine during the recommended pause. This review included two meetings of ACIP. Following a thorough safety review, FDA determined that the available data show that the Janssen COVID-19 vaccine's known and potential benefits outweigh its known and potential

[76] Janssen COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Sections 5.2 and 5.3 Warnings and Precautions Regarding Thrombosis with Thrombocytopenia and GBS, https://www.fda.gov/media/146304/download; Pfizer-BioNTech COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Section 5.2, Warning and Precautions Regarding Myocarditis and Pericarditis, https://www.fda.gov/media/144413/download; Moderna COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Section 5.2, Warning and Precautions Regarding Myocarditis and Pericarditis, https://www.fda.gov/media/144637/download.

[77] We note that Petitioner mentions that Denmark, among other nations, has "banned" the Janssen COVID-19 vaccine. To the extent Petitioner relies on this ban as support for Petitioner's request that FDA revoke the EUA for this vaccine, we note that Denmark and other nations' actions with respect to the use of this vaccine are outside purview of FDA's work, so we cannot comment on decisions they make under their public health regulatory framework.

risks in individuals 18 years of age and older. As a result of this review, the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) was updated to include a Warning pertaining to the risk of thrombosis with thrombocytopenia. The Fact Sheet for Recipients and Caregivers was also updated to include information about these serious adverse events. The FDA and CDC conducted extensive outreach to providers and clinicians to ensure they were made aware of the potential for these adverse events and could properly recognize and manage thrombosis with thrombocytopenia in individuals who receive the Janssen COVID-19 Vaccine.

- On June 25, 2021, following review of VAERS reports, FDA required revisions to the authorized labeling for the Pfizer-BioNTech COVID-19 vaccine and the Moderna COVID-19 vaccine to add a warning regarding the suggested increased risks of myocarditis and pericarditis. This update to the authorized labeling for these vaccines followed an extensive review of information and the discussion by CDC's ACIP meeting on June 23, 2021. As of July 26, 2021, the FDA and the Centers for Disease Control and Prevention (CDC) have received 1,194 reports of myocarditis or pericarditis occurring among people ages 30 and younger who received either Moderna or Pfizer-BioNTech COVID-19 vaccines, particularly following the second dose.[78] Through follow-up, including medical record reviews, the FDA and CDC had confirmed 699 cases of myocarditis or pericarditis.[79]
- On July 13, 2021, FDA required revisions to the vaccine recipient and vaccination provider fact sheets for the Janssen COVID-19 Vaccine to include information pertaining to a suggested increased risk of Guillain-Barré Syndrome (GBS) during the 42 days following vaccination. Based on an analysis of Vaccine Adverse Event Reporting (VAERS) data, at that time, there had been 100 reports of presumptive GBS following vaccination with the Janssen vaccine after approximately 12.5 million doses administered. Of these reports, 95 of them were serious and required hospitalization. There was one reported death. As noted in the Janssen Fact Sheet for Healthcare Providers Administering Vaccine, because these reactions are reported voluntarily, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. Each year in the United States, an estimated 3,000 to 6,000 people develop GBS. Most people fully recover from the disorder. FDA publicly presented this issue, and information regarding these 100 reports of presumptive GBS, to the ACIP on July 22, 2021.[80]

During each of these post-authorization reviews and labeling changes, the FDA has evaluated the available post-authorization information for the authorized COVID-19 Vaccines and continues to find the known and potential benefits clearly outweigh the known and potential risks.

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[78] CDC, COVID-19 Reported Adverse Events, https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html.

[79] Id.

[80] FDA, CDC ACIP Meeting Presentation, Guillain-Barré Syndrome (GBS) after Janssen COVID-19 Vaccine: Vaccine Adverse Event Reporting System (VAERS), July 22, 2021, https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/02-COVID-Alimchandani-508.pdf.

iv. Petitioner's Claims Regarding Anaphylaxis

Petitioner cites to a study of acute allergic reactions to mRNA COVID-19 vaccines in support of their argument that adverse event rates for COVID-19 vaccines have been miscalculated by CDC.[81] As stated above, questions relating to CDC are best directed to that Agency. We note, however, that this journal article states, immediately after the sentence quoted by Petitioner, "[h]owever, the overall risk of anaphylaxis to an mRNA COVID-19 vaccine remains extremely low and largely comparable to other common health care exposures. Although cases were clinically compatible with anaphylaxis, the mechanism of these reactions is unknown." The paper further states, in describing the limitations of the study, that "[a] northeastern US cohort may not be generalizable." Thus, Petitioner is inappropriately generalizing the results of this study in an attempt to compare the results to the CDC's reported data and conclude that the safety of COVID vaccines is "considerably worse than it currently appears." Petition at 4.

Additionally, we note that the authorized labeling for all the Authorized COVID-19 vaccines already contain warnings regarding the risk of anaphylaxis as a potential adverse event. Thus, the risk of anaphylaxis is a potential safety issue FDA is already aware of, and Petitioner's argument, and the article submitted in support of this argument, does not change FDA's conclusions regarding the safety of the Authorized COVID-19 vaccines.

v. Animal Toxicology and Pharmacokinetic Studies of COVID-19 Vaccines

Petitioner raises concerns regarding FDA's vaccine safety assessment. Specifically, Petitioner states that other "problems with vaccine safety assessment *may exist* because of inadequate animal toxicology and pharmacokinetic studies of COVID vaccines." Petition at 5; emphasis added. As an initial matter, we note that Petitioner's concerns regarding the vaccine safety assessment for COVID-19 vaccines involves speculation regarding whether problems actually exist ("problems with vaccine safety assessment *may exist* . . ."), and Petitioner fails to point to any specific problems that result or may result from the allegedly inadequate studies. Regarding Petitioner's claims, in general, when evaluating the safety data regarding a vaccine, FDA considers data from animal studies (if such pre-clinical studies were performed) as one part of the full body of evidence regarding the vaccine. In addition to data from animal studies, if available, FDA evaluates data from in vitro studies and conducts a safety assessment of data from clinical studies.

Thus, although Petitioner raises several concerns and cites to several articles regarding risks of COVID-19 vaccination, FDA is not aware of any information indicating that the known and potential benefits of the Authorized COVID-19 Vaccines are outweighed by their known and potential risks, nor has Petitioner provided any such information in the Petition. Therefore, the

[81] Blumenthal KG, Robinson LB, Camargo CA, et al., Acute Allergic Reactions to mRNA COVID-19 Vaccines, JAMA. 2021;325(15):1562–1565. doi:10.1001/jama.2021.3976, https://jamanetwork.com/journals/jama/fullarticle/2777417.

criterion under section 564(c)(2)(B) continues to be met with respect to the Authorized COVID-19 Vaccines.

4. No Alternatives

As noted above, Petitioner requests that "FDA should revoke all EUAs and refrain from approving any future EUA . . . for any COVID vaccine for all demographic groups because the current risks of serious adverse events or deaths outweigh the benefits, and because existing, approved drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs." Petition at 1. Section 564(c)(3) of the FD&C Act provides one of the required statutory factors that must be met in order for a product to be granted an EUA. This statutory provision requires that "there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating [the serious or life-threatening disease or condition]."[82] To the extent Petitioner's contention can be interpreted as an argument that there are adequate, approved, available drugs indicated for the prevention of COVID-19 (and that therefore the requirement in section 564(c)(3) of the FD&C Act that there is no "adequate, approved, and available alternative to the Authorized COVID-19 Vaccines for preventing COVID-19 is not met), this argument is erroneous.

As explained in the Decision Review Memoranda for the Authorized COVID-19 Vaccines, at the time each COVID-19 vaccine EUA was issued, there were no FDA-approved drugs or biological products indicated to prevent COVID-19 in any population because no vaccine or other medical product was the subject of an approved marketing application for prevention of COVID-19.[83] This is still true today, with the exception of the BLA for BioNTech's COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty), which is now approved for the prevention of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. The EUA for Pfizer-BioNTech COVID-19 Vaccine remains in effect. This EUA will continue to cover individuals 12 through 15 years of age, to cover the administration of a third dose to certain immunocompromised individuals 12 years of age and older, and to cover individuals 16 years of age and older until sufficient approved vaccine can be manufactured and distributed. Similarly, the EUA for the Moderna COVID-19 Vaccine and the Janssen COVID-19 Vaccine remain in effect for individuals 18 years of age and older. Although FDA has approved one new drug application (NDA) for remdesivir for use in adult and pediatric patients 12 years of age and older and weighing at least 40 kilograms for the treatment of COVID-19 requiring hospitalization, this drug is not for prevention of COVID-19. Several other therapies are currently available under EUA, but not FDA approved, for treatment of COVID-19, and one is available under EUA, but not FDA approved, for post-exposure prophylaxis in a limited population. These products that are available under EUA are not considered "approved" products for purposes of section

[82] The term "approved," for purposes of section 564(c) of the FD&C Act, means a product is approved, licensed, or cleared by FDA under section 505, 510(k), or 515 of the FD&C Act or section 351 of the PHS Act, as applicable, and this term is indication-specific. *See*, section 564(a)(2) of the FD&C Act. *See also*, EUA guidance at 3.
[83] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum (Dec. 11, 2020), at 8-9, https://www.fda.gov/media/144416/download; FDA, Moderna COVID-19 Vaccine EUA Decision Memorandum (Dec. 18, 2020), at 9, https://www.fda.gov/media/144673/download; FDA, Janssen COVID-19 Vaccine EUA Decision Memorandum (Feb. 27, 2021), at 9, https://www.fda.gov/media/146338/download.

564(c)(3) because they are not the subject of an approved marketing application (i.e., they are not approved under an NDA or BLA).

Thus, Petitioner's assertion that the EUAs for the Authorized COVID-19 Vaccines are "mooted" by the existence of drugs approved to prevent COVID-19 is incorrect.

5. No Other Circumstances Make A Revision or Revocation Appropriate to Protect the Public Health or Safety

As noted above, section 564(g)(2)(C) of the FD&C Act provides that FDA may revise or revoke an EUA if circumstances justifying its issuance (under section 564(b)(1)) no longer exist, the criteria for its issuance are no longer met, or other circumstances make a revision or revocation appropriate to protect the public health or safety. The EUA guidance explains that such other circumstances may include:

> significant adverse inspectional findings (e.g., when an inspection of the manufacturing site and processes has raised significant questions regarding the purity, potency, or safety of the EUA product that materially affect the risk/benefit assessment upon which the EUA was based); reports of adverse events (number or severity) linked to, or suspected of being caused by, the EUA product; product failure; product ineffectiveness (such as newly emerging data that may contribute to revision of the FDA's initial conclusion that the product "may be effective" against a particular CBRN agent); a request from the sponsor to revoke the EUA; a material change in the risk/benefit assessment based on evolving understanding of the disease or condition and/or availability of authorized MCMs; or as provided in section 564(b)(2), a change in the approval status of the product may make an EUA unnecessary.[84]

As of the date of this writing, FDA has not identified any such circumstances that would make revocation of any of the Authorized COVID-19 Vaccines appropriate to protect the public health or safety. As stated previously in this response, FDA determined the EUA standard is met for the three authorized COVID-19 vaccines because data submitted by the sponsors demonstrated in a clear and compelling manner that the known and potential benefits of these products, when used to prevent COVID-19, outweigh the known and potential risks of these products, and that there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating COVID-19.

As described in detail in section III.b.i.1.b above, FDA has identified circumstances that have made revision of the EUAs for the Authorized COVID-19 Vaccines appropriate, and,

[84] EUA Guidance at 29.

accordingly, has required changes to the authorized labeling for the Authorized COVID-19 Vaccines.[85]

Additionally, as explained above, FDA finds no basis in the information submitted in the Petition, or in any postmarket data regarding the Authorized COVID-19 Vaccines, to support a revocation of any of these EUAs, nor has Petitioner provided any such information in the Petition. FDA is not aware of any information indicating that the known and potential benefits of the Authorized COVID-19 Vaccines are outweighed by their known and potential risks, nor has Petitioner provided any such information in the Petition. Furthermore, there are no other circumstances that make a revision or revocation appropriate to protect the public health or safety, nor has Petitioner provided any information about such circumstances.

FDA therefore sees no justifiable basis upon which to take any action based on Petitioner's request with respect to the any of the Authorized COVID-19 Vaccines. Accordingly, as noted above, we deny Petitioner's request for FDA to "revoke all EUAs . . . for any COVID vaccine for all demographic groups because existing, approved drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs."

2. Petitioner's Request to Refrain from Granting any Future EUA for a COVID-19 Vaccine for any Population Because Approved Drugs Exist for COVID-19 Prevention

Petitioner also requests in the Petition that FDA "refrain from approving any future EUA . . . for any COVID vaccine for all demographic groups because the current risks of serious adverse events or deaths outweigh the benefits, and because existing, approved drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs."[86] Petition at 1.

Petitioner has provided no evidence that would provide a basis for FDA to conclude that no future COVID-19 vaccine candidate could meet the EUA standard. Indeed, FDA is not aware of any information indicating that the known and potential benefits of the Authorized COVID-19 Vaccines are outweighed by their known and potential risks, nor has Petitioner provided any such information in the Petition.

Additionally, as explained above in section III.b.i.1.b. of this letter, to the extent Petitioner's contention can be interpreted as an argument that there are FDA-approved drugs indicated for the prevention of COVID-19 (and that therefore the requirement in section 564(c)(3) of the FD&C Act that there is no "adequate, approved, and available alternative" could not be met), this

[85] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12 -15 Years of Age (May 10, 2021), Section 4.6, EUA Prescribing Information and Fact Sheets, https://www.fda.gov/media/148542/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of an Additional Dose in Certain Immunocompromised Individuals (August 12, 2021), https://www.fda.gov/media/151613/download; FDA, Moderna COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of an Additional Dose in Certain Immunocompromised Individuals (August 12, 2021), https://www.fda.gov/media/151611/download.

[86] FDA authorization of an EUA request is not FDA approval. FDA does not "approve" an EUA request. Rather, FDA *authorizes* the emergency use of a product following review of data and information submitted in an EUA request.

argument fails. Should FDA receive future requests for EUAs for COVID-19 vaccine candidates, FDA would consider such requests on a case-by-case basis.[87] Accordingly, Petitioner's request is denied.

3. Petitioner's Request to Refrain from Approving any Future NDA for any COVID-19 Vaccine for any Population

Petitioner's request regarding "any future…NDA … for any COVID Vaccine for all demographic groups" is moot because vaccines are biological products subject to licensure under the PHS Act and are not subject to approval under section 505 of the FD&C Act.

4. Petitioner's Request to Refrain from Licensing any Future BLA for any COVID-19 Vaccine for any Population

Petitioner requests that FDA "refrain from approving any future . . . BLA for any COVID vaccine for all demographic groups because the current risks of serious adverse events or deaths outweigh the benefits, and because existing, approved drugs provide highly effective prophylaxis and treatment against COVID, mooting the EUAs." Petition at 1. To the extent this request can be interpreted as asserting that the risks of serious adverse events or deaths associated with any COVID-19 vaccine would necessarily outweigh the benefits of any COVID-19 vaccine and therefore FDA should refrain from approving any BLA for any COVID-19 vaccine, this section explains why this argument is unavailing and why we are denying Petitioner's request.

To the extent this request can be interpreted as *also* asserting, in addition to the assertion above, that, because approved drugs provide effective prophylaxis and treatment of COVID-19, the approval of a BLA for a COVID-19 vaccine would be "moot," this section explains why such a position is flawed and why FDA is not granting this request.

a. Petitioner's Request that FDA Refrain from Approving any BLA for any COVID-19 Vaccine because the Current Risks Outweigh the Benefits

Petitioner requests that FDA "refrain from approving any future BLA . . . for any COVID vaccine for all demographic groups" because the risks of serious adverse events or deaths associated with any COVID-19 vaccine outweigh the benefits of any COVID-19 vaccine. Petitioner has provided no evidence that would provide a basis for FDA to conclude that no COVID-19 vaccine could meet the BLA approval standard, however. Indeed, FDA has now approved a BLA for BioNTech's COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty) because, among other things, the data and information in the application demonstrated the safety and effectiveness of the vaccine.[88] Thus, Petitioner's request that FDA refrain from approving any BLAs for COVID-19 vaccines is denied.

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[87] FDA has issued guidance describing factors the Agency intends to use in determining how to prioritize EUA requests for COVID-19 vaccine candidates. See October 2020 Guidance at 5 (citing EUA Guidance at 18-20).
[88] See FDA's Summary Basis for Regulatory Action (SBRA) for the BioNTech BLA. This memorandum will be posted on www.fda.gov.

In Appendix I to this letter, we have provided additional background information about FDA's regulatory framework for the review of vaccine BLAs.

b. Petitioner's Request that FDA Refrain from Approving any BLA for any COVID-19 Vaccine because the Current Risks Outweigh the Benefits and because Currently-Approved Drugs are Effective in Preventing COVID-19

To the extent Petitioner is arguing that FDA should *also* refrain from approving a BLA for any COVID-19 vaccine because of the existence of FDA-approved drugs that are effective in preventing COVID-19, this argument is unavailing. As described above in section III.b.i.1, there are no FDA-approved drugs that are effective in preventing COVID-19 (other than BioNTech'sCOVID-19 vaccine [COVID-19 Vaccine, mRNA; Comirnaty], which is now approved for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older.).

For the reasons outlined in this section, FDA denies Petitioner's requests to refrain from licensing any BLAs for a COVID-19 vaccine.

ii. Petitioner's Requests Regarding COVID-19 Vaccines in Children

1. Request to Immediately Refrain from Allowing COVID-19 Vaccine Trials to Include Pediatric Subjects

In the Petition, Petitioner requests that FDA "immediately refrain from allowing minors to participate in COVID vaccine trials . . . ." Petition at 1. To the extent that the Petition can be interpreted to request that FDA suspend any COVID-19 vaccine clinical trial that includes pediatric subjects, this section explains why FDA is not at this time ordering that these clinical trials be suspended.

As explained above in section III.a., with certain exceptions, clinical investigations in which a drug is administered to human subjects must be conducted under an IND submitted to FDA by the sponsor. FDA's review of an IND includes a review of the study protocol which describes, among other things, the design of the clinical study, including the identified endpoints and methods for assessing the safety and effectiveness of the investigational product. The Petition requests that FDA adopt a universal approach toward all clinical trials of COVID-19 vaccines. Under FDA's regulations, however, the Agency examines each Investigational New Drug (IND) Application individually and considers the IND in the context of the standards in the regulation.

The FD&C Act provides a specific mechanism, called a "clinical hold," for prohibiting sponsors of clinical investigations from conducting the investigation (section 505(i)(3) of the FD&C Act; 21 U.S.C. 355(i)(3)). FDA's implementing regulations in 21 CFR 312.42 identify the circumstances that may justify a clinical hold. In this section of this letter, we explain why, at this time, FDA has not granted Petitioner's request to place all proposed or ongoing studies of COVID-19 vaccines enrolling pediatric subjects on clinical hold under 21 CFR 312.42(b).

The grounds for placing a proposed or ongoing study, including an ongoing Phase 3 study, on clinical hold are provided in 21 CFR 312.42(b). Specifically, 21 CFR 312.42(b)(1)(i) through (b)(1)(v) provides grounds for imposition of a clinical hold of a Phase 1 study. Additionally, as stated in 21 CFR 312.42(b)(2), FDA may place a proposed or ongoing Phase 2 or 3 investigation on clinical hold if it finds that: (i) any of the conditions in 21 CFR 312.42(b)(1)(i) through (b)(1)(v) apply; or (ii) the plan or protocol for the investigation is clearly deficient in design to meet its stated objectives. As indicated in more detail below, at this time, FDA has not granted Petitioner's request to place all proposed or ongoing studies of COVID-19 vaccines enrolling pediatric subjects on clinical hold under 21 CFR 312.42(b).

- 21 CFR 312.42(b)(1)(i): Human subjects are or would be exposed to an unreasonable and significant risk of illness or injury.

  FDA continues to evaluate all available information and, based on this evaluation thus far, does not believe that human subjects in any COVID-19 vaccine study that includes pediatric subjects are or would be exposed to an unreasonable and significant risk of illness or injury. The Agency reviews the protocols for COVID-19 vaccine clinical trials proposing to enroll pediatric subjects when they are submitted to the IND, in addition to any subsequent protocol amendments. For those clinical trials that have proceeded to studying COVID-19 vaccines in pediatric populations, FDA has determined that, based on all information currently available to FDA, the studies do not expose subjects to unreasonable risks.

- 21 CFR 312.42(b)(1)(ii): The clinical investigators named in the IND are not qualified by reason of their scientific training and experience to conduct the investigation described in the IND.

  The Petitioner has not provided evidence and FDA is currently aware of no other information indicating that clinical investigators named in the IND for any COVID-19 vaccine clinical trial including pediatric subjects are not qualified by reason of their scientific training and experience to conduct the investigation described in the INDs.

- 21 CFR 312.42(b)(1)(iii): The investigator brochure is misleading, erroneous, or materially incomplete.

  The Petitioner has not provided evidence and FDA is currently aware of no other information indicating that the investigator brochures for any ongoing COVID-19 vaccine investigation which includes or proposes to include pediatric subjects are misleading, erroneous, or materially incomplete.

- 21 CFR 312.42(b)(1)(iv): The IND does not contain sufficient information required under 312.23 to assess the risks to subjects of the proposed studies.

  The Petitioner has not provided evidence and FDA is currently aware of no other information indicating that the IND for any ongoing COVID-19 vaccine in which

pediatric subjects are enrolled contains insufficient information required under 21 CFR 312.23 to assess the risks to pediatric subjects participating in the studies.

- 21 CFR 312.42(b)(1)(v) [provides, in part, that]: The IND is for the study of an investigational drug intended to treat a life-threatening disease or condition that affects both genders, and men or women with reproductive potential who have the disease or condition being studied are excluded from eligibility because of a risk or potential risk from use of the investigational drug of reproductive toxicity (*i.e.*, affecting reproductive organs) or developmental toxicity (*i.e.*, affecting potential offspring)….

  The Petitioner has not provided evidence and FDA is currently aware of no other information indicating that any COVID-19 vaccine studies enrolling pediatric subjects are excluding from eligibility men or women – including male and female adolescents and teenagers - with reproductive potential.

- 21 CFR 312.42(b)(2)(ii): The plan or protocol for the Phase 2 or Phase 3 investigation is clearly deficient in design to meet its stated objectives.

  The Agency reviewed the protocols for the COVID-19 vaccine investigations involving pediatric subjects at the time they were submitted to the INDs, as well as any subsequent amendments as they were submitted, and has determined that the study designs meets their stated objectives.

  At this time, the Agency is aware of no information to indicate that the protocols for any ongoing clinical investigations of COVID-19 vaccines involving pediatric subjects are clearly deficient in design to meet their stated objectives.

FDA has reviewed the issues raised in the Petition relating to the request to "immediately refrain from allowing minors to participate in COVID vaccine trials." Petition at 1. For the reasons outlined above, and in light of information currently available to FDA, FDA has determined that grounds do not exist to grant Petitioner's request to place all COVID-19 vaccine clinical investigations involving pediatric subjects on clinical hold pursuant to 21 CFR 312.42.

2. Request that FDA Refrain from Issuing EUA Amendments for Authorized COVID-19 Vaccines to Include Indications for Pediatric Populations

The Petition requests, among other things, that "[g]iven the extremely low risk of COVID illness in children, FDA should . . . immediately refrain from amending EUAs to include children. . . ." Petition at 1. To the extent that the Petition requests that FDA refrain from issuing EUA amendments for any of the Authorized COVID-19 Vaccines to include an indication for use in pediatric populations, this section explains why FDA is not granting this request.

In determining whether to issue an EUA for a product, including an amendment to an EUA in order to include additional populations within the indication, the FDA evaluates the available evidence and assesses, among other things, any known or potential risks and any known or potential benefits. Once a manufacturer submits an EUA request for a COVID-19 vaccine, the FDA then evaluates the request and determines whether the relevant statutory criteria are met,

taking into account the totality of the scientific evidence about the vaccine that is available to the agency.

As noted in Section II.b. above, in the October 2020 Guidance, FDA provided recommendations that describe key information that would support issuance of an EUA for a vaccine to prevent COVID-19.[89] In this guidance, FDA explained that, in the case of such vaccines, any assessment regarding an EUA will be made on a case-by-case basis considering the target population, the characteristics of the product, the preclinical and human clinical study data on the product, and the totality of the available scientific evidence relevant to the product.[90] FDA has also stated, in this guidance, that for a COVID-19 vaccine for which there is adequate manufacturing information to ensure its quality and consistency, issuance of an EUA would require a determination by FDA that the vaccine's benefits outweigh its risks based on data from at least one well-designed Phase 3 clinical trial that demonstrates the vaccine's safety and efficacy in a clear and compelling manner.[91]

a. Information Submitted by Petitioner Regarding the Safety of COVID-19 Vaccines in Pediatric Populations

Petitioner argues that, for children, the risks of COVID-19 vaccines outweigh the benefits because the risk of severe COVID in children is "extremely low." Petition at 1. Petitioner cites to several sources of information in support of this argument (Petition at 12-13), which FDA has reviewed and considered.

Petitioner cites to CDC data[92] regarding death rates of children in the United States due to COVID-19 and compares the number of children who have died involving COVID-19 to the number of Americans of all ages who have died of COVID-19. Petitioner's approach of simply comparing raw numbers of deaths involving COVID-19 in the U.S. pediatric population against the raw numbers of deaths involving COVID-19 in the overall U.S. population (all sexes and all ages), does not provide a sufficient scientific basis upon which to conclude, as Petitioner contends, that the "relative risk for children due to COVID is very low." Petition at 12. Additionally, as discussed in further detail below, based on available data and information, we have concluded that COVID-19 is a serious or life-threatening disease or condition in the 12-17 age group.

As a preliminary matter, we note that petitioner's claim that "the death rate following either vaccination in this age group, assuming these children were trial enrollees, is approximately 2 in 2,000 or 0.1%." (Petition at 13) is erroneous. Our review of the submitted clinical trial data associated with the Pfizer-BioNTech COVID-19 Vaccine has not identified any deaths among adolescent or young adult vaccinees.[93] Additionally, as described in a NEJM article regarding

[89] October 2020 Guidance at 6-7.
[90] Id. at 3.
[91] Id. at 4.
[92] CDC, National Center for Health Statistics, Weekly Updates by Select Demographic and Geographic Characteristics, https://www.cdc.gov/nchs/nvss/vsrr/covid_weekly/index.htm#SexAndAge.
[93] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum (Dec. 11, 2020), https://www.fda.gov/media/144416/download (stating that there were two deaths in vaccine recipients, both >55 years of age). FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for

the Moderna COVID-19 vaccine, no deaths were reported among vaccine recipients enrolled in the clinical trial of Moderna COVID-19 Vaccine.[94] Investigational New Drug (IND) application sponsors are required to notify FDA in a written safety report of any adverse experience associated with the use of the drug that is both serious and unexpected.[95] Any death that occurs in a vaccine clinical trial therefore must be reported to FDA and is then thoroughly evaluated by FDA to determine the cause and whether or not the death is plausibly related to the vaccine.

Additionally, we note that Petitioner raised concerns regarding VAERS reports in arguing that COVID-19 vaccines should not be authorized for pediatric populations because, Petitioner argues, "[a]vailable evidence strongly suggests that the vaccine is much more dangerous to children than the disease." Petition at 12. VAERS data reviewed to date has not identified risks related to vaccination that would cause the Agency to change its view that the benefits of vaccination with the Pfizer-BioNTech COVID-19 vaccine outweigh the risks of vaccination in individuals 12-17 years of age. VAERS data is evaluated thoroughly, and as described in greater detail above, FDA acts on safety signals. VAERS reports, however, are not used *in isolation* to draw an association between a vaccine and a possible adverse event.

Finally, we note that petitioner cites to an opinion piece published in the British Medical Journal, which presents the authors' opinion that the benefits of COVD-19 vaccination are outweighed by its risks in pediatric populations.[96] FDA has reviewed this article and determined it does not present evidence that the EUA standard could not be met for pediatric populations. Indeed, as explained in the FDA Decision Memorandum for the Pfizer-BioNTech COVID-19 Vaccine EUA, based on FDA's review of all available data regarding the benefits and risks of the use of the Pfizer-BioNTech COVID-19 vaccine in individuals 12 through 17 years of age, we have determined that this EUA meets the statutory criteria for individuals in this age range.[97]

Petitioner has failed to present data demonstrating that, for children, the risks of COVID-19 vaccines outweigh their benefits because the risk of severe COVID in children is "extremely low." Petition at 1. As explained in this section, the information submitted by Petitioner does not support this contention. As explained in further detail below, data reviewed by the Agency demonstrates that the Pfizer-BioNTech COVID-19 Vaccine, which is authorized for use in individuals 12 years of age and older, continues to demonstrate that the known and potential benefits of this vaccine outweigh its known and potential risks in this population. Any other EUA requests for COVID-19 vaccine candidates for use in pediatric populations will be reviewed on a case-by-case basis under the applicable statutory standards. Therefore, we deny

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Authorization in Individuals 12-15 Years of Age (May 10, 2021), https://www.fda.gov/media/148542/download (stating that there were no deaths among vaccine recipients 12-15 years of age during the follow-up period).

[94] K. Ali, et al., Evaluation of mRNA-1273 SARS-CoV-2 Vaccine in Adolescents, NEJM (Aug. 11, 2021), DOI: 10.1056/NEJMoa2109522, https://www.nejm.org/doi/10.1056/NEJMoa2109522.

[95] 21 CFR § 312.32(c)(1)(i).

[96] W. Pegden, V. Prasad, S. Baral, Covid vaccines for children should not get emergency use authorization, BMJ (May 7, 2021), https://blogs.bmj.com/bmj/2021/05/07/covid-vaccines-for-children-should-not-get-emergency-use-authorization/.

[97] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum (Dec. 11, 2020), https://www.fda.gov/media/144416/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age (May 10, 2021), https://www.fda.gov/media/148542/download.

Petitioner's request to refrain from amending any EUA for a COVID-19 vaccine to include a pediatric indication.

3. Request that FDA Immediately Revoke all EUAs for COVID-19 Vaccines with Pediatric Indications

Petitioner requests that FDA "immediately revoke all EUAs that permit vaccination of children under 16 for the Pfizer vaccine and under 18 for other COVID vaccines." Petition at 1. Currently, only the Pfizer-BioNTech COVID-19 vaccine is indicated for the prevention of COVID-19 in pediatric populations. This vaccine is indicated for individuals 12 years of age and older. As explained in section III.B.i.1.b above, in addressing this request, it is necessary to consider the EUA revocation standard provided in section 564(g)(2) of the FD&C Act. In this section, we assess whether any of these statutory conditions under which FDA may revoke an EUA are met with respect to the pediatric indication for the Pfizer-BioNTech COVID-19 Vaccine EUA and explain why the EUA revocation standard is not met for this vaccine.

a. Standard for Revocation of EUAs is not Met for the Authorized COVID-19 Vaccines with Pediatric Indications

As explained above in section III.b.i.1.b of this letter, Section 564(g)(2) of the FD&C Act provides the standard for revocation of an EUA. Under this statutory authority, FDA may revise or revoke an EUA if:

> (A) the circumstances described under [section 564(b)(1) of the FD&C Act] no longer exist;
> (B) the criteria under [section 564(c) of the FD&C Act] for issuance of such authorization are no longer met; or
> (C) other circumstances make such revision or revocation appropriate to protect the public health or safety.

As explained above in section II.b., the EUA Guidance notes that once an EUA is issued for a product, in general, that EUA will remain in effect for the duration of the EUA declaration under which it was issued, "unless the EUA is revoked because the criteria for issuance . . . are no longer met or revocation is appropriate to protect public health or safety (section 564(f),(g) [of the FD&C Act])."[98]

i. Circumstances Continue to Justify the Issuance of the EUAs for the Authorized COVID-19 Vaccine with Pediatric Indications

As explained in detail above in section III.b.i.1.b., section 564(b)(2) of the FD&C Act sets forth the statutory standard for termination of an EUA declaration. This provision provides that an EUA declaration remains in place until the earlier of: (1) a determination by the HHS Secretary, in consultation with the Secretary of Defense, that the circumstances that precipitated the declaration have ceased or (2) a change in the approval status of the product such that the authorized use(s) of the product are no longer unapproved. Neither of those statutory criteria is

[98] EUA Guidance at 28.

satisfied with respect to the Authorized COVID-19 Vaccine with a pediatric indication. Thus, the circumstances described under section 564(b)(1) of the FD&C Act continue to exist. FDA therefore is not revoking the EUA for the Authorized COVID-19 vaccine with a pediatric indication under the authority in section 564(g)(2)(A) of the FD&C Act.

1. The Criteria for The Issuance of the Authorized COVID-19 Vaccine with Pediatric Indications Continues to Be Met

This section describes in detail why the criteria under section 564(c) of the FD&C Act continue to be met with respect to the pediatric indication for the Pfizer-BioNTech COVID-19 Vaccine EUA and why, therefore, FDA may not revoke this EUA under the authority in section 564(g)(2)(B) of the FD&C Act.

a. Serious or life-threatening disease or condition.

As explained above in section III.b.i.1 of this letter, section 564(c)(1) of the FD&C Act requires that, for an EUA to be issued for a medical product, "the agent(s) referred to in [the HHS Secretary's EUA declaration] can cause a serious or life-threatening disease or condition." FDA has concluded that SARS-CoV-2, which is the subject of the EUA declaration, meets this standard. FDA is not aware of science indicating that there is any change in the ability of the SARS-CoV-2 virus to cause a serious or life-threatening disease or condition, namely COVID-19, nor has Petitioner provided any information about such a change.

The SARS-CoV-2 pandemic continues to present an extraordinary challenge to global health and, as of August 3, 2021, has caused more than 199 million cases of COVID-19 and claimed the lives of more than 4.2 million people worldwide.[99] In the United States, more than 34 million cases and over 611,000 deaths have been reported to the CDC.[100] On January 31, 2020, the U.S. Secretary of Health and Human Services (HHS) declared a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS, and the U.S. President declared a national emergency in response to COVID-19 on March 13, 2020. Additional background information on the SARS-CoV-2 virus and COVID-19 pandemic may be found in FDA Decision Memoranda for the Authorized COVID-19 Vaccines.[101]

Since March 1, 2020, approximately 1.7 million COVID-19 cases in individuals 12 to 17 years of age have been reported to the Centers for Disease Control and Prevention (CDC). Among these cases approximately 11,700 resulted in hospitalization, with more than 691 ICU admissions

[99] Johns Hopkins University School of Medicine, Coronavirus Resource Center, https://coronavirus.jhu.edu/map.html.
[100] CDC, COVID Data Tracker, https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases.
[101] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum (Dec. 11, 2020), https://www.fda.gov/media/144416/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age (May 10, 2021), https://www.fda.gov/media/148542/download; FDA, Moderna COVID-19 Vaccine EUA Decision Memorandum (Dec. 18, 2020), https://www.fda.gov/media/144673/download; FDA, Janssen COVID-19 Vaccine EUA Decision Memorandum (Feb. 27, 2021), https://www.fda.gov/media/146338/download.

and more than 100 deaths. It is difficult to estimate the incidence of COVID-19 among children and adolescents because they are frequently asymptomatic and infrequently tested. Children and adolescents appear less susceptible to SARS-CoV-2 infection and have a milder COVID-19 disease course as compared with adults. However, as with adults, children and adolescents with underlying conditions such as asthma, chronic lung disease, and cancer are at higher risk than their heathier counterparts for COVID-19-related hospitalization and death. Of the children who have developed severe illness from COVID-19, most have had underlying medical conditions. Multisystem inflammatory syndrome in children (MIS-C) is a rare but serious COVID-19-associated condition that can present with persistent fever, laboratory markers of inflammation and heart damage, and, in severe cases, hypotension and shock. As of June 28, 2021, the CDC received reports of 4196 cases and 37 deaths that met the definition for MIS-C.

Both FDA and CDC have convened advisory committee meetings to discuss the use of COVID-19 vaccines in pediatric populations. Overall, these advisory committees agreed that there is a serious risk of severe COVID-19 in the pediatric population. In particular, the June 23, 2021 ACIP meeting discussed the benefits and risks of the use of COVID-19 mRNA vaccines in adolescents and young adults.[102] This discussion raised the point that adolescents and young adults have the highest COVID-19 incidence rates, and that these populations are an increasing proportion of COVID-19 cases reported. COVID-19-associated deaths continue to occur in these populations; since April 2021, 316 deaths have been reported among persons aged 12-29 years. Additionally, post-COVID conditions -- such as Multisystem Inflammatory Syndrome in Children (MIS-C) and Multisystem Inflammatory Syndrome in Adults (MIS-A) -- can occur in these populations following COVID-19.

Therefore, the criterion under section 564(c)(1) continues to be met with respect to the Authorized COVID-19 Vaccines with Pediatric Indications.

b. Evidence of Effectiveness

As explained above in section III.b.i.1.b of this letter, Section 564(c)(2)(A) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude "based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled trials, if available, it is reasonable to believe that the product may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition that can be caused by SARS-CoV-2." FDA has determined that based on the totality of scientific evidence available, including data from adequate and well-controlled trials, it is reasonable to believe that the Pfizer-BioNTech COVID-19 vaccine may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition in the 12 through 17 years of age population.[103] The basis for this determination is explained in detail in FDA's decision memoranda regarding

[102] CDC, Megan Wallace and Sara Oliver, CDC ACIP Meeting Presentation, COVID-19 mRNA Vaccines in Adolescents and Young Adults: Benefit-Risk Discussion, (June 23, 2021), https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/05-COVID-Wallace-508.pdf; CDC, ACIP Meeting Slides, (June 23, 2021), https://www.cdc.gov/vaccines/acip/meetings/slides-2021-06.html.

[103] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum (Dec. 11, 2020), https://www.fda.gov/media/144416/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age (May 10, 2021), https://www.fda.gov/media/148542/download.

the Pfizer BioNTech COVID-19 Vaccine EUA.[104] Section III.b.ii of this letter explains why Petitioner's arguments regarding the effectiveness of the Authorized COVID-19 Vaccines, and the information submitted by Petitioner in support of this argument, does not change FDA's analysis regarding the effectiveness of the Pfizer-BioNTech COVID-19 vaccine in individuals 12 through 17 years of age.

Therefore, the criterion under section 564(c)(2)(A) continues to be met with respect to the Authorized COVID-19 Vaccines.

c. Benefit-Risk Analysis

Section 564(c)(2)(B) of the FD&C Act requires that, for an EUA to be issued for a medical product, FDA must conclude "the known and potential benefits of the product, when used to diagnose, prevent, or treat [the identified serious or life-threatening disease or condition], outweigh the known and potential risks of the product . . . ." Petitioner argues that the current risks of serious adverse events or deaths associated with the authorized COVID-19 vaccines outweigh the benefits of COVID-19 vaccines in the pediatric population. Section III.b.i.1.b.ii above addresses these arguments insofar as they apply to the Authorized COVID-19 Vaccines generally and explains why they are unavailing. Section III.b.ii above addresses Petitioner's arguments regarding the safety of COVID-19 vaccines in the pediatric population, and explains why the information submitted by Petitioner does not change FDA's analysis regarding the benefits and risks of the authorized COVID-19 vaccines in the pediatric population.

d. No Alternatives

Section 564(c)(3) of the FD&C Act provides one of the required statutory factors that must be met in order for a product to be granted an EUA. This statutory provision requires that "there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating [the serious or life-threatening disease or condition]." To the extent Petitioner's contention can be interpreted as an argument that there are FDA-approved drugs indicated for the prevention of COVID-19 in pediatric populations (and that therefore the requirement in section 564(c)(3) of the FD&C Act is not met with respect to the Authorized COVID-19 Vaccine with a pediatric indication), this argument is erroneous.

As described above in section III.b.i.1.b, there are no FDA-approved drugs or biological products indicated to prevent COVID-19 in any population, other than the newly-approved BioNTech COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty). That vaccine is approved for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older.[105] The EUA for Pfizer-BioNTech COVID-19 Vaccine remains in effect to cover those 12 through

[104] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum (Dec. 11, 2020), https://www.fda.gov/media/144416/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age (May 10, 2021), https://www.fda.gov/media/148542/download.

[105] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum (Dec. 11, 2020), at 8-9, https://www.fda.gov/media/144416/download; FDA, Moderna COVID-19 Vaccine EUA Decision Memorandum (Dec. 18, 2020), at 9, https://www.fda.gov/media/144673/download; FDA, Janssen COVID-19 Vaccine EUA Decision Memorandum (Feb. 27, 2021), at 9, https://www.fda.gov/media/146338/download.

15 years of age, the administration of a third dose to certain immunocompromised individuals 12 years of age and older, and until sufficient approved vaccine can be manufactured and distributed for use in those 16 years of age and older. Similarly, the EUA for the Moderna COVID-19 Vaccine and the Janssen COVID-19 Vaccine remain in effect for individuals 18 years of age and older. Therefore, there is no adequate, approved, and available alternative to the Authorized COVID-19 Vaccines for preventing COVID-19.

ii. No Other Circumstances Make A Revision or Revocation Appropriate to Protect the Public Health or Safety

As noted above in section III.b.i.1.b of this letter, section 564(g)(2)(C) of the FD&C Act provides that FDA may revise or revoke an EUA if circumstances justifying its issuance (under section 564(b)(1)) no longer exist, the criteria for its issuance are no longer met, or other circumstances make a revision or revocation appropriate to protect the public health or safety. The EUA guidance explains that such other circumstances may include:

> significant adverse inspectional findings (e.g., when an inspection of the manufacturing site and processes has raised significant questions regarding the purity, potency, or safety of the EUA product that materially affect the risk/benefit assessment upon which the EUA was based); reports of adverse events (number or severity) linked to, or suspected of being caused by, the EUA product; product failure; product ineffectiveness (such as newly emerging data that may contribute to revision of the FDA's initial conclusion that the product "may be effective" against a particular CBRN agent); a request from the sponsor to revoke the EUA; a material change in the risk/benefit assessment based on evolving understanding of the disease or condition and/or availability of authorized MCMs; or as provided in section 564(b)(2), a change in the approval status of the product may make an EUA unnecessary.[106]

As of the date of this writing, FDA has not identified any such circumstances that would make revocation of the pediatric indication for the Pfizer-BioNTech COVID-19 Vaccine EUA appropriate to protect the public health or safety. As stated previously in this response, FDA determined the EUA standard is met for the Pfizer-BioNTech COVID-19 Vaccine in individuals 12 through 17 years of age because data submitted by the sponsors demonstrated in a clear and compelling manner that the known and potential benefits of this vaccine, when used to prevent COVID-19, outweigh the known and potential risks of this vaccine in individuals 12 through 17 years of age, and that there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating COVID-19 in this population.

As described in detail in section III.b.i.1 above, FDA has identified circumstances that have made revision of the EUAs for the Authorized COVID-19 Vaccines appropriate, and,

[106] EUA Guidance at 29.

accordingly, has required changes to the authorized labeling for the Authorized COVID-19 Vaccines.[107]

Additionally, as explained above, FDA finds no basis in the information submitted in the Petition, or in any postmarket data regarding the Pfizer-BioNTech COVID-19 Vaccine, to support a revocation of the pediatric indication for the Pfizer-BioNTech COVID-19 Vaccine EUA, nor has Petitioner provided any such information in the Petition. FDA is not aware of any information indicating that the known and potential benefits of Pfizer-BioNTech COVID-19 Vaccine in the 12-17 years of age population are outweighed by their known and potential risks, nor has Petitioner provided any such information in the Petition. Furthermore, there are no other circumstances that make a revision or revocation of the pediatric indication for the Pfizer-BioNTech COVID-19 Vaccine EUA appropriate to protect the public health or safety, nor has Petitioner provided any information about such circumstances. FDA therefore sees no justifiable basis upon which to take any action based on Petitioner's request with respect to the pediatric indication for the Pfizer-BioNTech COVID-19 Vaccine EUA. Accordingly, as noted above, we deny Petitioner's request that FDA "immediately revoke all EUAs that permit vaccination of children under 16 for the Pfizer vaccine and under 18 for other COVID vaccines." Petition at 1.

iii. Petitioner's Request that FDA Immediately Revoke Tacit Approval that Pregnant Women may Receive any EUA or Licensed COVID-19 Vaccines and Immediately Issue Public Guidance

Petitioner requests that FDA "immediately revoke tacit approval that pregnant women may receive any EUA or licensed COVID vaccines and immediately issue public guidance to that effect." Petition at 1. Because "tacit approval," or revocation thereof, is not a concept that exists in applicable statutes or regulations governing FDA-regulated products, FDA interprets this as a request that the labeling for the Authorized COVID-19 Vaccines, and any COVID-19 vaccine that may be licensed in the future, contain a contraindication for use during pregnancy.
In addressing Petitioner's request for a contraindication, we first discuss the risks posed to pregnant women by COVID-19. We then provide an explanation of the regulatory framework for prescription drug labeling for approved and licensed products, including the standard for inclusion of contraindications in such labeling to inform health care providers of information such as known hazards in the use of a particular drug as well as the requirements for pregnancy and lactation information in such labeling. We then discuss labeling for products made available under an EUA and explain why a contraindication for use in pregnant women was not included in the labeling for the Authorized COVID-19 Vaccines. This section concludes with an explanation for why Petitioner's requests for a contraindication for use during pregnancy in the labeling for the Authorized COVID-19 Vaccines – and BioNTech's COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty) - is denied.

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[107] FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization in Individuals 12-15 Years of Age (May 10, 2021), https://www.fda.gov/media/148542/download; FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of an Additional Dose in Certain Immunocompromised Individuals (August 12, 2021), https://www.fda.gov/media/151613/download; FDA, Moderna COVID-19 Vaccine EUA Amendment Decision Memorandum for Authorization of an Additional Dose in Certain Immunocompromised Individuals (August 12, 2021), https://www.fda.gov/media/151611/download; FDA, Janssen COVID-19 Vaccine EUA Decision Memorandum (Feb. 27, 2021), https://www.fda.gov/media/146338/download.

1. COVID-19 in Pregnancy

As a preliminary matter, we note that COVID-19 poses significant risks to pregnant women. CDC explains that "observational data regarding COVID-19 during pregnancy demonstrate that pregnant people with COVID-19 have an increased risk of severe illness, including illness resulting in intensive care admission, mechanical ventilation, extracorporeal membrane oxygenation, or death, though the absolute risk for these outcomes is low. Additionally, they are at increased risk of preterm birth and might be at an increased risk of adverse pregnancy complications and outcomes, such as preeclampsia, coagulopathy, and stillbirth."[108]

2. Certain Content and Format Requirements for Prescription Drug Labeling for Products Approved Under NDAs or BLAs

As FDA explains in the draft guidance for industry, Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products – Content and Format, ("Pregnancy and Lactation Guidance") "[p]rescription drug labeling is a communication tool. Its principal objective is to make available to health care providers the detailed prescribing information necessary for the safe and effective use of a drug, in a manner that is clear and useful to providers when prescribing for and counseling patients."[109] In order to achieve this objective, prescription labeling must be based on scientific data, and it must not be inaccurate, false, or misleading.[110]

FDA regulations govern the content and format of prescription drug labeling for approved drugs and biological products (see, e.g., §§ 201.56 and 201.57 (21 CFR 201.57); see also 21 CFR 201.100(c)). The regulations are intended to organize labeling information to more effectively communicate to health care professionals the "information necessary for the safe and effective use of prescription drugs."[111] FDA regulations require that the labeling of most prescription drug products include Highlights of Prescribing Information, which are intended to summarize the information that is most important for prescribing the drug safely and effectively and to facilitate access to the more detailed information within product labeling (see § 201.57(a)). FDA regulations further require that the labeling for most prescription drugs include, among other information, the following sections: Contraindications; Warnings and Precautions; Adverse

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[108] CDC, Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Authorized in the United States, Vaccination of Pregnant or Lactating People, https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html#pregnant.

[109] Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products - Content and Format Guidance for Industry, Draft Guidance, July 2020, at 2, https://www.fda.gov/media/90160/download.

[110] 21 CFR § 201.56(a)(2) "The labeling must be informative and accurate and neither promotional in tone nor false or misleading in any particular. In accordance with §§ 314.70 and 601.12 of this chapter, the labeling must be updated when new information becomes available that causes the labeling to become inaccurate, false, or misleading."

[111] Preamble to final rule, "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products" (71 FR 3922 at 3928, January 24, 2006) (Physician Labeling Rule). For the content and format requirements for the labeling of older prescription drug products that are not subject to the labeling requirements in § 201.57, see § 201.80 (21 CFR 201.80). The specific labeling requirements for older drug products differ in certain respects, and generally are not referenced in this response.

Reactions; and Use in Specific Populations, which includes a subsection on Pregnancy (see § 201.57(c)(1), (5), (6), (7), and (9)(i)).

a. Contraindications

The Contraindications section must describe any situations in which the drug should not be used because the risk of use "clearly outweighs any possible therapeutic benefit" (§ 201.57(c)(5)). This section should include observed and anticipated risks, but not theoretical risks.[112] This could include, for example, a situation where animal data raise substantial concern about the potential for occurrence of the adverse reaction in humans (e.g., animal data demonstrate that the drug has teratogenic effects) and those risks do not outweigh any potential benefit of the drug to any patient.[113]

b. Pregnancy

The Pregnancy subsection is located under the Use in Specific Populations section (see § 201.57(c)(9)(i)). On December 4, 2014, FDA issued a final rule amending the regulations on the requirements for pregnancy and lactation information in prescription drug and biological product labeling (Pregnancy and Lactation Labeling Rule (PLLR)).[114] The PLLR revisions to the regulations were intended "to create a consistent format for providing information about the effects of a drug on pregnancy and lactation that would be useful for decision making by health care providers and their patients."[115] The labeling content and format requirements in § 201.57(c)(9)(i), as revised by the PLLR, took effect on June 30, 2015, with a phased implementation schedule for drugs (including biological products) that are the subject of NDAs, BLAs, and efficacy supplements that had been approved on or after June 30, 2001.[116] The PLLR also requires for all human prescription drug and biological products, including those for which an application was approved before June 30, 2001, that the Pregnancy subsection of labeling be revised to remove the pregnancy letter categories A, B, C, D, and X.[117]
Information in the Pregnancy subsection of labeling may present, in greater detail, a topic that is briefly summarized in another section of labeling (e.g., Warnings and Precautions).[118] FDA has explained that when a topic is discussed in more than one section of labeling, the section containing the most important information relevant to prescribing should typically include a succinct description and should cross-reference sections that contain additional detail.[119]

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[112] See § 201.57(c)(5); see also FDA guidance for industry, Warnings and Precautions, Contraindications, and Boxed Warning Sections of Labeling for Human Prescription Drug and Biological Products - Content and Format; Guidance for Industry, October 2011 (Warnings Guidance), at 8, https://www.fda.gov/media/71866/download.
[113] See Warnings Guidance at 8.
[114] Final rule, "Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling" (PLLR) (79 FR 72064, December 4, 2014), https://www.federalregister.gov/documents/2014/12/04/2014-28241/content-and-format-of-labeling-for-human-prescription-drug-and-biological-products-requirements-for.
[115] Id. at 72066.
[116] See §§ 201.56(b) and 201.57(c)(9)(i).
[117] §§ 201.57(c)(9) and 201.80; see also 79 FR 72064 at 72095 (December 4, 2014).
[118] PLLR, 79 FR 72064 at 72085 (December 4, 2014).
[119] See FDA guidance for industry, Labeling for Human Prescription Drug and Biological Products - Implementing the PLR Content and Format Requirements; Guidance for Industry, February 2013, https://www.fda.gov/media/71836/download.

Under current labeling requirements, information in the Pregnancy subsection of labeling is presented under the following subheadings: Pregnancy Exposure Registry; Risk Summary; Clinical Considerations; and Data.[120] The labeling for the Authorized COVID-19 Vaccines includes the Pregnancy Exposure Registry and the Risk Summary subheadings. We briefly describe these subheadings below.

i. Pregnancy Exposure Registry

If there is a scientifically acceptable pregnancy exposure registry for the drug, the labeling must state that fact and provide contact information needed for enrolling in or obtaining information about the registry.

ii. Risk Summary

The Risk Summary subheading is required under the Pregnancy subsection because certain statements must be included even when no product-specific data are available, given that all pregnancies have a background risk of birth defect, loss, or other adverse outcomes.[121] The Risk Summary must contain risk statement(s) that describe for the drug the risk of adverse developmental outcomes based on all relevant human data, animal data, and/or the drug's pharmacology.[122] When multiple data sources are available, the risk statements are required to be presented in the following order: human, animal, and pharmacologic.[123]

When human data are available that establish the presence or absence of any adverse developmental outcome(s) associated with maternal use of the drug, a risk statement based on human data must summarize the specific developmental outcome(s) and include its incidence and the effects of dose, duration of exposure, and gestational timing of exposure.[124] If human data indicate that there is an increased risk for a specific adverse developmental outcome in infants born to women exposed to the drug during pregnancy, the risk summary must contain a quantitative comparison of that risk to the risk for the same outcome in infants born to women who were not exposed to the drug, but who have the disease or condition for which the drug is indicated to be used.[125] When risk information is not available for women with the disease or condition(s) for which the drug is indicated, the risk summary must contain a comparison of the specific outcome in women exposed to the drug during pregnancy against the rate at which the outcome occurs in the general population.[126]

When animal data are available, the risk statement based on such data must describe the potential risk for adverse developmental outcomes in humans and summarize the available data.[127] This statement must include: the number and type(s) of species affected; timing of exposure; animal doses expressed in terms of human dose or exposure equivalents; and outcomes for pregnant animals and offspring.[128]

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[120] § 201.57(c)(9)(i).
[121] § 201.57(c)(9)(i)(B).
[122] Id.
[123] Id.
[124] § 201.57(c)(9)(i)(B)(1).
[125] Id.
[126] Id.
[127] § 201.57(c)(9)(i)(B)(2).
[128] Id.

With respect to pharmacology, when the drug has a well-understood pharmacologic mechanism of action that may result in adverse developmental outcomes, the Risk Summary must explain the mechanism of action and the potential associated risks.[129]

3. Inclusion of Contraindications and Pregnancy Information in the Labeling for the Authorized COVID-19 Vaccines

For the emergency use of an unapproved product, section 564(e)(1)(A)(i) of the FD&C Act requires that FDA must—to the extent practicable given the applicable circumstances of the emergency, and as FDA finds necessary and appropriate to protect the public health—establish appropriate conditions designed to ensure that health care professionals administering the authorized product are informed:

- That FDA has authorized the emergency use of the product (including the product name and an explanation of its intended use);
- Of the significant known and potential benefits and risks of the emergency use of the product, and the extent to which such benefits and risks are unknown; and
- Of available alternatives and their benefits and risks.

Therefore, as explained in the EUA Guidance, FDA recommends that "a request for an EUA include a 'Fact Sheet' for health care professionals or authorized dispensers that includes essential information about the product. In addition to the required information, Fact Sheets should include . . . any contraindications or warnings."[130] The EUA guidance also recommends that, for unapproved drugs that do not have "FDA-approved labeling for any indication . . . in addition to the brief summary information found in a Fact Sheet, the sponsor also develop more detailed information similar to what health care professionals are accustomed to finding in FDA-approved package inserts."[131]

The sponsors for all the Authorized COVID-19 Vaccines submitted such prescribing information in the EUA requests, and FDA reviewed and authorized this labeling. The Fact Sheets for Healthcare Providers Administering Vaccine for all of the Authorized COVID-19 Vaccines contain Contraindications and Warnings and Precautions sections because FDA determined that sufficient data existed for inclusion of such information in the authorized labeling for these vaccines.[132]

FDA did not, however, require inclusion of a contraindication for pregnancy in the authorized labeling. The authorized COVID-19 vaccines are authorized for use in an age range that includes women of childbearing age and are not contraindicated for use in pregnant women because FDA

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[129] § 201.57(c)(9)(i)(B)(3).
[130] EUA Guidance at 22.
[131] EUA Guidance at 23.
[132] Janssen COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Sections 5.2 and 5.3 Warnings and Precautions Regarding Thrombosis with Thrombocytopenia and GBS, https://www.fda.gov/media/146304/download; Pfizer-BioNTech COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Section 5.2, Warning and Precautions Regarding Myocarditis and Pericarditis, https://www.fda.gov/media/144413/download Moderna COVID-19 Vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers), Section 5.2, Warning and Precautions Regarding Myocarditis and Pericarditis, https://www.fda.gov/media/144637/download.

is not aware of any evidence that suggests the risk of use of the Authorized COVID-19 Vaccines in pregnant women would clearly outweigh any possible therapeutic benefit.[133] Nor has the Petitioner presented any such evidence in the Petition. Accordingly, this request is denied.

4. Inclusion of Contraindications and Pregnancy Information in the Labeling for Licensed COVID-19 Vaccines

With respect to Petitioner's request that FDA "immediately revoke tacit approval that pregnant women may receive any EUA or licensed COVID vaccines and immediately issue public guidance to that effect" (Petition at 1; emphasis added), as explained above in this section, FDA regulations require the Contraindications section of the labeling for an approved drug or biological product to describe any situations in which the drug or biological product should not be used because the risk of use "clearly outweighs any possible therapeutic benefit" (§ 201.57(c)(5)). This section should include observed and anticipated risks, but not theoretical risks.[134] The approved COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty) is indicated for use in an age range that includes women of childbearing age and is not contraindicated for use in pregnant women because FDA is not aware of any evidence that suggests the risk of use of BioNTech's COVID-19 vaccine in pregnant women would clearly outweigh any possible therapeutic benefit,[135] nor has the Petitioner presented any such evidence in the Petition.

In its review of a BLA for any future COVID-19 vaccine candidate, FDA will apply the regulatory standards outlined above in determining, on a case-by-case basis, whether to include a contraindication in pregnancy, or any other contraindications, in the approved labeling for such a vaccine. Accordingly, Petitioner's request is denied.

iv. Petitioner's Request that FDA Immediately Amend its Guidance regarding Certain Approved Drugs [chloroquine drugs, ivermectin, "and any other drugs demonstrated to be safe and effective against COVID"]

Petitioner requests that the Agency "immediately amend its existing guidance for the use of the chloroquine drugs, ivermectin, and any other drugs demonstrated to be safe and effective against COVID, to comport with current scientific evidence of safety and efficacy at currently used doses and immediately issue notifications to all stakeholders of this change." Petition at 2. FDA has not issued "guidance for the use of chloroquine drugs, ivermectin, and other drugs

[133] FDA's decision memoranda for the Authorized COVID-19 Vaccines discuss FDA's analysis of all available data regarding the use of the Authorized COVID-19 Vaccines in pregnancy. *See*, FDA, Pfizer-BioNTech COVID-19 Vaccine EUA Decision Memorandum (Dec. 11, 2020), https://www.fda.gov/media/144416/download; FDA, Moderna COVID-19 Vaccine EUA Decision Memorandum (Dec. 18, 2020), https://www.fda.gov/media/144673/download; FDA, Janssen COVID-19 Vaccine EUA Decision Memorandum (Feb. 27, 2021), https://www.fda.gov/media/146338/download.

[134] See § 201.57(c)(5); see also Warnings Guidance at 8.

[135] See FDA's Summary Basis for Regulatory Action (SBRA) for the BioNTech BLA. This memorandum will be posted on www.fda.gov.

demonstrated to be safe and effective against COVID."[136] FDA has, however, analyzed adverse event information and made publicly available safety issues regarding the use of hydroxychloroquine and chloroquine to treat patients with COVID-19.[137] FDA has also informed the public that it has received multiple reports of patients who have required medical support and been hospitalized after self-medicating with ivermectin intended for horses, that taking large doses of ivermectin can cause serious harm, that ivermectin is not authorized or approved by FDA to treat COVID-19, and that using any treatment for COVID-19 that is not approved or authorized by the FDA, unless part of a clinical trial, can cause serious harm.[138] You have not provided any evidence to suggest that the safety information in these communications is inaccurate. Thus, to the extent you are requesting that FDA withdraw or revise these previous safety communications, that request is denied.

v. Petitioner's Request that FDA Issue Guidance to the Secretary of Defense and the President

Petitioner requests that FDA "issue guidance to the Secretary of the Defense and the President not to grant an unprecedented Presidential waiver of prior consent regarding COVID vaccines for Servicemembers under 10 U.S.C. § 1107(f) or 10 U.S.C. § 1107a." Petition at 2.

FDA denies this request because FDA, an agency within the U.S. Department of Health and Human Services, does not issue guidance of the type requested to the President of the United States or to other Departments in the executive branch of the U.S. federal government.

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[136] Under FDA's good guidance practices regulations, a "guidance document" is defined as "documents prepared for FDA staff, applicants/sponsors, and the public that describe the agency's interpretation of or policy on a regulatory issue." 21 CFR 10.115(a)(b)(1). The regulation provides further that "[g]uidance documents include, but are not limited to, documents that relate to: The design, production, labeling, promotion, manufacturing, and testing of regulated products; the processing, content, and evaluation or approval of submissions; and inspection and enforcement policies." Importantly, the provision at 21 CFR 10.115(b)(3), excludes from the definition of "guidance document" general information documents provided to consumers or health professionals, such as those communications that have been provided to the public regarding the use of hydroxychloroquine, chloroquine, and ivermectin to treat patients with COVID-19. 21 CFR 10.115(b)(3) states: "[g]uidance documents do not include: Documents relating to internal FDA procedures, agency reports, general information documents provided to consumers or health professionals, speeches, journal articles and editorials, media interviews, press materials, warning letters, memoranda of understanding, or other communications directed to individual persons or firms." (Emphasis added.)

[137] FDA Drug Safety Communication, FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems, April 24, 2020, updated June 15, 2020 and July 1, 2020, https://www.fda.gov/drugs/drug-safety-and-availability/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-covid-19-outside-hospital-setting-or; FDA, CDER Office of Surveillance and Epidemiology Pharmacovigilance Memorandum, May 19, 2020, https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/OSE%20Review_Hydroxychloroquine-Cholorquine%20-%2019May2020_Redacted.pdf.

[138] FDA Consumer Update, Why You Should Not Use Ivermectin to Treat or Prevent COVID-19, March 5, 2021, https://www.fda.gov/consumers/consumer-updates/why-you-should-not-use-ivermectin-treat-or-prevent-covid-19; FDA Letter to Stakeholders, Do Not Use Ivermectin Intended for Animals as Treatment for COVID-19 in Humans, April 10, 2020, https://www.fda.gov/animal-veterinary/product-safety-information/fda-letter-stakeholders-do-not-use-ivermectin-intended-animals-treatment-covid-19-humans.

vi. Petitioner's Request that FDA Issue Guidance to Stakeholders Regarding the Option to Refuse or Accept Administration of Investigational COVID-19 Vaccines

Petitioner requests that FDA "issue guidance to all stakeholders in digital and written formats to affirm that all citizens have the option to accept or refuse administration of investigational COVID vaccines without adverse work, educational or other non-health related consequences, under 21 U.S.C. § 360bbb-3(e)(1)(a)(ii)(III) 1 and the informed consent requirements of the Nuremberg Code."[139] We interpret this request to relate to the Authorized COVID-19 Vaccines and third parties' decisions with respect to unvaccinated individuals' participation in certain activities. Such decisions by third parties with respect to employment, education, and other non-FDA-regulated activities would not be within FDA's purview. Accordingly, FDA denies Petitioner's request.

vii. Petitioner's Request that FDA Issue Guidance Regarding Marketing and Promotion of COVID-19 Vaccines

FDA notes that your Petition discusses statements made by CDC. For requests intended for CDC, you should contact CDC directly.

As explained above in section III.b.i.1.b of this response, the EUA revocation standard in section 564(g)(2) of the FD&C Act is not met for any of the Authorized COVID-19 Vaccines. With respect to Petitioner's request to issue guidance pending revocation of the EUAs for the Authorized COVID-19 Vaccines, we note that the EUA Guidance contains a section regarding advertising for EUA products. As explained in the EUA guidance, FDA may, under section 564(e)(1)(B) of the FD&C Act, on a case-by-case basis and to the extent feasible given the circumstances of a particular public health emergency, establish certain additional conditions that FDA finds to be necessary or appropriate to protect the public health.[140] The EUA guidance explains that, under section 564(e)(4) of the FD&C Act, FDA may place conditions on "advertisements and other promotional descriptive printed matter (e.g., press releases issued by the EUA sponsor) relating to the use of an EUA product, such as requirements applicable to prescription drugs under section 502(n) . . . ."[141] FDA's authority under section 564(e)(4) ordinarily does not extend to statements by third parties who have no direct connection with the EUA sponsor.

For the Authorized COVID-19 Vaccines, FDA has determined that such conditions are necessary to protect the public health. Accordingly, the Letter of Authorization for each of the Authorized COVID-19 Vaccines contains conditions related to printed matter, advertising, and promotion.[142] Given the current public health emergency, FDA does not see a need to expend the resources

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[139] Concerns about potential State vaccine requirements are better directed to the States. FDA does not mandate use of vaccines.
[140] EUA Guidance at 26.
[141] Id. at 27.
[142] FDA, Pfizer-BioNTech COVID-19 Vaccine Letter of Authorization (Aug. 12, 2021), https://www.fda.gov/media/150386/download; FDA, Moderna COVID-19 Vaccine Letter of Authorization (Aug. 12, 2021), https://www.fda.gov/media/144636/download; FDA, Janssen COVID-19 Vaccine Letter of Authorization (June 10, 2021), https://www.fda.gov/media/146303/download.

necessary to develop and issue additional guidance on this topic. Thus, because FDA has already issued guidance addressing advertising and promotion of EUA products, and because FDA has established conditions related to printed matter, advertising, and promotion for all of the Authorized COVID-19 Vaccines, FDA denies Petitioner's request to issue additional guidance on this issue.

c. Conclusion

FDA has considered Petitioner's requests as they relate to the Authorized COVID-19 Vaccines and the approved COVID-19 Vaccine. For the reasons given in this letter, FDA denies the requests in Petitioner's citizen petition. Therefore, we deny the Petition in its entirety.

Sincerely,

Peter Marks, MD, PhD
Director
Center for Biologics Evaluation and Research

cc: Dockets Management Staff

Appendix I: Aspects of Vaccine Development and Process for Licensure

A. Vaccines are Biologics and Drugs

Vaccines are both biological products under the Public Health Service Act (PHS Act) (42 U.S.C. § 262) and drugs under the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. § 321). The PHS Act defines a "biological product" as including a "vaccine…or analogous product…applicable to the prevention, treatment, or cure of a disease or condition of human beings." 42 U.S.C. § 262(i)(1). The FD&C Act defines drug to include "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man." 21 U.S.C. § 321(g)(1)(B).

Under the PHS Act, a biological product may not be introduced or delivered for introduction into interstate commerce unless a biologics license is in effect for the product. 42 U.S.C. § 262(a)(1)(A).

B. Clinical Investigations of Vaccines

Before a vaccine is licensed (approved) by FDA and can be used by the public, FDA requires that it undergo a rigorous and extensive development program that includes laboratory research, animal studies, and human clinical studies to determine the vaccine's safety and effectiveness.

The PHS Act and the FD&C Act provide FDA with the authority to promulgate regulations that provide a pathway for the study of unapproved new drugs and biologics. 42 U.S.C. § 262(a)(2)(A) and 21 U.S.C. § 355(i). The regulations on clinical investigations require the submission of an Investigational New Drug application (IND), which describes the protocol, and, among other things, assures the safety and rights of human subjects. These regulations are set out at 21 CFR Part 312. See 21 CFR § 312.2 (explaining that the IND regulations apply to clinical investigations of both drugs and biologics).

The regulations provide that, once an IND is in effect, the sponsor may conduct a clinical investigation of the product, with the investigation generally being divided into three phases. With respect to vaccines, Phase 1 studies typically enroll fewer than 100 participants and are designed to look for very common side effects and preliminary evidence of an immune response to the candidate vaccine. Phase 2 studies may include up to several hundred individuals and are designed to provide information regarding the incidence of common short-term side effects, such as redness and swelling at the injection site or fever, and to further describe the immune response to the investigational vaccine. If an investigational new vaccine progresses past Phase 1 and Phase 2 studies, it may progress to Phase 3 studies. For Phase 3 studies, the sample size is often determined by the number of subjects required to establish the effectiveness of the new vaccine, which may be in the thousands or tens of thousands of subjects. Phase 3 studies are usually of sufficient size to detect less common adverse events.

If product development is successful and the clinical data are supportive of the proposed indication, the completion of all three phases of clinical development can be followed by submission of a Biologics License Application (BLA) pursuant to the PHS Act (42 U.S.C. § 262(a)), as specified in 21 CFR § 601.2.

C. Biologics License Applications

A BLA must include data demonstrating that the product is safe, pure, and potent and that the facility in which the product is manufactured "meets standards designed to assure that the biological product continues to be safe, pure, and potent." 42 U.S.C. § 262(a)(2)(C)(i). FDA does not consider an application to be filed until FDA determines that all pertinent information and data have been received. 21 CFR § 601.2. FDA's filing of an application indicates that the application is complete and ready for review but is not an approval of the application.

Under § 601.2(a), FDA may approve a manufacturer's application for a biologics license only after the manufacturer submits an application accompanied by, among other things, "data derived from nonclinical laboratory and clinical studies which demonstrate that the manufactured product meets prescribed requirements of safety, purity, and potency." The BLA must provide the multidisciplinary FDA reviewer team (medical officers, microbiologists, chemists, biostatisticians, etc.) with the Chemistry, Manufacturing, and Controls (CMC)[143] and clinical information necessary to make a benefit-risk assessment, and to determine whether "the establishment(s) and the product meet the applicable requirements established in [FDA's regulations]." 21 CFR § 601.4(a).

FDA generally conducts a pre-license inspection of the proposed manufacturing facility, during which production of the vaccine is examined in detail. 42 U.S.C. § 262(c). In addition, FDA carefully reviews information on the manufacturing process of new vaccines, including the results of testing performed on individual vaccine lots.

FDA scientists and physicians evaluate all the information contained in a BLA, including the safety and effectiveness data and the manufacturing information, to determine whether the application meets the statutory and regulatory requirements. FDA may also convene a meeting of its advisory committee to seek input from outside, independent, technical experts from various scientific and public health disciplines that provide input on scientific data and its public health significance.

As part of FDA's evaluation of a vaccine as a whole, FDA takes all of a vaccine's ingredients into account (including preservatives and adjuvants). FDA licenses a vaccine only after the Agency has determined that the vaccine is safe and effective for its intended use, in that its benefits outweigh its potential risks.

[143] Also referred to as Pharmaceutical Quality/CMC.

Marks Decl. Exhibit F

July 23, 2021

Electronic Submission

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

This petition for administrative action is submitted on behalf of CAALM, the Coalition Advocating for Adequately Licensed Medicines ("Petitioner") pursuant to 21 C.F.R. § 10.30 and related relevant provisions of the Federal Food, Drug, and Cosmetic Act or the Public Health Service Act to request that the Commissioner of Food and Drugs (the "Commissioner") require that the vaccine manufacturers provide the FDA with the data outlined in the "Actions Requested" section below before approval of any COVID-19 vaccine.

The Food and Drug Administration (FDA) has granted Emergency Use Authorizations (EUAs) to three COVID-19 vaccines, enabling rapid, and widespread vaccine rollout across the United States. These EUAs do not have any built-in expiration date, and therefore vaccines can continue to be lawfully distributed under EUA even after a future date when a public health emergency no longer exists.

Approximately seven months have passed since the first EUAs were granted, and two vaccine manufacturers now seek licensure (approval) and have submitted Biologics License Applications (BLAs). Other manufacturers have indicated similar intentions, as well as intentions for EUAs for additional pediatric populations.

We believe the FDA should not prematurely grant a license to any COVID-19 vaccine until all necessary efficacy and safety studies are completed and substantial evidence demonstrates the benefits of an individual COVID-19 vaccine product outweigh the harms for the indicated, recipient population. We are concerned that the premature licensure of a COVID-19 vaccine can seriously undermine public confidence in regulatory authorities, particularly if long-term safety issues were to emerge following licensure.

In this petition, we outline **efficacy and safety measures that must be met before serious consideration is given to granting a BLA of any COVID-19 vaccine**. These measures include:

1. **Completing at least 2 years of follow-up** of participants originally enrolled in pivotal clinical trials, even if the trials were unblinded and now lack a placebo control. All vaccine manufacturer phase 3 trials were already designed with this planned duration.

2. Ensuring, prior to including in the list of populations for which a vaccine is approved, that there is **substantial evidence of clinical effectiveness that outweighs harms in special populations** such as: infants, children, and adolescents; those with past SARS-CoV-2 infection; immunocompromised; pregnant women; nursing women; frail older adults; and individuals with cancer, autoimmune disorders, and hematological conditions.
3. Requiring thorough **safety assessment of spike proteins** being produced in-situ by the body tissues following vaccine administration, and spike proteins' full biodistribution, pharmacokinetics, and tissue specific toxicity.
4. Completion of **vaccine biodistribution studies** from administration site and safety implications of mRNA translation in distant tissues.
5. **Thorough investigation of all severe adverse reactions reported following COVID-19 vaccination**, such as deaths, reported in the United States and global pharmacovigilance systems.
6. Assessment of **safety in individuals receiving more than two doses.**
7. **Inclusion of gene delivery and therapy experts in the Vaccines and Related Biological Products Advisory Committee (VRBPAC)**, in recognition of the fact that the novel COVID vaccines work on the premise of gene delivery, in contrast to conventional vaccines.
8. **Enforcing stringent conflict of interest requirements** to ensure individuals involved in data analysis and BLA-related decision making processes have no conflict of interests with vaccine manufacturers.

A COVID-19 vaccine BLA should be approved when—and only when—substantial evidence demonstrates the benefits of a specific product outweigh the harms for the indicated, recipient population.

This means that the following are **invalid reasons** to approve a COVID-19 vaccine:

- **To ensure vaccines are accessible after the public health emergency has ended.** COVID-19 vaccines granted an emergency use authorization (EUA) can be lawfully used after the expiry of the SARS-CoV-2 public health emergency declaration. (This is made clear by the many products for Ebola and Zika viruses which still have active EUAs.[1])

- **To ensure adequate access to vaccines across the population.** A BLA is not necessary to assure access to COVID-19 vaccines. Unlike normal licensing, in which widespread use of a drug or vaccine follows approval, EUAs for COVID-19 vaccines have enabled, and continue to enable, their widespread use. Ensuring access to vaccines is irrelevant to the considerations for issuance of a BLA because broad access to COVID-19 vaccines has already been accomplished.

- **To enable vaccine mandates.** Consideration of vaccine mandates is outside of FDA's purview. Furthermore, a mandate should only be considered once the evidentiary conditions are met for a BLA (demonstrating that benefits outweigh harms).

- **To bolster public confidence.** Like mandates, approving a medical product in order to bolster public confidence is backward logic and is outside the FDA's purview. Approving before substantial evidence that population-based evidence of clinical effectiveness is superior to harms may contribute to public wariness and hesitancy, not only about COVID-19 vaccines, but other vaccines and public health authorities more broadly. An approval may bolster public confidence, but it is not a valid reason to approve.

Regardless of any legitimacy of each of the above reasons, none provides grounds to approve a COVID-19 vaccine.

The widespread use of a COVID-19 vaccine under EUA, particularly for a limited amount of time, also is not a valid reason to approve a product. Even if vaccine recipients are followed up within observational studies, such studies may have important design biases and flaws, and their conclusions, especially concerning clinical effectiveness outcomes, may not be reliable.

Premature FDA approval of any COVID-19 vaccine could negatively impact the health and safety of US residents, with global ramifications considering the international importance of FDA decisions. It also could set a precedent of lowered standards for future vaccine approvals. For these reasons and due to the compelling need to ensure the safety and efficacy of any COVID-19 vaccine licensed by the FDA and to allow Petitioner the opportunity to seek emergency judicial relief should the instant Petition be denied, it is respectfully requested that FDA act on the instant Amended Petition by July 30, 2021.

I. ACTIONS REQUESTED

Petitioner request that the FDA, prior to granting any license for a COVID-19 vaccine:

1. Confirm, in revised Guidance, that the FDA expects a minimum of 2 years of follow-up of participants enrolled in pivotal clinical trials, even if trials are unblinded and lack a placebo control.

2. Require data demonstrating substantial evidence of clinical effectiveness that outweighs harms, in all special populations, as a condition of consideration of including these populations among the indicated populations. Special populations include: infants, children, and adolescents; those with past SARS-CoV-2 infection; immunosuppressed individuals; those with history of or current cancer; individuals with hematological disorders or autoimmune diseases; pregnant or nursing women; and frail older adults.

3. Require data on the safety and pharmacokinetic profiles of the spike protein.

4. Require data from biodistribution studies investigating the actual COVID-19 vaccines.

5. Require data from pharmacovigilance systems in the US and globally documenting a thorough investigation of serious adverse events, carried out by independent, impartial individuals.

6. Clarify in revised Guidance that safety data from individuals receiving more than 2 vaccine doses must be submitted.

7. Ensure the inclusion of experts in gene therapy in the VRBPAC.

8. Ensure that the analysis of data and decisions regarding any COVID-19 vaccine BLA application are informed by experts with no financial or research relationships with any vaccine manufacturers within the last 36 months, both within FDA and amongst the composition of the VRBPAC.

II. STATEMENT OF GROUNDS

Here, in the order as above, we set out the rationale for each requested action.

1. **Confirm, in revised Guidance, that the FDA expects a minimum of 2 years of follow-up of participants enrolled in pivotal clinical trials, even if trials are unblinded and lack a placebo control. Rationale:**
    a. Requiring at least 2 years is consistent with the 2 year follow-up duration prospectively proposed by the manufacturers when they registered their ongoing phase 3 trials of COVID-19 vaccines (Moderna: NCT04470427, Pfizer: NCT04368728, Janssen: NCT04505722) and consistent with the June 2020 FDA guidance on COVID-19 vaccines which stated participants should be followed for COVID-19 outcomes for "as long as feasible, ideally at least one to two years."[2]
    b. Important adverse event signals can be detected in clinical trials. This is true despite enrolling tens of thousands of participants, which is still too few to assess rare adverse events. For example, a serious blood clot occurring in the phase 3 Janssen clinical trial led to an initial trial pause in October 2020.[3]
    c. Two year follow-up from trials allows the detection of commonly experienced longer-term adverse effects that may not manifest until many months following vaccination.
    d. Two year follow-up from trials would also allow for more detailed assessment of infection, re-infection, infectiousness, and the monitoring of immune response over time, among all vaccinated participants.
    e. The quality of data collection in clinical trials can be expected to be superior to passive data collection systems like the Vaccine Adverse Event Reporting System (VAERS). Therefore, trials of at least 2 years duration provide a valuable chance to develop a more complete understanding of the adverse event profile in the general population as well as in specific groups, such as individuals of

reproductive age, immunocompromised individuals, and different age groups, including adolescents and young children.

f. The quality of data on adverse events during an ongoing trial can be improved while the trial is ongoing (e.g., improving the range of types of adverse events that are systematically assessed), as and when evidence from other data sources (e.g., pre-clinical or pharmacovigilance) show any trends or indicate specific types of adverse events of special interest.

g. Finally, the expectation of at least 2 years of follow-up prior to BLA also carries the advantage of longer-term data collection from other available sources (e.g., MedWatch/VAERS, V-safe, Vaccine Safety Datalink, FDA-CMS, BEST & PRISM, VA Electronic Health Records & data warehouse, Department of Defense DMSS, and Genesis HealthCare (Brown University & NIH-National Institute of Aging), as well as other medical claims databases).

2. **Require data demonstrating substantial evidence of clinical effectiveness that outweighs harms, in all special populations, as a condition of consideration of including these populations among the indicated populations. Special populations include: infants, children, and adolescents; those with past SARS-CoV-2 infection; immunosuppressed individuals; those with history of or current cancer; individuals with hematological disorders or autoimmune diseases; pregnant or nursing women; and frail older adults. Rationale:**

   a. The efficacy and safety of medicines often differs amongst populations such as healthy young adults vs. older adults, men vs. women, or SARS-CoV-2 survivors vs. never-exposed individuals.

   b. For example, the relative risks of SARS-CoV-2 infection, hospitalization, and death are considerably lower in infants, children, and adolescents in comparison to adults.[4,5]

   c. For example, individuals who experienced past SARS-CoV-2 infection (which are now believed to be a significant minority of many subpopulations[6]) are likely to have immunity to subsequent infections for as long or longer than immunity conferred by vaccine,[7–10] and may also be at heightened risk for adverse effects.[11–14]

   d. The ongoing phase 3 trials of COVID-19 vaccines (Moderna: NCT04470427, Pfizer: NCT04368728, Janssen: NCT04505722) largely (or wholly) excluded the following important populations in which there is reason to believe the effects of the product may differ from the populations enrolled in the trial:

      i. Infants, children, and adolescents
      ii. Those with past SARS-CoV-2 infection
      iii. Those who are immunosuppressed
      iv. Those with history of or current cancer
      v. Those with hematological disorders
      vi. Those with autoimmune diseases
      vii. Those who are pregnant or nursing
      viii. Frail older adults (including those living in nursing homes)

e. The question is not simply whether there is efficacy, but how much efficacy exists in these populations, what kind of efficacy (e.g. reduction in risk of symptomatic COVID-19 vs. reduction in risk of hospitalization or death), and do efficacy advantages outweigh potential harms in these populations.
f. Before these special populations can be considered for inclusion amongst the approved indicated populations, data demonstrating substantial evidence of clinical effectiveness that outweighs harms in these specific populations, are needed.

3. **Require data on the safety and pharmacokinetic profiles of the spike protein.**
Rationale:
   a. In-situ production of SARS-CoV-2 spike protein is the target mechanism of action of all COVID-19 vaccines with an EUA at present. Therefore, the safety profile of spike protein itself (i.e., in the absence of virus) must be thoroughly understood in the range of populations on the indications list.
   b. Recently, evidence of systemic circulation of spike protein or its components in subjects post-immunization was reported.[15] All studies we are aware of to date raise concerns about the safety of spike protein,[16–28] and the concentration of circulatory spikes was correlated to the disease severity in COVID-19 patients.[29]
   c. Required studies must, at a minimum, address these concerns:
      i. Coagulopathy issues, including blood clots, hemorrhage, thrombocytopenia, heart attack, and strokes. According to the VAERS, as of May 21, 2021, there have been a total of 1,222 reports of thrombocytopenia/low platelets; and 6,494 (112 in 0-24 year-olds) reports of blood clots/strokes.
      ii. Reproductive issues, including menstrual irregularities, reduced fertility, miscarriages, and preterm births. According to VAERS, as of May 21, 2021, there were 511 reports of miscarriage and 522 reports of uterine hemorrhage (including 88 in women older than 50 years). The vaccines induce the generation of antibodies to attack spike protein, which are genetically similar to proteins produced by the placenta.[30] To date, no vaccine sponsors have conducted immunologic studies of spike protein involvement with proteins involved in placental development.
      iii. Carcinogenesis. There is preliminary and theoretical evidence that the spike protein may promote cancer.[31,32] Considering the potential for annual booster vaccinations, COVID-19 vaccines should be treated similarly to medication taken for chronic conditions on a long term basis. Carcinogenic potential is important to characterize.
      iv. Transmission of spike protein (or its fragments) from vaccinated individuals, such as through breast milk and associated risk in neonates and infants. According to the UK Medicines & Healthcare products Regulatory Agency, there are 921 reports of exposure via breast milk following AstraZeneca's vaccine and 215 reports following Pfizer's vaccine.

v. Neurological disorders, including Guillain-Barré syndrome, acute disseminated encephalomyelitis, transverse myelitis, encephalitis, myelitis, encephalomyelitis, meningoencephalitis, meningitis, encephalopathy, demyelinating diseases, and multiple sclerosis.
vi. Cardiac issues, including myocardial infarction, myocarditis and pericarditis, among others. According to the VAERS, as of May 21, 2021, there have been a total of 1,598 reports of heart attacks (24 reported in 0-24 year-olds; 501 resulted in death).
vii. Autoimmune diseases, including thyroiditis and diabetes mellitus, immune thrombocytopenia, autoimmune hepatitis, primary biliary cholangitis, systemic sclerosis, autoimmune disease for skeletal muscles (myasthenia gravis, myositis such as polymyositis, dermatomyositis, or other inflammatory myopathies)
viii. Studies should be conducted in individuals of both sexes[33] and all ages. We cannot assume that the effects of spike protein are the same across populations of all ages, sex, and across pre-existing conditions.

4. **Require data from biodistribution studies investigating the actual COVID-19 vaccines. Rationale:**
   a. Data from the biodistribution studies submitted by Moderna and Pfizer suggests that the vaccines distribute widely in the body, including to the liver, brain, heart, lung, adrenals, ovaries, and testes, among many other tissues.[34,35] (**See Tables 1a, 1b, and 2 below for studies R-[?]-0072 and 185350 submitted by Pfizer and study 5002121 submitted by Moderna.**)
   b. However these were not studies of the currently authorized products: Pfizer's BNT162b2, Moderna's mRNA-1273, or Janssen's Ad26.COV2.S.[34–36]
   c. Instead of presenting novel biodistribution studies of the COVID-19 vaccine formulations, sponsors presented substitute studies to FDA for an EUA during the pandemic.[34–36]
   d. Therefore, novel biodistribution studies investigating the actual COVID-19 vaccines are necessary.
   e. Biodistribution studies would be required for any small molecule pharmaceutical drug submitted for approval (i.e. New Drug Application), and should be conducted on the COVID-19 vaccines as well as these novel vaccines which work on the premise of gene delivery--very different to conventional vaccines.
   f. Biodistribution studies help inform an understanding of vaccine transfection to various tissues (away from injection site) spurring various distant tissues to produce spike proteins and consequent autoimmune response against the body's cells. These studies will therefore help enhance our understanding of the nature of potential short and long term adverse events. At this point in time, in which other data sources exist to characterize short term harms of COVID-19 vaccines with an EUA, the utility of biodistribution studies to characterize long term adverse effects and better understand potential mechanism(s) of action of short and long term harms, remains critically important.

g. Necessary studies must, at a minimum, address these concerns related to biodistribution, as well as the effects of vaccines in the body:
    i. The need to know basic pharmacokinetic parameters, including absorption, distribution, metabolism, and excretion (ADME).
    ii. Effects of multiple doses. ADME may change depending on dose and cumulative dose and should be investigated. This is more important than usual as the whole purpose of all COVID-19 vaccines with an EUA at present is to change the body's way of processing spike protein, and therefore repeated injections should result in different rates of clearance of spike protein from the blood, and different rates of immune attack on spike protein producing cells.
    iii. The impact of body mass index (size of deltoid muscle) and vaccine distribution away from injection site, implications for dose estimation for lean or younger age groups or frail older adults.
    iv. The duration of the studies must be sufficient to fully understand the complete distribution and elimination of the injected vaccine and its carrier and other constituents. For example, data from the substitute study submitted for Pfizer's vaccine (**see Tables 1a, 1b, and 2 below for studies R-[?]-0072 and 185350 submitted by Pfizer and study 5002121 submitted by Moderna**) showed levels of drug product increasing at the 48 hour mark, but it is unknown what occurred after 48 hours as this was apparently the study cut off.[37]
    v. Potential side effects (safety review) in those organs/tissues with a detectable proportion of injected vaccine (antigen or novel excipients) from the circulatory system.

5. **Require data from pharmacovigilance systems in the US and globally documenting a thorough investigation of serious adverse events, carried out by independent, impartial individuals. Rationale:**
    a. A major testament to the overall short-term safety of a medical product is the absence of serious adverse events (SAEs) when administered to millions. COVID-19 vaccines have now been administered to hundreds of millions of individuals, and it is vital that all reports of SAEs are thoroughly investigated to determine whether the vaccine played any role in the SAE.
    b. The most serious of all SAEs is death, and a CDC webpage on VAERS discusses 4,863 reports of death after COVID-19 vaccination reported between December 14, 2020 and May 24, 2021.[38] CDC states that:
        i. "CDC follows up on any report of death to request additional information to learn more about what occurred and to determine whether the death was a result of the vaccine or was unrelated."
        ii. "CDC and FDA physicians review each case report of death as soon as notified and CDC requests medical records to further assess reports."

iii. "A review of available clinical information, including death certificates, autopsy, and medical records has not established a causal link to COVID-19 vaccines."[38]

c. However, the FDA has stated that VAERS staff do not contact family members to learn more about the deaths. It stated: "Because the VAERS system is not designed to determine causality of adverse events, there is not a mechanism to follow-up with families for additional details. The determination of the cause of death is done by the certifying official who completes the death certificate or the pathologist who conducts the autopsy."[39]

d. Regulators in other countries have conducted detailed case investigations (e.g. Norway's investigation of 100 deaths amongst frail elderly following COVID-19 vaccination[40,41]).

e. FDA must require evidence of a thorough investigation into deaths and other SAEs—investigations that include contacting families to obtain a full medical history and personal accounts (in the case of deaths) and those who experienced the adverse event (in the case of other SAEs). Event adjudication, as done on data safety monitoring boards, must be in place in order to carry out detailed case investigations, and must be carried out by independent, impartial individuals.

6. **Clarify in revised Guidance that safety data from individuals receiving more than 2 vaccine doses must be submitted by vaccine manufacturers. Rationale:**

a. There is wide speculation that COVID-19 vaccines may become offered as annual vaccines, much like influenza vaccines, and regulators have already released guidance to this effect.[42]

b. Some manufacturers, such as Pfizer and Moderna, have indicated that a third dose may be necessary within the first 12 months. Other manufacturers may present similar claims in the future.[43]

c. The safety profile of multiple doses, possibly more than 70 doses across an average lifetime, must be considered at the time of licensure. Phase 3 trial data make clear that the safety profile differs by dose (e.g. dose 2 of the Pfizer and Moderna vaccines induce more severe systemic adverse events than dose 1).[44,45]

d. Information on the types and severity of adverse events that emerge following the administration of additional doses is necessary to better characterize long term safety.

7. **Ensure the inclusion of experts in gene therapy in the VRBPAC.** Rationale:

a. The COVID-19 vaccines produced by Pfizer, Moderna, and Janssen (as well as AstraZeneca, CanSinoBio (China) and Gamaleya Research Institute (Russia)) are gene based vaccines. Their mechanism of action differs substantially from all other vaccines that have been used on populations globally, as these novel vaccines work on the premise of gene delivery, and may therefore be considered a type of gene therapy. These gene based vaccines involve entering the cell, where the overwhelming majority of critical body activities occur, and utilizing

the host's cells to produce spike protein. This is an entirely different mechanism than that utilized by traditional vaccines such as inactivated, attenuated, subunit or protein-based (that are not intended to invade cells). Therefore, there is a need to consider safety with the informed perspectives of those with expertise in gene therapies.

8. **Ensure that the analysis of data and decisions regarding any COVID-19 vaccine BLA application are informed by experts with no financial or research relationships with any vaccine manufacturers within the last 36 months, both within FDA and amongst the composition of the VRBPAC. Rationale:**
    a. The public interest weighs strongly in favor of the evaluation of data and all decision making to be performed by competent individuals with independence from vaccine manufacturers (institutions that stand to gain or lose from a BLA decision on a COVID-19 vaccine). Disclosure requirements should be at least as stringent, if not more, than what is expected for writing a manuscript in a medical journal—namely, disclosure of relationships within the last 36 months, as requested by the International Committee of Medical Journal Editors (ICMJE). Insisting on this level of disclosure, and transparency of the disclosures, can publicly demonstrate the independence of the FDA's decision making process.[46]

Table 1a. Pfizer study report R-[?]-0072, biodistribution study submitted by Pfizer to Japanese regulator (PMDA).

2.6.5.5A. PHARMACOKINETICS: ORGAN DISTRIBUTION		**Test Article: modRNA encoding luciferase in LNP Report Number: R-[redacted]-0072**
Species (Strain):	Mice (BALB/c)	
Sex/Number of Animals:	Female/3 per group	
Feeding Condition:	Fed ad libitum	
Vehicle/Formulation:	Phosphate-buffered saline	
Method of Administration:	Intramuscular injection	
Dose (mg/kg):	1 µg/hind leg in gastrocnemius muscle (2 µg total)	
Number of Doses:	1	
Detection:	Bioluminescence measurement	
Sampling Time (hour):	6, 24, 48, 72 hours; 6 and 9 days post-injection	

Time point	**Total Mean Bioluminescence signal (photons/second)**		**Mean Bioluminescence signal in the liver (photons/second)**
	Buffer control	**modRNALuciferase in LNP**	**modRNALuciferase in LNP**
6 hours	1.28×10^{5}	1.26×10^{9}	4.94×10^{7}
24 hours	2.28×10^{5}	7.31×10^{8}	2.4×10^{6}
48 hours	1.40×10^{5}	2.10×10^{8}	Below detection[a]
72 hours	1.33×10^{5}	7.87×10^{7}	Below detection[a]
6 days	1.62×10^{5}	2.92×10^{6}	Below detection[a]
9 days	7.66×10^{4}	5.09×10^{5}	Below detection[a]

LNP = Lipid nanoparticle; modRNA = Nucleoside modified messenger RNA.
a. At or below the background level of the buffer control.

Source: Japan PMDA (PDF page 15).[37]

Table 1b. Pfizer study report 185350, biodistribution study submitted by Pfizer to Japanese regulator (PMDA).

2.6.5.5B. PHARMACOKINETICS: ORGAN DISTRIBUTION CONTINUED

Test Article: [^{3}H]-Labelled LNP-mRNA formulation containing ALC-0315 and ALC-0159
Report Number: 185350

Species (Strain):	Rat (Wistar Han)
Sex/Number of Animals:	Male and female/3 animals/sex/timepoint (21 animals/sex total for the 50 µg dose)
Feeding Condition:	Fed ad libitum
Method of Administration:	Intramuscular injection
Dose:	50 µg [^{3}H]-08-A01-C0 (lot # NC-0552-1)
Number of Doses:	1
Detection:	Radioactivity quantitation using liquid scintillation counting
Sampling Time (hour):	0.25, 1, 2, 4, 8, 24, and 48 hours post-injection

Sample	Mean total lipid concentration (µg lipid equivalent/g (or mL) (males and females combined)							% of administered dose (males and females combined)						
	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h
Adipose tissue	0.057	0.100	0.126	0.128	0.093	0.084	0.181	--	--	--	--	--	--	--
Adrenal glands	0.271	1.48	2.72	2.89	6.80	13.8	18.2	0.001	0.007	0.010	0.015	0.035	0.066	0.106
Bladder	0.041	0.130	0.146	0.167	0.148	0.247	0.365	0.000	0.001	0.001	0.001	0.001	0.002	0.002
Bone (femur)	0.091	0.195	0.266	0.276	0.340	0.342	0.687	--	--	--	--	--	--	--
Bone marrow (femur)	0.479	0.960	1.24	1.24	1.84	2.49	3.77	--	--	--	--	--	--	--
Brain	0.045	0.100	0.138	0.115	0.073	0.069	0.068	0.007	0.013	0.020	0.016	0.011	0.010	0.009
Eyes	0.010	0.035	0.052	0.067	0.059	0.091	0.112	0.000	0.001	0.001	0.002	0.002	0.002	0.003
Heart	0.282	1.03	1.40	0.987	0.790	0.451	0.546	0.018	0.056	0.084	0.060	0.042	0.027	0.030
Injection site	128	394	311	338	213	195	165	19.9	52.6	31.6	28.4	21.9	29.1	24.6
Kidneys	0.391	1.16	2.05	0.924	0.590	0.426	0.425	0.050	0.124	0.211	0.109	0.075	0.054	0.057
Large intestine	0.013	0.048	0.093	0.287	0.649	1.10	1.34	0.008	0.025	0.065	0.192	0.405	0.692	0.762
Liver	0.737	4.63	11.0	16.5	26.5	19.2	24.3	0.602	2.87	7.33	11.9	18.1	15.4	16.2
Lung	0.492	1.21	1.83	1.50	1.15	1.04	1.09	0.052	0.101	0.178	0.169	0.122	0.101	0.101
Sample	**Total Lipid concentration (µg lipid equivalent/g [or mL]) (males and females combined)**							**% of Administered Dose (males and females combined)**						
	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h
Lymph node (mandibular)	0.064	0.189	0.290	0.408	0.534	0.554	0.727	--	--	--	--	--	--	--
Lymph node (mesenteric)	0.050	0.146	0.530	0.489	0.689	0.985	1.37	--	--	--	--	--	--	--
Muscle	0.021	0.061	0.084	0.103	0.096	0.095	0.192	--	--	--	--	--	--	--
Ovaries (females)	0.104	1.34	1.64	2.34	3.09	5.24	12.3	0.001	0.009	0.008	0.016	0.025	0.037	0.095
Pancreas	0.081	0.207	0.414	0.380	0.294	0.358	0.599	0.003	0.007	0.014	0.015	0.015	0.011	0.019
Pituitary gland	0.339	0.645	0.868	0.854	0.405	0.478	0.694	0.000	0.001	0.001	0.001	0.000	0.000	0.001
Prostate (males)	0.061	0.091	0.128	0.157	0.150	0.183	0.170	0.001	0.001	0.002	0.003	0.003	0.004	0.003
Salivary glands	0.084	0.193	0.255	0.220	0.135	0.170	0.264	0.003	0.007	0.008	0.008	0.005	0.006	0.009
Skin	0.013	0.208	0.159	0.145	0.119	0.157	0.253	--	--	--	--	--	--	--
Small intestine	0.030	0.221	0.476	0.879	1.28	1.30	1.47	0.024	0.130	0.319	0.543	0.776	0.906	0.835
Spinal cord	0.043	0.097	0.169	0.250	0.106	0.085	0.112	0.001	0.002	0.002	0.003	0.001	0.001	0.001
Spleen	0.334	2.47	7.73	10.3	22.1	20.1	23.4	0.013	0.093	0.325	0.385	0.982	0.821	1.03
Stomach	0.017	0.065	0.115	0.144	0.268	0.152	0.215	0.006	0.019	0.034	0.030	0.040	0.037	0.039
Testes (males)	0.031	0.042	0.079	0.129	0.146	0.304	0.320	0.007	0.010	0.017	0.030	0.034	0.074	0.074
Thymus	0.088	0.243	0.340	0.335	0.196	0.207	0.331	0.004	0.007	0.010	0.012	0.008	0.007	0.008
Thyroid	0.155	0.536	0.842	0.851	0.544	0.578	1.00	0.000	0.001	0.001	0.001	0.001	0.001	0.001
Uterus (females)	0.043	0.203	0.305	0.140	0.287	0.289	0.456	0.002	0.011	0.015	0.008	0.016	0.018	0.022
Whole blood	1.97	4.37	5.40	3.05	1.31	0.909	0.420	--	--	--	--	--	--	--
Plasma	3.97	8.13	8.90	6.50	2.36	1.78	0.805	--	--	--	--	--	--	--
Blood:Plasma ratio[a]	0.815	0.515	0.550	0.510	0.555	0.530	0.540	--	--	--	--	--	--	--

Source: Japan PMDA (PDF page 16).[37]

Table 2. Modern study report 5002121, biodistribution study submitted by Moderna to Japanese regulator (PMDA).

表 2.6.4.4-3　雄性 Sprague Dawley ラットに mRNA-1647 100 µg を単回筋肉内接種したときの各組織における薬物動態パラメータ

Matrix	mRNA Construct	T_{max} (h)[a]	C_{max} (ng/mL)[a]	$AUC_{(0-t)}$ (ng × h/mL)[a,b]	$T_{1/2}$ (h)[a,c]	$AUC_{(0-t)}$ Ratio (Tissue/Plasma)[d]	$AUC_{(0-t)}$ Ratio (Tissue/Plasma) Average
Bone marrow	gB	NC	NC	NC	NC	NC	NR
	gH	8.0	0.254 ± 0.0871	7.85 ± 2.03	NC	0.316	
	gL	8.0	0.224 ± 0.0920	2.78 ± 1.03	NC	0.119	
	UL128	8.0	0.292 ± 0.120	3.53 ± 1.33	NC	0.147	
	UL130	NC	NC	NC	NC	NC	
	UL131A	8.0	0.186 ± 0.0829	2.05 ± 0.912	NC	0.0825	
Brain	gB	NC	NC	NC	NC	NC	NR
	gH	24.0	0.0800 ± 0.0491	2.19 ± 1.08	NC	0.0880	
	gL	2.0	0.0360 ± 0.0360	0.144 ± 0.144	NC	0.00615	
	UL128	2.0	0.0340 ± 0.0340	0.136 ± 0.136	NC	0.00564	
	UL130	NC	NC	NC	NC	NC	
	UL131A	NC	NC	NC	NC	NC	
Distal lymph node	gB	8.0	108 ± 101	1,460 ± 1,110	31.6	64.1	62.8
	gH	8.0	110 ± 102	1,490 ± 1,130	36.2	59.8	
	gL	8.0	117 ± 109	1,460 ± 1,200	30.6	62.6	
	UL128	8.0	125 ± 117	1,620 ± 1,290	32.1	67.1	
	UL130	8.0	129 ± 121	1,630 ± 1,330	27.9	64	
	UL131A	8.0	114 ± 108	1,470 ± 1,190	28.5	59.2	
Eye	gB	2.0	4.72 ± 2.77	26.7 ± 13.6	NC	1.18	1.24
	gH	2.0	3.92 ± 2.19	37.6 ± 11.0	NC	1.51	
	gL	2.0	3.23 ± 1.84	29.2 ± 9.75	NC	1.25	
	UL128	2.0	3.91 ± 2.19	34.5 ± 12.2	NC	1.43	
	UL130	2.0	3.61 ± 2.14	21.3 ± 11.0	NC	0.838	
	UL131A	2.0	3.43 ± 1.96	31.1 ± 10.2	NC	1.26	
Heart	gB	NC	NC	NC	NC	NC	NR
	gH	8.0	0.548 ± 0.107	9.94 ± 1.85	NC	0.400	
	gL	8.0	0.220 ± 0.0907	2.96 ± 1.05	NC	0.127	
	UL128	8.0	0.276 ± 0.113	4.49 ± 1.51	NC	0.186	
	UL130	NC	NC	NC	NC	NC	
	UL131A	8.0	0.312 ± 0.0896	3.71 ± 1.02	NC	0.150	
Injection site, muscle	gB	2.0	1,770 ± 803	27,100 ± 4,880	13.5	1190	939
	gH	2.0	1,720 ± 828	26,100 ± 4,700	17.1	1050	
	gL	2.0	1,310 ± 638	20,900 ± 3,720	15.2	893	
	UL128	2.0	1,620 ± 720	25,300 ± 4,090	14.9	1050	
	UL130	2.0	1,630 ± 777	24,500 ± 4,240	13.8	961	
	UL131A	8.0	427 ± 210	12,100 ± 2,830	15.0	487	
Jejunum	gB	NC	NC	NC	NC	NC	NR
	gH	8.0	0.0800 ± 0.0490	2.06 ± 1.04	NC	0.0827	
	gL	2.0	0.0700 ± 0.0429	0.720 ± 0.472	NC	0.0308	
	UL128	NC	NC	NC	NC	NC	
	UL130	NC	NC	NC	NC	NC	
	UL131A	NC	NC	NC	NC	NC	
Kidney	gB	NC	NC	NC	NC	NC	NR
	gH	NC	NC	NC	NC	NC	
	gL	NC	NC	NC	NC	NC	
	UL128	NC	NC	NC	NC	NC	
	UL130	NC	NC	NC	NC	NC	
	UL131A	NC	NC	NC	NC	NC	
Liver	gB	2.0	2.16 ± 1.21	8.65 ± 4.83	NC	0.381	0.499
	gH	2.0	2.12 ± 0.982	16.8 ± 4.15	NC	0.674	
	gL	2.0	1.30 ± 0.432	11.0 ± 2.37	NC	0.470	
	UL128	2.0	2.00 ± 0.814	13.7 ± 3.72	NC	0.570	
	UL130	2.0	1.87 ± 1.01	7.46 ± 4.04	NC	0.293	
	UL131A	2.0	1.99 ± 0.928	13.9 ± 4.04	NC	0.562	
Lung	gB	NC	NC	NC	NC	NC	NR
	gH	8.0	0.442 ± 0.130	8.04 ± 1.96	NC	0.323	
	gL	8.0	0.274 ± 0.0984	3.45 ± 1.12	NC	0.148	
	UL128	8.0	0.340 ± 0.129	5.40 ± 1.74	NC	0.224	
	UL130	8.0	0.188 ± 0.188	2.07 ± 2.07	NC	0.0812	
	UL131A	8.0	0.310 ± 0.111	4.86 ± 1.49	NC	0.196	

Proximal lymph nodes	gB	2.0	260 ± 121	5,850 ± 949	33.5	257	201
	gH	8.0	206 ± 51.6	4,860 ± 722	38.2	195	
	gL	2.0	175 ± 81.9	3,460 ± 538	36.3	148	
	UL128	8.0	246 ± 66.6	5,190 ± 875	32.8	215	
	UL130	8.0	252 ± 67.2	5,240 ± 881	35.7	206	
	UL131A	2.0	225 ± 106	4,600 ± 719	32.2	185	
Spleen	gB	2.0	7.36 ± 3.81	460 ± 52.9	46.9	20.2	13.4
	gH	24.0	5.63 ± 1.28	371 ± 39.5	83.0	14.9	
	gL	8.0	3.83 ± 1.04	196 ± 21.0	68.2	8.36	
	UL128	24.0	4.87 ± 1.22	297 ± 34.8	68.8	12.3	
	UL130	8.0	5.03 ± 1.41	288 ± 33.0	64.9	11.3	
	UL131A	2.0	5.10 ± 2.64	277 ± 33.1	46.2	11.2	
Stomach	gB	NC	NC	NC	NC	NC	NR
	gH	8.0	0.110 ± 0.0696	3.49 ± 1.59	NC	0.140	
	gL	8.0	0.0800 ± 0.0499	2.07 ± 1.19	NC	0.0886	
	UL128	24.0	0.102 ± 0.0648	2.85 ± 1.47	NC	0.118	
	UL130	NC	NC	NC	NC	NC	
	UL131A	24.0	0.0980 ± 0.0634	2.53 ± 1.39	NC	0.102	
Testes	gB	2.0	1.16 ± 0.719	4.64 ± 2.88	NC	0.204	0.209
	gH	2.0	1.11 ± 0.480	5.52 ± 2.20	NC	0.222	
	gL	8.0	0.420 ± 0.335	6.08 ± 3.73	NC	0.260	
	UL128	2.0	0.946 ± 0.397	4.73 ± 1.85	NC	0.196	
	UL130	2.0	0.682 ± 0.442	2.73 ± 1.77	NC	0.107	
	UL131A	2.0	0.872 ± 0.380	4.54 ± 1.85	NC	0.183	

Abbreviations: gB = glycoprotein B; gH = glycoprotein H; gL = glycoprotein L; IM = intramuscular; NC = not calculable (insufficient data points above the lower limit of quantitation); NR = not reported (some constructs measured all samples as below limit of quantitation).

[a] T_{max} and $T_{1/2}$ data reported as the mean; C_{max} and $AUC_{(0-t)}$ data reported as the mean ± standard error.

[b] For the bone marrow, brain, jejunum, heart, liver, lung, stomach, and testes, $AUC_{(0-t)}$ was calculated using less than 3 quantifiable mean concentrations and therefore is an estimate.

[c] Due to the lack of a distinct elimination phase in plasma, the $T_{1/2}$ of the mRNA constructs could not be calculated; however, the $T_{1/2}$ was estimated to range from 2.7 to 3.8 hours.

[d] For $AUC_{(0-t)}$ Ratio, samples listed as NC were not calculable because all samples were below limit of quantitation.

Source: Report 5002121 Amendment 1 (Appendix 8, Table 2 and Table 3)

Source: Japan PMDA (PDF page 7).[47]

III. ENVIRONMENT IMPACT

The petitioner hereby states that the relief requested in this petition will have no environmental impact and therefore an environmental assessment is not required under 21 C.F.R. Sections 25.30 and 25.31.

IV. ECONOMIC IMPACT

Economic impact information will be submitted upon request of the commissioner.

V. CERTIFICATION

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

Linda Wastila

Linda Wastila, BSPharm, MSPH, PhD
Representative
Coalition Advocating for Adequately Licensed Medicines (CAALM)

Coalition Advocating for Adequately Licensed Medicines (CAALM), current members as of July 23, 2021:

Peter Aaby, MSc, DMSc†
Head of Bandim Health Project, Guinea-Bissau
University of Southern Denmark
Copenhagen, Denmark
† Dr. Aaby's organizational affiliation is included for identification purposes only.

Christine Stabell Benn, MD, PhD, DMSc†
Professor of Global Health
University of Southern Denmark
Copenhagen, Denmark
† Dr. Benn's organizational affiliation is included for identification purposes only.

Aditi Bhargava, PhD†
Professor
University of California, San Francisco
San Francisco, California, U.S.A.
† Dr. Bhargava's organizational affiliation is included for identification purposes only.

Dick Bijl, PhD, MD, MSc†
Pharmacoepidemiologist, former GP
Utrecht, the Netherlands
† President, International Society of Drug Bulletins

Florence T. Bourgeois MD, MPH†
Associate Professor of Pediatrics
Harvard Medical School
Boston, Massachusetts, U.S.A.
† Dr. Bourgeois's organizational affiliation is included for identification purposes only.

Anthony J Brookes, PhD†
Professor of Genetics
University of Leicester
Leicester, United Kingdom
† Dr. Brookes's organizational affiliation is included for identification purposes only.

Byram W. Bridle, PhD†
Associate Professor of Viral Immunology
University of Guelph
Ontario, Canada
† Dr. Bridle's organizational affiliation is included for identification purposes only.

Peter Collignon AM, MB, BS(Hons), BSc(Med), FRACP, FRCPA, FASM†
Professor
Australian National University Medical School
Canberra, Australia
† Dr. Collignon's organizational affiliation is included for identification purposes only.

Peter Doshi, PhD†
Associate Prof., Pharmaceutical Health Services Research
University of Maryland School of Pharmacy
Baltimore, Maryland, U.S.A.
† Dr. Doshi's organizational affiliation is included for identification purposes only.

Juan Erviti, PharmD, PhD†
Unit of Innovation and Organization
Navarre Health Service, Spain
Pamplona, Spain
† Dr. Erviti's organizational affiliation is included for identification purposes only.

Peter C. Gøtzsche, Professor, DrMedSci, MD, MSc
Director
Institute for Scientific Freedom
Copenhagen, Denmark

Janice E. Graham, PhD, FCAHS, FRSC†
University Research Professor
Dalhousie University
Halifax, Canada
† Dr. Graham's organizational affiliation is included for identification purposes only

David Healy, MD FRCPsych†
Professor of Psychiatry
McMaster University
Ontario, Canada
† Dr. Healy's organizational affiliation is included for identification purposes only.

Iona Heath, CBE FRCGP†
Past president of the Royal College of General Practitioners
London, United Kingdom
† Dr. Heath's former affiliation is included for identification purposes only.

Matthew Herder, JSM LLM†
Director, Health Law Institute
Dalhousie University
Nova Scotia, Canada
† *Prof. Herder's organizational affiliation is included for identification purposes only.*

Tom Jefferson, MD MRCGP FFPHM†
Senior Associate Tutor
University of Oxford
† *Dr. Jefferson's organizational affiliation is included for identification purposes only.*

Mark Jones, PhD†
Associate Professor of Biostatistics
Bond University
Gold Coast, Queensland, Australia
† *Dr. Jones's organizational affiliation is included for identification purposes only.*

Robert M. Kaplan, PhD†
Distinguished Research Professor
UCLA Fielding School of Public Health
Los Angeles, California, U.S.A.
† *Dr. Kaplan's organizational affiliation is included for identification purposes only.*

Ulrich Keil, MD, PhD, FRCP (London)†
Professor Emeritus
University of Muenster
Muenster, Germany
† *Dr. Keil's organizational affiliation is included for identification purposes only.*

Joseph A. Ladapo, MD, PhD†
Associate Prof. of Medicine
David Geffen School of Medicine at UCLA
Los Angeles, California, U.S.A.
† *Dr. Ladapo's organizational affiliation is included for identification purposes only.*

Trudo Lemmens, LicJur, LLM bioethics, DCL†
Professor and Scholl Chair in Health Law and Policy
University of Toronto
Toronto, Canada
† *Dr. Lemmens' organizational affiliation is included for identification purposes only*

Tianjing Li, MD, MHS, PhD†
Associate Professor
University of Colorado Anschutz Medical Campus
Aurora, Colorado, U.S.A.
† *Dr. Li's organizational affiliation is included for identification purposes only.*

Donald W. Light, PhD†
Professor of Comparative Health Policy and Psychiatry
Rowan University School of Osteopathic Medicine
Glassboro, New Jersey, U.S.A.
† *Dr. Light's organizational affiliation is included for identification purposes only.*

Peter A. McCullough, MD, MPH†
Professor of Medicine
Texas A & M College of Medicine
Dallas, Texas, U.S.A.
† *Dr. McCullough's organizational affiliation is included for identification purposes only.*

Hamid A. Merchant, BPharm, MPharm, PhD, RPh, CQP, PGCertHE, FHEA, SRPharmS†
Subject Leader in Pharmacy
University of Huddersfield
Huddersfield, United Kingdom
† *Dr. Merchant's organizational affiliation is included for identification purposes only.*

Barbara Mintzes, BA, MSc, PhD†
Associate Professor, School of Pharmacy
The University of Sydney
Sydney, Australia
† *Dr. Mintzes' organizational affiliation is included for identification purposes only.*

Huseyin Naci, MHS, PhD†
Associate Professor of Health Policy
London School of Economics and Political Science
London, United Kingdom
† *Dr. Naci's organizational affiliation is included for identification purposes only.*

Allyson M Pollock, MBChB, FRCPH, FRCP (Ed) FRCGP†
Clinical Professor of Public Health
Institute of Health and Society, Newcastle University
Newcastle upon Tyne, United Kingdom
† *Dr. Pollock's organizational affiliation is included for identification purposes only.*

Angela Spelsberg, MD, SM[†]
Comprehensive Cancer Center Aachen
Aachen, Germany
[†] *Dr. Spelsberg's organizational affiliation is included for identification purposes only.*

Erick Turner, MD[†]
Associate Professor of Psychiatry
Oregon Health & Science University
Portland, Oregon, U.S.A.
[†] *Dr. Turner's organizational affiliation is included for identification purposes only.*

Linda Wastila, BSPharm, MSPH, PhD[*†]
Professor, Pharmaceutical Health Services Research
University of Maryland School of Pharmacy
220 Arch Street, Baltimore, Maryland 21201, U.S.A.
[*] *Dr. Wastila is serving as the Representative of CAALM*
[†] *Dr. Wastila's organizational affiliation is included for identification purposes only.*

Patrick Whelan, MD PhD[†]
Associate Clinical Professor of Pediatrics
David Geffen School of Medicine at UCLA
Los Angeles, California, U.S.A.
[†] *Dr. Whelan's organizational affiliation is included for identification purposes only.*

Kim Witczak
President/Co-Founder
Woodymatters
Minneapolis, Minnesota, U.S.A.

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Marks Decl. Exhibit G

August 23, 2021

Linda Wastila, BSPharm, MSPH, PhD
Representative
Coalition Advocating for Adequately Licensed Medicines (CAALM)

Re: Citizen Petition (Docket Number FDA-2021-P-0786)

Dear Petitioner,

This letter responds to the citizen petition that the Coalition Advocating for Adequately Licensed Medicines (CAALM) (the Petitioner, you) submitted to the Food and Drug Administration (FDA, the Agency, we) relating to licensure of vaccines to prevent Coronavirus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (the CP).

In the CP, Petitioner requests that FDA:

1. "Confirm, in revised Guidance, that the FDA expects a minimum of 2 years of follow-up of participants enrolled in pivotal clinical trials, even if trials are unblinded and lack a placebo control";
2. "Require data demonstrating substantial evidence of clinical effectiveness that outweighs harms, in all special populations, as a condition of consideration of including these populations among the indicated populations" including the special populations "infants, children, and adolescents; those with past SARS-CoV-2 infection; immunosuppressed individuals; those with history of or current cancer; individuals with hematological disorders or autoimmune diseases; pregnant or nursing women; and frail older adults";
3. "Require data on the safety and pharmacokinetic profiles of the spike protein";
4. "Require data from biodistribution studies investigating the actual COVID-19 vaccines";
5. "Require data from pharmacovigilance systems in the US and globally documenting a thorough investigation of serious adverse events, carried out by independent, impartial individuals";
6. "Clarify in revised Guidance that safety data from individuals receiving more than 2 vaccine doses must be submitted";
7. "Ensure the inclusion of experts in gene therapy in the VRBPAC"; and
8. "Ensure that the analysis of data and decisions regarding any COVID-19 vaccine BLA application are informed by experts with no financial or research relationships with any vaccine manufacturers within the last 36 months, both within FDA and amongst the composition of the VRBPAC."

CP at 3-4.

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

This letter responds to the CP in full. FDA has carefully reviewed the CP and other relevant information available to the Agency. Based on our review of these materials and for the reasons described below, we conclude that the CP does not contain facts demonstrating any reasonable grounds for the requested action. In accordance with 21 CFR § 10.30(e)(3), and for the reasons stated below, FDA is denying the CP.

In this letter, we discuss the requirements for licensed vaccines. We then turn to the requests contained in the CP. We consider each of your requests in light of the legal standards for FDA action, and provide our conclusions based on the facts, the science, and the law.

I. Background

There is currently a pandemic of respiratory disease, COVID-19, caused by a novel coronavirus, SARS-CoV-2. The COVID-19 pandemic presents an extraordinary challenge to global health. On January 31, 2020, the Department of Health and Human Services (HHS) issued a declaration of a public health emergency related to COVID-19.[1] On February 4, 2020, pursuant to section 564 of the FD&C Act, the Secretary of HHS determined that there is a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad, and that involves the virus that causes COVID-19.[2] On the basis of such determination, on March 27, 2020, the Secretary then declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic ("COVID-19 EUA Declaration"), pursuant to section 564(b)(1) of the FD&C Act.[3] In addition, on March 13, 2020, the Presidential declared a national emergency in response to COVID-19.[4]

Commercial vaccine manufacturers and other entities are developing COVID-19 vaccine candidates, and clinical studies of these vaccines are underway and/or have been completed. Between December 11, 2020 and February 27, 2021, FDA issued emergency use authorizations for three vaccines to prevent COVID-19, including vaccines sponsored by Pfizer Inc. (Pfizer); ModernaTX, Inc. (Moderna); and Janssen Biotech, Inc. (Janssen), a pharmaceutical company of Johnson & Johnson. FDA received a Biologics License Application (BLA) for the COVID-19 vaccine, BNT162b2, intended to prevent COVID-19 in individuals 16 years of age and older. As announced by FDA on August 23, 2021, the Agency is issuing a biologics license

[1] Secretary of Health and Human Services Alex M. Azar, Determination that a Public Health Emergency Exists (Originally issued Jan. 31, 2020, and subsequently renewed), https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx.
[2] HHS, Determination of Public Health Emergency, 85 FR 7316, February 7, 2020, https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.
[3] HHS, Emergency Use Authorization Declaration, 85 FR 18250, April 1, 2020, https://www.federalregister.gov/documents/2020/04/01/2020-06905/emergency-use-authorization-declaration.
[4] Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak, issued March 13, 2020, https://trumpwhitehouse.archives.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/.

for this COVID-19 vaccine (COVID-19 Vaccine, mRNA; Comirnaty) to BioNTech Manufacturing GmbH.[5,6]

II. Vaccines That Are FDA-Licensed Meet Relevant Statutory Requirements

1. Vaccines Are Shown to Be Safe, Pure, and Potent at the Time of Licensure

FDA has a stringent regulatory process for licensing vaccines.[7,8] The Public Health Service Act (PHS Act) authorizes FDA to license biological products, including vaccines, if they have been demonstrated to be "safe, pure, and potent."[9] Prior to approval by FDA, vaccines are extensively tested in non-clinical studies and in humans. FDA's regulations describe some of the extensive data and information that each sponsor of a vaccine must submit to FDA in order to demonstrate the product's safety before FDA will consider licensing the vaccine. FDA requires that the sponsor's BLA include, among other things, data derived from nonclinical and clinical studies showing the product's safety, purity, and potency; a full description of manufacturing methods for the product; data establishing the product's stability through the dating period; and a representative sample of the product and summaries of results of tests performed on the lot(s) represented by the sample.[10]

As is evident from the language of the PHS Act and FDA's regulations, the licensure process for a vaccine requires the sponsor to establish, through carefully controlled laboratory and clinical studies, as well as through other data, that the product is safe and effective for its approved indication(s) and use. FDA's multidisciplinary review teams then rigorously evaluate the sponsor's laboratory and clinical data, as well as other information, to help assess whether the safety, purity, and potency of a vaccine has been demonstrated.[11] Only when FDA's standards are met is a vaccine licensed.

FDA regulations explicitly state that "[a]pproval of a biologics license application or issuance of a biologics license shall constitute a determination that the establishment(s) and the product meet applicable requirements to ensure the continued safety, purity, and potency of such products."[12] Therefore, the manufacturers of vaccines that have been licensed in the U.S. have necessarily demonstrated the safety of the vaccines within the meaning of the applicable statutory and regulatory provisions before the vaccines were licensed and allowed to be marketed.

For more information on FDA's thorough process for evaluating the safety of vaccines, see Appendix I of this letter, *Aspects of Vaccine Development and Process for Licensure*.

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[5] BioNTech Manufacturing GmbH is the biologics license holder for this vaccine, which is manufactured by Pfizer Inc. for BioNTech Manufacturing GmbH (hereinafter "BioNTech").
[6] The basis for FDA's licensure decision is set forth in FDA's Summary Basis for Regulatory Action for the BioNTech application. This memorandum will be posted on fda.gov. We incorporate by reference the SBRA for the BLA.
[7] CDC, Ensuring the Safety of Vaccines in the United States, February 2013, https://www.cdc.gov/vaccines/hcp/patient-ed/conversations/downloads/vacsafe-ensuring-bw-office.pdf.
[8] Vaccine Safety Questions and Answers, last updated March 2018, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/vaccine-safety-questions-and-answers.
[9] 42 U.S.C. § 262(a)(2)(C)(i)(I).
[10] 21 CFR § 601.2(a).
[11] Vaccines, last updated January 2021, https://www.fda.gov/vaccines-blood-biologics/vaccines.
[12] 21 CFR § 601.2(d) (emphasis added).

2. Vaccine Safety Continues to Be Monitored Post-Licensure

FDA's oversight of vaccine safety continues after licensure of the product. Once the licensed vaccine is on the market, post-marketing surveillance of vaccine safety is conducted in order to detect any rare, serious, or unexpected adverse events, as well as to monitor vaccine lots. FDA employs multiple surveillance systems and databases to continue to evaluate the safety of these vaccines. In certain cases, FDA may require the manufacturer to conduct post-marketing studies to further assess known or potential serious risks.

For more information on post-licensure safety monitoring of vaccines, see Appendix II of this letter, *Aspects of Vaccine Postmarketing Safety Monitoring*.

III. Discussion

The CP makes a series of requests regarding the data to be submitted in support of licensure of vaccines to prevent COVID-19. Much of the key data supporting licensure applications is developed during the clinical trial process, which is subject to FDA's investigational new drug process.[13]

A. Investigational New Drugs

Before a vaccine is licensed (approved) by FDA for use by the public, FDA requires that it undergo a rigorous and extensive development program to determine the vaccine's safety and effectiveness. This development program encompasses preclinical research (laboratory research, animal studies[14]) and clinical studies. At the preclinical stage, the sponsor focuses on collecting the data and information necessary to establish that the product will not expose humans to unreasonable risks when used in limited, early-stage clinical studies. Clinical studies, in humans, are conducted under well-defined conditions and with careful safety monitoring through all the phases of the investigational new drug process. FDA's regulations governing the conduct of clinical investigations are set out at 21 CFR Part 312.

Before conducting a clinical investigation in the U.S. in which a new drug or biological product is administered to humans, a sponsor must submit an investigational new drug application (IND) to FDA.[15] The IND describes the proposed clinical study in detail and, among other things, helps protect the safety and rights of human subjects.[16] In addition to other information, an IND must contain information on clinical protocols and clinical investigators. Detailed protocols for proposed clinical studies permit FDA to assess whether the initial-phase trials will expose subjects to unnecessary risks. Information on the qualifications of clinical investigators (professionals, generally physicians, who oversee the administration of the experimental drug) permits FDA to assess whether they are qualified to fulfill their clinical trial duties. The IND

[13] See 21 CFR § 312.2 (explaining that the IND regulations apply to clinical investigations of both drugs and biologics).

[14] We support the principles of the "3Rs," to reduce, refine, and replace animal use in testing when feasible. We encourage sponsors to consult with us if they wish to use a non-animal testing method they believe is suitable, adequate, validated, and feasible. We will consider if such an alternative method could be assessed for equivalency to an animal test method.

[15] See 21 CFR § 312.20(a).

[16] For additional information regarding the IND review process and general responsibilities of sponsor-investigators related to clinical investigations see Investigational New Drug Applications Prepared and Submitted by Sponsor-Investigators; Draft Guidance for Industry, May 2015, https://www.fda.gov/media/92604/download.

includes commitments to obtain informed consent from the research subjects, to obtain review of the study by an institutional review board (IRB),[17] and to adhere to the investigational new drug regulations.

Once the IND is submitted, the sponsor must wait 30 calendar days before initiating any clinical trials, unless FDA informs the sponsor that the trial may begin earlier. During this time, FDA reviews the IND. FDA's primary objectives in reviewing an IND are, in all phases of the investigation, to assure the safety and rights of subjects, and, in Phase 2 and Phase 3, to help assure that the quality of the scientific evaluation of drugs is adequate to permit an evaluation of the drug's effectiveness and safety.[18]

FDA's regulations provide that, once an IND is in effect, the sponsor may conduct a clinical investigation of the product, with the investigation generally being divided into three phases. With respect to vaccines, the initial human studies, referred to as Phase 1 studies, are generally safety and immunogenicity studies performed in a small number of closely monitored subjects. Phase 2 studies may include up to several hundred individuals and are designed to provide information regarding the incidence of common short-term side effects such as redness and swelling at the injection site or fever and to further describe the immune response to the investigational vaccine. If an investigational new vaccine progresses past Phase 1 and Phase 2 studies, it may progress to Phase 3 studies. For Phase 3 studies, the sample size is often determined by the number of subjects required to establish the effectiveness of the new vaccine, which may be in the thousands or tens of thousands of subjects. Phase 3 studies provide the critical documentation of effectiveness and important additional safety data required for licensing.

At any stage of development, if data raise significant concerns about either safety or effectiveness, FDA may request additional information or studies; FDA may also halt ongoing clinical studies. The FD&C Act provides a specific mechanism, called a "clinical hold," for prohibiting sponsors of clinical investigations from conducting the investigation (section 505(i)(3) of the FD&C Act; 21 U.S.C. § 355(i)(3)), and FDA's IND regulations in 21 CFR § 312.42 identify the circumstances that may justify a clinical hold. Generally, a clinical hold is an order issued by FDA to the sponsor of an IND to delay a proposed clinical investigation or to suspend an ongoing investigation.[19]

B. The Citizen Petition

In the CP, Petitioner requests that before FDA licenses any vaccine[20] for COVID-19, the agency require certain data be submitted. Because much of the relevant data is the kind that would be

[17] The IRB is a panel of scientists and non-scientists in hospitals and research institutions that oversees clinical research. IRBs approve clinical study protocols, which describe the type of people who may participate in the clinical study; the schedule of tests and procedures; the medications and dosages to be studied; the length of the study; the study's objectives; and other details. IRBs make sure that the study is acceptable, that participants have given consent and are fully informed of the risks, and that researchers take appropriate steps to protect patients from harm. See The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective web page, last updated November 2017, https://www.fda.gov/drugs/drug-information-consumers/fdas-drug-review-process-ensuring-drugs-are-safe-and-effective.

[18] 21 CFR § 312.22(a).

[19] 21 CFR § 312.42(a).

[20] The CP refers to "granting" a license. See, e.g., CP at 1. FDA generally refers to *issuing* licenses, or *approving* a BLA. See 21 CFR § 601.2(d); 21 CFR § 601.4(a).

gathered during clinical trials, we interpret the CP as asking that FDA require the sponsors to make the requested changes to their investigations, as well as, in some cases, to submit certain other data. As explained above, with certain exceptions, clinical investigations in which a drug is administered to human subjects must be conducted under an IND submitted to FDA by the sponsor. FDA's review of an IND includes a review of the study protocol which describes, among other things, the design of the clinical study, including the identified endpoints and methods for assessing the safety and effectiveness of the investigational product.

Below, we discuss the requested changes to the study design and other data submissions.

1. Petitioner's request to require data demonstrating "substantial evidence of clinical effectiveness that outweighs harms" in all "special populations"

Petitioner asks that, prior to issuing a license for a COVID-19 vaccine, FDA require certain types of *clinical* data, specifically:

> data demonstrating substantial evidence of clinical effectiveness that outweighs harms, in all special populations, as a condition of consideration of including these populations among the indicated populations. Special populations include: infants, children, and adolescents; those with past SARS-CoV-2 infection; immunosuppressed individuals; those with history of or current cancer; individuals with hematological disorders or autoimmune diseases; pregnant or nursing women; and frail older adults.

CP at 3.

Petitioner refers to the ongoing phase 3 trials of COVID-19 vaccines for the Moderna, Pfizer, and Janssen products, and states that the trials "largely (or wholly) excluded" certain identified populations. CP at 5. Petitioner states that there should be information about "what kind of efficacy" exists for these populations, and refers to "reduction in risk of symptomatic COVID-19 vs. reduction in risk of hospitalization or death." CP at 6.

Thus, Petitioner appears to request that FDA require evidence derived from clinical trials to provide evidence of effectiveness for each of the identified populations, and also that clinical trials be designed and conducted in each population to assess the effectiveness of these vaccines to prevent COVID-19 disease of varying severity in the specified populations.

In support of Petitioner's request, Petitioner asserts that "efficacy and safety of medicines often differs amongst populations" and that the risks of SARS-CoV-2 infection are "considerably lower in infants, children, and adolescents in comparison to adults." CP at 5.

FDA addressed trial populations in the guidance.[21] In the June 2020 guidance, FDA noted that while certain exclusions were recommended, for example "[e]xclusion of participants at higher risk of severe COVID-19 from early phase studies" in order "to mitigate potential risk of vaccine associated [enhanced respiratory disease] until additional data to inform that potential risk becomes available through ongoing product development,"[22] FDA in general "encourages the

[21] Development and Licensure of Vaccines to Prevent COVID-19; Guidance for Industry, June 2020 (June 2020 Guidance), https://www.fda.gov/media/139638/download.
[22] June 2020 Guidance at 10.

inclusion of diverse populations in all phases of vaccine clinical development."[23] FDA also noted in the June 2020 Guidance that "vaccine safety and COVID-19 outcomes in individuals with prior SARS-CoV-2 infection, which might have been asymptomatic, is also important to examine because pre-vaccination screening for prior infection is unlikely to occur in practice with the deployment of licensed COVID-19 vaccines."[24]

With respect to the pediatric population, the June 2020 Guidance acknowledged that "the safety and effectiveness of COVID-19 vaccines, may be different in children compared with adults"[25] and recommended that "considerations on the prospect of direct benefit and acceptable risk to support initiation of pediatric studies, and the appropriate design and endpoints for pediatric studies, should be discussed in the context of specific vaccine development programs."[26]

Although the June 2020 Guidance includes various recommendations, ultimately FDA licensure decisions are based on an evaluation of the entirety of the data contained in a BLA and a finding that a vaccine's benefits outweigh its potential risks.

In assessing benefits and risks, FDA takes into account a number of factors including, but not limited to, the evidence for benefit, the requested indication, severity of the disease or condition, treatment alternatives, and the type and severity of adverse events. In general, the evidence for benefit is based on the results of clinical trials. In some cases, vaccine clinical trials assess clinical disease endpoints. In other cases, it may be scientifically acceptable to utilize immunogenicity endpoints.

In assessing benefits for particular populations, FDA is not limited to considering evidence of effectiveness based on clinical trial studies with disease endpoints. In some cases, FDA may conclude that pediatric effectiveness can be extrapolated from adequate and well-controlled studies in adults.[27] Furthermore, a study may not be needed in each pediatric age group if data from one age group can be extrapolated to another age group.[28] There are times where it is scientifically appropriate to demonstrate effectiveness using scientifically accepted immune marker(s) of protection or to infer effectiveness for a population through immunobridging.

In assessing risks, FDA takes into account the type, frequency, and severity of any adverse events.

The benefit-risk assessment will be informed by the body of evidence about the vaccine's safety and effectiveness submitted by an applicant in the BLA, the severity of the target disease, and the target population. Thus, in approving or authorizing a vaccine for use in a particular population (such as children), FDA will take into account the severity of the disease in the population as well as the benefits of the vaccine.

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[23] Id. at 11.
[24] Id.
[25] Id.
[26] Id.
[27] See section 505B(a)(2)(B)(i) of the FD&C Act (21 U.S.C. 355c(a)(2)(B)(i)) (providing that "[i]f the course of the disease and the effects of the drug are sufficiently similar in adults and pediatric patients, the Secretary may conclude that pediatric effectiveness can be extrapolated from adequate and well-controlled studies in adults, usually supplemented with other information obtained in pediatric patients, such as pharmacokinetic studies").
[28] See section 505B(a)(2)(B)(ii) of the FD&C Act (21 U.S.C. 355c(a)(2)(B)(ii)) (providing that "[a] study may not be needed in each pediatric age group if data from one age group can be extrapolated to another age group").

To require the Petitioner's proposed across-the-board approach—i.e., of requiring effectiveness data from clinical trials specific to each population group and specifically designed to evaluate disease endpoints of varying severity (e.g., hospitalization and death) in all of the specified populations—would not reflect the scientifically valid methods of assessing safety and effectiveness described above. Petitioner has not provided a scientific justification for why such tools as immunobridging or extrapolation across population groups cannot be used. Therefore, we deny Petitioner's request[29] to require effectiveness data from clinical trials specifically designed to assess disease endpoints of varying severity (e.g., hospitalization and death) for each of the identified populations as a condition of licensing a COVID-19 vaccine.[30,31]

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[29] In denying Petitioner's request, we do not dispute Petitioner's statement that the risks of SARS-CoV-2 infection can differ across population groups. That has been a feature of the pandemic's effects thus far, with children and adolescents generally experiencing a milder disease course compared to older adults. But as with adults, children and adolescents with underlying conditions such as asthma, chronic lung disease, and cancer are at higher risk than their healthier counterparts for COVID-19-related hospitalization and death. See generally Emergency Use Authorization (EUA) Amendment for an Unapproved Product Review Memorandum (pertaining to FDA's authorization of the Pfizer-BioNTech COVID-19 Vaccine for individuals 12 years and older), https://www.fda.gov/media/148542/download. These are features of COVID-19 that FDA may consider in weighing the risks and benefits of COVID-19 vaccines for different populations.

[30] With respect to Petitioner's statement that it is important to consider "how much efficacy exists" (CP at 6) for different populations, with the example of reduction of risk of hospitalization or death vs. reduction of risk of symptomatic COVID-19, we agree that severity of disease experienced by different groups is an important consideration that may be accounted for in a risk-benefit analysis. What we disagree with is Petitioner's apparent request that FDA only accept the results of clinical trials that have different endpoints for different populations (e.g., hospitalization or death for a younger population and symptomatic COVID-19 for older populations). A clinical trial endpoint of symptomatic disease for all populations included in the trial may provide sufficient information for FDA to adequately assess the risks and benefits of the vaccine, and FDA may evaluate the effectiveness of the vaccine in different populations by considering subgroup analyses of the data including analyses of vaccine effectiveness against disease of varying severity using pre-specified case definitions.

[31] With respect to Petitioner's statement that individuals with past SARS-CoV-2 infection "are likely to have immunity to subsequent infections for as long or longer than immunity conferred by vaccine," and that they "may also be at heightened risk for adverse effects," (CP at 5) we note that there is scientific uncertainty about the duration of protection provided by previous natural infection, but that the scientific community believes that vaccines may provide a longer duration of protection than that provided by natural infection. See CDC, COVID-19 Frequently Asked Questions, last updated August 2021, https://www.cdc.gov/coronavirus/2019-ncov/vaccines/faq.html; Boyton, R. and D Altmann, 2021, Risk of SARS-CoV-2 reinfection after natural infection, Lancet, 397(10280):1161-1163, https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00662-0/fulltext

In addition, you state that individuals with previous infection "may also be at heightened risk for adverse effects." CP at 5. The sources that you cite for this proposition are unavailing. First, the Krammer et al. publication (http://medrxiv.org/lookup/doi/10.1101/2021.01.29.21250653) does not assert safety problems with this population receiving COVID-19 vaccines; rather, the publication asserts that these individuals could receive only one dose of vaccine without negatively impacting their antibody titers and sparing them from unnecessary local and systemic adverse reactions (e.g., pain, swelling, fatigue, headache, chills, fever, muscle or joint pains) while also freeing up many urgently needed vaccine doses. The Samanovic et al. publication (http://dx.doi.org/10.1101/2021.02.07.21251311) similarly does not identify safety concerns, but rather concludes that prior history of COVID-19 affects adaptive immune responses to mRNA vaccination. The Camara et al. publication (https://www.biorxiv.org/content/10.1101/2021.03.22.436441v1) asserts only that the second dose may not be necessary in individuals with prior infection and that a second dose may cause a "possible contraction of their spike-specific memory T cell immunity," while also noting that "[o]ur study has clear limitations" and that "more detailed analysis of the phenotype of the spike-specific T cells induced by COVID-19 vaccines both in naïve and

2. Petitioner's request to require data on the safety and pharmacokinetic profiles of the spike protein

Petitioner asks FDA to "[r]equire data on the safety and pharmacokinetic profiles of the spike protein" prior to licensing any COVID-19 vaccine. CP at 6. In support of this request, Petitioner states that "[i]n-situ production of SARS-CoV-2 spike protein is the target mechanism of action of all COVID-19 vaccines with an EUA at present. Therefore, the safety profile of the spike protein itself (i.e., in the absence of virus) must be thoroughly understood in the range of populations on the indications list." CP at 6.

This request relates to the technology used to make the COVID-19 vaccines that have been authorized by FDA for emergency use. The Pfizer-BioNTech and Moderna vaccines contain a piece of mRNA that instructs cells in the body to make the distinctive "spike" protein of the SARS-COV-2 virus. The Janssen COVID-19 vaccine is manufactured using a specific type of virus called adenovirus type 26 (Ad26) that delivers a piece of the DNA that is used to make the distinctive "spike" protein of the SARS-CoV-2 virus.

Your request appears to be premised on the notion that licensure should be contingent on sponsors' conducting safety studies of a specific protein produced by the COVID-19 vaccines that is designed to elicit an immune response. Contrary to the assumption underlying your request, it is not scientifically necessary to require toxicological or pharmacokinetic studies in individuals to evaluate specific features of a vaccine outside the context of evaluating the vaccine as a whole. In making a licensure decision, FDA determines whether the data and information provided by a manufacturer have demonstrated that a vaccine is safe, pure, and potent. In making a determination about the safety of a vaccine, the agency evaluates the complete manufacturing process and whether specific features of a vaccine are such that the finished product itself, when used at the recommended dose, is safe for the recipient. FDA applies its

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recovered individuals are needed to answer these questions." Petitioner also references a preprint by Levi et al. (https://www.medrxiv.org/content/10.1101/2021.02.01.21250923v2). In the published version of that study, the authors conclude that "[o]ne vaccine dose is sufficient in symptomatic SARS-CoV-2-exposed subjects to reach a high titer of antibodies, suggesting no need for a second dose, particularly in light of current [sic] vaccine shortage." Levi et al. One Dose of SARS-CoV-2 Vaccine Exponentially Increases Antibodies in Individuals Who Have Recovered from Symptomatic COVID-19, J Clin Invest. 2021;131(12):e149154: https://www.jci.org/articles/view/149154). Levi et al. does not identify safety concerns with COVID-19 vaccines.

We note that history of infection prior to vaccination is not usually known in adverse event reports (either because it wasn't reported, or because it could have been asymptomatic and the patient never knew they had infection). Likewise, there could be a reporting bias for a reporting system like VAERS, which relies on vaccine recipients, healthcare providers, or others to initiate reports to the system, because individuals who were infected previously might be more likely to report adverse events. However, FDA, together with CDC, has not become aware of data from VAERS to suggest an increased frequency of adverse events in vaccinees who were infected with SARS-CoV-2 prior to vaccination. FDA and CDC Medical Officers conduct on-going review of certain, serious adverse events of special interest for the COVID vaccines. These reviews often include examination of the narrative and other fields which would contain information about past infection, if provided. Additionally, CDC and the VAERS Program contractor collect follow-up medical records for certain serious reports. Teams of physicians, nurses, and other reviewers abstract key clinical details, including medical history, from these records. The reviewers conducting these on-going surveillance efforts have not identified patterns of adverse events associated with prior infection.

sound scientific judgment in evaluating vaccines and other biological products, and ensures that vaccines licensed by the agency are safe within the meaning of the PHSA, the FD&C Act, and implementing regulations.

With respect to the spike protein feature of vaccines for COVID-19, while there have been numerous claims on social media suggesting that the spike protein is toxic,[32] there are in fact no reliable scientific data to indicate that the spike protein is toxic or that it lingers at any toxic level in the body after vaccination. Below, we list the publications you cite in footnotes 15-28 of your petition in support of what you describe as "safety concerns" with the spike protein feature of authorized vaccines.[33] The left column identifies the relevant footnote in your petition and the accompanying citation, and the right column describes FDA's analysis of the publication. The information in the right column explains why you have not in fact presented data showing safety problems with the spike protein feature of vaccines that would cause the vaccines to be unsafe.

Publication cited by Petitioner in support of "safety concerns" regarding spike protein	**FDA analysis**
Footnote 15: Ogata AF, Cheng C-A, Desjardins M, Senussi Y, Sherman AC, Powell M, et al. Circulating SARS-CoV-2 Vaccine Antigen Detected in the Plasma of mRNA-1273 Vaccine Recipients. Clin Infect Dis [Internet]. 2021 May 20; Available from: http://dx.doi.org/10.1093/cid/ciab465	This work conducted in a small number of individuals (n=13) documents that shortly following administration of the mRNA-1273 COVID-19 vaccine, SAR-CoV-2 spike protein was detectible in the plasma of 11 of the 13. Clearance of the protein from the circulation was associated with the development of IgG and IgA antibodies. The authors suggest a mechanism that might have led to the findings, based on the immune response to the vaccine. This paper documents the appearance of spike protein in plasma and its clearance with development of an immune response. This publication does not provide evidence that authorized COVID-19 vaccines are unsafe.
Footnote 16: Kuba K, Imai Y, Rao S, Gao H, Guo F, Guan B, et al. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. Nat Med [Internet]. 2005 Aug;11(8):875–9. Available from: http://dx.doi.org/10.1038/nm1267	This article relates to SARS-CoV, the causative agent of SARS, an atypical pneumonia that occurred in several countries in 2002-2003. It was published in 2005 before the discovery of SARS-CoV-2 and the development of vaccines to prevent COVID-19. Therefore, the reports in this publication do not present safety concerns about the use of the spike protein in vaccines.
Footnote 17: Chen I-Y, Chang SC, Wu H-Y, Yu T-C, Wei W-C, Lin S, et al. Upregulation of the chemokine (C-C motif) ligand 2 via a severe acute respiratory syndrome coronavirus spike-ACE2 signaling pathway. J	This 2010 publication describes in vitro studies with SARS-CoV. It was published in 2010 before the discovery of SARS-CoV-2 and the development of vaccines to prevent COVID-19. The publication therefore does not present any evidence of safety

[32] See, e.g., FactCheck.org, COVID-19 Vaccine-Generated Spike Protein is Safe, Contrary to Viral Claims, https://www.factcheck.org/2021/07/scicheck-covid-19-vaccine-generated-spike-protein-is-safe-contrary-to-viral-claims/ (describing spread of social media claims about the spike protein); Lin, R., 2021, Busted: 3 dangerous social-media myths about COVID-19 vaccines, LA Times, https://www.latimes.com/california/story/2021-06-03/covid-19-vaccine-myths-busted (same); Dupuy, B., 2021, Spike protein produced by vaccine not toxic, AP, https://apnews.com/article/fact-checking-377989296609 (same).

[33] See Sec. 3(b) of the CP, which refers to footnotes 15-28 as support for asserted safety concerns with the spike protein.

Virol [Internet]. 2010 Aug;84(15):7703–12. Available from: http://dx.doi.org/10.1128/JVI.02560-09	concerns related to the formulation of COVID-19 vaccines.
Footnote 18: Patra T, Meyer K, Geerling L, Isbell TS, Hoft DF, Brien J, et al. SARS-CoV-2 spike protein promotes IL6 trans-signaling by activation of angiotensin II receptor signaling in epithelial cells. PLoS Pathog [Internet]. 2020 Dec;16(12):e1009128. Available from: http://dx.doi.org/10.1371/journal.ppat.1009128	This publication pertains to SARS-CoV-2 infection and disease progression, but does not relate to vaccines to prevent COVID-19. The publication therefore does not present any evidence of safety concerns related to the formulation of COVID-19 vaccines.
Footnote 19: Zhang S, Liu Y, Wang X, Yang L, Li H, Wang Y, et al. SARS-CoV-2 binds platelet ACE2 to enhance thrombosis in COVID-19. J Hematol Oncol [Internet]. 2020 Sep 4;13(1):120. Available from: http://dx.doi.org/10.1186/s13045-020-00954-7	This publication pertains to SARS-CoV-2 infection and disease progression, but does not relate to vaccines to prevent COVID-19. The publication therefore does not present any evidence of safety concerns related to the formulation of COVID-19 vaccines.
Footnote 20: Suresh SJ, Suzuki YJ. SARS-CoV-2 Spike Protein and Lung Vascular Cells. Journal of Respiration [Internet]. 2020 Dec 31 [cited 2021 May 25];1(1):40–8. Available from: https://www.mdpi.com/2673-527X/1/1/4	This publication states that "it is critical to understand the biological effects of this [spike] protein on human cells to ensure that it does not promote long-term adverse health consequences" and that "[f]urther work is needed to understand the effects of various SARS-CoV-2 spike protein segments" used in vaccines. But the publication does not in fact report any adverse effects of authorized vaccines. Nor does it conclude that use of spike protein in authorized vaccines causes the vaccines to be unsafe.
Footnote 21: Angeli F, Spanevello A, Reboldi G, Visca D, Verdecchia P. SARS-CoV-2 vaccines: Lights and shadows. Eur J Intern Med [Internet]. 2021 Apr 30; Available from: http://dx.doi.org/10.1016/j.ejim.2021.04.019	This article summarizes the features of several COVID-19 vaccines and discusses potential interactions between the spike protein of vaccines with the cardiovascular system. The article notes "[t]he basic mechanisms …require further research…" and that newer vaccines might be developed; however, it does not state that the spike protein itself should be studied in people.
Footnote 22: Han M, Pandey D. ZMPSTE24 Regulates SARS-CoV-2 Spike Protein-enhanced Expression of Endothelial Plasminogen Activator Inhibitor-1. Am J Respir Cell Mol Biol [Internet]. 2021 May 18; Available from: http://dx.doi.org/10.1165/rcmb.2020-0544OC	This publication pertains to COVID-19 disease, but does not relate to vaccines to prevent COVID-19. The publication therefore does not present any evidence of safety concerns related to the formulation of COVID-19 vaccines.
Footnote 23: Rhea EM, Logsdon AF, Hansen KM, Williams LM, Reed MJ, Baumann KK, et al. The S1 protein of SARS-CoV-2 crosses the blood-brain barrier in mice. Nat Neurosci [Internet]. 2021 Mar;24(3):368– 78. Available from: http://dx.doi.org/10.1038/s41593-020-00771-8	This publication pertains to COVID-19 disease, but does not relate to vaccines to prevent COVID-19. The publication therefore does not present any evidence of safety concerns related to the formulation of COVID-19 vaccines.
Footnote 24: Idrees D, Kumar V. SARS-CoV-2 spike protein interactions with amyloidogenic proteins: Potential clues to neurodegeneration. Biochem Biophys Res Commun [Internet]. 2021 May 21;554:94–8. Available from: http://dx.doi.org/10.1016/j.bbrc.2021.03.100	This publication pertains to COVID-19, but does not relate to vaccines to prevent COVID-19. The publication therefore does not present any evidence of safety concerns related to the formulation of COVID-19 vaccines.
Footnote 25: Lei Y, Zhang J, Schiavon CR, He M, Chen L, Shen H, et al. SARS-CoV-2 Spike Protein Impairs Endothelial Function via Downregulation of ACE 2. Circ Res [Internet]. 2021 Apr 30;128(9):1323–6. Available	This publication pertains to the S protein, but does not relate to vaccines to prevent COVID-19. The publication therefore does not present any evidence of safety concerns related to the formulation of COVID-19 vaccines. In fact, the publication

from: http://dx.doi.org/10.1161/CIRCRESAHA.121.318902	concludes by stating: "vaccination-generated antibody and/or exogenous antibody against S protein not only protects the host from SARS-CoV-2 infectivity but also inhibits S protein-imposed endothelial injury."
Footnote 26: Zhang L, Richards A, Barrasa MI, Hughes SH, Young RA, Jaenisch R. Reverse-transcribed SARS-CoV-2 RNA can integrate into the genome of cultured human cells and can be expressed in patientderived tissues. Proc Natl Acad Sci U S A [Internet]. 2021 May 25;118(21). Available from: http://dx.doi.org/10.1073/pnas.2105968118	This publication pertains to SARS-CoV-2 infection, but does not relate to vaccines to prevent COVID-19. The publication therefore does not present any evidence of safety concerns related to the formulation of COVID-19 vaccines.
Footnote 27: Suzuki YJ, Nikolaienko SI, Dibrova VA, Dibrova YV, Vasylyk VM, Novikov MY, et al. SARS-CoV-2 spike protein-mediated cell signaling in lung vascular cells. Vascul Pharmacol [Internet]. 2021 Apr;137:106823. Available from: http://dx.doi.org/10.1016/j.vph.2020.106823	This publication pertains to SARS-CoV-2 infection, but does not relate to vaccines to prevent COVID-19. The publication therefore does not present any evidence of safety concerns related to the formulation of COVID-19 vaccines.
Footnote 28: Suzuki YJ, Gychka SG. SARS-CoV-2 Spike Protein Elicits Cell Signaling in Human Host Cells: Implications for Possible Consequences of COVID-19 Vaccines. Vaccines (Basel) [Internet]. 2021 Jan 11;9(1). Available from: http://doi.org/10.3390/vaccines901003	This publication states that "it is important to consider the possibility that the SARS-CoV-2 spike protein produced by the new COVID-19 vaccines triggers cell signaling events that promote [pulmonary arterial hypertension]," and that it important to monitor vaccinees for long-term consequences. While the publication advocates experimental animal studies, it does not provide any data suggesting that the vaccines cause any harm.

In sum, you have not demonstrated why FDA is scientifically or legally obligated to require "data on the safety and pharmacokinetic profiles of the spike protein." In other words, you have not demonstrated why it is scientifically or legally faulty for FDA to make licensure determinations without requiring the specific requested safety data on the isolated spike protein in individuals. Therefore, we deny your request.[34]

3. Petitioner's request to require data from biodistribution studies

Petitioner asks FDA to require "data from biodistribution studies investigating the actual COVID-19 vaccines." CP at 7. Petitioner asserts that data submitted thus far by Moderna and Pfizer "suggests that the vaccines distribute widely in the body, including to the liver, brain, heart, lung, adrenals, ovaries, and testes, among many other tissues." CP at 7. Petitioner further states that "instead of presenting novel biodistribution studies of the COVID-19 vaccine formulations, sponsors presented substitute studies to FDA for an EUA during the pandemic." CP at 7. Therefore, according to Petitioner, "novel biodistribution studies investigating the

[34] We note that in addition to generally requesting "data on the safety and pharmacokinetic profiles of the spike protein," you request that studies investigate the spike protein's link to certain identified health outcomes (e.g., related to coagulopathy, reproduction, etc.). See Sec. 3(c) of the CP. Because we conclude that you have not supported the need for the requested type of data that is specific to the isolated spike protein, we deny your requests that FDA require that the studies producing such data examine the identified health outcomes. It is worth pausing to acknowledge that you premise some of the health outcome data requests on information that you attribute to VAERS. While VAERS is a critical part of FDA's post-market safety monitoring system for vaccines, reports to VAERS are not confirmed to be associated with vaccination.

actual COVID-19 vaccines are necessary." CP at 7. Petitioner further states that the studies are important "to characterize long term adverse effects and better understand potential mechanism(s) of action of short and long term harms. . . " CP at 7.

FDA addressed biodistribution studies in the June 2020 Guidance in the section regarding toxicity studies. FDA recommended biodistribution studies "if the vaccine construct is novel in nature and there are no existing biodistribution data from the platform technology."[35] FDA specified that biodistribution studies may not be necessary in certain situations "if the COVID-19 vaccine candidate is made using a platform technology utilized to manufacture a licensed vaccine or other previously studied investigational vaccines and is sufficiently characterized."[36]

Petitioner has not demonstrated the need for biodistribution studies of "the actual COVID-19 vaccines." For example, it is not scientifically inappropriate to support a BLA with biodistribution data for a surrogate protein produced using the platform technology, for example if imaging on such protein can be performed to visualize the location of the protein expression. Because Petitioner has not explained why such alternative approaches cannot be used, we deny Petitioner's request.

4. Petitioner's Request to Require Data from Pharmacovigilance Systems Documenting an Investigation into Serious Adverse Events

Petitioner asks FDA to require "data from pharmacovigilance systems in the US and globally documenting a thorough investigation serious adverse events, carried out by independent, impartial individuals." CP at 8. Petitioner states that "COVID-19 vaccines have now been administered to hundreds of millions of individuals, and it is vital that all reports of SAEs [significant adverse events] are thoroughly investigated to determine whether the vaccine played any role in the SAE." CP at 8. Petitioner also states that the investigation "must be carried out by independent, impartial individuals." CP at 9. Thus, Petitioner appears to be asking for "thorough investigation" into serious adverse events.

It is unclear whether Petitioner is requesting that individual manufacturers perform the pharmacovigilance, or if Petitioner asks that FDA do so. Given that post-marketing surveillance systems are conducted both by sponsors and FDA, we interpret the request as asking that FDA ensure that both the agency and sponsors conduct the requested investigations.

Petitioner has not demonstrated any failures to conduct "thorough investigations" into post-marketing serious adverse events, so it is unclear what additional action FDA could take in response to the CP. Therefore, we deny this request.

FDA agrees that post-marketing surveillance plays an important role. FDA is monitoring the safety of the Authorized COVID-19 Vaccines through both passive and active safety surveillance systems. FDA is doing so in collaboration with the Centers for Disease Control and Prevention (CDC), the Centers for Medicare and Medicaid Services (CMS), the Department of Veterans Affairs (VA), and other academic and large non-government healthcare data systems.

[35] June 2020 Guidance, at 7.
[36] Id.

In addition, FDA participates actively in ongoing international pharmacovigilance efforts, including those organized by the International Coalition of Medicines Regulatory Authorities (ICMRA) and the World Health Organization (WHO). These efforts are in addition to the pharmacovigilance efforts being undertaken by the individual manufacturers for authorized vaccines. A coordinated and overlapping approach using state-of the art technologies has been implemented. As part of our efforts to be transparent about our COVID-19 vaccine safety monitoring activities, FDA is posting summaries of the key safety monitoring findings on the FDA website.[37]

Passive Surveillance

VAERS is a national passive surveillance vaccine safety database that receives unconfirmed reports of possible adverse events following the use of a vaccine licensed or authorized in the United States. Passive surveillance is defined as unsolicited reports of adverse events that are sent to a central database or health authority. In the United States, these are received and entered into VAERS, which is co-managed by FDA and CDC. In the current pandemic, these reports are being used to monitor the occurrence of both known and unknown adverse events, as providers of COVID-19 vaccines are required to report serious adverse events to VAERS.

As part of FDA and CDC's multi-system approach to post-licensure and post-authorization vaccine safety monitoring, VAERS is designed to rapidly detect unusual or unexpected patterns of adverse events, also known as "safety signals." VAERS reports generally cannot be used to determine if a vaccine caused or contributed to an adverse event or illness. If the VAERS data suggest a possible link between an adverse event and vaccination, the relationship may be further studied in a controlled fashion.[38]

Anyone can make a report to VAERS, including vaccine manufacturers, private practitioners, state and local public health clinics, vaccine recipients, and their parents or caregivers. Surveillance programs like VAERS perform a critical function by generating signals of potential problems that may warrant further investigation.

Active Surveillance

Active surveillance involves proactively obtaining and rapidly analyzing information related to millions of individuals and recorded in large healthcare data systems to verify safety signals identified through passive surveillance or to detect additional safety signals that may not have been reported as adverse events to passive surveillance systems. FDA is conducting active surveillance using the Sentinel BEST (Biologics Effectiveness and Safety) System and the CMS system, and is also collaborating with other federal and non-federal partners.

BEST

[37] https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines?

[38] FDA, VAERS Overview, available at https://www.fda.gov/vaccines-blood-biologics/vaccine-adverse-events/vaers-overview

To elaborate further, the BEST system,[39] which is part of the Sentinel initiative,[40] comprises large-scale claims data, electronic health records (EHR), and linked claims-EHR databases with a data lag of approximately three months. The system makes use of multiple data sources and enables rapid queries to detect or evaluate adverse events as well as studies to answer specific safety questions for vaccines. The linked claims-EHR database makes it possible to study the safety of vaccines in sub-populations with pre-existing conditions or in pregnant women. The major partners for BEST currently are Acumen, IBM Federal HealthCare, IQVIA, and Columbia University and many affiliated partners such as MedStar Health, BlueCross BlueShield of America, the Observational Health Data Sciences and Informatics (OHDSI), OneFlorida, University of California and several others.[41]

Using BEST, CBER plans to monitor about 15 adverse events[42] that have been seen with the deployment of previous vaccines but have yet to be associated with a safety concern for an authorized COVID-19 vaccine at this time. CBER further plans to use the BEST system to conduct more in-depth analyses should a safety concern be identified from sources such as VAERS.

CMS

FDA has worked over the past several years with CMS to develop capabilities for routine and time-sensitive assessments of the safety of vaccines for people 65 years of age and older using the Medicare Claims database.[43] Because it was already in place, this system was immediately put into use for COVID-19 vaccine surveillance to monitor for adverse events.[44]

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[39] Biologics Effectiveness and Safety (BEST) System, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-biologics-effectiveness-and-safety-best-system

[40] FDA's Sentinel Initiative, https://www.fda.gov/safety/fdas-sentinel-initiative

[41] To confirm the utility of the BEST system for situations such as COVID-19 vaccine surveillance, a test case was conducted. This study aimed to replicate a previous study by the CDC's Vaccine Safety Datalink (VSD) (Klein et al. Pediatrics 2010) that examined the databases and analytic capabilities of the new system. The objective of this study was to test the new system's ability to reproduce the increased risk of febrile seizures in children receiving the first dose of measles-mumps-rubella-varicella (MMRV) vaccine, compared to that of MMR and varicella vaccines separately but on the same day. The results of the study met the objectives and demonstrated the ability of the BEST Initiative data network to run a complex study protocol at multiple sites using a distributed data network and the Observational Medical Outcomes Partnership Common Data Model (organizing disparate data sources into the same database design using a common format).

[42] CBER, Background Rates of Adverse Events of Special Interest for COVID-19 Vaccine Safety Monitoring, Draft Protocol (December 31, 2020), https://www.bestinitiative.org/wp-content/uploads/2021/01/C19-Vaccine-Safety-AESI-Background-Rate-Protocol-2020.pdf

[43] CMS, Standard Analytical Files (Medicare Claims) – LDS, https://www.cms.gov/Research-Statistics-Data-and-Systems/Files-for-Order/LimitedDataSets/StandardAnalyticalFiles

[44] As one example of the capabilities of this system, FDA, CMS, and CDC evaluated the risk of Guillain-Barré syndrome (GBS) following influenza vaccination after CDC's Vaccine Safety Datalink, identified safety signals suggesting an increased risk of GBS following high-dose influenza vaccinations and Shingrix vaccinations during the 2018-2019 influenza season. CBER, CDC, and CMS formed working groups in February 2019 to refine these safety signals in the CMS data.

During the current pandemic, FDA, CMS, and CDC have already used the Medicare data to publish a study showing that frailty, comorbidities, and race/ethnicity were strong risk factors of COVID-19 hospitalization and death among the U.S. elderly.[45]

In summary, in collaboration and coordination with several different partners, FDA has assembled passive surveillance systems – including VAERS – and active surveillance systems that can detect and refine safety findings with the Authorized COVID-19 Vaccines in a relatively rapid manner. These systems can also potentially be leveraged to assess safety in specific subpopulations and to assess vaccine effectiveness.

Petitioner points to a CDC webpage on COVID-19 vaccines that discusses 4,863 reports to VAERS of death after COVID-19 vaccination that describes the monitoring that is conducted in connection with such reports.[46] Petitioner suggests that this is inadequate because of an FDA response to a question posed by one of the CP signatories on the proportion of VAERS death reports for which FDA/CDC staff had reached out to families to collect follow-up information. In that response, FDA stated that "the VAERS system is not designed to determine causality of adverse events" and thus "there is not a mechanism to follow-up with families for additional details."[47] However, there are indeed procedures in place to conduct continuous monitoring of VAERS data, including deaths (though the procedures do not involve following up *with families*). When FDA and CDC receive reports of deaths in VAERS, there is a mechanism for requesting and evaluating other types of follow-up information, including associated health records, such as hospital discharge summaries, and medical and laboratory results, death certificates, and autopsy reports.[48]

5. Petitioner's Request to Include Gene Therapy Experts on the Vaccines and Related Biological Products Advisory Committee (VRBPAC)

Petitioner requests that FDA ensure the inclusion of gene therapy experts on the VRBPAC because "there is a need to consider safety with the informed perspectives of those with expertise in gene therapies." CP at 9-10. In support of this request, Petitioner states that the vaccines produced by several manufacturers are gene based and that "[t]heir mechanism of action differs substantially from all other vaccines that have been used on populations globally, as these novel

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[45] Hector S Izurieta, David J Graham, Yixin Jiao, Mao Hu, Yun Lu, Yue Wu, Yoganand Chillarige, Michael Wernecke, Mikhail Menis, Douglas Pratt, Jeffrey Kelman, Richard Forshee, Natural History of Coronavirus Disease 2019: Risk Factors for Hospitalizations and Deaths Among >26 Million US Medicare Beneficiaries, *The Journal of Infectious Diseases*, 223: 6: 945–956 (2021), https://doi.org/10.1093/infdis/jiaa767 https://academic.oup.com/jid/article/223/6/945/6039057

[46] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html.

[47] Petitioner refers to a Letter to the Editor authored by one of the CP signatories that includes questions the signatory posed to FDA, and FDA's responses. See https://www.bmj.com/content/372/bmj.n149/rr-25.

[48] See Shimabukuro et al., Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/ (stating that "For reports classified as serious, the VAERS contractor requests associated health records, including hospital discharge summaries, medical and laboratory results, and death certificates and autopsy reports for deaths. Additional MedDRA terms might be added based on information obtained through follow-up. Also, for serious reports where the patient has not recovered from the adverse event by the time the report was filed or recovery status was unknown, a follow-up letter is sent to the reporter at one year requesting information on recovery status if that information is still not known").

vaccines work on the premise of gene delivery, and may therefore be considered a type of gene therapy." CP at 9.

The VRBPAC's members are selected "among authorities knowledgeable in the fields of immunology, molecular biology, rDNA, virology; bacteriology, epidemiology or biostatistics, vaccine policy, vaccine safety science, federal immunization activities, vaccine development including translational and clinical evaluation programs, allergy, preventive medicine, infectious diseases, pediatrics, microbiology, and biochemistry."[49] Additionally, an advisory committee may consult with experts.[50] FDA may also add temporary voting members to the VRBPAC, for example to provide relevant expertise.[51] The VRBPAC's role is to advise FDA. The VRBPAC does not make regulatory decisions.

The premise of the CP is that certain actions need to be taken "before serious consideration is given to granting a BLA of any COVID-19 vaccine." CP at 1. But it is FDA, not VRBPAC, that is authorized to determine whether to approve a BLA. Indeed, the Public Health Service Act confers this authority to the Secretary of the Department of Health and Human Services, and this authority has been delegated to the Commissioner of FDA. Because FDA is authorized to approve a BLA, we do not agree that the composition of an advisory committee is determinative of whether to approve or seriously consider approving a BLA. Accordingly, we deny your request.

6. Petitioner's Request that FDA Ensure That Experts Within FDA and Amongst VRBPAC Have No Financial or Research Relationships With Any Vaccine Manufacturer's Within 36 Months

Petitioner requests that FDA "[e]nsure that the analysis of data and decisions regarding any COVID-19 vaccine BLA application are informed by experts with no financial or research relationships[52] with any vaccine manufacturers within the last 36 months, both within FDA and amongst the composition of the VRBPAC."[53] CP at 10. In support of this request, Petitioner states disclosure and transparency would demonstrate the independence of FDA decision making and that an evaluation of data by "competent individuals with independence from vaccine manufacturers" would be in the public interest.[54] CP at 10.

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[49] See FDA's Website on Vaccines and Related Biological Products Advisory Committee, https://www.fda.gov/advisory-committees/blood-vaccines-and-other-biologics/vaccines-and-related-biological-products-advisory-committee.

[50] 21 CFR § 14.31.

[51] See https://www.fda.gov/advisory-committees/vaccines-and-related-biological-products-advisory-committee/charter-vaccines-and-related-biological-products-advisory-committee.

[52] You do not describe what you mean for there to be a conflict related to "research relationships." You refer only to disclosure requirements established by the International Committee of Medical Journal Editors (ICMJE) (presumably that organization's document related to providing readers of manuscripts with information about interests that could influence how they receive scientific work), but an online form we found for ICMJE does not use or define the term "research relationship." See https://cdn-links.lww.com/permalink/jbjs/d/jbjs_2017_03_30_tashjian_e15_sdc1.pdf. That form does describe financial conflicts of interests, see id., and given the CP's statement that decisions should be made by individuals with "independence" we assume you refer to financial or employment-type conflicts.

[53] CP at 10.

[54] CP at 10.

FDA acknowledges the value in maintaining a positive public perception of how FDA conducts its activities and ensuring that the decisions FDA employees make, and actions they take, neither are, nor appear to be, tainted by any conflict of interest. Ethical requirements for both advisory committee and staff are described in statute and regulation.[55]

FDA has addressed the evaluation of financial interests by special Government employees (SGEs) and FDA employees in the 2014 Guidance for the Public, FDA Advisory Committee Members, and FDA Staff: Public Availability of Advisory Committee Members' Financial Interest Information and Waivers[56] (Financial Issues Guidance) and has addressed the evaluation of appearance issues in the 2016 draft Guidance for the Public, FDA Advisory Committee Members, and FDA Staff: Procedures for Evaluating Appearance Issues and Granting Authorizations for Participation in FDA Advisory Committees (Appearance Issues Draft Guidance).[57] The 2016 draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. As described in the Appearance Issues Draft Guidance, "[t]o protect the credibility and integrity of advisory committee advice, FDA screens advisory committee members carefully for two categories of potentially disqualifying interests or relationships: (1) current financial interests that may create a recusal obligation under Federal conflict of interest laws; and (2) other interests and relationships that do not create a recusal obligation under Federal conflict of interest laws but that may create the appearance that a member lacks impartiality, known as 'appearance issues.'" The Appearance Issues Guidance explicitly contemplates that a Research Relationship might raise an appearance issue.[58]

FDA employees also are subject to strict ethical requirements.[59] FDA employees, as well as their spouses and minor children, are prohibited from holding financial interests, like stock, in certain businesses regulated by FDA. This includes many companies working in the drug, biologic, medical device, food, and tobacco industries, among others.[60] In addition, certain restrictions apply to FDA employees working on particular matters involving parties with whom the employee has served as officer, director, trustee, general partner, agent, attorney, consultant, contractor or employee.[61]

Although both the VRBPAC members and FDA employees are subject to ethical requirements, the requirements do not involve a 36-month prohibition. For example, FDA is authorized by statute to grant waivers to allow individuals with potentially conflicting financial interests to participate in meetings where it concludes, after close scrutiny, that certain criteria are met.[62] In addition, the restrictions that apply to FDA employees working on particular matters involving parties with whom the employee has served as officer, director, trustee, general partner, agent,

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[55] See, e.g., 18 U.S.C. § 208; See also the description of Ethics Laws and Regulations on FDA's website, available at: https://www.fda.gov/about-fda/ethics/ethics-laws-and-regulations

[56] https://www.fda.gov/media/83188/download. "Most FDA advisory committee members are appointed as SGEs." Financial Issues Guidance at 3.

[57] https://www.fda.gov/media/98852/download.

[58] See Appearance Issues Draft Guidance at 14-15.

[59] For a summary of relevant requirements, see the description of Ethics Laws and Regulations on FDA's website https://www.fda.gov/about-fda/ethics/ethics-laws-and-regulations.

[60] See Prohibited Financial Interests for FDA Employees, https://www.fda.gov/about-fda/ethics/prohibited-financial-interests-fda-employees.

[61] 5 CFR § 2635.502.##

[62] See 18 U.S.C. § 208(b)(1) and (b)(3).

attorney, consultant, contractor or employee apply when the employee has served *within the last year*--but not longer.

In evaluating your request, we are guided by these laws and regulations, which do not contain a 36-month prohibition. We also note that you have not demonstrated that any FDA employees or members of the VRBPAC have been improperly involved in the agency's review of COVID-19 vaccines. We are also guided by our consideration of one of the purposes served by an FDA advisory committee, which is that it permits the agency access to a range of perspectives from experts with the most current knowledge. We believe that applying our existing standards for conflict of interest will address the perception concern that the CP articulates, while appropriately balancing the agency's need for current outside expertise. Accordingly, we deny your request.

7. Petitioner's Request to Revise the 2020 Guidance to Require 2 Years of Follow-Up

Petitioner requests that FDA "[c]onfirm, in revised Guidance, that the FDA expects a minimum of 2 years of follow-up of participants enrolled in pivotal clinical trials, even if trials are unblinded and lack a placebo control." CP at 4. You state that "two year follow-up from trials allows the detection of commonly experienced longer-term adverse effects that may not manifest until many months following vaccination" and would add to the data collection in clinical trials in certain ways that you identify. CP at 4.

FDA's June 2020 Guidance describes FDA's expectations for follow-up of participants enrolled in clinical trials.[63] FDA does not at this time see a need to revise its guidance documents, because FDA may communicate to individual sponsors whether there is a need to support a BLA with a particular duration of follow-up for a clinical trial. While guidance documents allow the agency to articulate its interpretation of or policy on a regulatory matter (21 CFR § 10.115(b)), there are also times where FDA's advice would be specific to an individual manufacturer.

In addition, we note that there are many reasons why it may be appropriate to license some vaccines based on follow-up of participants for less than two years. For example, if a clinical trial enrolls subjects rapidly and the primary endpoint is the incidence of a disease such as COVID-19 which occurs frequently, cases may accumulate quickly and may allow FDA to assess the benefit-risk profile of the vaccine based on a shorter clinical trial duration and participant follow-up. By contrast, if a clinical trial enrolls subjects more slowly and assesses a disease with lower incidence, more time may be needed to accumulate a database that allows statistically meaningful comparisons to be drawn between the vaccine and control groups. FDA's benefit-risk analysis may reasonably take into account the historical experience with vaccines, and the fact that most adverse events that are plausibly linked to vaccination occur within two months of vaccination.[64] Furthermore, vaccine trials involve different types of endpoints, with some trials focusing on immunogenicity endpoints and some focusing on disease endpoints. All of these features impact the type and duration of data needed to evaluate the benefits and risks of a vaccine.

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[63] See, e.g., June 2020 Guidance at 12.

[64] Table VI. National Vaccine Injury Compensation Program. Rockville, MD: Health Resources and Services Administration, 2017 (https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/vaccine-injury-table.pdf. opens in new tab).

For all of these reasons, we deny Petitioner's request.

8. **Petitioner's Request that FDA Revise its Guidance Document to Address Safety Data from Individuals Receiving more than 2 Doses**

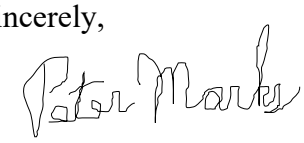
Petitioner states that FDA should "[c]larify in revised Guidance that safety data from individuals receiving more than 2 vaccine doses must be submitted by vaccine manufacturers." CP at 9. Petitioner states that the safety profile of multiple doses must be considered. CP at 9.

FDA does not at this time see a need to revise its guidance documents, because FDA may communicate to individual sponsors whether there is a need to provide the agency with data to support the possible use of more than 2 vaccine doses. While guidance documents allow the agency to articulate its interpretation of or policy on a regulatory matter (21 CFR § 10.115(b)), there are also times where FDA's advice would be specific to an individual manufacturer. Accordingly, we deny Petitioner's request.

a. Conclusion

FDA has considered Petitioner's requests. For the reasons given in this letter, FDA denies the requests in Petitioner's citizen petition. Therefore, we deny the CP in its entirety.

Sincerely,



Peter Marks, MD, PhD
Director
Center for Biologics Evaluation and Research

cc: Dockets Management Staff

Appendix I: Aspects of Vaccine Development and Process for Licensure

A. Vaccines are Biologics and Drugs

Vaccines are both biological products under the Public Health Service Act (PHS Act) (42 U.S.C. § 262) and drugs under the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. § 321). The PHS Act defines a "biological product" as including a "vaccine…or analogous product…applicable to the prevention, treatment, or cure of a disease or condition of human beings." 42 U.S.C. § 262(i)(1). The FD&C Act defines drug to include "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man." 21 U.S.C. § 321(g)(1)(B).

Under the PHS Act, a biological product may not be introduced or delivered for introduction into interstate commerce unless a biologics license is in effect for the product. 42 U.S.C. § 262(a)(1)(A).

B. Clinical Investigations of Vaccines

Before a vaccine is licensed (approved) by FDA and can be used by the public, FDA requires that it undergo a rigorous and extensive development program that includes laboratory research, animal studies, and human clinical studies to determine the vaccine's safety and effectiveness.

The PHS Act and the FD&C Act provide FDA with the authority to promulgate regulations that provide a pathway for the study of unapproved new drugs and biologics. 42 U.S.C. § 262(a)(2)(A) and 21 U.S.C. § 355(i). The regulations on clinical investigations require the submission of an Investigational New Drug application (IND), which describes the protocol, and, among other things, assures the safety and rights of human subjects. These regulations are set out at 21 CFR Part 312. See 21 CFR § 312.2 (explaining that the IND regulations apply to clinical investigations of both drugs and biologics).

The regulations provide that, once an IND is in effect, the sponsor may conduct a clinical investigation of the product, with the investigation generally being divided into three phases. With respect to vaccines, Phase 1 studies typically enroll fewer than 100 participants and are designed to look for very common side effects and preliminary evidence of an immune response to the candidate vaccine. Phase 2 studies may include up to several hundred individuals and are designed to provide information regarding the incidence of common short-term side effects, such as redness and swelling at the injection site or fever, and to further describe the immune response to the investigational vaccine. If an investigational new vaccine progresses past Phase 1 and Phase 2 studies, it may progress to Phase 3 studies. For Phase 3 studies, the sample size is often determined by the number of subjects required to establish the effectiveness of the new vaccine, which may be in the thousands or tens of thousands of subjects. Phase 3 studies are usually of sufficient size to detect less common adverse events.

If product development is successful and the clinical data are supportive of the proposed indication, the completion of all three phases of clinical development can be followed by submission of a Biologics License Application (BLA) pursuant to the PHS Act (42 U.S.C. § 262(a)), as specified in 21 CFR § 601.2.

C. Biologics License Applications

A BLA must include data demonstrating that the product is safe, pure, and potent and that the facility in which the product is manufactured "meets standards designed to assure that the biological product continues to be safe, pure, and potent." 42 U.S.C. § 262(a)(2)(C)(i). FDA does not consider an application to be filed until FDA determines that all pertinent information and data have been received. 21 CFR § 601.2. FDA's filing of an application indicates that the application is complete and ready for review but is not an approval of the application.

Under § 601.2(a), FDA may approve a manufacturer's application for a biologics license only after the manufacturer submits an application accompanied by, among other things, "data derived from nonclinical laboratory and clinical studies which demonstrate that the manufactured product meets prescribed requirements of safety, purity, and potency." The BLA must provide the multidisciplinary FDA reviewer team (medical officers, microbiologists, chemists, biostatisticians, etc.) with the Chemistry, Manufacturing, and Controls (CMC)[65] and clinical information necessary to make a benefit-risk assessment, and to determine whether "the establishment(s) and the product meet the applicable requirements established in [FDA's regulations]." 21 CFR § 601.4(a).

FDA generally conducts a pre-license inspection of the proposed manufacturing facility, during which production of the vaccine is examined in detail. 42 U.S.C. § 262(c). In addition, FDA carefully reviews information on the manufacturing process of new vaccines, including the results of testing performed on individual vaccine lots.

FDA scientists and physicians evaluate all the information contained in a BLA, including the safety and effectiveness data and the manufacturing information, to determine whether the application meets the statutory and regulatory requirements. FDA may also convene a meeting of its advisory committee to seek input from outside, independent, technical experts from various scientific and public health disciplines that provide input on scientific data and its public health significance.

As part of FDA's evaluation of a vaccine as a whole, FDA takes all of a vaccine's ingredients into account (including preservatives and adjuvants). FDA licenses a vaccine only after the Agency has determined that the vaccine is safe and effective for its intended use, in that its benefits outweigh its potential risks.

[65] Also referred to as Pharmaceutical Quality/CMC.

Appendix II: Aspects of Vaccine Postmarketing Safety Monitoring

Post-marketing surveillance of vaccine safety is crucial to detect any rare, serious, or unexpected adverse events, as well as to monitor vaccine lots. Manufacturers often conduct post-marketing observational studies. However, FDA also uses multiple tools and databases to evaluate the safety of vaccines after they have been licensed and used in the general population.

The Vaccine Adverse Event Reporting System (VAERS) is a national passive surveillance vaccine safety database that receives unconfirmed reports of possible adverse events following the use of a vaccine licensed in the United States. VAERS is co-administered by FDA and the Centers for Disease Control and Prevention (CDC). Anyone can make a report to VAERS, including vaccine manufacturers, private practitioners, State and local public health clinics, vaccine recipients, and their parents or caregivers. Surveillance programs like VAERS perform a critical function by generating signals of potential problems that may warrant further investigation.

It is often difficult to determine with certainty if a vaccine caused an adverse event reported to VAERS. Many events that occur after vaccination can happen by chance alone. Some adverse events are so rare that their association with a vaccine is difficult to evaluate. In addition, VAERS often receives reports where there is no clear clinical diagnosis. FDA draws upon multiple sources of data and medical and scientific expertise to assess the potential strength of association between a vaccine and a possible adverse event.

Monitoring and analysis of VAERS reports typically includes daily in-depth medical review of all serious reports, statistical data mining techniques, and epidemiological analysis. We look for patterns and similarities in the onset timing and clinical description. We review published literature to understand possible biologic hypotheses that could plausibly link the reported adverse event to the vaccine. We review the pre-licensure data and any other post-marketing studies that have been conducted. We also consider "background rate," meaning the rate at which a type of adverse event occurs in the unvaccinated general population. When necessary, we discuss the potential adverse event with our federal and international safety surveillance partners. We also carefully evaluate unusual or unexpected reports, as well as reports of "positive re-challenges" (adverse events that occur in the same patient after each dose received). When there is sufficient evidence for a potential safety concern we may proceed to conduct large studies, and we may coordinate with our federal, academic and private partners to further assess the potential risk after vaccination. In addition, when potential safety issues arise, they are often presented to various U.S. government advisory committees, including the Vaccines and Related Biological Products Advisory Committee, the Advisory Committee on Immunization Practices, the Vaccines Advisory Committee, and the Advisory Committee on Childhood Vaccines, and are often discussed with experts from other countries and from the World Health Organization (WHO). Federal agencies that assist in population-based vaccines safety studies include the Centers for Medicaid and Medicare (CMS), the Department of Defense (DoD), and the Indian Health Services (IHS). In addition, we generally communicate and work with international regulatory authorities and international partners to conduct studies in vaccine safety.

The Vaccine Safety Datalink (VSD) project has actively monitored vaccine safety in more than 9.1 million people nationwide, over 3% of the US population. The VSD can monitor vaccine safety with near real-time surveillance systems, which is particularly important for new vaccines. If there is a vaccine safety signal in the VSD, chart reviews and case series analyses are done

when assessing the possible association between a vaccine and an adverse event. If needed, VSD is able to use its large health care database to further evaluate specific vaccine safety concerns.

The Clinical Immunization Safety Assessment (CISA) is a national network of six medical research centers with expertise conducting clinical research related to vaccine safety. The goals of CISA are: to study the pathophysiologic basis of adverse events following immunization using hypothesis-driven protocols; to study risk factors associated with developing an adverse event following immunization using hypothesis-driven protocols, including genetic host-risk factors; to provide clinicians with evidence-based guidelines when evaluating adverse events following immunization; to provide clinicians with evidence-based vaccination or revaccination guidelines; and to serve as a regional referral center to address complex vaccine safety inquiries. Advances in genetics and immunology continue to help us further assess the safety of vaccines, and FDA has established a genomics evaluation team for vaccine safety.

Finally, the Sentinel Initiative is a national electronic system that will continue to improve FDA's ability to track the safety of medical products, including vaccines. Launched in May 2008 by FDA, the Sentinel System will enable FDA to actively query diverse automated healthcare data holders – like electronic health record systems, administrative and insurance claims databases, and registries – to evaluate possible safety issues quickly and securely. The Sentinel Initiative will cover 100 million people in the U.S. It is also anticipated that Sentinel will facilitate the development of active surveillance methodologies related to signal detection, strengthening, and validation.

Exhibit 9

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
CINCINNATI DIVISION

HUNTER DOSTER, *et al.*,	)	
Plaintiffs,	)	
v.	)	No. 1:22-cv-00084
FRANK KENDALL, et al.,	)	
Defendants.	)	

DECLARATION OF COLONEL TONYA RANS

I, Colonel Tonya Rans, hereby state and declare as follows:

1. I am currently employed by the U.S. Air Force as the Chief, Immunization Healthcare Division, Defense Health Agency – Public Health Directorate, located in Falls Church, Virginia. I have held the position since June 2017. I am a medical doctor and have been board certified in Allergy/Immunology since 2008 and was a board certified Pediatrician from 2001-2015.

2. In my current role, my responsibilities include directing a responsive, evidence-based, patient-centered organization promoting optimal immunization healthcare for all DoD beneficiaries and those authorized to receive immunization from DoD. This includes assisting in policy development, providing implementation guidance and education, and engaging in clinical studies and research through clinical collaboration. The Defense Health Agency-Immunization Healthcare Division (DHA-IHD) routinely engages with the medical representatives from the military departments, U.S. Coast Guard, Joint Staff, Combatant Commands, and others to develop

standardized immunization implementation guidance in accordance with published policy for consistency across DoD where possible.

3. I am aware of the allegations set forth in the pleadings filed in this matter. This declaration is based on my personal knowledge, as well as information made available to me during the routine execution of my official duties.

Coronavirus Disease 2019 (COVID-19)

4. As part of my official duties, I served as a member of the COVID-19 Vaccine Distribution Operational Planning Team (OPT), which was directed to develop and implement DoD's COVID-19 Vaccine Distribution plan. The Coronavirus Task Force (CVTF) provided overarching guidance to the OPT. The OPT provided routine and ad hoc updates on COVID-19 vaccine deliveries, administration, and adverse events to the CVTF.

5. The virus that causes COVID-19 disease is SARS-CoV-2, a ribonucleic acid (RNA) virus from the Coronavirus family. Like any RNA virus, the SARS-CoV-2 virus mutates and evolves constantly and regularly as it infects and replicates in host cells. Mutations that are beneficial to the virus (i.e., make the virus more easily spread between hosts, evade the immune system) are integrated into the viral genome, thereby increasing "survival" and replication opportunity. This has been seen with the SARS-CoV-2 "Delta" variant, which is twice as contagious as previous variants.[1] However, not all mutations are beneficial to the virus – some can result in virus death and therefore do not infect the host. This is part of the normal biology cycle of all viruses.

[1] https://www.yalemedicine.org/news/5-things-to-know-delta-variant-covid, last accessedMarch 4, 2022.

6. The latest reports from the U.S. Centers for Disease Control and Prevention (CDC) indicate that the SARS-CoV-2 virus spreads when an infected person breathes out droplets and very small particles that contain the virus.[2] These droplets and particles can be inhaled by other people or land on their eyes, noses, or mouth. In some circumstances, viral particles may contaminate surfaces. People who are closer than 6 feet from the infected person are most likely to get infected, especially in areas where there is poor ventilation.

7. COVID-19 disease can cause acute symptoms such as fever/chills, cough, shortness of breath, fatigue, muscle aches, headache, nausea, vomiting, diarrhea, loss of sense of smell or taste and/or sore throat. Symptoms appear 2-14 days (usually within 4-5 days) after viral exposure.[3] The infection can affect people in different ways: from asymptomatic, to limited and mild (for 2-3 days) to more severe (such as trouble breathing, chest pain, inability to think straight and inability to stay awake). Even with the availability of aggressive medical management and ventilator support in an intensive care setting for those with severe symptoms, hundreds of thousands with COVID-19 disease have died. As of March 2, 2022, CDC reports that over 78 million individuals in the U.S. have been diagnosed with COVID-19 disease, over 4.5 million have been hospitalized, and over 952,000 have died (approximately 1 in 500 in the total U.S. population of 330 million).[4] Per the CDC, the elderly and those with underlying medical history of cardiovascular disease, diabetes, chronic respiratory disease, smoking, being overweight or obese,

[2] https://www.cdc.gov/coronavirus/2019-ncov/faq.html, last accessed March 4, 2022.

[3] https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html, last accessed March 4, 2022.

[4] https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html, last accessed March 4, 2022.

pregnancy, immunocompromising conditions, or cancer are more likely to develop serious illness.[5] However, it is a misguided belief that those who are otherwise young and healthy could not develop severe, or even fatal, disease. During the acute infectious stage, the virus causes inflammatory cell death, resulting in the release of pro-inflammatory cytokines (proteins which are important in cell signaling). Pro-inflammatory cytokines can cause inflammatory cell death within multiple organs. Cell death releases cellular and viral fragments, which results in production and release of more inflammatory cytokines.[6] Disease progression can be curtailed by controlling the inflammatory process through immune system clearing of the virus. However, as depicted in the figure below, if the immune system is overwhelmed, either by viral immune evasive mechanisms or by an impaired host response, the pro-inflammatory cytokine process may continue unabated, causing increasingly severe disease such as acute respiratory distress syndrome and cytokine storm. Recognition of the viral and hyperinflammatory phases informs treatment strategies for those with COVID-19 disease, including, but not limited to anti-SARS-CoV-2 monoclonal antibodies, and effective pooled antibodies (convalescent plasma) for prevention/mitigation and antivirals for treatment in the viral phase, and targeted immunobiologics and systemic steroids for those in the hyper-inflammatory phase.[7]

[5] https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html, last accessed March 4, 2022.

[6] Bordallo B, et al. Severe COVID-19: What Have We Learned With the Immunopathogenesis? *Adv Rheumatol* (2020) 60(1):50. doi: 10.1186/s42358-020-00151-7.

[7] https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/, last accessed March 5, 2022.

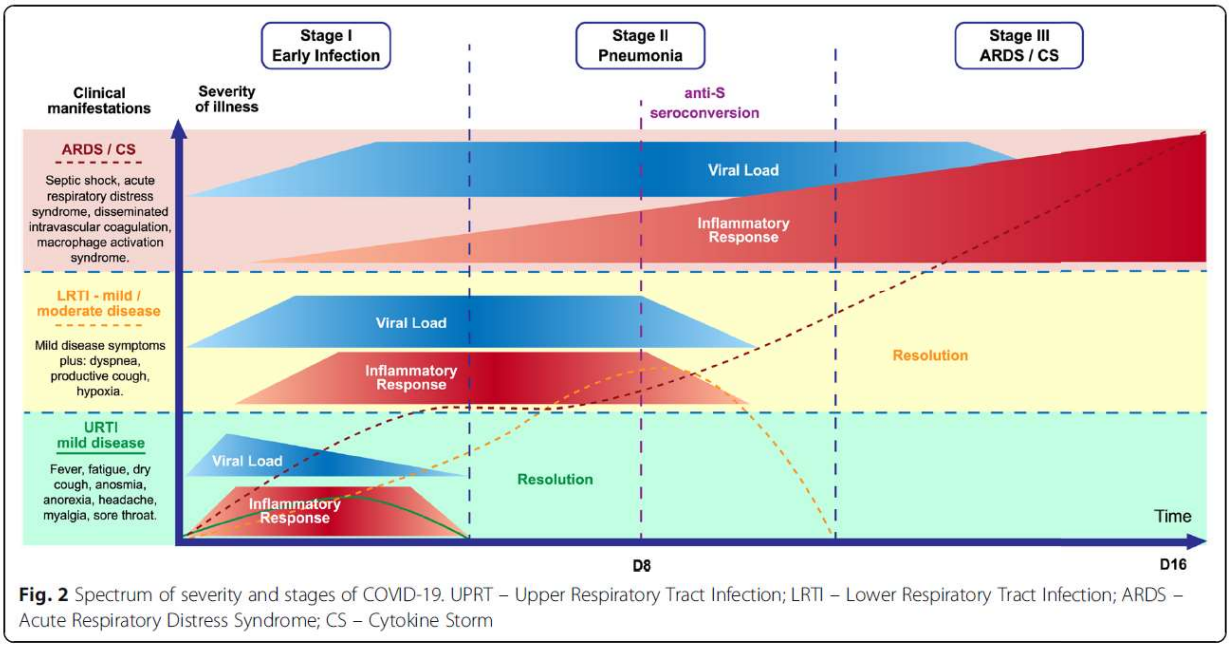


Fig. 2 Spectrum of severity and stages of COVID-19. UPRT – Upper Respiratory Tract Infection; LRTI – Lower Respiratory Tract Infection; ARDS – Acute Respiratory Distress Syndrome; CS – Cytokine Storm

8. Treatment for COVID-19 disease, even in the outpatient environment, is not without risks. The strongest recommendation for pre-exposure to COVID-19 disease remains vaccination, with highest level of evidence demonstrated through robust randomized control trials.[8] Although anti-SARS-CoV-2 monoclonal antibody combinations may be prescribed in the outpatient setting, the indication and level of evidence in use differs when considering pre-exposure prophylaxis, post-exposure prophylaxis, or treatment. Additionally, effectiveness of monoclonal antibodies is impacted by the variant in the infected person. Currently, few treatments are effective against the omicron variant, resulting in inadequate supply to meet demand nationwide. What this means to DoD is that even if otherwise healthy service members develop COVID-19 disease, an individual's immune system response may not be able to adequately manage the virus, resulting in a hyperinflammatory state, with variable outcomes, depending on the individual's genetics, medical history, and immune response. Just as it is acknowledged that

[8] https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management// last accessed March 5, 2022.

there have been adverse events following COVID-19 vaccine receipt, it should also be understood that there are risks to treatment of COVID-19 disease, even in those who can be managed in the outpatient setting. A non-exhaustive list includes cardiovascular events, liver toxicity, and drug interactions. Further, some treatments must be administered shortly after diagnosis – within a matter of days – in order to be effective.[9]

9. Although most people with COVID-19 are better within weeks of illness, some people experience post-COVID-19 conditions (aka long/long-haul COVID, Postacute Sequelae of COVID-19 (PASC), long-term effects of COVID, or chronic COVID). Post-COVID-19 conditions include a wide range of new, returning, or ongoing health problems four or more weeks after infection. Those who were asymptomatic during their COVID-19 infection may still develop post-COVID-19 conditions. One systematic review assessing short and long-term rates of long-COVID in more than 250,000 COVID-19 survivors from 57 studies with an average age of 54 years demonstrated that more than 50% of these COVID-19 survivors continued to have a broad range of symptoms six months after resolution of the acute COVID-19 infection, of which the most common were functional mobility impairments, respiratory abnormalities, and mental health disorders.[10] Another study comparing outcomes in patients referred to outpatient rehabilitation clinics after COVID-19 reported poorer general, mental, and physical health and functioning compared with patients with no previous diagnosis of COVID-19 referred for cancer rehabilitation. Those referred for rehabilitation following COVID-19 were more likely to be male, younger, and

[9] https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/ last accessed March 5, 2022.

[10] Groff, et al, *JAMA Network Open*, Short-term and Long-term Rates of Postacute Sequelae of SARS-CoV-2 Infection, https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2784918.

employed.[11] A study assessing clinical patterns and recovery time from COVID-19 illness in 147 international-level Paralympic and Olympic athletes showed that 86% had symptoms lasting ≤ 28 days, whereas 14% had symptoms of longer duration. In both groups, fatigue, dry cough, and headache were the predominant symptoms.[12] A recent study, conducted within the Department of Veterans Affairs, described long-term cardiovascular outcomes of 153,760 people with COVID-19 who survived the first 30 days after infection as compared with controls[13]. They provided evidence that, beyond the first 30 days of infection, people with a history of COVID-19 exhibited "increased risks and 12-month burdens of incident cardiovascular diseases, including cerebrovascular disorders (i.e. stroke), dysrhythmias (abnormal heart rhythms), inflammatory heart disease (i.e. myocarditis, pericarditis), ischemic heart disease (decreased blood flow to the heart), heart failure, thromboembolic disease (blood clots that can break loose and occlude a blood vessel), and other cardiac disorders. For example, among those with a history of COVID-19, there was an 85% greater risk of pericarditis (HR, 1.85; 95% CI, 1.61-2.13) and a 438% greater risk of myocarditis (HR, 5.38; 95% CI, 3.80-7.59) compared to controls. The authors report that the risks were evident regardless of age, race, sex, and other cardiovascular risk factors, including obesity, hypertension (high blood pressure), diabetes, chronic kidney disease, and hyperlipidemia (high cholesterol); they were also evident in people without any cardiovascular disease before exposure

[11] Rogers-Brown JS, et al. CDC Morbidity and Mortality Weekly Report, Vol 70(27) 9 July 2021 https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7027a2-H.pdf.

[12] Hull JH, et al. Clinical patterns, recovery time and prolonged impact of COVID-19 illness in international athletes: the UK experience. *Br J Sports Med* 2021;0:1-8. Doi 10.1136/bjsports-2021-104392.

[13] Xie, Y., Xu, E., Bowe, B. *et al.* Long-term cardiovascular outcomes of COVID-19. *Nat Med* (2022). https://doi.org/10.1038/s41591-022-01689-3

to COVID-19, "providing evidence that these cardiovascular risks might manifest even in people at low risk for cardiovascular disease".

COVID-19 Impacts on the Force

10. Infectious diseases have been the single greatest threat to the health of those involved in military operations. As the standard military unit shrinks and becomes more mobile to rapidly respond to global threats, any decrease in personal or unit readiness can significantly decrease operational efficiency and result in military ineffectiveness. Similar to other viruses, SARS-CoV-2 virus can be easily transmitted to others prior to symptom development and therefore may infect significant numbers before being identified. DoD personnel, including service members, especially those in an operational setting (such as those working on ships, submarines, or engaged in the operation of aircraft and vehicles; those deployed to austere environments; or those engaged in routine field training and airborne exercises), work in environments where duties may limit the ability to strictly comply with mitigation measures such as wearing a face mask, avoiding crowded areas, maintaining physical distancing of at least 6 feet, increasing indoor ventilation, maintaining good hand hygiene, and quarantining if in close contact with a COVID-19 case. Therefore, upon exposure, these individuals may be at higher risk to be diagnosed with COVID-19 compared to those who can robustly maintain all recommended mitigation strategies. Further, although the elderly population and those with medical conditions are more likely to have severe disease, otherwise healthy Service members have developed "long-haul" COVID-19, potentially impacting their long-term ability to perform their missions. Data presented from DoD's COVID-19 registry has demonstrated that of 111,767 active duty service members who had COVID-19 disease between February 1, 2020 to August 12, 2021, 37,838 (33.9%) had diagnoses for conditions requiring a healthcare visit 30-180 days following their

illness, the most common being joint/muscle pain (15,614 or 14%) followed by chest pain/cough (7,887 or 7.1%). In comparison, only 8.3% and 1.81%, respectively, of active duty service members had a healthcare visit for those diagnoses 30-180 days after vaccination. All diagnoses associated with "Long-COVID-19 Syndrome" were found to be more common after COVID-19 disease than after COVID-19 vaccination. Some service members have unfortunately succumbed to the disease, as described further below. Service members and federal civilian employees are the military's most valuable asset; without a medically ready force and ready medical force, the military mission is at high risk of failure. Recommendations from evidence-based medicine must remain the core approach to medical readiness. These evidence-based recommendations will continue to be updated as our understanding of the disease, complications, and impact from vaccination continues to evolve.

11. Between February 2020 and January 2022, there were 350,833 new and repeat cases of COVID-19 among active duty service members (see "Table" below). The largest monthly peak in cases occurred in January 222, with 113,266 cases identified, followed by the second highest peak in January 2021 with 28,416 cases identified (see "Figure" below). The percentage of cases that were hospitalized was highest at the start of the pandemic and trended downward through January 2021. The percentage of hospitalized cases then increased from 0.9% in January 2021 to 2.1% in May 2021 and 2.0% in July 2021, and decreased to 0.2% in January 2022. However, this trend should be interpreted with caution due to data lags. In total, 31 active duty service members have died from COVID-19 as of the end of January 2022. The number of active duty service members who died from COVID-19 remained very low throughout the first year of the pandemic, with a slight increase in the numbers of deaths occurring between December 2020 and February 2021, and a greater increase occurring between August and

October 2021, coinciding with the increased spread of the Delta variant. More than one-half of the 31 deaths in active duty service members occurred between August and October 2021 (n=17). The most recently reported active duty service member death occurred in November 2021.

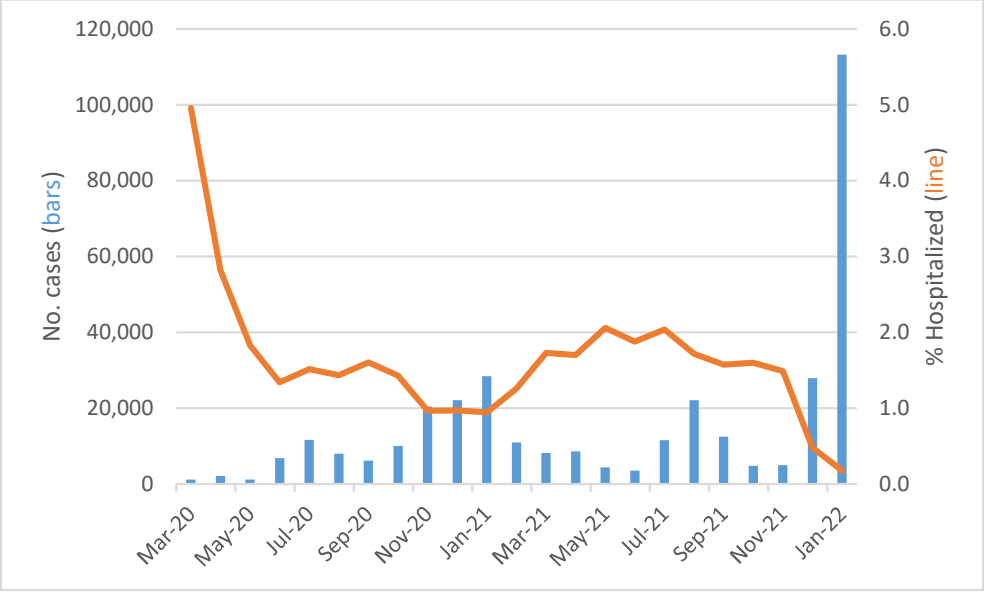
Table. COVID-19 cases, hospitalizations, and deaths among active duty service members, February 2020 - January 2022

	No. cases	No. hospitalizations	% hospitalizations	No. deaths
Feb-20	7	2	28.6	0
Mar-20	1,150	57	5.0	0
Apr-20	2,126	60	2.8	1
May-20	1,204	22	1.8	0
Jun-20	6,791	91	1.3	0
Jul-20	11,609	176	1.5	0
Aug-20	8,011	115	1.4	0
Sep-20	6,119	98	1.6	0
Oct-20	10,058	144	1.4	1
Nov-20	20,429	197	1.0	0
Dec-20	22,129	215	1.0	2
Jan-21	28,416	269	0.9	2
Feb-21	10,984	138	1.3	5
Mar-21	8,148	141	1.7	0
Apr-21	8,582	146	1.7	1
May-21	4,424	91	2.1	0
Jun-21	3,572	67	1.9	0
Jul-21	11,588	236	2.0	1

Aug-21	22,090	379	1.7	5
Sep-21	12,446	196	1.6	6
Oct-21	4,811	77	1.6	6
Nov-21	4,963	74	1.5	1
*Dec-21	27,910	134	0.5	0
*Jan-22	113,266	200	0.2	0

*Hospitalization and death data not complete due to data lags

Figure. COVID-19 cases among active duty service members and percentage of cases that were hospitalized, March 2020 – January 2022



Note: February 2020 is not shown due to the very small number of cases. Hospitalization data for December 2021-January 2022 not complete due to data lags

12. The DoD regularly updates its information concerning the number of vaccinations provided by DoD, the vaccination of the force, and health impact of those who developed COVID-19 infections.[14] As depicted below, data through March 2, 2022 demonstrated that of the 603,736

[14] https://www.defense.gov/Spotlights/Coronavirus-DOD-Response/, last accessedMarch 5, 2022.

COVID-19 cases within the DoD, 6,180 individuals were hospitalized and 679 have died, including 93 military service members (service members include Active Duty, Reserves, and National Guard personnel). In both the civilian sector and in the military, the overwhelming majority of individuals hospitalized or who died were unvaccinated or not fully vaccinated.

DOD COVID-19 CUMULATIVE TOTALS

	Cases	Hospitalized	Recovered	Deaths
Military	388,151	2,543	359,343	93
Civilian	119,302	2,340	100,535	412
Dependent	61,236	552	54,168	35
Contractor	35,047	745	30,800	139
Total	603,736	6,180	544,846	679

13. The bed capacity at DoD's military medical treatment facilities (MTFs) has generally followed local civilian hospital utilization, with some MTFs having high admission rates and a need to temporarily curtail medical services. Throughout the pandemic, the National Guard has been called on extensively to provide medical support to the civilian population. During the winter months, DoD had increasingly been deploying military doctors, nurses, paramedics and other personnel to U.S hospitals to assist in preventing the country's medical system from collapsing from demand.

Vaccine Impacts

14. Immunization is a global health and development success story, saving millions of lives across the age spectrum annually from illness, chronic conditions, and potentially death. Immunizations provide benefit at both the individual and community level. First, by stimulating an active immune response, vaccinated individuals are largely protected from the disease of

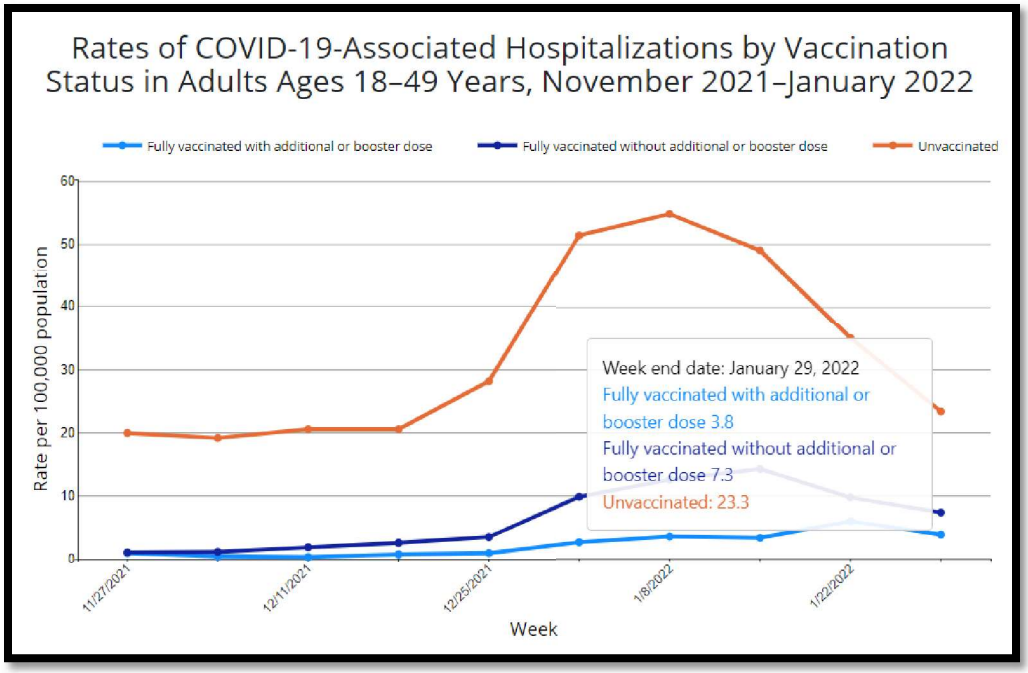
concern. Second, when a high proportion of individuals are immune (i.e., herd immunity) human-to-human transmission is disrupted, thereby protecting those who remain susceptible (i.e., those who may not be able to receive a vaccine or do not mount an adequate antibody response). Disease prevention through immunization also mitigates the need for pharmacologic treatment (antibiotics for sepsis, etc.), reducing the risk of drug-resistant pathogen development.

15. A key component of primary health care, the U.S. Food and Drug Administration (FDA) provides regulatory allowance for immunizations and has licensed vaccines for over 20 different infectious diseases. The Advisory Committee on Immunization Practices (ACIP), an advisory committee of the CDC, develops recommendations on how to use vaccines to control diseases in the United States. The military also maintains awareness, surveillance, and provides guidance to DoD personnel and beneficiaries on vaccine-preventable diseases in the global setting.

16. According to the CDC, over 553 million doses of COVID-19 vaccine have been given in the United States from December 14, 2020, through February 28, 2022.[15] Evidence consistently shows that the incidence of SARS-CoV-2-associated, hospitalizations and deaths are higher in unvaccinated than vaccinated persons. During the week ending January 29, 2022, the rate of COVID-19 associated hospitalization was 3.8 per 100,000 in those who were fully vaccinated with an additional or booster dose; 7.3 per 100,000 in those who were fully vaccinated without an additional or booster dose; and 23.3 per 100,000 in those who were unvaccinated. , 2022.[16]

[15] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/safety-of-vaccines.html, last accessed March 5, 2022.

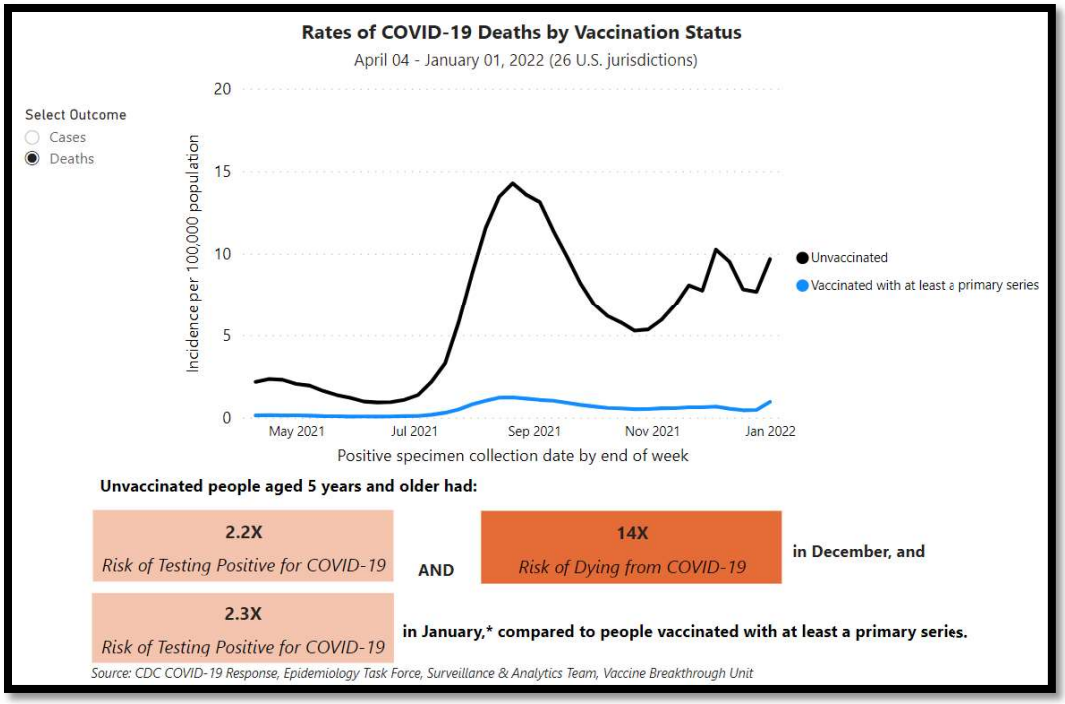
[16] https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination, last accessed March 5, 2022.

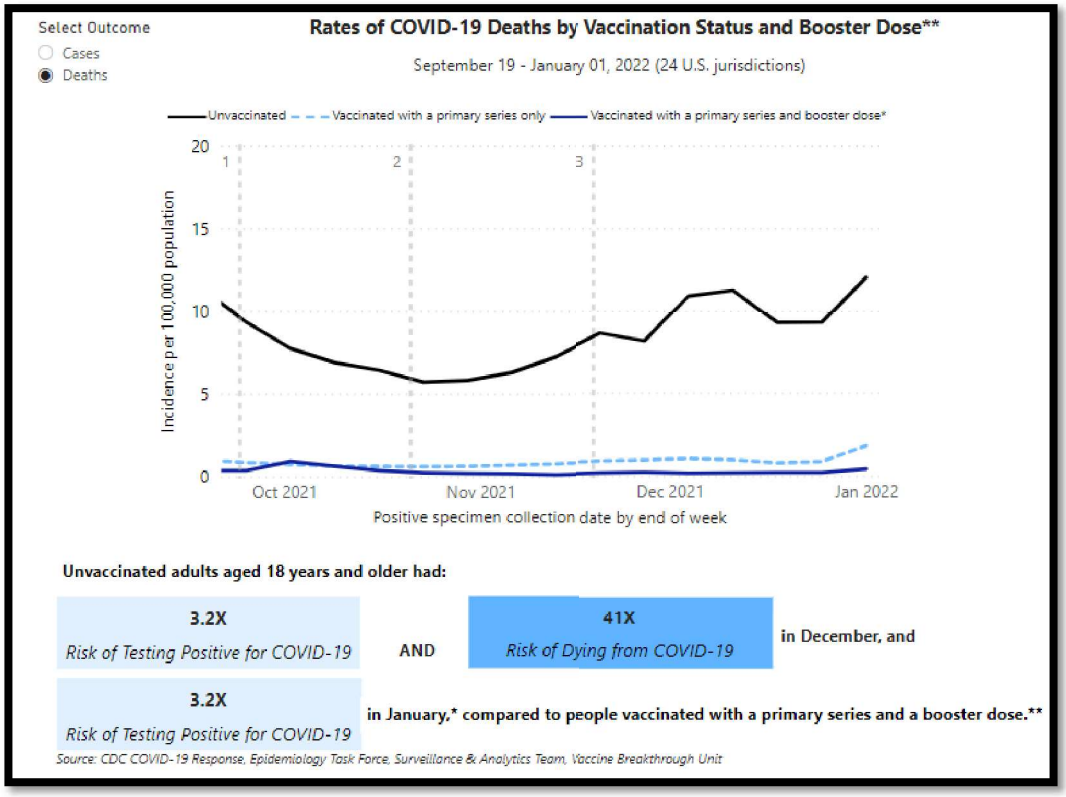


According to CDC data in December 2021, unvaccinated persons 5 years of age and older had a 2.2 times greater risk of testing positive for COVID-19 and a 14 times greater risk of dying from COVID-19 compared to fully vaccinated individuals, and unvaccinated persons 18 years of age and older had a 3.2 times greater risk of testing positive for COVID-19 and 41 times greater risk of dying from COVID-19 compared to fully vaccinated adults with a booster dose.[17] In January 2022,, unvaccinated adults aged 5 years and older had a 2.3 times greater risk of testing positive for COVID-19 compared to fully vaccinated adults and a 3.2 times greater risk of testing positive for COVID-19 compared to fully vaccinated adults with booster doses.[18]

[17] https://covid.cdc.gov/covid-data-tracker/#rates-by-vaccine-status, last accessed March 5, 2022.

[18] Id.


Rates of COVID-19 Deaths by Vaccination Status
April 04 - January 01, 2022 (26 U.S. jurisdictions)
Select Outcome
Cases
Deaths
Incidence per 100,000 population
20
15
10
5
0
May 2021
Jul 2021
Sep 2021
Nov 2021
Jan 2022
Positive specimen collection date by end of week
Unvaccinated
Vaccinated with at least a primary series
Unvaccinated people aged 5 years and older had:
2.2X
Risk of Testing Positive for COVID-19
AND
14X
Risk of Dying from COVID-19
in December, and
2.3X
Risk of Testing Positive for COVID-19
in January,* compared to people vaccinated with at least a primary series.
Source: CDC COVID-19 Response, Epidemiology Task Force, Surveillance & Analytics Team, Vaccine Breakthrough Unit


Select Outcome
Cases
Deaths
Rates of COVID-19 Deaths by Vaccination Status and Booster Dose**
September 19 - January 01, 2022 (24 U.S. jurisdictions)
Unvaccinated
Vaccinated with a primary series only
Vaccinated with a primary series and booster dose*
Incidence per 100,000 population
20
15
10
5
0
1
2
3
Oct 2021
Nov 2021
Dec 2021
Jan 2022
Positive specimen collection date by end of week
Unvaccinated adults aged 18 years and older had:
3.2X
Risk of Testing Positive for COVID-19
AND
41X
Risk of Dying from COVID-19
in December, and
3.2X
Risk of Testing Positive for COVID-19
in January,* compared to people vaccinated with a primary series and a booster dose.**
Source: CDC COVID-19 Response, Epidemiology Task Force, Surveillance & Analytics Team, Vaccine Breakthrough Unit

17. As of March 4, 2022, DoD immunization sites have administered over 7.83 million doses of COVID-19 vaccine. Adverse events temporally associated with vaccine administration are centrally captured by CDC and FDA's Vaccine Adverse Event Reporting System (VAERS) through passive surveillance, meaning that information is voluntarily reported by health care providers and the public. VAERS is not designed to determine whether a vaccine caused a health issue of concern, but it is useful for detecting unexpected patterns of adverse event reporting that might indicate a possible safety problem with a vaccine. As of February 26, 2022, a total of 8,384 unique VAERS reports (approximately 11 VAERS reports/10,000 doses administered) were submitted by DoD beneficiaries or those authorized to receive vaccine from DoD. Note that the number of VAERS reports/10,000 doses administered for DoD beneficiaries is likely to be lower, as the denominator does not take into account beneficiaries who receive vaccine in the civilian sector though DoD would still receive their VAERS report if the submitter indicated military affiliation. Additionally, individuals who had an adverse event but did not submit a VAERS would not be known and therefore would not be counted. It must be stressed that a VAERS submission to the CDC does not mean that the vaccine of concern caused or contributed to the medical issue reported.

18. The DoD has received hundreds of thousands of Pfizer-BioNTech BLA-manufactured, EUA-labeled COVID-19 vaccine doses and continues to use them.

19. Approach to immunizations within DoD are outlined in DoD Instruction 6205.02, "DoD Immunization Program" dated June 19, 2019, which states that it is DoD policy that all DoD personnel and other beneficiaries required or eligible to receive immunizations will be offered immunizations in accordance with recommendations from the CDC and its ACIP. Army Regulation 40-562, Navy Bureau of Medicine and Surgery Instruction 6230.15B, Air Force

Instruction 48-110_IP, Coast Guard Commandants Instruction M6230.4G, "Immunizations and Chemoprophylaxis for the Prevention of Infectious Diseases," October 7, 2013, further states the Military Service policy concerning immunizations follows the recommendations of the CDC, ACIP, and the prescribing information on the manufacturer's package inserts, unless there is a military-relevant reason to do otherwise. This document also describes general examples of medical exemptions, which include "evidence of immunity based on serologic tests, documented infection, or similar circumstances." Some interpret this as a diagnosis of COVID-19 disease and/or results of a COVID-19 serologic test means that a medical exemption should be granted. However, of significance is the phrase "evidence of immunity." CDC defines immunity as "protection from an infectious disease. If you are immune to a disease, you can be exposed to it without becoming infected."[19] There are two major types of testing available for COVID-19: diagnostic tests, which assess for current infection, and antibody tests, which assess for antibody production, which is indicative of past infection and (in some tests) a history of vaccination. The FDA states, "Antibody tests should not be used to diagnose a current SARS-CoV-2 infection or COVID-19 and, at this time, should also not be used to check for immunity. More research is needed to determine what, if anything, antibody tests can tell us about a person's immunity."[20] As described below, lab tests for serology also state that it is unclear at this time if a positive antibody result infers immunity against future COVID-19 infection. Therefore, given the scientific evidence available, a medical exemption based on the history of COVID-19 disease or serology

[19] https://www.cdc.gov/healthyschools/bam/diseases/vaccine-basics.htm, accessed February 16, 2022.

[20] https://www.fda.gov/consumers/consumer-updates/coronavirus-disease-2019-testing-basics, accessed March 6, 2022.

results does not meet "evidence of immunity". The presence of antibodies is not the same thing as being immune.

20. The CDC states that "COVID-19 vaccination is recommended for everyone aged 5 years and older, regardless of a history of symptomatic or asymptomatic SARS-CoV-2 infection. This includes people with prolonged post-COVID-19 symptoms and applies to primary series doses and booster doses. This recommendation also applies to people who experience SARS-CoV-2 infection before or after receiving any COVID-19 dose… Current evidence demonstrates a robust immune response to vaccination after infection, but information is lacking about whether and how the amount of time since infection affects the immune response to vaccination. Growing epidemiologic evidence from adults and adolescents indicates that vaccination following infection further increases protection from subsequent infection, including in the setting of increased circulation of more infectious variants. Viral testing to assess for acute SARS-CoV-2 infection or serologic testing to assess for prior infection is not recommended for the purpose of vaccine decision-making"[21].

21. Further, CDC states "antibody testing is not currently recommended to assess the need for vaccination in an unvaccinated person or to assess immunity to SARS-CoV-2 following COVID-19 vaccination. If antibody testing was done, vaccination with the primary series, an additional dose, or a booster dose should be completed as recommended regardless of the antibody test result. SARS-CoV-2 antibody tests currently authorized under an Emergency Use Authorization have variable performance characteristics and limitations. Furthermore, serologic

[21] https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html, accessed March 6, 2022

correlates of protection have not been established and antibody testing does not evaluate the cellular immune response"[22]

22. Although natural infection for some diseases, in some cases, can result in long-standing immunity (e.g., measles), there is risk of untoward outcomes from the disease itself, which can be chronic or even fatal. Examples include Pneumonia or invasive group B Strep from chickenpox, meningitis or epiglottitis from *Haemophilis influenza* type B, birth defects from rubella, liver cancer from Hepatitis B, and death from measles.

23. Examples of natural infections that do not mount long-standing immunity include, in addition to COVID-19, Influenza, Respiratory Syncytial Virus, Malaria, Whooping cough, and rotavirus. In other words, re-infection is possible. Multiple serotypes of a pathogen like influenza, pneumococcus, and possibly with the COVID-19 variants, also make determination of a protective serologic level more difficult, especially to say there is lifelong immunity.

24. "Herd immunity" is an epidemiologic concept that explains how a community may be protected from an infectious disease that is human-to-human transmitted.[23]-[24] Herd immunity can be achieved through vaccination or through natural infection, if enough individuals 1) survive the disease and 2) mount a life-long immune response. Safe and effective vaccines are unequivocally considered the safer approach to a vaccine-preventable disease as compared to the

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[22] https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html, accessed March 6, 2022.

[23] Desai AN, Majumder MS. What Is Herd Immunity? *JAMA.* 2020;324(20):2113. doi:10.1001/jama.2020.20895

[24] McDermott A. Core Concept: Herd immunity is an important-and often misunderstood-public health phenomenon. *Proc Natl Acad Sci U S A*. 2021;118(21):e2107692118. doi:10.1073/pnas.2107692118

unpredictable response that an individual may have to exposure to disease, as described above. When a large proportion of a community is immune, vulnerable members of the community are indirectly protected because their chance of infection exposure is very low. Herd immunity does not eliminate risk, but the phenomenon means that population risk is greatly reduced. Herd immunity is only possible when humans are the only source of infection transmission, when immunity can be clearly established to prevent lifelong infection and transmission, and when an adequate proportion of the population can safely develop immunity to protect all others. Measles (rubeola virus infection) is a classic example of the successful application of the concept of herd immunity. It is important to recognize that there is no disease where a vaccination program would cease once a certain level of immunity is reached, unless the disease is considered eradicated (i.e. smallpox in humans). Children continue to receive routine immunizations for diseases that we have not seen in this country for many years (i.e., polio) or rarely see (i.e. epiglottitis from *Haemophilus influenza*) so the vaccine preventable disease does not resurge. The Department of Defense vaccine program follows these same principles.

25. The percentage of the population needing to be immune to drive herd immunity varies from disease to disease. Generally, the more contagious a disease is, the greater proportion of the population needs to be immune to stop its spread. For example, with regards to the highly contagious measles disease, approximately 95% immunity within a population is needed to interrupt the chain of transmission. When the immunity levels of a population falls, local outbreaks can, and have, occurred. In 2019, 1,282 individual cases of measles were confirmed in 31 states,

the highest level since 1992. The majority of those cases were among those who were not vaccinated.[25,26]

26. This herd immunity threshold – the level above which the spread of disease will decline – is currently unknown for COVID-19. As described above, in order to interpret an antibody response as it pertains to immunity, a correlate of protection (i.e. what antibody result do I need to be considered immune?) must be determined and validated. No FDA antibody test has validated a correlate of protection at this time and none of them are licensed. Nonetheless, it is generally agreed that the more severe the COVID-19 disease is in an individual, the more antibodies a survivor would produce and therefore likely would have a higher degree of protection and possibly be protected longer than those who are asymptomatic or with mild symptoms.

27. Those who receive the COVID-19 vaccine contribute to the information available from studying the outcomes from 553 million doses administered in the US and over the 10.85 billion doses administered globally.[27] Responses to vaccination are more consistent and there is minimal risk compared to the potential long-term complications and treatments needed to treat COVID-19 disease. Although breakthrough infections do occur depending on the circulating variant and the longer the interval from vaccination, vaccines (especially when a booster is also received) remain highly effective in preventing hospitalizations and death.[28]

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[25] https://www.cdc.gov/measles/cases-outbreaks.html, accessed March 6, 2022.

[26] https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6840e2-H.pdf, accessed March 6, 2022.

[27] https://ourworldindata.org/covid-vaccinations?country=OWID_WRL, accessed March 6, 2022.

[28] Ferdinands JM, et al Waning 2-Dose and 3-Dose Effectiveness of mRNA Vaccines Against COVID-19-Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and Omicron Variant Predominance – VISION Network, 10 States, August 2021-January 2022. MMWR Morb Mortal Wkly Rep

28. In October 2021, prior to the presentation of the Omicron variant, the newest SARS-CoV2 variant of concern, CDC summarized a review of 96 peer-reviewed and preprint publications, providing an overview of current scientific evidence regarding infection-induced immunity.[29] Key findings include the following:

- Available evidence shows that fully vaccinated individuals and those previously infected with SARS-CoV-2 each have a low risk of subsequent infection for at least 6 months. Data are presently insufficient to determine an antibody titer threshold that indicates when an individual is protected from infection. At this time, there is no FDA-authorized or approved test that providers or the public can use to reliably determine whether a person is protected from infection.
    - The immunity provided by vaccine and prior infection are both high but not complete (i.e., not 100%).
    - Multiple studies have shown that antibody titers correlate with protection at a population level, but protective titers at the individual level remain unknown.
    - Whereas there is a wide range in antibody titers in response to infection with SARS-CoV-2, completion of a primary vaccine series, especially with mRNA vaccines, typically leads to a more consistent and higher-titer initial antibody response.
    - For certain populations, such as the elderly and immunocompromised, the levels of protection may be decreased following both vaccination and infection.

2022:71:1-9 https://www.cdc.gov/mmwr/volumes/71/wr/mm7107e2.htm, accessed February 16, 2022.

[29] https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/vaccine-induced-immunity.html, accessed March 6, 2022.

- Current evidence indicates that the level of protection may not be the same for all viral variants.
- The body of evidence for infection-induced immunity is more limited than that for vaccine-induced immunity in terms of the quality of evidence (e.g., probable bias towards symptomatic or medically-attended infections) and types of studies (e.g., observational cohort studies, mostly retrospective versus a mix of randomized controlled trials, case-control studies, and cohort studies for vaccine-induced immunity). There are insufficient data to extend the findings related to infection-induced immunity at this time to persons with very mild or asymptomatic infection or children.

29. Debate continues about whether natural immunity versus vaccine-induced immunity is more protective against breakthrough infections (a reinfection in someone who was previously infected versus an infection in a previously not infected individual who was fully immunized). A frequently cited, though not peer-reviewed, retrospective study from Israel found that the rates of SARS-CoV-2 breakthrough infections in vaccinated individuals, while very low (highest rate = 1.5%) were 13 times higher than the rates of reinfection and hospitalization in previously infected individuals[30]. These findings have not been reproduced in a peer-reviewed or prospective publication. However, an observational study,[31] also out of Israel, compared adverse events in Pfizer-BioNTech vaccinated versus unvaccinated

[30] https://www.medrxiv.org/content/10.1101/2021.08.24.21262415v1, last accessed March 6, 2022.

[31] Barda N, et al. Safety of the BNT162b2 mRNA COVID-19 Vaccine in a Nationwide Setting N Engl J Med 2021; 385:1078-1090.

individuals in addition to those who had a history of COVID-19 disease versus those who did not. As previously identified in multiple studies, vaccination with an mRNA vaccine like Pfizer-BioNTech was associated with an elevated risk of myocarditis compared to those unvaccinated (risk difference 2.7 events/100,000 people). However, when assessing the relative risk in those with a history of COVID-19 disease with those who did not have disease, the risk of myocarditis was substantially higher in those who had COVID-19 disease (risk difference of 11 events/100,000 persons). The risk difference is calculated as the difference between the observed risks in the two groups.

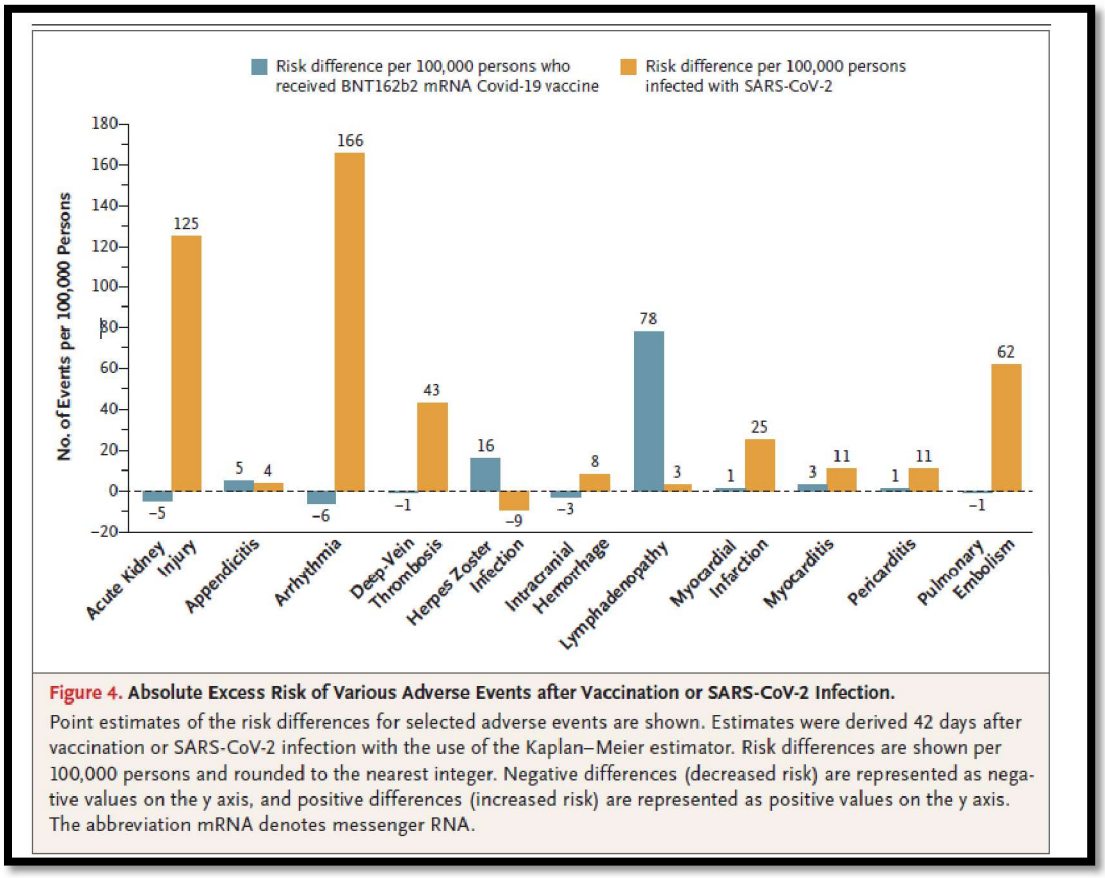


Figure 4. Absolute Excess Risk of Various Adverse Events after Vaccination or SARS-CoV-2 Infection.
Point estimates of the risk differences for selected adverse events are shown. Estimates were derived 42 days after vaccination or SARS-CoV-2 infection with the use of the Kaplan–Meier estimator. Risk differences are shown per 100,000 persons and rounded to the nearest integer. Negative differences (decreased risk) are represented as negative values on the y axis, and positive differences (increased risk) are represented as positive values on the y axis. The abbreviation mRNA denotes messenger RNA.

The Omicron variant

30. On November 26, 2021, the World Health Organization (WHO) designated the Omicron variant (Pango lineage B.1.1.529), first identified in November 2021 in Botswana and South Africa, a "variant of concern" upon recommendations of the Technical Advisory Group on SARS-CoV-2 Virus Evolution, which assesses if specific mutations and combinations of mutations alter the behavior of the virus.[32] The United States designated Omicron as a variant of concern on November 30, 2021, and following first detection in the United States on December 1, 2021, it has been found to spread more easily than the original and Delta variants.[33] Those infected with the Omicron variant in South Africa were initially reported in the media as not having severe outcomes and therefore concluding that this would be a "mild" variant. In attempt to address that misconception, on January 6, 2022, Dr. Tedros Adhanom Ghebreyesus, the WHO Director-General, stated that "while Omicron does appear to be less severe compared to Delta, especially in those vaccinated, it does not mean it should be categorized as 'mild'. Hospitals are becoming overcrowded and understaffed, which further results in preventable deaths from not only COVID-19 but other diseases and injuries where patients cannot receive timely care. First-generation vaccines may not stop all infections and transmission but they remain highly effective in reducing hospitalization and death from this virus."[34]

[32] https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern, last accessed March 6, 2022.

[33] https://www.cdc.gov/coronavirus/2019-ncov/variants/omicron-variant.html, last accessed March 6, 2022.

[34] https://twitter.com/WHO/status/1479167003109859328, posted January 6, 2022.

31. The Omicron variant has approximately 32 mutations on the spike (S) protein with approximately 15 of the 32 occurring within the receptor binding domain (RBD). The RBD is what the virus uses to bind to our cells and initiate viral infection process. Antibodies produced from previous infection or vaccination, as well as the monoclonal antibodies (mAb) given to treat those infected, target the RBD. The degree to which antibodies bind or "neutralize" the virus, determines the degree of resultant illness – the better antibodies bind, the less likely a person will become ill. This is why any mutation on the S protein RBD would cause concerns about the efficacy of existing vaccines, antibodies produced from previous infection, and the mAb given to treat people in preventing Omicron infection. One study, using an artificial intelligence (AI) model, revealed that "Omicron may be over 10 times more contagious than the original virus or about 2.8 times as infectious as the Delta variant."[35]

32. Multiple investigators turned their attention to assessing the effectiveness of antibodies following COVID-19 disease and current vaccines against Omicron. One study assessed the neutralization of 9 monoclonal antibodies (mAb), sera from 34 COVID-19 vaccine (Pfizer or Astra Zeneca) primary series recipients who had not previously been infected, sera from 20 recipients who had received a Pfizer-BioNTech booster dose, and sera from 40 convalescent sera (blood serum obtained from individuals who had a history of infection) donors, 22 of whom had also been vaccinated.[36] The better the neutralization, the better the protection. Results showed that Omicron was totally or partially resistant to neutralization by all mAbs tested. Sera

[35] Chen J, et al. Omicron Variant (B.1.1.529): Infectivity, Vaccine Breakthrough, and Antibody Resistance J. Chem. Inf. Model. 2022, 62, 2, 412-422 https://doi.org/10.1021/acs.jcim.1c01451.

[36] Planas, D. et al. Considerable escape of SARS-CoV-2 Omicron to antibody neutralization. *Nature* https://doi.org/10.1038/s41586-021-04389-z (2021).

from those vaccinated, sampled 5 months after being fully vaccinated, had limited inhibition of Omicron. Blood sera from those with a history of COVID-19 disease demonstrated no or low neutralizing activity against Omicron. Those who received a booster COVID-19 vaccine dose did generate an anti-Omicron neutralizing response, though lower than what has been seen against the Delta variant. A second study[37] also demonstrated that those who had a history of infection and were fully vaccinated (whether disease then vaccinated or vaccinated then disease (i.e., a breakthrough infection) were better able to neutralize the Omicron variant as compared to those who had only a history of disease or had a history of being fully vaccinated. An additional small study investigated the neutralizing activity of sera from convalescent patients, mRNA double vaccinated (BNT162b2 = Pfizer-BioNTech; mRNA-1273 = Moderna), mRNA boosted, convalescent double vaccinated, and convalescent boosted individuals against the original SARS-CoV-2 strain, Beta variant (B.1.351), and Omicron (B1.1.529) variant in a laboratory (in vitro) setting.[38] In the figures depicted below, Figures 1c–1j provide the results of different combinations of sera studied. What would be interpreted as the "best" combination to work against the Omicron variant is the highest level of red dots on the y-axis seen with the B.1.1.529 on the x-axis. For example, Figure 1c shows the results of those individuals with a history of COVID-19 disease. In an oversimplified interpretation, Figure 1c shows that those with a history of COVID-19 disease had no measurable neutralizing activity for Omicron. In Figures 1d and 1e, (2 doses of either Pfizer-BioNTech or Moderna), there is some neutralization against Omicron. Those who received

[37] Rossler A., et al SARS-CoV-2 Omicron Variant Neutralization in Serum from Vaccinated and Convalescent Persons NEJM, published January 12, 2022 doi:10.1056/NEJMc2199236.

[38] Carreno, J.M. et al. Activity of convalescent and vaccine serum against SARS-CoV-2 Omicron. *Nature* https://doi.org/10.1038/s41586-022-04399-5 (2021).

a booster (Figure 1f and 1g) had higher levels of neutralization against Omicron compared to the two-dose primary series. Those who had a history of disease and were then vaccinated with a two-dose primary series or a two-dose primary series and a booster (Figures 1h-1j) had better Omicron neutralization. In summary, the study found that neutralizing activity against Omicron "is most impacted in unvaccinated, convalescent individuals and in naïve individuals who acquired immunity through two mRNA COVID-19 vaccine doses" and that "boosted individuals had, at least within the short time after the booster dose, significant protection against symptomatic disease in the range of 75%."[39]

[39] *Id.* at 2.

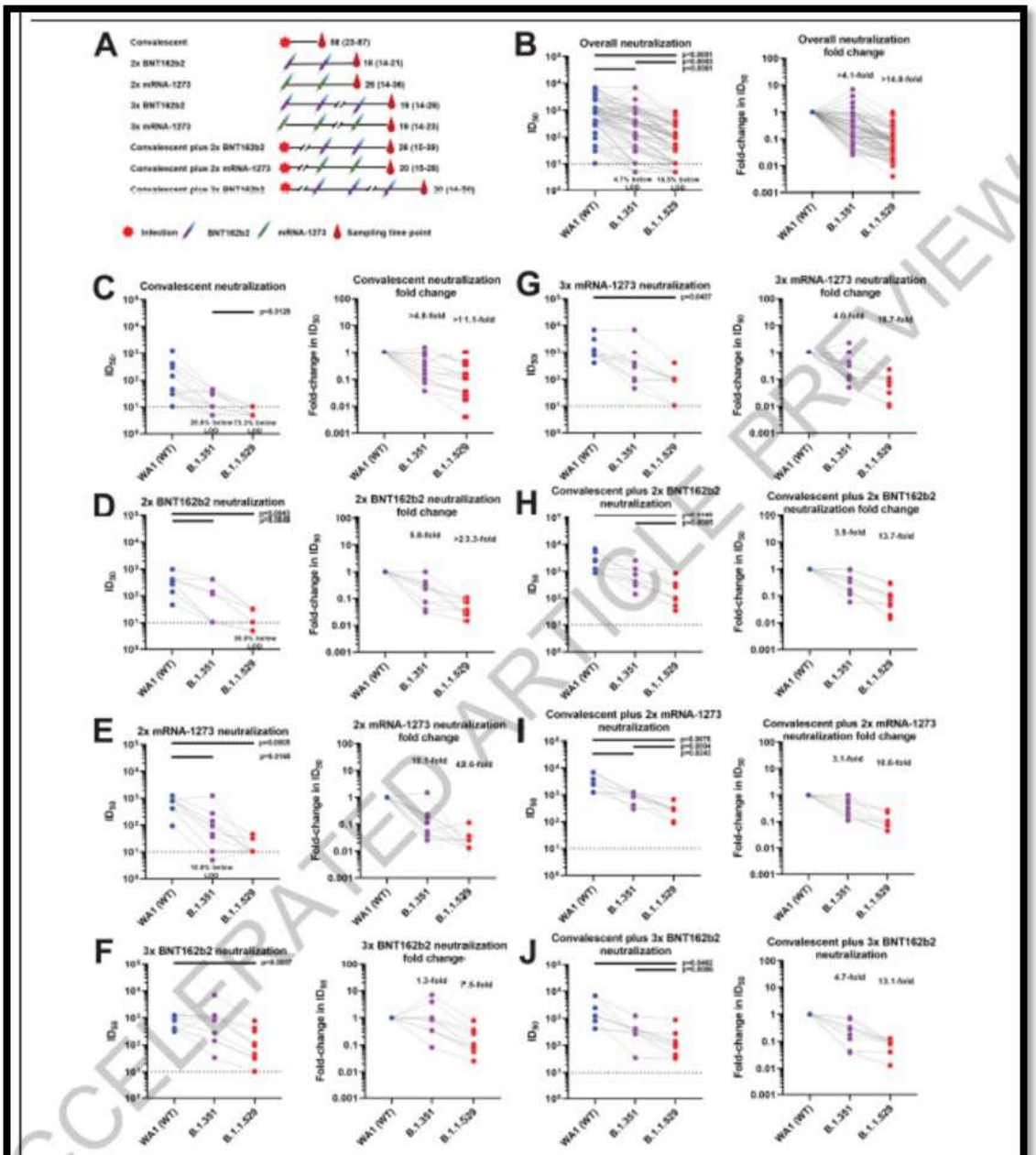
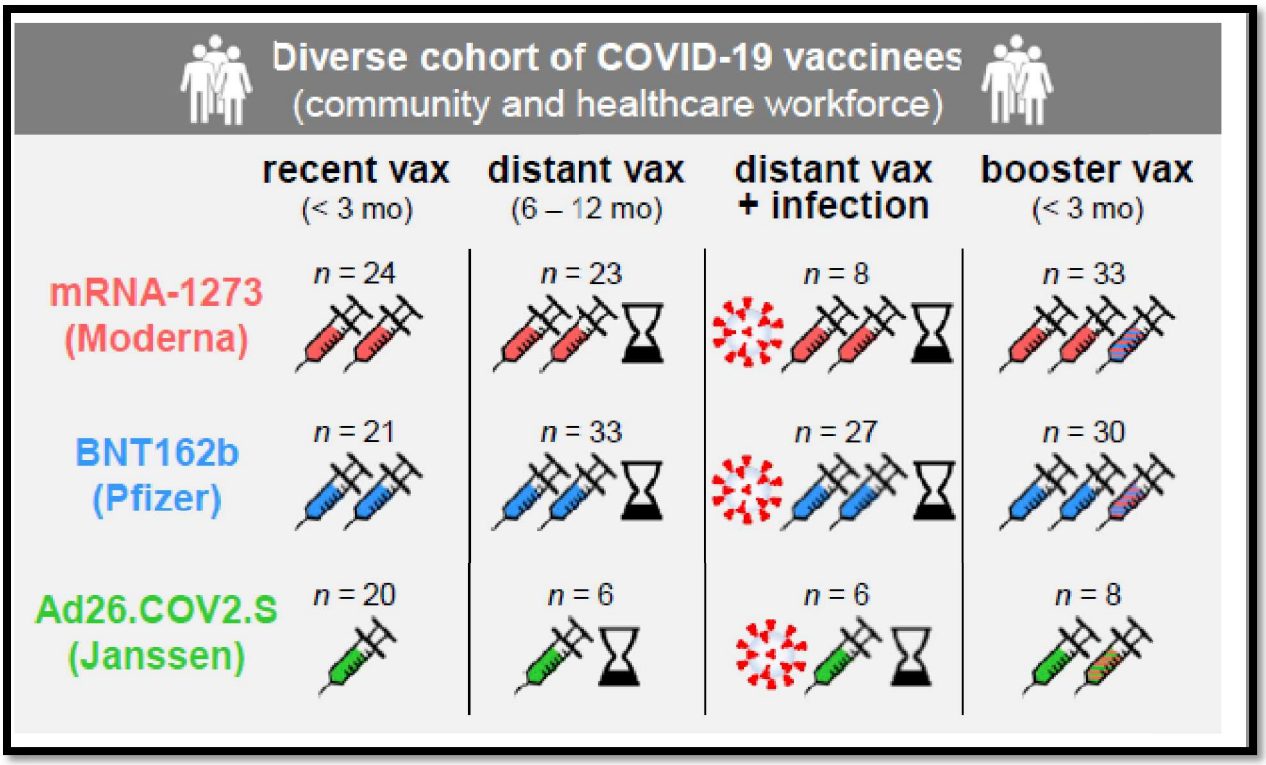


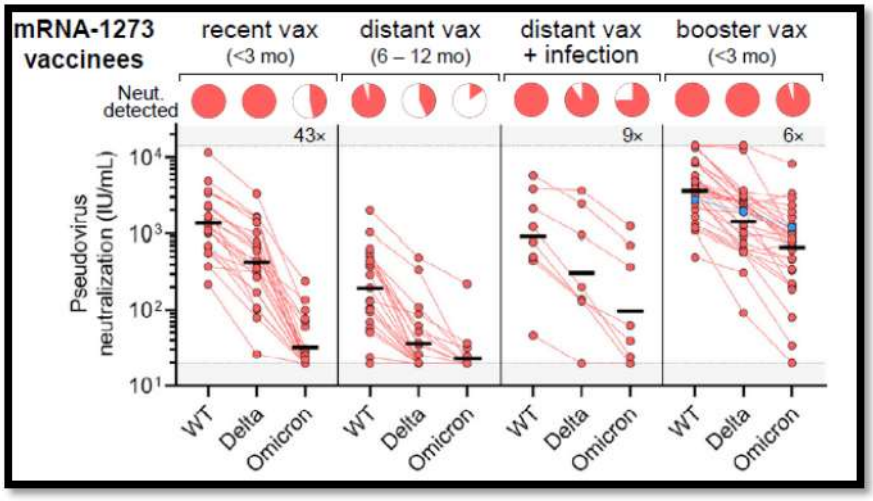
Fig. 1 | Sera of convalescent and vaccinated individuals have strongly reduced neutralizing activity against Omicron as compared to wild type SARS-CoV-2. A Overview of different exposure groups from whom samples were obtained. Further details are provided in Supplemental Table 1 and 2. **B** shows absolute titers (left) and fold reduction (right) for the combined samples, **C** to **J** shows the different groups. A one-way ANOVA with Tukey's multiple comparisons test was used to compare the neutralization titers and significant p values (<0.05) are indicated in the figure. Data in panel B is based on 85 samples, data in panel C is based on 15 samples and data in all other panels is based on 10 samples each. The dotted line represents the limit of detection (10), negative samples were assigned half the limit of detection (5). Each dot represents a biological replicate and the assays were performed once. Fold change is defined as geometric mean fold change.

33. An additional study[40] assessed the neutralizing potency of sera from 88 mRNA-1273 (Moderna), 111 BNT162b (Pfizer-BioNTech), and 40 Ad26.COV2.S (Janssen) vaccine recipients against wild-type, Delta, and Omicron COVID-19 variants, based on recent vaccination, distant vaccination (6-12 months), history of infection and distant vaccination, and recent booster vaccination, as depicted below.

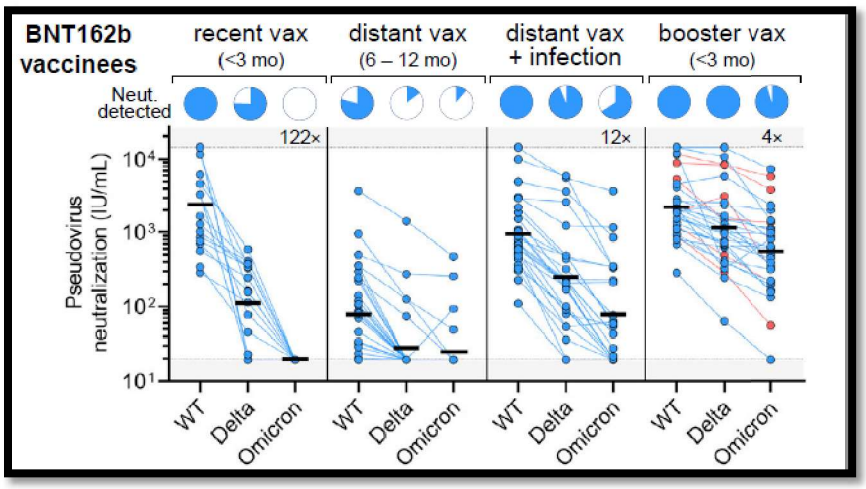


34. Against the Omicron variant, recent (< 3 months) vaccine recipients exhibited a 43-fold lower neutralization than against the wild type (WT) strain. Those with a history of vaccination and infection had a 9-fold decrease in neutralization than WT, whereas those who received a booster dose less than 3 months ago had a 6-fold decrease in neutralization compared to WT.

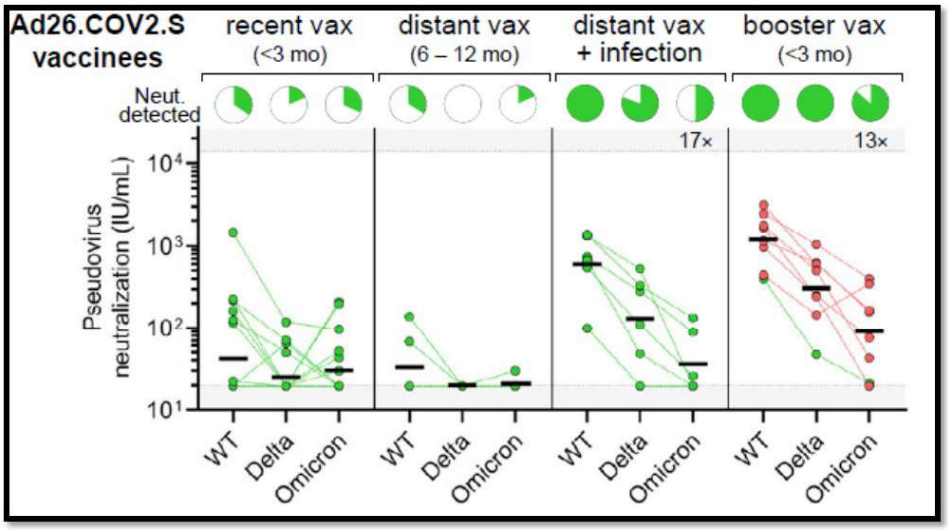
[40] Garcia-Beltran WF, et al mRNA-based COVID-19 vaccine boosters induce neutralizing immunity against SARS-CoV-2 Omicron variant. Cell 185, 1-10..



35. Similar results were seen in Pfizer-BioNTech recipients, with the best protection against Omicron seen in those who recently received a booster dose.



36. Of the three vaccines, Janssen recipients had the least neutralization against the Omicron variant, with those who recently received a booster dose demonstrating a 13-fold decrease in neutralization as compared to the WT.



37. Finally, two recent CDC publications described vaccine effectiveness during periods of Delta and Omicron dominance. The first study evaluated the benefit of a third COVID-19 vaccine dose in those who were and were not immunocompromised between August and December 2021. In those who were not immunocompromised vs immunocompromised, vaccine effectiveness (VE) was 82% and 69%, respectively, in those who were fully vaccinated and 97% and 88%, respectively in those who had received 3 doses of COVID-19 vaccine[41]. The second publication reported on the waning 2- and 3-dose effectiveness of mRNA vaccines against COVID-19 associated emergency department (ED) and urgent care (UC) encounters and hospitalizations among adults during Delta and Omicron between August 2021 and January 2022. During the Delta period, those who sought ED or UC care and received 2 doses versus 3 doses of a mRNA vaccine had an overall VE of 80% and 96%, respectively. Of those admitted to the hospital, COVID-19 vaccine VE was 85% and 95%, respectively. During the Omicron period,

[41] Tenforde MW, et al Effectiveness of a Third Dose of Pfizer-BioNTech and Moderna Vaccines in Preventing COVID-19 Hospitalization Among Immunocompetent and Immunocompromised Adults – United States, August-December 2021 MMWR Morb Mortal. Wkly Rep 2022;71(4) :118-121. DOI: https://www.cdc.gov/mmwr/volumes/71/wr/mm7104a2.htm

those who sought ED or UC care and received 2 doses versus 3 doses of a mRNA vaccine had an overall VE of 41% and 83%, respectively. Those who were admitted to the hospital demonstrated overall VE of 55% and 88%, respectively[42]. Although there was a noticeable decrease in VE during the Omicron period, comparatively mRNA COVID-19 vaccine VE is higher than annual influenza vaccine, where VE ranged between 29-48% over the last 5 seasons.[43]

38. In contrast to the above studies, the CDC recently published a study examining the impact of primary COVID-19 vaccination and previous SARS-CoV-2 infection on COVID-19 incidence and hospitalization rates from California and New York.[44] The findings demonstrated that prior to Delta variant, being vaccinated with or without a history of COVID-19 resulted in lower incidence of laboratory-confirmed COVID-19 disease and hospitalizations as compared to those who were unvaccinated with a history of disease. However, after the Delta variant became dominant, those with a history of COVID-19 disease, with or without a history of vaccination, had a lower incidence of laboratory-confirmed COVID-19 disease than those who were vaccinated without a history of COVID-19. Excluded in the study was discussion of severity of COVID-19 disease and outcomes of those who had disease (complications, etc). CDC concludes with reminding readers that more than 130,000 California and New York residents died from COVID-

[42] Ferdinands JM, et al. Waning 2-Dose and 3-Dose Effectiveness of mRNA Vaccines Against COVID-19-Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and Omicron Variant Predominance – VISION Network, 10 States, August 2021-January 2022. MMWR Morb Mortal. Wkly Rep 2022;71:1-9. DOI: https://www.cdc.gov/mmwr/volumes/71/wr/mm7107e2.htm.

[43] https://www.cdc.gov/flu/vaccines-work/past-seasons-estimates.html, last accessed March 6, 2022.

[44] Leon TM, Dorabawila V., Nelso L, et al. COVID-19 Cases and Hospitalizations by COVID-19 Vaccination Status and Previous COVID-19 Diagnosis – California and New York, May-November 2021. MMWR Morb Mortal. Wkly Rep 2022;71:125-131. DOI: http://dx.doi.org/10.15585/mmwr.mm7104e1.

19 through November 30, 2021, and that "vaccination remains the safest and primary strategy to prevent SARS-CoV-2 infections, associated complications, and onward transmission."

39. Clinical data of DoD breakthrough rates and hospitalizations as of January 20, 2022, taking into account the prior 6 weeks (where 78.8% of all breakthrough cases were seen) revealed the following results: Of the 1,578,364 active duty fully vaccinated individuals without a booster dose, 116,513 (7.38%) had a breakthrough infection. The hospitalization rate in active duty after full vaccination without a booster was 12 per 100,000 active duty service members. Of those active duty service members who were unvaccinated, the hospitalization rate was 782 per 100,000. Those who were unvaccinated had a higher percentage of critical and severe disease.

40. In summary, unvaccinated persons without a history of COVID-19 are most vulnerable to COVID-19 disease. Vaccination was highly effective against the initial SARS-CoV-2 strain it was developed to protect against. The longer the interval from vaccination, the increased risk for breakthrough disease, although vaccination continues to be protective against severe disease, hospitalization, and death. Vaccination and a history of disease was shown to be less protective than vaccination and booster dose against both the Delta and Omicron variants. Clinically, breakthrough infections during the time of Omicron dominance have been increasingly seen in those fully vaccinated. Hospitalization rates during Omicron dominance in the unvaccinated active duty population was 65 times higher than the hospitalization rate in those fully vaccinated without a booster. CDC states "primary COVID-19 vaccination, additional doses, and booster doses are recommended by CDC's Advisory Committee on Immunization Practices to ensure that all eligible persons are up to date with COVID-19 vaccine, which proves the most

robust protection against initial infection, severe illness, hospitalization, long-term sequelae, and death."[45]

Risks from COVID-19 Vaccination

41. Risks from immunization, including COVID-19 vaccines are rare. CDC provides routine updates on specific adverse events temporally associated with COVID-19 vaccines.[46] CDC updates as of March 1, 2022, include the following:

A. **Anaphylaxis after COVID-19 vaccination is rare** and has occurred in approximately 5 people per million vaccinated in the United States.

B. **Thrombosis with thrombocytopenia syndrome (TTS) after Johnson & Johnson's Janssen (J&J/Janssen) COVID-19 vaccination is rare.** As of February 24, 2022, more than 18.4 million doses of the J&J/Janssen COVID-19 Vaccine have been given in the United States. CDC and FDA identified 57 confirmed reports of people who got the J&J/Janssen COVID-19 Vaccine and later developed TTS. Women 30-49 years of age, especially, should be aware of the rare but increased risk of this adverse event. There are other COVID-19 vaccine options available for which this risk has not been seen.

C. Guillain-Barre Syndrome - CDC and FDA are monitoring reports of Guillain-Barré Syndrome (GBS) in people who have received the J&J/Janssen COVID-19 Vaccine. GBS is a rare disorder where the body's immune system damages nerve cells, causing

[45] Leon TM, Dorabawila V., Nelso L, et al. COVID-19 Cases and Hospitalizations by COVID-19 Vaccination Status and Previous COVID-19 Diagnosis – California and New York, May-November 2021. MMWR Morb Mortal. Wkly Rep 2022;71:125-131. DOI: http://dx.doi.org/10.15585/mmwr.mm7104e1.

[46] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html, last accessed March 6, 2022.

muscle weakness and sometimes paralysis. Most people fully recover from GBS, but some have permanent nerve damage. After more than 18.4 million J&J/Janssen COVID-19 Vaccine doses administered, there have been around 303 preliminary reports of GBS identified in VAERS as of February 24, 2022. These cases have largely been reported about 2 weeks after vaccination and mostly in men, many 50 years and older. CDC will continue to monitor for and evaluate reports of GBS occurring after COVID-19 vaccination and will share more information as it becomes available.

D. **Myocarditis and pericarditis after COVID-19 vaccination are rare.** As of February 24, 2022, VAERS has received 2,261 reports of myocarditis or pericarditis among people ages 30 years and younger who received COVID-19 vaccines. Most cases have been reported after mRNA COVID-19 vaccination (Pfizer-BioNTech or Moderna), particularly in male adolescents and young adults. Through follow-up, including medical record reviews, CDC and FDA have confirmed 1,328 reports of myocarditis or pericarditis.

E. **Reports of death after COVID-19 vaccination are rare**. More than 553 million doses of COVID-19 vaccines were administered in the United States from December 14, 2020, through February 22, 2022. During this time, VAERS received 12,775 reports of death (0.0023%) among people who received a COVID-19 vaccine. FDA requires healthcare providers to report any death after COVID-19 vaccination to VAERS, even if it's unclear whether the vaccine was the cause. **Reports of adverse events to VAERS following vaccination, including deaths, do not necessarily mean that a vaccine caused a health problem.** A review of available clinical information, including death certificates, autopsy, and medical records, has not established a causal

link to COVID-19 vaccines. CDC has identified nine deaths that have been caused by or were directly attributed to TTS following J&J/Janssen COVID-19 vaccination.

42. Additionally, on October 27 2021, the COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety (GACVS) provided an updated statement regarding myocarditis and pericarditis reported with COVID-19 mRNA vaccines, stating, in part: The GACVS COVID-19 subcommittee notes that myocarditis can occur following SARS-CoV-2 infection (COVID-19 disease) and that mRNA vaccines have clear benefit in preventing hospitalisation and death from COVID-19. Countries should continue to monitor reports of myocarditis and pericarditis following vaccination by age, sex, dose and vaccine brand. Countries should consider the individual and population benefits of immunization relevant to their epidemiological and social context when developing their COVID-19 immunisation policies and programs.[47]

COVID-19 Antibody Tests

43. As described above, testing to assess for acute SARS-CoV-2 infection or serologic testing to assess for prior infection is not recommended for the purposes of vaccine decision-making. Last updated December 3, 2021, the FDA's EUA Authorized Serology Test Performances[48] lists approximately 90 products, of which all of them had one of the following three statements about immunity interpretation:

[47] https://www.who.int/news/item/27-10-2021-gacvs-statement-myocarditis-pericarditis-covid-19-mrna-vaccines-updated, last accessed March 6, 2022.

[48] https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/eua-authorized-serology-test-performance, last accessed March 6, 2022.

A. "You should not interpret the results of this test as an indication or degree of immunity or protection from reinfection."[49]

B. "It is unknown how long antibodies to SARS-CoV-2 will remain present in the body after infection and if they confer immunity to infection. Incorrect assumptions of immunity may lead to premature discontinuation of physical distancing requirements and increase the risk of infection for individuals, their households and the public."[50]

C. "It is unknown how long (IgA, IgM or IgG) antibodies to SARS-CoV-2 will remain present in the body after infection and if they confer immunity to infection. A positive result for XXX test may not mean that an individual's current or past symptoms were due to COVID-19 infection."[51]

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Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge.

Executed on March 6, 2022, in Falls Church, Virginia

RANS.TONYA.SUE.1081263031 Digitally signed by RANS.TONYA.SUE.1081263031 Date: 2022.03.06 09:30:37 -05'00'

Tonya S. Rans
Colonel, Medical Corps, U.S. Air Force
Chief, Immunization Healthcare Division
Public Health Directorate
Falls Church, Virginia

[49] https://www.fda.gov/media/146369/download, last accessed March 6, 2022.

[50] https://www.fda.gov/media/138627/download, last accessed March 6, 2022.

[51] https://www.fda.gov/media/137542/download, last accessed March 6, 2022.

Exhibit 10

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
CINCINNATI DIVISION

HUNTER DOSTER, *et al.*,	)	
Plaintiffs,	)	
v.	)	No. 1:22-cv-00084
FRANK KENDALL, et al.,	)	
Defendants.	)	

DECLARATION OF MAJOR SCOTT STANLEY

I, Major Scott Stanley, hereby state and declare as follows:

1. I am an Army Preventive Medicine Officer. I hold a PhD in genetics and have over 10 years of experience working in novel drug and vaccine development prior to joining the Army. I am currently employed by the U.S. Army as the Joint Force Health Protection Officer. I have held this position since June of 2021. I previously served as the Medical Advisor to the Assistant Secretary of State for the Bureau of Population, Refugees, and Migration, Department of State. My responsibilities as the Joint Force Health Protection Officer include: coordinating with the Office of the Secretary of Defense, the Combatant Commands, and the Services on health service support and preventive medicine; providing expert analyses and medical recommendations impacting the Joint Force; providing Military medical advice to the Chairman of the Joint Chiefs of Staff through the Joint Staff Surgeon on all matters related to force health protection, including: Public Health, comprehensive health surveillance and risk management, laboratory services, and veterinary services; and providing expertise across the continuum of force health protection

activities including medical intelligence, health threat analysis, infectious disease prevention, industrial hygiene, chemical, biological and toxic materials and medical countermeasures.

2. I am generally aware of the allegations set forth in the pleadings filed in this matter. I am generally aware of the allegations set forth in the pleadings filed in this matter. This declaration is based on my personal knowledge, as well as information made available to me during the routine execution of my official duties.

COVID-19 IM ACTS ON THE FORCE

3. As of March 1, 2022, there have been 387,621 cases of Coronavirus Disease 2019 (COVID-19) in service members across the Department of Defense (DoD) which have led to 94 deaths (89 were unvaccinated, 3 were partially vaccinated, and 2 fully vaccinated but not boosted). There have been no deaths among active duty personnel since the vaccination deadlines when approximately 98% of active duty personnel are at least partially vaccinated.

4. COVID-19 impacted all elements of DoD simultaneously, and required significant operational oversight by the Secretary of Defense, the Chairman of the Joint Chiefs of Staff, Secretaries of the Military Departments, the Under Secretaries of Defense, and all geographic and functional combatant commands (CCMD) (i.e., military commands that carry out broad missions and are composed of forces from the military departments) to execute their statutory responsibilities.

5. On March 25, 2020, then-Secretary of Defense Mark Esper enacted a 60-day stop movement order for all DoD uniformed and civilian personnel and their sponsored family members overseas. This measure was taken to aid in further prevention of the spread of COVID-19, to protect U.S. personnel and preserve the operational readiness of our global force.

6. Building upon previously enacted movement restrictions governing foreign travel, permanent change of station moves, temporary duty and personal leave, this stop movement order

also impacted exercises, deployments, redeployments, and other global force management activities. Approximately 90,000 service members slated to deploy or redeploy within 60 days of its issuance were impacted by this stop movement order.

7. Specific examples of cancelled or curtailed training resulting from the dangers posed by the SARS-CoV-2 virus, which causes COVID-19, include the following. In March of 2020, 63 Fort Jackson recruits in a class of 940 had tested positive for the virus and caused a rescheduling of basic training activities. Also in March 2020, the United States Military Academy at West Point was on spring break when the seriousness of the pandemic came to light, forcing a pause in the academic year until a plan could be developed to bring the cadets back to campus safely. In early April 2020, Secretary Esper authorized the Secretaries of the Military Departments to pause accessions training (i.e., training for new recruits) for two weeks. In May 2020, the Defender Europe 2020 exercise was originally supposed to deploy the largest force (20,000 service members) from the United States to Europe in over 20 years, but the event was modified to about 6,000 service members to limit troop movement. Reserve and National Guard units suspended monthly battle assemblies and drill as early as March and April 2020, and moved to virtual training. For instance, the Army Reserve announced on March 18, 2020, that it was suspending monthly battle assemblies. The Navy Reserve announced about the same time the suspension of drill weekends, and then on April 16 it announced that suspension would be extended. In Korea, United States Forces Korea (the command responsible for military operations in the country) was forced to limit travel outside of the country, and travel to and from Daegu was limited to mission-essential personnel only. In addition, the spread of the virus caused the DoD Education Activity (DoDEA) to cancel school for children in all of the schools in Daegu, and military commanders were forced to cancel all meetings, formations, and training events greater than 20 people, which severely

impacted unit training which routinely requires service members to practice maneuvers and operations in large group settings.

8. Perhaps one of the more well-known examples of how the spread of COVID-19 could impact military operations, particularly among unvaccinated service members, is that of the U.S.S. Theodore Roosevelt, a nuclear-powered aircraft carrier with 4,779 personnel onboard. While conducting operations in the Pacific Ocean, the U.S.S. Theodore Roosevelt had to be diverted to the U.S. Naval Base Guam after an outbreak of SARS-CoV-2 occurred in an estimated 1,331 crew members, killing one, and resulting in the ship becoming non-operational.[1] Since the U.S. Navy only has 11 aircraft carriers in the total inventory, this event represented a significant reduction in the Navy's operational capacity. This example highlights not only the operational impact unmitigated spread of SARS-CoV-2 could have on the military's ability to carry out operations, but also the increased risk of transmission to those who must carry out their duties in close-quarters environments, such as service members who must work in close contact with others, sleep in open bays with tightly packed bunks, or must work in the confined areas of a ship where it is believed that such close, confined working environments contributed to higher exposure to the virus and a higher risk of infection.

9. Over the past twenty months, approximately 19 major training events, many of which involved preparedness and readiness training with our foreign partners, had to be canceled as a result of COVID-19. These included major training events involving tens of thousands of personnel that focus on readiness and response to events spanning a wide range of national security and international objectives, including: responses to catastrophic natural disasters, multi-national

[1] The New England Journal of Medicine, An Outbreak of Covid-19 on an Aircraft Carrier, https://www.nejm.org/doi/full/10.1056/NEJMoa2019375.

exercises with international partners to defend against military aggression, training symposiums and exercises to enhance defenses to information infrastructures, and partner capacity training for security and stability operations.

10. Further, unvaccinated individuals were unable to participate in some international training events because some partner nations had COVID-19 vaccination requirements or additional testing and quarantine requirements for country entry that degraded training value and involvement for unvaccinated individuals. There are still countries with vaccine requirements or quarantine requirements for unvaccinated individuals which would preclude an unvaccinated individual from participating in a military-to-military engagement with partner nations.

11. The loss of these training opportunities not only inhibited the development and sustainment of intra- and international relationship development that would otherwise allow for increased cooperation and understanding, but it prevented invaluable training opportunities that allow our forces, and our foreign partners, to practice interoperability and to strengthen their abilities to plan and execute combat, humanitarian, and security operations that are vital to the preservation of national security and the protection of our foreign interests.

12. As in the civilian health care system, in the early weeks and months of the pandemic, the DoD cancelled all non-essential medical procedures and surgeries and was further limited in its ability to provide medical appointments due to access restrictions to military treatment facilities (MTFs), the lack of available beds in the MTFs, and the burden on the military health system associated with caring for COVID-19 patients. This had the effect of reducing readiness as service members were, in some cases, unable to receive the care they needed to address non-emergency conditions and undergo routine medical and health assessments that are required under military directives to maintain medical readiness.

13. The military health system was also called on to support the COVID-19 response in the United States. In April of 2020, the Department of Defense converted the Jacob K. Javits Center in New York into an alternative care facility for more than 2,000 COVID-19 patients. The United States Naval Ship (USNS) Comfort arrived in New York Harbor on March 30, 2020, while the USNS Mercy arrived in Los Angeles on March 27, 2020, to relieve pressure on local hospital systems so they could focus on life-saving COVID-19 related care. In December of 2021, the President announced plans to send an additional 1,000 military medical personnel to U.S. hospitals to join the roughly 240 personnel already deployed to seven states. These and other examples of DoD support to civil authorities served as a resource drain on the military health system and obviously directly exposed DoD personnel to the SARS-CoV-2virus.

14. Vaccinations for COVID-19 enabled the return to higher levels of occupancy in DoD facilities, and hold in-person training, meetings, conferences, and other events. Vaccinations also permit service members to engage in joint training exercises with other countries that have vaccine requirements. It also reduced the testing burden on the DoD since in many instances individuals who are fully vaccinated are not required to submit to COVID-19 testing.

15. On May 26, 2020, the Secretary of Defense issued conditions-based guidance that enabled the resumption of some unrestricted official DoD travel based on the White House's Opening Up America Guidelines. On April 12, 2021, the Under Secretary of Defense for Personnel and Readiness published guidance removing some travel restrictions for fully vaccinated individuals and on September 24, 2021, the Deputy Secretary of Defense lifted travel restrictions for fully vaccinated DoD personnel.

16. According to the Director of the National Institute of Allergy and Infectious Diseases (NIAID), Dr. Anthony Fauci, the latest statistics for the U.S. population show that an

unvaccinated person has a 10-times greater chance of getting infected, a 17-times greater chance of getting hospitalized, and a 20-times chance of dying compared to a vaccinated person.[2] Rates of COVID-19 cases between October and November of 2021 were lowest among fully vaccinated persons with a booster dose compared to those with just the primary series, and much lower than rates among unvaccinated persons (25.0, 87.7, and 347.8 per 100,000 population, respectively). In December of 2021, when Omicron was circulating widely, the same pattern holds (148.6, 254.8, and 725.6 per 100,000 population, for boosted, primary series only, and unvaccinated, respectively).

17. Although COVID-19 vaccine effectiveness (VE) has decreased in terms of preventing infections with the emergence of the new variants and with the waning of vaccine-induced immunity, protection against hospitalization and death has remained high. The CDC published a study on January 19, 2022 that showed VE in terms of preventing hospitalization during the period when Omicron has been the dominant variant was 81% following the initial 2-shot series and 90% in those who were up to date with the recommended booster dose, compared to only 57% in those who were not up to date (meaning beyond the recommended time for booster dose eligibility without receiving a booster dose). In November of 2021, the CDC found that unvaccinated individuals were 4-times more likely to test positive and 15-times more likely to die than a fully vaccinated individual. In December of 2021, unvaccinated individuals were 16 times more likely to be hospitalized with COVID-19. For hospitalized adults, the CDC found that unvaccinated people with a previous COVID-19 diagnosis were more than 5 times more likely to get re-infected than fully vaccinated people with no prior history of SARS-CoV-2 infection. This

[2] 20 January 2022 Blue Star Families forum. Panel Speakers: Dr. Anthony Fauci, NIAID; LTG Ronald Place, Defense Health Agency; and Maj Gen Paul Friedrichs, Joint Staff Surgeon.

demonstrates that COVID-19 vaccines are effective reducing the risk of becoming infected but, more importantly, are highly effective at preventing hospitalizations and deaths and highlights the importance of being up to date with your COVID-19 vaccine.

18. DoD specific data is equally compelling in terms of demonstrating the value of vaccinations. Between July and November of 2021, non-fully-vaccinated active-duty service members had a 14.6-fold increased risk of being hospitalized when compared to fully vaccinated active-duty service members. In December 2021 unvaccinated adults were 16-times more likely to be hospitalized than vaccinated adults. Furthermore, unvaccinated adults over 50 years of age were 44 times more likely to be hospitalized than individuals who were vaccinated and received a booster dose. Of all active duty personnel hospitalized with COVID-19 since December of 2020 thru this month, only 0.012% were vaccinated. This amounts to 13 active duty personnel with boosters and breakthrough infections requiring hospitalization – an extremely rare occurrence. And as mentioned previously, of the 94 deaths among uniformed service members, only two had completed a primary series of a COVID-19 vaccine (one with Moderna and one with J&J) and neither had received a booster dose. It is also worth noting that there have been no COVID-19 related deaths among active duty personnel since the vaccination deadlines have passed.

19. While some have pointed to the increase in the number of breakthrough cases in general, and with the Delta and Omicron variants in particular, as a reason to question the effectiveness of the vaccines, it is important to keep in mind that as vaccination rates increase among service members, vaccinated service members will make up a larger percentage of the population available to become infected. In other words, vaccinated personnel are disproportionately represented in the pool of individuals exposed to the virus that causes COVID-19. Taken to the extreme, if *ever* service member were vaccinated, only vaccinated service

members *could* have infections. So it is important to view the number of breakthrough infections in this light and not as a reflection of vaccine effectiveness.

20. Given the tangible protection the vaccines afford service members against infection, serious illness, hospitalization, and death, it is clear that COVID-19 vaccines improve readiness and preserve the DoD's ability to accomplish its mission. If an individual tests positive for COVID-19, they are required to isolate and are unavailable to perform their duties, even if they are asymptomatic or have mild symptoms. They also put their fellow service members at risk of infection and hospitalization and further degrade the readiness of their units, their service, and the DoD. Additionally, if an unvaccinated service member in a hostile area becomes seriously ill and requires a medical evaluation, it may risk the lives of other service members or may ultimately not be possible, thus endangering the member's life and affecting the unit's mission.

****

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct.

Executed on March 7, 2022 in Washington, DC.

STANLEY.SCOTT.E.1169637659 Digitally signed by STANLEY.SCOTT.E.1169637659 Date: 2022.03.07 09:13:04 -05'00'

Scott Stanley, PhD
Major, United States Army
Joint Staff Force Health Protection Officer
Office of the Joint Staff Surgeon

Exhibit 11

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
CINCINNATI DIVISION

HUNTER DOSTER, *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	No. 1:22-cv-00084
	)	
FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	
	)	

DECLARATION OF COLONEL ARTEMIO C. CHA A

I, Artemio C. Chapa, hereby state and declare as follows:

1. I am a Colonel in the United States Air Force currently assigned as the Division Chief for Medical Operations at the Air Force Medical Readiness Agency. I have been in this position since July 2018. As a part of my duties, I am responsible for medical operations in the COVID-19 pandemic policy.

2. I am generally aware of the allegations set forth in the pleadings filed in this matter. I make this declaration in my official capacity as the Division Chief for Medical Operations and based upon my personal knowledge and upon information that has been provided to me in the course of my official duties.

3. Medical exemptions from immunization requirements are accomplished in accordance with Air Force Instruction (AFI) 48-110_IP, *Immunizations and hemoproph la is for the Prevention of Infectious iseases*, dated October 7, 2013 (certified current February 16, 2018).[1]

[1] AFI 48-110_IP is an inter-service publication. The Army identifies is at Army Regulation (AR) 40-562, Navy as Bureau of Medicine and Surgery Instruction (BUMEDINST) 6230.15B, and Coast Guard (CG) Commandant Instruction (COMDTINST) M6230.4G.

I am familiar with the medical exemption policy and process as it falls within the scope of my professional duties. Medical exemptions are vaccine-specific and are determined "based on the health of the vaccine candidate and the nature of the immunization under consideration."[2] Accordingly, there is no automatic presumptive exemption from a vaccine.

4. A service member may request a medical exemption from the COVID-19 immunization requirement by notifying their commander.[3] The service member must make an appointment with the Military Treatment Facility (MTF) to be evaluated by a military medical provider. The provider will counsel the service member to ensure the member is making an informed decision, including providing specific information about COVID-19, Centers for Disease Control scientific recommendations, the potential risks of infection, benefits of vaccination, and vaccine-specific information about the product constituents, risks, and benefits.

5. Additionally, the military medical provider will evaluate the service member to determine if a medical exemption is warranted. The military medical provider's decision to grant or deny a medical exemption request is based on the provider's individualized assessment of the service member's medical situation. By way of example, individuals who are granted a medical exemption from the COVID-19 vaccine may include (1) people who previously received passive antibody therapy within the last 90 days, including treatment with monoclonal antibodies or convalescent plasma;[4] (2) Multisystem Inflammatory Syndrome in Adults (MIS-A); (3) acute current COVID-19 infection; (4) pregnancy; (5) myocarditis or pericarditis following first dose or current unresolved myocarditis/pericarditis; (6) prior anaphylaxis to Pfizer COVID vaccine or

[2] AFI 48-110_IP, paragraph 2-6.(a).
[3] A military medical provider can be a military service member, civilian, or contractor so long as they are privileged at a "Military Treatment Facility."
[4] As of February 11th, 2022, the CDC has updated the guidance that it is no longer necessary to delay COVID-19 vaccination following receipt of monoclonal antibodies or convalescent plasma. The AF Medical Service is evaluating removing this as a medical exemption criteria.

a component of the vaccine;[5] or (7) immediate allergic reaction of any severity to a previous dose or known (diagnosed) allergy to a component of the COVID-19 vaccine.[6] A military medical provider may seek further consultation if medically indicated.

6. If a military medical provider makes a determination that a medical exemption applies to a service member, the provider documents the exemption in the Aeromedical Services Information Management System (ASIMS),[7] which is used to track Individual Medical Readiness,[8] and the Electronic Health Record. At this time, all medical exemptions to the COVID-19 vaccination requirement granted by the Air Force are temporary. The duration of a medical exemption depends on the underlying reason for the medical exemption. It may be as short as 30 days and as long as one year. Scientific information can also be updated to remove a medical exemption criteria, such as the February 11th, 2022, CDC notice that it is no longer recommended to delay COVID-19 vaccination following receipt of monoclonal antibodies or convalescent plasma. Additionally, because new or additional COVID-19 immunization products may be approved, permanent medical exemptions are not permitted at this time. After the medical exemption expires, the member may be reevaluated to determine if a new exemption is warranted. Additionally, a military medical provider may revoke a medical exemption when it is no longer clinically warranted. The military medical provider will also submit a Memorandum For Record to the service member's commander notifying them if the medical exemption was approved or denied. The number of medical exemptions fluctuates as temporary exemptions are

[5] This is defined as the onset within 4 hours of urticarial, wheezing/dyspnea, vomiting or diarrhea, hypotension, or angioedema.
[6] Air Force Medical Readiness Agency, "COVID-19 Vaccine Exemptions Guidance for AFMS Medical Personnel" (Sept. 3, 2021).
[7] An alternative database it can be entered is Military Health System Genesis.
[8] The Individual Medical Readiness displays a member's medical readiness, including what immunization requirements have been accomplished, which are coming due, and which are outstanding.

granted and expire, but the overall trend has been a decrease in the number of active medical exemptions and the Air Force expects that trend to continue. Indeed, as data submitted in response to a court order in a related case reflect, the number of temporary medical exemptions dropped from 1,723 to 1,513 in the span of one month.[9]

7. A service member's commander may review the member's Individual Medical Readiness to ensure the member has met all the medical requirements directed. Once a medical exemption is annotated in ASIMS, the service member's Individual Medical Readiness will display that the member is medically exempt for the COVID-19 vaccination requirement and it will no longer display the member as coming due or overdue for the requirement.

8. If a military medical provider determines that a service member does not meet the criteria for a medical exemption, the provider will document the denial in the member's Electronic Health Record and provide the rationale for disapproval. Like any other medical condition, a service member may seek a second opinion.[10] To qualify for a medical exemption, the second opinion must come from a military medical provider, whether at the same or different Medical Treatment Facility. If the second medical evaluation denies the medical exemption as well, the provider annotates this denial in the Electronic Health Record and it is considered a final medical exemption disposition. If the medical evaluations conflict, the Chief of Medical Staff and military medical provider may consult with the facility's allergist or with the Defense Health Agency Immunization Healthcare Division for resolution and final adjudication by the Chief of the Medical Staff for the Military Treatment Facility.

[9] *See Nav S A v. Biden*, No. 21-cv-2429 (M.D. Fla.), ECF No. 47-5 (Holbrook Decl. Ex. 1), ECF No. 73-5 (Holbrook Decl.).

[10] This is true of any medical condition, including if the service member was granted a medical exemption.

9. The timeline for resolution of a medical exemption request will vary depending on the purported medical issues involved and the appointment availability at the individual Military Treatment Facilities.

Temporary Nature of Medical Exemptions

10. Medical exemptions are granted based on concerns that a COVID-19 vaccine would place the individual service member at a heightened health risk. Healthcare determinations are based upon individual provider encounters with each patient, with the provider assessing the service member's medical history and considering all relevant aspects of that patient's unique medical circumstances and needs. Decisions concerning vaccination, to include the medical necessity to issue a temporary exemption are no exception to this rule and are tailored to the individual patient.

11. As previously noted, Department of the Air Force policy is to only grant temporary medical exemptions from immunization requirements. The majority of medical conditions warranting an exemption for the COVID-19 vaccine are temporary in nature. The duration of these exemptions necessarily vary based on the medical conditions and history of the patient at the time of evaluation, along with the specifics of the vaccine. Circumstances under which a temporary exemption could be granted are wide-ranging. A temporary medical exemption for allergic reaction to the vaccine or components of the vaccine is a good example. While a service member may have a severe allergic reaction to an ingredient, it may not occur with a future COVID-19 vaccine of a different formulation. A temporary exemption allows the Air Force to reassess individuals with allergies or severe adverse reactions to determine whether an updated or new vaccine has been approved with constituents the member can safely take.[11] An

[11] For example, the FDA's recent approval of the Moderna vaccine, now marketed under the name "SPIKEVAX."

exemption may also be temporarily granted for other medical reasons and conditions, such as when receiving the vaccine caused myocarditis or pericarditis following the first dose, or when the vaccine could create a confusing clinical diagnostic assessment during an active COVID-19 infection (e.g., is a fever due to a side effect from a COVID-19 vaccine or due to the COVID-19 infection), or for a pregnancy (which is time limited).

12. The period of an exemption is dependent on the underlying medical reason, but can be as short as 30 days (or less) for someone who has an acute COVID-19 infection to 365 days for an individual with a severe allergic reaction. Many exemptions are limited to 30, 60, or 90 days.

13. Denying medical exemptions where they are not warranted protects the member, unit, and mission by ensuring the member gets vaccinated and is medically ready. Granting medical exemptions when warranted also serves the military interests in readiness and promoting the health of the force. If giving the vaccine would undermine the health of that particular service member, the military's interests in readiness and force health protection would be degraded in that circumstance by vaccination. After the individual health risk to vaccination has subsided, the member is again required to vaccinate.

14. A service member with a medical exemption is still subject to restrictions and/or limitations related to the fact that they are unvaccinated (e.g., deployment eligibility, foreign country entry restrictions, frequent COVID-19 testing or extended quarantine requirements, restrictions from all non-mission essential travel, etc.). Therefore, receipt of a medical exemption does not permit the recipient to continue to freely perform any and all duties without consequences. To the extent necessary for the mission and commander decision-making, that member may be reassigned and/or likely categorized as non-deployable just as any other unvaccinated person with or without a pending religious accommodation. Moreover, receiving

any type of exemption from the vaccine requirement may require an additional medical waiver in order to deploy overseas, go on sea duty, or engage in other special duties or assignments.

15. As a physician, this process of individual service member review with individual vaccine medical review to adjudicate proper temporary medical exemption clearly consolidates an un-biased alignment with policy,[12] occupational health, member protection and military interest. Both granting a temporary medical exemption and requiring service members without a medical condition to be vaccinated are evidence of the goal of the military interest in preserving a healthy, responsive force and medical readiness.

16. On March 08, 2022, the numbers of exemptions from the COVID-19 vaccine in the ASIMS data was 1,211 Total Force Service Members (595 U.S. Air Force, 11 U.S. Space Force, 385 Air National Guard and 220 Air Force Reserve Command).[13] The "Medical Temporary" code documents all exemptions due to medical conditions (e.g., pregnancy, allergic reaction, participation in vaccine trial). The Department of the Air Force cannot readily ascertain how many Service members, if any at all, have medical exemptions for each particular medical condition.

Administrative Exemption for Vaccine Clinical Trials

17. I am familiar with the administrative exemption policy and process for Vaccine Clinical Trials as part of my professional duties. Pursuant to Force Health Protection Guidance (Supplement 23), Revision 3, *epartment of efense uidance for oronavirus isease accination Attestation Screenin estin and accination erification*, service members who

[12] Per AFI 48-110, medical exemptions are vaccine-specific and are determined "based on the health of the vaccine candidate and the nature of the immunization under consideration."

[13] This is a snapshot in time. Medical exemptions from COVID-19 are all temporary in nature. The period of an exemption is dependent on the underlying medical reason, but can be as short as 30 days (or less) for someone who has an acute COVID-19 infection to 365 days for an individual with a severe allergic reaction. Many exemptions are limited to 30, 60, or 90 days.

are "actively participating in COVID-19 vaccine clinical trials begun prior to November 22, 2021, are exempt from mandatory vaccination against COVID-19 until the trial is complete in order to avoid invalidating the such clinical trial results." Although not a medical condition, a temporary exemption from the COVID-19 vaccination requirement for a Service member while they are actively participating in a vaccine clinical trial is annotated in ASIMS as "Medical Temporary." If a Service member is not actively participating (e.g., chose not to continue the trial, etc.) or if the clinical trial is not for a vaccine, the service member is not exempt. This exemption would be temporary and the Service member would be required to vaccinate at the end of the trial.

18. Service members shall follow their command policies regarding the requirement to obtain command permission to participate in a clinical trial. If approved, the Service member would be required to provide the study information and proof of participation to the MTF for review of a medical temporary exemption. There are different types of vaccine clinical trials, included blinded (where the member is unaware if they received the actual vaccine or a placebo) and not blinded (where member knows if they received the vaccine). If the member received a placebo and was blinded, the MTF would document a "Medical Temporary" exemption in ASIMS. The member would be temporarily exempt until the study was unblinded or until the study ends. If the member received the actual vaccine, and not a placebo, and it was EUA-authorized or on the World Health Organization (WHO) EUL, the MTF would document the immunization in ASIMS showing the member had been vaccinated.

19. ASIMS is unable to identify in a searchable format how many service members are actively participating in a vaccine clinical trial and have a temporary medical exemption. This "Medical Temporary" code is the same code used to document exemptions due to medical

conditions (e.g., pregnancy, allergic reaction) as described above. As such, the Department of the Air Force is not readily able to ascertain how many Service members, if any at all, in the pool of "Medical Temporary" ASIMS data are participating in a vaccine clinical trial.

20. Moreover, even if an individual participates in a vaccine clinical trial, it does not mean they are unvaccinated. For example, during a blinded trial, an individual's vaccination status is unknown, even to that person.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

CHAPA.ARTEMIO.CERDA.1169367589

Digitally signed by CHAPA.ARTEMIO.CERDA.1169367589
Date: 2022.03.08 12:47:19 -05'00'

ARTEMIO C. CHAPA, Colonel, USAF
Division Chief, Medical Operations,
AFMRA SG3

Exhibit 12

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
CINCINNATI DIVISION

HUNTER DOSTER, *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	No. 1:22-cv-00084
	)	
FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	
	)	

DECLARATION OF CHA LAIN, MAJOR MATTHE J. STREETT

I, Matthew J. Streett, hereby state and declare as follows:

1. I am a Major in the United States Air Force currently assigned as a Staff Chaplain at the Office of the Chief of Chaplains. I have been in this position since June 2021. As a part of my duties, I am responsible for coordinating Chaplain Corps policy, publications, and religious accommodation concerns for the United States Air Force and the United States Space Force, lead the Policy branch of the Plans and Programs division, and I serve as one of the chaplain representatives on the Headquarters Air Force Religious Resolution Team advising the Air Force Surgeon General on religious accommodation appeals for vaccination exemption requests.

2. I make this declaration in my official capacity as a Staff Chaplain and based upon my personal knowledge and upon information that has been provided to me in the course of my official duties.

3. The Air Force policy and procedures for addressing religious accommodation requests are outlined in Department of the Air Force Instruction (DAFI) 52-201, *Reli ious reedom in the epartment of the Air orce*, dated June 23, 2021 and Air Force Instruction (AFI) 48-110_IP,

Immunizations and hemoproph la is for the Prevention of Infectious iseases, dated October 7, 2013 (certified current February 16, 2018).[1] DAFI 52-201 implements Department of the Air Force Policy Directive 52-2, *Accommodation of Reli ious Practices in the Air orce*, which implements Department of Defense Instruction (DoDI) 1300.17, *Reli ious i ert in the Militar Services*, in the Air Force. DoDI 1300.17 implements requirements in the "Religious Freedom Restoration Act[2] and other applicable laws.[3] I am familiar with the religious accommodation policy and process as they fall within the scope of my professional duties.

4. A service member may request a religious accommodation from an immunization requirement by submitting a written request addressed to the approval authority to his or her unit commander. The request will include, in addition to other identifying information, "the religious basis for the request; a comment on the sincerity of the request; and the substantial burden on the member's expression of religion."[4] The approval authority indicated in DAFI 52-201 is the Major Command (MAJCOM), Field Command (FIELDCOM), Direct Reporting Unit (DRU), or Field Operating Agency (FOA) commander over the service member. The appeal authority for any disapproved request is the Air Force Surgeon General.

5. The DoD will accommodate individual expressions of sincerely held beliefs (conscience, moral principles, or religious beliefs) which do not have an adverse impact on military readiness, unit cohesion, good order and discipline, or health and safety.[5] Accommodations will be granted unless they encounter these issues. Not all religious accommodation requests are the same.

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[1] AFI 48-110_IP is an inter-service publication. The Army identifies it as Army Regulation (AR) 40-562, Navy as Bureau of Medicine and Surgery Instruction (BUMEDINST) 6230.15B, and Coast Guard (CG) Commandant Instruction (COMDTINST) M6230.4G.
[2] 42 U.S.C. § 2000bb-1.
[3] Note that because of publication dates, AFI 48-110_IP does not reflect the recent, significant changes in DoDI 1300.17, while DAFI 52-201 does reflect those changes. When there are conflicts between AFI 48-110_IP and DAFI 52-201 on the same subject, DAFI 52-201 will reflect more recent guidance.
[4] DAFI 52-201, paragraph 5.3.
[5] DoDI 1300.17, paragraph 1.2.b.

Each request is reviewed individually by both the initial approval level decision authority and the appellate authority, if applicable to determine (1) if there is a sincerely held religious (as opposed to moral or conscience) belief, (2) if the vaccination requirement substantially burdens the applicant's religious exercise based upon a sincerely held religious belief, and if so, (3) whether there is a compelling government interest in requiring that specific requestor to be vaccinated, and (4) whether there are less restrictive means in furthering that compelling government interest.

6. When evaluating a religious accommodation request, DAFI 52-201 states that " t he Department of the Air Force has a compelling government interest in mission accomplishment and will take this into account when considering members' requests for accommodation of religious beliefs. This interest includes military readiness, unit cohesion, good order and discipline, and health and safety for both the member and the unit."[6] Commanders may only deny a religious accommodation request (in full or in part) "when there is a real (not theoretical) adverse impact on military readiness, unit cohesion, good order and discipline, or public health and safety for both the individual and unit levels."[7] Any substantial burden imposed "will employ the least restrictive means possible on expressions of sincerely held religious beliefs."[8]

7. To ensure commanders are properly informed of the facts and circumstances of the request and able to make an informed recommendation and/or decision, the Air Force uses a Religious Resolution Team, which "is a multidisciplinary team that advises commanders regarding resolution of religious liberty matters."[9] At the installation level, the team is comprised of the commander (or designee), Senior Installation Chaplain, a public affairs officer,

[6] DAFI 52-201, paragraph 2.1.
[7] Id.
[8] Id.
[9] Id., paragraph 3.8.1.

a member of the Staff Judge Advocate's office (i.e., the legal office). Teams addressing immunization requests also include a medical provider.

8. Most units that fall under Air Force Reserve Command (AFRC) operate on a part-time basis and are not fully staffed for the entirety of a month. Typically, these units only fully convene one weekend per month. As such, it is logistically difficult for AFRC units to assemble the members required for a Religious Review Team to address the number of COVID-related religious accommodation packages that have been submitted. Accordingly, the AFRC temporarily waived the requirement for AFRC units to hold a Religious Review Team, with the AFRC-level Religious Review Team fulfilling the requirement instead.[10] This waiver was made pursuant to the AFRC Commander's authority in Department of the Air Force Instruction 33-360, which delegated waiver authority for such matters to Air Force Major Command commanders. That waiver was valid from September 1, 2021 to December 31, 2021.

9. Prior to review by the Religious Resolution Team, the member will have three consultations, in no particular order. First, a chaplain is appointed to interview the service member. The interview addresses the type of request, the sincerity of an asserted religious or moral/conscience belief, any substantial burden imposed by the policy in question on a sincere religious practice, and potential alternative means of accommodating the practice, and the substantial burden. Second, the service member's unit commander must also counsel the service member concerning the impact not receiving the specified vaccine may have on "readiness for deployment, assignment, international travel, or result in other administrative consequences."[11] Third, a military physician must ensure the service member is making an informed decision and

[10] Per DAFI 52-201, paragraph 3.8.1.2, the Religious Resolution Team at a Major Command is comprised of representatives from the Deputy Chief of Staff for Manpower, Personnel, and Services; Chaplain Corps, Public Affairs, Judge Advocates General, and the Surgeon General.
[11] DAFI 52-201, paragraph 6.6.1.1.

consult with the member on "at a minimum, specific information about the diseases concerned; specific vaccine information including product constituents, benefits, and risks; and potential risks of infection incurred by unimmunized individuals."[12] The chaplain, commander, and medical provider each provide written memoranda of their respective meetings to include in the request package.

10. The chaplain's memorandum must address whether the requestor's beliefs seem to be sincere and based upon religion (as opposed to moral or conscience), alternative means explored for religious accommodation, the substantial burden infringing on religious exercise, and a recommendation to the decision authority.[13] The chaplain's role is to provide inputs based on the interview to ensure the approval authority is able to make an informed decision. Additionally, the recommendation is not necessarily whether the accommodation should be granted or not. While the chaplain is not prohibited from saying whether an accommodation should or should not be granted, the chaplain could also recommend that alternative means be explored, or that a belief should be viewed as a religious versus ethical/moral case involving different standards of burden. For example, in appeals, the chaplain recommendation is either that the request appears to be religious or moral/conscience in nature, the vaccination does or does not constitute a substantial burden, more information should be requested before further chaplain analysis, or further group discussion is requested.

11. The Religious Resolution Team reviews the package (i.e., written request and other submitted endorsements/letters, chaplain memorandum, medical provider memorandum, unit commander memorandum, and any other pertinent information) and provides a written recommendation from the team, including dissenting views of any members of the team. If

[12] AFI 48-110_IP, paragraph 2-6.(b)(3)(a)(2).
[13] DAFI 52-201, Attachment 5.

necessary to making a recommendation, the team may request additional information. Separately, a written legal review for the package is provided.

12. The package is then routed through each commander in the chain of command, from the unit commander up to the approval authority, with each commander providing an endorsement with a recommendation to approve or disapprove the request. "Endorsements must address if there is a compelling government interest and any effect the accommodation will have on readiness, unit cohesion, good order and discipline, health, or safety, and impact on the duties of the member. . . . The endorsement must also address whether less restrictive means can be used to meet the government's compelling government interest."[14]

13. Depending on the chain of command for a specific service member, the commanders endorsing a request may include a squadron command, group command, wing command/delta commander,[15] Numbered Air Force commander,[16] and MAJCOM/FIELDCOM/DRU/FOA commander. In addition, as the package is routed through the chain of command, Religious Resolution Teams at the MAJCOM (or equivalent) level also review the package and advise the commander. The MAJCOM (or equivalent) commander is the final approval authority.

14. A religious accommodation request where the policy, practice or duty in question substantially burdens a sincerely held religious belief will be approved unless there is a compelling government interest and the policy, practice or duty causing the substantial burden is the least restrictive means to achieve the compelling governmental interest.[17] "Using the least restrictive means necessary may include partial approval, approval with specified conditions, or

[14] DAFI 52-201, paragraph 6.6.1.5.
[15] A Delta is the Space Force equivalent of an Air Force Wing.
[16] A Numbered Air Force is a level of command directly under a MAJCOM with other organizational units, such as Wings, Groups, and Squadrons assigned as subordinate units.
[17] DAFI 52-201, paragraph 2.4; DoDI 1300.17, paragraph 1.2.(e)(2).

other means that are less burdensome on the member's religious beliefs."[18] An accommodation request based on the government substantially burdening a sincerely held belief based on conscience or moral principle (as opposed to religious beliefs) is not evaluated under the compelling government interest standard; in these cases, the needs of the member are balanced against the needs of mission accomplishment.[19]

15. Requests for religious accommodation from an immunization requirement made by an active duty service member within the continental United States should be reviewed with final action and notification to the member within thirty business days from the date the service member submitted the request. For requests from a member outside the continental United States or reserve component service members, the timeline is extended to 60 business days.[20] If there is a large influx of religious accommodation requests, these timelines may not be met. However, even if the timelines are not met, a service member is temporarily exempted from the relevant immunization requirement while their religious accommodation request is pending.[21] The temporary exemption applies to both the approval process and any appeal from a denial, if applicable. No administrative or disciplinary action is to be taken for failure to comply with the vaccination requirement during that exemption period.

16. If the final approval authority approves a religious accommodation request, a written approval is provided to the member's servicing Force Support Squadron to include in the member's electronic personnel record. The member's unit commander will inform the member of the approved request. If a request is disapproved, the member may elect to appeal the request

[18] DAFI 52-201, paragraph 2.4.
[19] DoDI 1300.17, paragraph 1.2.d. Para. 2.2.b directs the services to establish regulations and policies addressing conscience and moral principles ("Accommodation of practices reflecting a Service member's sincerely held conscience or moral principles will be governed by the policies of the DoD Component concerned."); DAFI 52-201, paragraph 2.5 describes that policy.
[20] DAFI 52-201, Table 2.1; DoDI 1300.17, Table 1.
[21] DAFI 52-201, paragraph 2.12.

to each level of command and ultimately to the final appeal authority, the Air Force Surgeon General.[22] An appeal must be submitted within five (5) calendar days of receiving notification of the disapproval.[23] To file an appeal, the member addresses the appeal memorandum to the appeal authority and provides a copy to the unit commander. The unit commander will provide the request to both the prior approval authority and the appeal authority.[24] An appeal should be resolved within 30 business days following the member's written notification of intent to appeal.[25] As noted, if the timeline is not met the service member continues to be exempt from the immunization requirement, and no administrative or disciplinary action is to be taken for failure to comply with the vaccination requirement during that exemption period.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

STREETT.MATTHEW.JAMES.1147844570 Digitally signed by STREETT.MATTHEW.JAMES.1147844570 Date: 2022.03.08 11:15:45 -05'00'

MATTHEW J. STREETT, Maj, USAF
Staff Chaplain

Attachments:
1. DoDI 1300.17, *Reli ious i ert in the Militar Services*, dated 1 September 2020
2. DAFI 52-201, *Reli ious reedom in the epartment of the Air orce*, dated 23 June 2021
3. Air Force Policy Directive (AFPD) 52-2, *Accommodation of Reli ious Practices in the Air orce*, dated 28 July 2020

[22] DAFI 52-201, paragraph 5.8.1. While the DAFI discusses appealing to the next higher decision authority, absent a delegation of approval authority from the MAJCOM to a lower level, in this case the next higher authority for immunization requirements is the Air Force Surgeon General with no intermediate appeal authority.
[23] Secretary of the Air Force Memo, *Supplemental oronavirus isease accination Polic* , dated December 7, 2021.
[24] DAFI 52-201, paragraph 5.8.2. – 5.8.3.
[25] DAFI 52-201, paragraph 5.8.4.

Exhibit 13

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
CINCINNATI DIVISION

HUNTER DOSTER, *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	No. 1:22-cv-00084
	)	
FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	
	)	

DECLARATION OF COLONEL ELI A ETH M. HERNANDE

I, Elizabeth M. Hernandez, hereby state and declare as follows:

1. I am a Colonel in the United States Air Force currently assigned as the Chief of the Military Justice Law and Policy Division in the Military Justice and Discipline Directorate at Joint Base Andrews, Maryland. I have been in this position since July 2021. As a part of my duties, I am responsible for providing counsel on military justice matters to senior leaders, as well as guidance on military justice policy and processes to legal offices at every level of command. The Division also represents the Air Force on the Joint Service Committee on Military Justice: an inter-agency, joint body dedicated to ensuring the Manual for Courts-Martial and Uniform Code of Military Justice constitute a comprehensive body of criminal law and procedure.

2. I make this declaration in my official capacity as the Chief of the Military Justice Law and Policy Division and based upon my personal knowledge and upon information that has been provided to me in the course of my official duties.

3. Department of the Air Force commanders approach every instance of a military member's refusal to obey a lawful order to receive the COVID-19 vaccination on a case-by-case basis. This is the same as it would be for allegations of misconduct or issues in work performance. In the case of COVID-19 vaccine refusals, the Secretary of the Air Force withheld authority to take action in order to ensure consistency and uniformity in disposition. Accordingly, before any administrative or disciplinary action can be taken based on a COVID-19 vaccine refusal, the case must be reviewed by a Colonel (O-6) with special court-martial convening authority, or higher.

4. If the member has failed to obey a lawful order, disciplinary action may be appropriate. Each commander must look at all the facts and circumstances and evaluate each case individually to determine the appropriate disposition. Generally, more minor misconduct should be addressed at the lowest possible level, as soon as possible, to ensure a service member's career is not negatively affected unnecessarily. More serious misconduct is typically addressed by more serious disciplinary action.

5. Potential dispositions for failing to obey a lawful order to receive the COVID-19 vaccination include adverse administrative actions, non-judicial punishment, administrative demotions, administrative discharges, and courts-martial. Each action follows its own timeline, specific to the needs of the Department of the Air Force, the member, and the commander.

6. Administrative actions are non-punitive tools, intended to improve, correct, and instruct service members who violate established Department of Air Force standards.[1] These actions include, from least severe to most severe: Records of Individual Counseling, Letters of Counseling, Letters of Admonishment, and Letters of Reprimand. Each of these actions are

[1] Air Force Instruction (AFI) 36-2907, *Adverse Administrative Actions*, dated May 22, 2020 (certified current January 15, 2021).

administered in a manner to protect the service member's due process rights. These protections include an ability to consult with a free defense counsel, provide a response, and provide other relevant information to the issuing authority. If the administrative paperwork is filed in the service member's Personnel information file or Unfavorable Information File, the service member may appeal to the issuing authority or a superior authority for removal. There is no available data on the average processing time for these actions, but normally, the process could be expected to take anywhere from two to three weeks.

7. Non-judicial punishment provides commanders with a means of maintaining good order and discipline. It is intended to promote positive behavior changes in service members without subjecting the service member to a criminal (i.e., court-martial) conviction. This type of action has significant due process protections and an appeal process. As always, the service member has access to free defense counsel services to assist in responding to these actions. For calendar year 2021, the average processing time for cases involving service members on Active Duty was 60 days. The average processing time for cases involving Reserve service members was 173 days.

8. Adverse administrative action (e.g., Letter of Reprimand), Non-Judicial Punishment, or Courts-martial conviction may be placed in an Unfavorable Information File (UIF). Depending on the rank of the service member and the type of action, placing the document in the UIF may be mandatory in accordance with AFI 36-2907. The UIF is an official record of unfavorable information about an individual. It documents administrative, judicial, and nonjudicial actions.

9. An administrative demotion is a quality force management tool available to Department of the Air Force commanders to help ensure a quality enlisted force. This process does not apply to commissioned officers. Administrative demotions are intended to place service members at a

rank commensurate with their skill level and ability; they are not intended to be punitive. The process starts when the service member's immediate commander notifies the service member of a recommendation for demotion. The service member has an opportunity to access free defense services and respond to the demotion recommendation before it goes to the demotion authority (a commander senior to the initiating commander) for decision. The service member can appeal the demotion authority's decision to the commander senior to the demotion authority. There is no available data on the average processing time for these actions.

10. Administrative discharges are appropriate when a service member does not show potential for further service. In the case of a refusal to comply with the COVID-19 vaccination mandate, absent an exemption, regular service members will be subject to initiation of administrative discharge proceedings. The characterization of an administrative discharge is dependent upon many factors, to include duty performance, prior misconduct, and basis of the discharge. Although there are different processes for enlisted and officer members, the service characterizations and bases for discharge are generally the same. The process starts when the service member's immediate commander notifies the service member of a recommendation for administrative discharge. The service member has an opportunity to access free defense services and respond before the discharge recommendation goes to the separation authority, often the senior commander in the unit (O-6/Colonel) for decision. Depending on the characterization of the service separation, the decision may move to a higher level review (General Officer). Additionally, depending on the service member's time in service, they may be entitled to a formal administrative hearing before a decision is made regarding their discharge from the service. For calendar year 2021, the average discharge processing time for cases involving Active Duty enlisted members not entitled to a board was 38 days. The average discharge

processing time for cases involving Reserve enlisted members not entitled to a board is longer than that of Active Duty cases. For both Active Duty and Reserve enlisted members entitled to a board, the average discharge processing time is longer than that of non-board cases. Finally, the average discharge processing time for all forms of officer discharges is longer than that of enlisted discharge cases.

11. In the case of a refusal to comply with the COVID-19 vaccination mandate, absent an exemption, the Secretary of the Air Force has mandated Traditional Reservists and Individual Mobilization Augmentees will be placed in a no pay/no points status and involuntarily reassigned to the Individual Ready Reserve (IRR). Similarly, Active Guard and Reserve (AGR) members who refuse to comply with the COVID-19 vaccination mandate, absent an exemption, will have their AGR tour curtailed and involuntarily reassigned to the IRR. Reassigning a member to the IRR is not a discharge or separation. Currently, there is no policy mandating administrative separation for Traditional Reservists, Individual Mobilization Augmentees, or AGR members.

12. A court-martial is a criminal trial for military members and is reserved for serious criminal offenses. There are three levels of courts-martial – general, special, and summary. If a service member were to face a court-martial for failing to obey a lawful order, the service member would be able to challenge the lawfulness of the order during the proceedings.

13. Possible sentences in a court-martial include confinement, reduction in grade (enlisted only), and punitive discharges. For enlisted members, punitive discharges include bad conduct or dishonorable discharges. For commissioned officers, the punitive discharge available is a dismissal (the equivalent of a dishonorable discharge). Punitive discharges are adjudged in cases where a service member has committed serious misconduct.

14. A service member who receives a punitive discharge and/or at least two years of confinement automatically receives appellate review of the conviction and/or sentence by the Air Force Court of Criminal Appeals. If the service member does not receive a punitive discharge and/or at least two years of confinement, the service member receives appellate review of the conviction and/or sentence by the Office of The Judge Advocate General of the Air Force. For calendar year 2021, the average processing time from offense to trial for a special court-martial was 270 days. For calendar year 2021, the average processing time from offense to trial for a general court-martial was 526 days.

15. Air Force Review Boards Agency (AFRBA) is responsible for the adjudication of military personnel matters through a number of statutory and secretarial boards. There are two subsets of the AFRBA. First, the Secretary of the Air Force Personnel Council (SAFPC) acts for, recommends to, and announces decisions on behalf of the Secretary of the Air Force for a variety of military personnel issues. SAFPC is comprised of five boards, one of which is the Air Force Discharge Review Board (AFDRB), which has discretionary authority to review administrative discharges. A service member who received an administrative discharge or a bad conduct discharge from a special court-martial may appeal the characterization of the discharge to the AFDRB. The AFDRB estimates a records review decision will take six to 12 months to process.

16. A second subset of the AFRBA includes the Air Force Board for Correction of Military Records (AFBCMR), which is a statutory board of civilians considering applications for correction of military records submitted by Air Force members, former Air Force members, or persons with a proper interest in the correction of a person s military record. The AFBCMR is the highest level of administrative review within the Department of the Air Force. Its decisions

are final and binding on all Department of Air Force officials and other government agencies. The AFBCMR determines whether the service member has demonstrated the existence of a material error or injustice that can be remedied effectively through correction of the applicant's military record and, if so, what corrections are needed to provide full and effective relief. Prior to applying to the AFBCMR, a service member must exhaust all other available administrative remedies. This means any service member seeking relief from an administrative discharge or a bad conduct discharge from a special court-martial first must have applied to the AFDRB and been denied relief. Service members with punitive discharges from a general court-martial may apply directly to the AFBCMR. Administrative applications take about three months to complete. Cases involving formal AFBCMR consideration take an average of 12 months.

17. Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

HERNANDEZ.ELIZABETH.MARIE.1279606660
Digitally signed by HERNANDEZ.ELIZABETH.MARIE.1279606660
Date: 2022.03.08 11:08:40 -05'00'

ELIZABETH M. HERNANDEZ, Colonel, USAF
Chief, Military Justice Law and Policy Division

Attachment:
AFI 36-2907, *Adverse Administrative Actions*, dated May 22, 2020 (certified current January 15, 2021).

Exhibit 14

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
CINCINNATI DIVISION

HUNTER DOSTER, *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	No. 1:22-cv-00084
	)	
FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	
	)	

DECLARATION OF LIEUTENANT COLONEL ETHEL M. ATSON

I, Ethel M. Watson, hereby state and declare as follows:

1. I am a Lieutenant Colonel in the United States Air Force currently assigned as the Chief, Force Support Policy at the Department of the Air Force Directorate of Personnel Policy for the Director of Personnel, Air Force Reserve (REP). I have been in this position since December 2020. As a part of my duties, I am responsible for liaising with the Air Force and Air Force Reserve Personnel Centers on military readiness programs. As an REP officer, I serve as the focal point for developing and interpreting both policy and guidance for Air Force Reserve (AFR) military readiness programs.

2. I have reviewed the allegations set forth in the pleadings filed in this matter. I make this declaration in my official capacity as the Chief, Force Support Policy and based upon my personal knowledge and upon information that has been provided to me in the course of my official duties.

3. On August 24, 2021, the Secretary of Defense issued a mandate for all members of the Armed Forces on active duty or in the Ready Reserve to immediately begin full vaccination

against Coronavirus Disease 2019 (COVID-19). Thereafter, the Secretary of the Air Force provided additional mandatory vaccination guidance for Department of the Air Force (DAF) commanders that they take all steps necessary to ensure all uniformed service members receive the COVID-19 vaccine, which included issuing unit-wide and individual orders to their Ready Reserve members to become fully vaccinated no later than December 2, 2021 (Secretary of the Air Force Mem., Sept. 3, 2021, Mandatory Coronavirus Disease 19 Vaccine of Department of the Air Force Military Members).

4. Since the Secretary of the Air Force's initial mandatory vaccination order, the Chief of Air Force Reserve, who also serves as the Commander, Air Force Reserve Command, began developing guidance to enable compliance for Reserve members serving in both full-time and part-time reserve categories. In instances where Reserve specific guidance was necessary, implementation guidance has been issued separately and is available to all Reserve members at https://www.afrc.af.mil/COVID-19/.

5. Additionally, on December 7, 2021, the Secretary of the Air Force issued a memorandum, "*Supplemental oronavirus isease accination Polic* ." The memorandum established specific policy and provided guidance applicable to regular Air Force and Space Force members, Air Force Reserve (AFR) and Air National Guard (ANG) members. The memorandum included supplemental guidance concerning those who requested separation or retirement prior to November 2, 2021, whose request for medical, religious or administrative exemption from the COVID-19 vaccination requirement is denied, and those who refuse to take the COVID-19 vaccine.

6. Additional separation and retirement guidance was provided for members of the Air Force Reserve. Effective December 2, 2021, all Air Force Reserve members were required to fall into one of the following categories to comply with the vaccination mandate:

a. Completed a vaccination regimen.

b. Have requested or received a medical exemption.

c. Have requested or received a religious accommodation request.

d. Have requested or received an administrative exemption.

7. Unvaccinated members who request a medical exemption or a religious accommodation request will be temporarily exempt from the COVID-19 vaccination requirement while their exemption request is under review. For those members who have declined to be vaccinated, or have not otherwise complied with the guidance above, they are potentially in violation of the Uniform Code of Military Justice (UCMJ) by refusing to obey a lawful order.

8. Traditional Reservists who fail to be vaccinated, have not submitted an exemption request, or have not been granted an exemption will be placed in a no pay/no points status and involuntarily reassigned to the Individual Ready Reserve (IRR). The IRR is part of the Ready Reserve of the Armed Forces Reserve Component and is composed of former active-duty, national guard, and reserve military personnel, who, though not actively participating in the military, are still affiliated with the Reserve Component. Placing a member in a no pay/no points status means that the member will not be drilling with the member's unit and thus will not be earning pay for that work or credit toward retirement.

9. Members whose medical exemption or religious accommodation request is denied have five (5) calendar days from receipt of their denial to do one of the following:

a. Begin a COVID-19 vaccination regimen, or

b. If the member submitted a medical exemption request, request a second medical opinion, or

c. If the member submitted a religious accommodation request, submit an appeal to the final appeal authority (the Air Force Surgeon General).

10. If a final appeal is denied, the member will have five (5) calendar days from notice of denial to begin the COVID-19 vaccination regimen.

11. If the member's appeal is denied, and the member continues to refuse to take the COVID-19 vaccine, they may be subject to adverse administrative action, such as the placement of a Letter of Reprimand in their personnel file or their actions may be punishable under the UCMJ. They will also be involuntarily reassigned to the Individual Ready Reserve (IRR).

12. Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

WATSON.ETHEL.M.1013814330 Digitally signed by WATSON.ETHEL.M.1013814330 Date: 2022.03.08 12:30:34 -05'00'

ETHEL M. WATSON, Lt Col, USAF
Chief, Force Support Policy

Attachment:

Secretary of the Air Force Memorandum, *Supplemental oronavirus isease accination Polic* , dated 7 December 2021

Exhibit 15

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
CINCINNATI DIVISION

HUNTER DOSTER, *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	No. 1:22-cv-00084
	)	
FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	
	)	

DECLARATION OF LIEUTENANT COLONEL NE ITHA M. LITTLE

I, Nekitha M. Little, hereby state and declare as follows:

1. I am a Lieutenant Colonel in the United States Air Force currently assigned as the Deputy Division Chief, Military Compensation Policy, Force Management for Military Personnel (A1P). I have been in this position since approximately August 1, 2019. As a part of my duties, I am responsible for developing and interpreting policy related to military pay and compensation guidance, which includes leave policy, to ensure consistency with Congressional statutes and the Office of the Secretary of Defense and Department of the Air Force Instructions, enhance the Air Force mission, and improve the quality of life for Airmen and Guardians.

2. I make this declaration in my official capacity as the Deputy Division Chief, Military Compensation Policy, and based upon my personal knowledge and upon information that has been provided to me in the course of my official duties.

3. After the Secretary of Defense mandated the COVID-19 vaccine for all service members, the Department of the Air Force developed and promulgated a departmental-wide

implementation guide, which included guidance on administrative exemptions available. The Air Force has granted administrative exemptions to certain service members on terminal leave because the members do not normally return to duty when terminal leave begins. The Air Force has decided to grant administrative exemptions for members on terminal leave because it has assessed that its interest in military readiness and mission accomplishment is not served by requiring members to be vaccinated when they are no longer anticipated to return to duty.

4. "Terminal leave" is considered a valid administrative exemption to the vaccine mandate. I am familiar with this terminal leave policy as it falls within the scope of my professional duties. In accordance with Air Force Guidance Memorandum to Department of Air Force Instruction 36-3003, *Militar eave Pro ram*, dated April 7, 2021, terminal leave is defined as "…chargeable leave taken in conjunction with retirement or separation from active duty. Member's last day of leave coincides with the last day of active duty." Terminal leave is not automatic, and members must request the leave from their unit commanders via the LeaveWeb system, which is the system of record for all leave requests. Once a member is on terminal leave, they are no longer considered on active duty, hence the acceptance of this as an administrative exemption as referenced in 48-110, Immunizations and Chemoprophylaxis for the Prevention of Infectious Diseases, 16 February 2018.

5. Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

LITTLE.NEKITHA.M.1103890892 Digitally signed by LITTLE.NEKITHA.M.1103890892 Date: 2022.03.08 22:34:05 -05'00'

NEKITHA M. LITTLE, Lt Col, USAF
Deputy Division Chief
Military Compensation Policy

Attachment:

AFI 36-3003, paragraph 1.2.5.3

Exhibit 16

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
CINCINNATI DIVISION

HUNTER DOSTER, *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	No. 1:22-cv-00084
	)	
FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	
	)	

DECLARATION OF COLONEL JAMES R. OEL

I, James R. Poel, hereby state and declare as follows:

1. I am a Colonel in the United States Air Force currently assigned as the Chief of Public Health at the Air Force Medical Readiness Agency (AFMRA). I have been in this position since July 31, 2018. As a part of my duties, I am responsible for developing and directing Department of the Air Force (DAF) Public Health and Preventive Medicine policy, directing accessions and assignments for DAF Public Health Officers, and advising the DAF Surgeon General on Public Health matters.[1] I also develop DAF policy for force health protection, immunization recommendations and community health programs to ensure they are consistent with national medical standards and guidelines, improve the health of Airmen and Guardians, and enhance the mission.

[1] The Department of the Air Force includes the U.S. Air Force (including the Air National Guard and the Air Force Reserve) and the U.S. Space Force.

2. I make this declaration in my official capacity as the Chief of Public Health and based upon my personal knowledge and upon information that has been provided to me in the course of my official duties.

3. The Air Force depends on healthy personnel to complete its mission to "fly, fight and win . . . airpower anytime, anywhere."[2] When service members become ill, are hospitalized, or die from an infectious disease, they are unable to fulfill their role in achieving the Air Force's mission. Just as important, an infected service member can spread disease to other service members, further undermining the Air Force's ability to accomplish its mission. Any treatment of infected service members impacts the Air Force's ability to meet the medical needs of other service members. The Air Force relies on its vaccine program to protect service members from potential health risks, including infectious disease threats.

4. The Air Force requires vaccination because vaccines are the most effective way of mitigating the risk of spreading infectious diseases to other members, both in non-deployed and deployed environments, and preventing service members from becoming ill and dying. Vaccination has been ranked among the top 10 "Great Public Health Achievements" since 1900[3,4] and has dramatically decreased the number of infectious diseases world-wide over the last century. The main causes of death in the early 1900s were infectious diseases.[5] However,

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[2] U.S. Air Force, *Air orce unveils new mission statement* (Apr. 8, 2021), https://www.af.mil/News/Article-Display/Article/2565837/air-force-unveils-new-mission-statement/. "Airmen work to support all aspects of airpower, which includes five core missions: air superiority; global strike; rapid global mobility; intelligence, surveillance and reconnaissance; and command and control." *Id.*

[3] Centers for Disease Control and Prevention (CDC), *en reat Pu lic Health Achievements United States*, Morbidity and Mortality Weekly Report (MMWR), Vol. 48 (12), pages 241–243 (Apr. 2, 1999), *availa le at* https://www.cdc.gov/mmwr/pdf/wk/mm4812.pdf.

[4] CDC, *en reat Pu lic Health Achievements United States*, Morbidity and Mortality Weekly Report, (MMWR), Vol. 60 (19), pages 619–623 (May 20, 2011), *availa le at* https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6019a5.htm.

[5] CDC, *Achievements in Pu lic Health ontrol of Infectious iseases*, MMWR, Vol. 48(29), pages 621-629 (July 30, 1999), *availa le at* https://www.cdc.gov/mmwr/preview/mmwrhtml/mm4829a1.htm.

since the introduction of vaccines, many previously deadly diseases are rarely seen today. Cases of measles and polio, for example, have been dramatically reduced by 80–99%.[6,7] But these diseases have not been entirely eradicated, so continued vaccination is necessary. For example, 159 cases of measles were reported in the United States over an eight month period in 2013, and 11% of those cases required hospitalization. The majority of those cases were unvaccinated individuals (82%).[8] Vaccines are therefore crucial to keeping diseases at bay. As the number of unvaccinated people increases, the risk of resurgence of such diseases and their associated morbidity and mortality, increases.

5. Vaccines prevent infectious disease and have long been a cornerstone of military strategy. Disease and non-battle injury have historically been a greater threat to military personnel than battle injuries. There are numerous examples where the use of vaccines has enhanced the U.S. military mission by drastically curtailing morbidity and mortality among U.S. military personnel.[9, 10] "Influenza vaccine development was a high priority for the U.S. military after the deaths of approximately 1 in every 67 soldiers from influenza during the 1918-1919 pandemic."[11] The first influenza vaccine was first adopted for use by the Army in 1943, but out of fear for a winter outbreak of influenza, the Army directed influenza vaccination for all Army personnel on September 3, 1945.[12] Today, all active duty and reserve component personnel are

[6] World Health Organization (WHO), *acts on Polio radication* (Apr. 1, 2017), https://www.who.int/news-room/photo-story/photo-story-detail/10-facts-on-polio-eradication.
[7] Centers for Disease Control and Prevention (CDC), *Measles ata and Statistics* (Apr. 16, 2019), https://www.cdc.gov/measles/downloads/measlesdataandstatsslideset.pdf.
[8] CDC, *Measles United States Januar Au ust* , MMWR, Vol. 62(36), pages 741-43 (Sept. 13, 2013), https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6236a2.htm.
[9] Gaberstein J, Pittman P, Greenwood J, Engler R, Immunization to Protect the US Armed Forces: Heritage, Current Practice and Prospects. *pidemiolo ic Reviews*, Vol 28, 2006, pgs. 3-26.
[10] Lemon S, Thaul S, Fisseha S, O'Maonaigh H, editors, Protecting Our Forces: Improving Vaccine Acquisition and Availability in the US Military, National Academies Press, 2002.
[11] College of Physicians of Philadelphia; The History of Vaccines: Influenza, https://www.historyofvaccines.org/content/articles/influenza; last updated 25 Jan 2018.
[12] War Department Circular No. 267, Influenza – Vaccination of Army Personnel 5 September 1945.

required to receive the annual seasonal influenza immunization or obtain an exemption. AFI 48-110, 4–7(a). Although the efficacy of the influenza immunization is typically less than 50%[13], the Department of Defense continues to require the immunization in order to minimize the potential impact to military operations.

6. Vaccines are vital to ensuring the health and safety of the force, maintaining mission readiness, and essential to protecting the individual from infectious diseases and preventing transmission to other military members with whom he or she interacts. This is even more important for those military duties and positions, like the plaintiff's, which require interaction with others in close quarters or travel, whether to an austere, deployed setting or for training at another location in the US.

7. Vaccinations are also important in providing protection for Service members who are unable to receive one or more vaccines due to medical issues. Those issues can be temporary (e.g., during pregnancy) or permanent (e.g., allergic or severe adverse reaction to ingredients in a vaccine).[14] Medical exemptions are provided in those situations. Maximizing vaccinations within the Air Force for those medically able helps protect those that cannot otherwise receive the vaccine. The greater the number of required medical exemptions, the more important maximizing vaccinations becomes.

8. Other medical means of accommodating a request for an exemption from the COVID-19 vaccine would not be as effective and would hinder the Air Force mission. Evaluating his request entails evaluating whether practices, other than immunizations, to reduce the member's

[13] CDC, Past Seasons Vaccine Effectiveness Estimates, last updated 26 Apr 2021, https://www.cdc.gov/flu/vaccines-work/past-seasons-estimates.html

[14] The Department of the Air Force only granted temporary medical exemptions from the COVID-19 vaccine. This allows individuals who have a temporary medical condition (e.g., pregnancy) to get vaccinated after that temporary condition has resolved. This also allows the Air Force to reassess individuals with allergies or severe adverse reactions to determine whether a vaccine has been approved with constituents the member can safely take.

risk of infectious diseases and transmission can would be as effective as if he were fully immunized. Unfortunately, short of fully isolating the member from any contact with others both on the job and off – which is not practicable – I am not aware of any way to reduce the risks of contracting, transmitting, and physically combatting COVID-19 to the same level as if he were fully immunized.

9. Vaccinated members clear the virus faster and therefore are contagious for fewer days than those unvaccinated.[15,16,17] Transmission of COVID-19 can occur in vaccinated individuals,[18] but vaccinated individuals are much less likely to develop severe disease, be hospitalized, or die.[19,20] With the Delta variant (which was the primary variant in the United States when Air Force Officer's request was denied), fully-vaccinated individuals had a 5-fold decreased risk of infection, a 13-fold decreased risk of hospitalization, and a 14-fold decreased risk of death compared to unvaccinated individuals.[21] Early studies from South Africa of vaccine effectiveness against the Omicron variant indicated the Pfizer vaccine was effective,

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[15] Singanayagam, A., et al., Community transmission and viral load kinetics of the SARS-CoV-2 delta (B. 1.617. 2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study," *he ancet Infectious iseases* (2021).

[16] Chia, PY., et al., "Virological and serological kinetics of SARS-CoV-2 delta variant vaccine-breakthrough infections: a multi-center cohort study," *medR iv* 2021 (July 31,2021), https://doi.org/10.1101/2021.07.28.21261295 (preprint).

[17] Kissler, SM., et al., "Viral Dynamics of SARS-CoV-2 Variants in Vaccinated and Unvaccinated Individuals," *medR iv* 2021 (Aug. 25, 2021), https://doi.org/10.1101/2021.02.16.21251535.

[18] One study found that the infection rate among vaccinated people from a family member or roommate infected with the Delta variant was 25% with prolonged, close contacts. *See* Singanayagam, Anika, et al., "Community transmission and viral load kinetics of the SARS-CoV-2 delta (B. 1.617. 2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study," *he ancet Infectious iseases* (2021).

[19] CDC, *he Possi ilit of O I After accination Breakthrou h Infections* (Nov. 9, 2021), https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness/why-measure-effectiveness/breakthrough-cases.html

[20] Tenforde, Mark W., et al., "Association Between mRNA Vaccination and COVID-19 Hospitalization and Disease Severity," *JAMA* (2021).

[21] Two websites, https://covid.cdc.gov/covid-data-tracker/#rates-by-vaccine-status and https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination, provide updated data regarding the effectiveness of vaccination against a) testing positive, b) being hospitalized, and c) dying from COVID-19. The data analyzed is from April through November 2021 and thus addresses vaccine efficacy during the Fall 2021 Delta variant wave.

although at a reduced level, against hospital admissions for COVID-19.[22] Similarly, the United Kingdom Security Agency published a recent technical report, indicating reduced efficacy against symptomatic disease from the Omicron variant after 2 doses of Pfizer or Moderna COVID-19 vaccines; however, vaccine efficacy increased to levels comparable to the Delta variant effectiveness after a third or booster dose.[23] Protection against hospitalization is much greater, in particular after a booster dose. In summary, a fully vaccinated service member is less likely to contract COVID-19 than an unvaccinated Service member and, if infected, is more likely to recover quicker and get back to the fight, minimizing the impact to mission accomplishment.

10. I have reviewed the declaration of Colonel Tonya Rans, dated March 6, 2022, regarding the effectiveness of the COVID-19 vaccine. My understanding of the effectiveness of the COVID-19 vaccine comports with the information in Colonel Rans's declaration.

Masks

11. Masking is a critical public health measure for preventing the spread of respiratory diseases, like COVID-19. However, while wearing a mask may decrease transmission of some diseases, such as COVID-19, masking is not as effective as vaccination. The effectiveness of face masks depends upon the behavior of the wearer. Face masks are less effective if they are not tight fitting, not double layered, worn only around the mouth, taken off frequently, and adjusted frequently increasing hand/finger contact with one's face.

12. Cloth face coverings and surgical masks provide source control (reduction of virus shed by someone infected) and personal protection (filtering out of virus for the mask wearer) against

[22] Collie, S, et al, Effectiveness of BNT162b2 Vaccine against Omicron Variant in South Africa, New England Journal of Medicine, DOI: 10.1056/NEJMc2119270; 29 Dec 2021.
[23] United Kingdom Health Security Agency, (UKHSA) SARS-CoV-2 variants of concern and variants under investigation in England, Technical briefing 34, pages 1-36, Publishing Reference: GOV-10924 (14 Jan 2022).

small inhalable infectious particles. The Centers of Disease Control and Prevention (CDC) recently updated mask guidance by (a) clarifying that people can choose respirators such as N95s and KN95s, (b) removing concerns related to supply shortages for N95s, (c) clarifying that the "surgical N95s" are reserved for healthcare settings, and (d) some types of masks and respirators provide more protection than others.[24] Regarding types of masks to use, the CDC explained that N95 and KN95 masks work better than cloth masks which are better than no masks. They acknowledged human behavior limits the effectiveness of masks when they are not worn consistently and correctly and recommended wearing a mask with the best fit, protection, and for comfort for the individual. As source control, consistent and correct wear of multiple-layered cloth masks filter out 50–70% of viral particles and limit the distance of spread for the remaining virus. For the wearer, consistent and correct wear of a multiple-layered cloth mask can filter out up to 50% of viral particles. When near others, many people do not constantly wear their mask and when wearing it, many do not wear a clean (or new) mask daily with a snug fit (no gaps) over the mouth and nose. Even when worn consistently and correctly, extended durations in close contact with an infectious person can still lead to transmission. Data suggest that consistent, correct mask wear decreases COVID-19 incidence by 10–79%,[25] but typical use in the general population is not nearly this effective. Mask mandates only decrease transmission by 2–29% and mortality by 45.7%.[26]

[24] CDC, Types of Masks and Respirators, https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/types-of-masks.html.
[25] CDC, *Science Brief ommunit Use of Masks to ontrol the Spread of SARS o* (Dec. 6, 2021), https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/masking-science-sars-cov2.html.
[26] Talic S, et al., Effectiveness of Public Health Measures in Reducing the Incidence of COVID-19, SARS-CoV Transmission, and COVID-19 Mortality: Systematic Review and Meta-Analysis. *British Medical Journal* 2021; 375: e068302. https://www.bmj.com/content/375/bmj-2021-068302

13. If two individuals in an indoor environment are wearing a typical cloth mask, the receiver's time to an infectious dose increases by minutes. If both people are wearing a surgical mask, the time to receive an infectious dose increases to an hour. If both people are wearing a non-fit-tested N-95, the time to an infectious dose increases to over 6 hours.[27] The protection provided, however, varies based on human behavior – type of mask worn, how the mask is worn, in what settings it is worn, etc. Accordingly, mask wear is a supplement to, but not an effective substitute for, vaccination.

14. Additionally, masks are limited to controlling the spread of the virus. Masks provide no protection to a service member who is infected with COVID-19. Unlike vaccination, a mask does not decrease the risk of serious illness, complications (e.g., hospitalization, long COVID), or death, and does not shorten recovery time.

Temperature Checks & Testing

15. Checking a service member's temperature alone to screen for COVID-19 is not an adequate screening tool for several reasons. Temperature checks only identify if a service member has a fever; they do not identify if a member is infected with SARS-CoV-2. A fever is a symptom of many illnesses or conditions, including influenza, common cold, injury, side effect from medication, or over exertion. Additionally, an individual infected with COVID-19 may be asymptomatic or not have fever as one of their symptoms. Finally, non-contact thermometers and thermal cameras may not provide an accurate reading of the individual's core body

[27] Brosseau, LM., et al., *ommentar hat an Masks o Part he Science Behind O I Protection* (Oct. 14, 2021), https://www.cidrap.umn.edu/news-perspective/2021/10/commentary-what-can-masks-do-part-1-science-behind-covid-19-protection.

temperature, have not been accurate when evaluating multiple people over time, or have mixed results when used to reduce the spread of disease a points of entry to countries.[28, 29]

16. Two primary tests are used to detect infection with SARS-CoV-2: PCR tests and antigen tests. Each test detects different parts of the virus in different ways and vary by cost, resources required, and speed or turn-around-time of the results. PCR tests are highly sensitive and accurate. However, they are expensive, may take an hour or more from start to finish and must be accomplished by skilled lab technicians in a certified lab. Antigen tests, on the other hand, do not require special skills to complete them, are less expensive and provide results in a quarter of the time required for a PCR test. However, antigen tests may provide less accurate results if not done properly or if the person is in the early stages of COVID-19 and asymptomatic with a small amount of virus in their body.

17. Antigen tests have a 52.5% chance in those asymptomatic and a 76.7% chance in those symptomatic to identify individuals with COVID-19.[30] With twice weekly testing, the sensitivity increased to 76.3% without regard to symptoms, to 83.8% within the first week of symptoms, and 95.8% for those with a high viral load.[31] As most Service members who are using the antigen test for workplace entry or travel will likely be asymptomatic for the required weekly testing (symptomatic service members are more likely to get tested in a medical setting at

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[28] Nuertey, BD, et al *Performance of O I associated s mptoms and temperature checkin as a screenin tool for SARS o infection* PLOS One, (Sep 17, 2021) https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0257450

[29] US Food and Drug Administration, Thermal Imaging Systems (Infrared Thermographic Systems / Thermal Imaging Cameras), (updated 12 Jan 2021) https://www.fda.gov/medical-devices/general-hospital-devices-and-supplies/thermal-imaging-systems-infrared-thermographic-systems-thermal-imaging-cameras

[30] Brummer LE., et al., (2021) Accuracy of Novel Antigen Rapid Diagnostics for SARS-CoV-2: A Living Systematic Review and Meta-Analysis. *P OS Medicine* 18(8): e1003735. https://doi.org/10.1371/journal.pmed.1003735

[31] More frequent antigen testing increases the chance of detecting the optimal amount of virus at the earliest possible moment. For example, if an individual is infected on Sunday, takes an antigen test on Monday, but has an optimal amount of viral antigen on Wednesday, Monday's test will likely be a false negative.

the onset of symptoms with a PCR test), the chance to identify a member that is actually infected is a little better than 50% with a single antigen test.[32]

18. Most instructions for antigen tests direct at least twice a week, serial testing followed by confirmatory testing (PCR test) in case of a positive antigen test. Research indicates testing with an antigen test at least every three days increases the probability of detecting a true positive to a level closer to a weekly PCR test (98.7% accuracy), but detection may not be prior to infectivity. For example, serial antigen testing at least every three days detected true positives with a 95.9% accuracy within a 14-day period from infection. The rate of antigen test detection prior to the first day of infectivity is 37.5%. On the day of peak infectivity viral detection is only 90%.[33]

19. Overall, serial antigen testing of asymptomatic members will detect most infections, but the member will likely be infectious prior to the test becoming positive. Serial testing will curtail the exposure in the unit after the infection is detected, but this is not as effective as preventing the original infection.

20. Additionally, testing can only identify the virus and does not prevent the Service member from becoming infected in the first place. Likewise, temperature checks identify only if a member has a fever and do not prevent a member from becoming infected. As with masking, testing and temperature checks provide no protection for an individual who is already infected and do not reduce the risk of illness, complications (e.g., long COVID, hospitalization), or death.

[32] Brummer LE., et al., Accuracy of Novel Antigen Rapid Diagnostics for SARS-CoV-2: A Living Systematic Review and Meta-Analysis. *P OS Medicine* 18(8): e1003735 (2021); https://doi.org/10.1371/journal.pmed.1003735.

[33] Smith, Rebecca L., et al., "Longitudinal assessment of diagnostic test performance over the course of acute SARS-CoV-2 infection," *medR iv* (2021).

Nor do temperature checks and testing reduce the length of recovery time after infection. As such testing is not an effective substitute for vaccinating service members.

Natural Immunity"

21. While evidence of prior infection is considered adequate documentation for some vaccine requirements such as measles, mumps, rubella, varicella (chickenpox), and hepatitis B virus, there are other vaccine-preventable pathogens where previous infection does not induce life-long sterilizing immunity, and prior infection is not considered an acceptable medical exemption (e.g., influenza, adenovirus).[34] AFI 48-110 recognizes that "for *some* vaccine-preventable diseases, serologic or other tests can be used to identify pre-existing immunity from prior infections or immunizations that may eliminate unnecessary immunizations"[35] (emphasis added), but notes that " h ealth care providers will determine a medical exemption based on the health of the vaccine candidate *and the nature of the immunization under consideration*."[36] (emphasis added)

22. Although COVID-19 disease does provide some degree of natural immunity to SARS-CoV-2 virus, the length and completeness of protection varies. Current evidence has not determined an antibody threshold indicative of protection from re-infection. Nor is there an FDA-authorized or FDA-approved test to assess this. Evidence is also inadequate to associate specific antibody levels with the degree of re-infection risk for an individual.[37] One to ten percent of people do not develop long-lasting (IgG-type) antibodies following confirmed COVID-19 infection (vs. 100% developing antibodies for the mRNA vaccines and 90% for

[34] Defense Health Agency Procedural Instruction, *uidance for the o Influenza accination Pro ram* (Aug. 21, 2020).
[35] AFI 48-110, para. 2-1(g).
[36] AFI 48-110, para. 2-6(a).
[37] CDC, *Science Brief SARS o Infection Induced and accine Induced Immunit* (Oct. 29, 2021), https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/vaccine-induced-immunity.html.

Johnson & Johnson/Janssen).[38, 39] Antibody titers, a measurement of the amount of antibody in a person's blood, peak at 3 to 5 weeks after infection and then begin to wane. Neutralizing antibodies, or antibodies which eliminate a pathogen before an infection takes place, demonstrate approximately a 50% reduction within 2 to 3 months and become undetectable in up to 30% of people within 10 months post-infection.[40] Mild or asymptomatic COVID-19 infections tend to generate lower antibody levels than those with severe disease.[41] Overall, the duration of protection varies depending on disease severity, person's age, antibody assay utilized, and variants of the virus.[42] After infections with the original SARS-CoV-2 strain, detectable neutralizing antibodies were found in 84% of people for the Alpha variant, 68% for the Delta variant, and 55% for the Beta variant.[43]

23. Both natural and vaccine immunity decrease the risk of re-infection. Studies vary on their conclusions regarding whether the infection rate is equivalent, lower, or higher in those fully vaccinated compared to those previously infected. The varying conclusions show there is still a lot that is unknown about the strength, consistency, and duration of protection from prior SARS-CoV-2 infection. In light of these unknowns, the Department of the Air Force has determined the best way to minimize the risk to service members and the Air Force mission is to require vaccination. These studies are not conclusive and it is not prudent to rely on isolated

[38] World Health Organization, *O I Natural Immunit Scientific Brief* (2021), https://apps.who.int/iris/handle/10665/341241.
[39] CDC, *Science Brief SARS o Infection Induced and accine Induced Immunit* (Oct. 29, 2021), https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/vaccine-induced-immunity.html.
[40] CDC, *Science Brief SARS o Infection Induced and accine Induced Immunit* (Oct. 29, 2021), https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/vaccine-induced-immunity.html.
[41] Long, .X., Tang, X.J., Shi, .L., Li, ., Deng, H.J., Yuan, J., Hu, J.L., Xu, W., Zhang, Y., Lv, F.J., et al., Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections, *Nat. Med*. 26, 1200-1204, (2020).
[42] World Health Organization, *O I Natural Immunit Scientific Brief* (2021), https://apps.who.int/iris/handle/10665/341241.
[43] CDC, *Science Brief SARS o Infection Induced and accine Induced Immunit* (Oct. 29, 2021), https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/vaccine-induced-immunity.html.

studies as authoritative. In two studies, prior infection (without subsequent vaccination) was associated with 2.3 times the odds of reinfection and 5.49 times the rate of hospitalization with re-infection compared with being fully vaccinated.[44,45] In contrast, another study showed that at six months from vaccination or infection, the rate of breakthrough or re-infection was 13-fold higher for those vaccinated without prior infection than those with only prior infection,[46] indicating prior infection imparts some additional protection. Similarly, a recent study indicates during the Delta wave, both COVID-19 vaccination and surviving a prior infection provided protection against infection and hospitalization from COVID-19 as case rates and related hospitalizations increased at a lower rate among both vaccinated and unvaccinated persons with prior COVID-19 diagnosis. This study, however, did not include information on the severity of initial infection[47] and does not reflect the risk of morbidity and mortality from COVID-19 infection.[48] Both latter studies, while indicating prior infection impart some protection, show the added benefit of vaccination for those previously infected. Vaccination provides a strong boost in protection for people who have recovered from COVID-19, resulting in a 1.85 to 2.34-fold

[44] Cavanaugh, A. M., Reduced Risk of Reinfection with SARS-CoV-2 After COVID-19 Vaccination Kentucky, May–June 2021, *MM R. Mor idit and Mortalit eekl Report*, 70(32) (Aug. 13, 2021), *availa le at* https://www.cdc.gov/mmwr/volumes/70/wr/mm7032e1.htm.

[45] Bozio CH., et al. Laboratory-Confirmed COVID-19 Among Adults Hospitalized with COVID-19-Like Illness with Infection-Induced or mRNA Vaccine-Induced SARS-CoV-2 Immunity Nine States, January-September 2021, *MM R. Mor idit and Mortalit eekl Report*, 70(44) (Nov. 5, 2021), *availa le at* https://www.cdc.gov/mmwr/volumes/70/wr/mm7044e1.htm.

[46] Gazit S., et al., Comparing SARS-CoV-2 Natural Immunity to Vaccine-Induced Immunity: Reinfections Versus Breakthrough Infections (Aug. 25, 2021), https://doi.org/10.1101/2021.08.24.21262415.

[47] Personnel with more severe infection have a larger antibody response. In a study of SARS-CoV-2 infected individuals, a more severe disease indicated a larger memory B cell response to the SARS-CoV-2 spike protein. Guthmiller JJ, Stovicek O, Wang J, et al. SARS- *o Infection Severit Is inked to Superior Humoral Immunit a ainst the Spike*. mBio. 2021;12(1):e02940-20. Published 2021 Jan 19. doi:10.1128/mBio.02940-20,

[48] Le n TM, Dorabawila V, Nelson L, et al., *O I ases and Hospitalizations O I accination Status and Previous O I ia nosis alifornia and New ork Ma Novem er* MMWR Morb Mortal Wkly Rep. (Jan. 19, 2022), https://www.cdc.gov/mmwr/volumes/71/wr/mm7104e1.htm?s_cid=mm7104e1_w.

decreased risk of re-infection.[49,50,51] Overall, boosting the immune system with a vaccine after infection or initial vaccine series is effective for decreasing the risk of subsequent infection.

Isolation & Social Distancing

24. Effectiveness of social distancing depends on the specific activity being conducted (e.g., sitting quietly vs. yelling orders or speaking loudly in a meeting vs. constant intermingling during a social event, such as a holiday party). A systematic review of physical distancing of at least three feet to prevent SARS-CoV-2 transmission demonstrated a 25% reduction in transmission.[52] Although infections through inhalation at distances greater than three to six feet from an infectious source are less likely than at closer distances, infections even at these distances have been repeatedly documented under certain preventable circumstances.[53,54,55] These transmission events have involved the presence of an infectious person exhaling virus indoors for an extended time (more than 15 minutes and in some cases hours) leading to virus concentrations in the air space sufficient to transmit infections to people more than six feet away, and in some cases to people who have passed through that space soon after the infectious person left.

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[49] Cavanaugh, A. M., Reduced Risk of Reinfection with SARS-CoV-2 After COVID-19 Vaccination Kentucky, May–June 2021. *MM R. Mor idit and Mortalit eekl Report*, (32) (Aug. 13, 2021), *availa le at* https://www.cdc.gov/mmwr/volumes/70/wr/mm7032e1.htm.

[50] Stamatatos L., et al., mRNA Vaccination Boosts Cross-Variant Neutralizing Antibodies Elicited by SARS-CoV-2 Infection, *Science* 372 (6549): at 1413–1418 (Mar. 25, 2021), https://doi.org/10.1126/science.abg9175.

[51] Gazit S., et al., Comparing SARS-CoV-2 Natural Immunity to Vaccine-Induced Immunity: Reinfections Versus Breakthrough Infections (Aug. 25, 2021), https://doi.org/10.1101/2021.08.24.21262415.

[52] Talic S, et al. Effectiveness of Public Health Measures in Reducing the Incidence of COVID-19, SARS-CoV Transmission, and COVID-19 Mortality: Systematic Review and Meta-Analysis. *British Medical Journal* 2021; 375: e068302. https://www.bmj.com/content/375/bmj-2021-068302.

[53] Lendacki F, et al., COVID-19 Outbreak Among Attendees of an Exercise Facility Chicago, Illinois, August–September 2020. MMWR, 70(9):321-325 (Mar. 5, 2021), https://pubmed.ncbi.nlm.nih.gov/33661859/.

[54] Katelaris AL, et al., Epidemiologic Evidence for Airborne Transmission of SARS-CoV-2 during Church Singing, Australia, 2020. Emerg Infect Dis. 27(6) (June 6, 2021), https://doi:10.3201/eid2706.210465.

[55] Hamner L, Dubbel P, Capron I, et al. High SARS-CoV-2 Attack Rate Following Exposure at a Choir Practice – Skagit County, Washington, March 2020. MMWR 69(19): 606-610 (May 15, 2020), https://www.cdc.gov/mmwr/volumes/69/wr/mm6919e6.htm.

25. United States data shows isolation/lock-downs have been associated with a 4.9% to 14-fold decrease in transmission.[56] But even if an individual works in an isolated environment by full-time teleworking, an individual still interacts with others in the local community and their household. Thus, working in an isolated environment removes risk from viral transmission to others at work, but it does not eliminate risk of infection and disease complications to the individual to include long-COVID symptoms, hospitalizations, ICU admissions, and deaths.

Herd Immunity

26. Herd immunity is not as effective in preventing and controlling the spread of a virus as being vaccinated. Herd immunity occurs when a large portion of the community becomes immune to a disease, thus reducing the spread and impact of the disease. Early in 2020, as the COVID-19 vaccine was being developed, many estimated a vaccine rate of 60-70% would impart herd immunity upon the population and thus end the pandemic. However, there are many reason why this has proven to be a faulty assumption.[57] First, vaccine roll-out and vaccine acceptance rates vary among populations in the community. The vaccination rate among the military cannot be viewed in isolation for determining "herd immunity." For example, while 97% of Active Duty Service members and 92% of Reservists in the Department of the Air Force are fully vaccinated, the vaccination rate for the U.S. population is 64.5%.[58, 59] Considering only one subset of the population (e.g., the U.S. military or Department of the Air Force) to determine herd immunity would be erroneous, since these populations intermingle with other less-

[56] Talic S, et al. Effectiveness of Public Health Measures in Reducing the Incidence of COVID-19, SARS-CoV Transmission, and COVID-19 Mortality: Systematic Review and Meta-Analysis. *British Medical Journal* 2021; 375: e068302. https://doi.org/10.1136/bmj-2021-068302.
[57] Aschwanden, Christine, Five Reasons why COVID Herd Immunity is Probably Impossible, Nature Vol. 591 (Mar. 25, 2021).
[58] Official site for the AF's Aeromedical Services Information Management System (ASIMS) Reports, Data current as of 21 Jan 2022; https://asimsimr.health.mil/main/main.aspx
[59] CDC COVID Data Tracker (data current as of Jan. 24, 2022), https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-total-admin-rate-total.

vaccinated populations, thus increasing the risk the disease will continue to spread and mutate. The community vaccination rate also varies based on region. For example, as of March 7, 2022 (0600 EST), the metropolitan corridor from Dayton, Ohio to Cincinnati, OH includes about 9 counties with COVID-19 vaccination rates as low as 50.2% for Miami County to a high of 67.8% for Hamilton County.[60] Similarly, the vaccine rate in the counties were the plaintiffs who reside outside of Ohio is as follows: Comel County, TX has a 61.5% vaccination rate; Guadalupe County, TX is at 54.6%; Hillsborough County, FL is at 62.0%, and Santa Rosa County, FL is at 53.6%. These vaccination rates are lower than the vaccination rate among Airmen and Guardians; the vaccination rate may be even lower among small cohorts of people in the community. Thus, while the military may have a higher rate of vaccination, community and social groups, with which military service members associate, may not have as high of a vaccination rate, thus presenting a greater risk of disease.

27. Second, the COVID-19 disease continues to mutate, which degrades the overall effectiveness of herd immunity. The Delta and Omicron variants developed in populations which had low rates of vaccination – India for the Delta variant and South Africa for the Omicron variant. Within months, both variants spread throughout the world causing increases in cases, hospitalizations, and deaths. Herd immunity does not necessarily provide protection against these variants. For example, although Israel and the United Kingdom have higher vaccine rates than the United States and likely decreased the rate of hospitalization and death for

[60] CDC COVID Tracker, COVID-19 Integrated County View, Data current as of 6am, 8 Mar 2022 at https://covid.cdc.gov/covid-data-tracker/#county-view?list_select_state=Ohio&data-type=Vaccinations&metric=Administered_Dose1_Pop_Pct.

the vaccinated, herd immunity was insufficient to protect them from increases in COVID-19 cases.[61]

28. The impact of mutations is demonstrated with seasonal influenza, where a new vaccine is required each year to protect against the changing influenza virus. The current COVID-19 vaccines, developed for the Alpha variant, provide better protection than being unvaccinated, but are slightly less effective for the Delta variant, and less effective for the Omicron variant. As the viruses mutate, any herd immunity gained may be lost with subsequent mutations. Persistent mutations, or viral changes which increase the viruses chance of surviving and being transmitted to others, have a greater risk of developing in an unvaccinated, unprotected population. The lower the rate of vaccination, the greater the chance of infection and subsequent mutations.

29. Additionally, although the original belief was that 60%-70% vaccination would help end the pandemic, the Air Force's vaccine program is not meant to prevent a pandemic. Instead, as previously noted, the Air Force relies on the Department of Defense vaccine program (and medical readiness program as a whole) to protect Service members from potential health risks to ensure a healthy fighting force and mission readiness. Military medical readiness requirements aim to mitigate risk. The Department of Defense requires vaccination for many diseases unrelated to the COVID-19 pandemic, including, for example, influenza, measles, and diphtheria. These requirements include vaccination from diseases that are not contagious through human-to-human transmission, such as tetanus. This is similar to the requirement for Service members to undergo annual dental examinations and meet specific dental requirements (e.g., root canals) in order to be considered medically ready. The need for a root canal could

[61] COVID-19 case, vaccination, hospitalization and death rate data for this statement taken from (a) Johns Hopkins University, Center for Systems Science and Engineering (CSSE) as used by Google search engine (i.e., www.google.com, search terms "Israel COVID case graph") (last accessed Jan. 27, 2022) and (b) Our World Data In Data (https://ourworldindata.org/coronavirus).

result in a medical evacuation from a deployed environment. As such, the Department of Defense has determined that these requirements are the best method of ensuring mission accomplishment because the vaccine program maximizes the number of Service members vaccinated for each immunization requirement in order to minimize the risk to the individual Service member and to the force of illness, hospitalization, transmission, and adversely impacting the mission of the United States military to protect and defend the nation.

30. Finally, while herd immunity may eventually reduce some of the risk to unvaccinated Service members, it would not be as effective as the member being vaccinated. An unvaccinated individual increases risk of disease to themselves, their colleagues, their family and community. Increased risk of disease in any of these groups may impact the mission by either eliminating the service member, depleting medical resources, or distracting the service member from focusing their work.

Saniti ation

31. Improved sanitation also cannot replace vaccination. Many vaccine-preventable diseases are spread through fomites. Fomites are objects or surfaces that, when exposed to infectious agents from bodily secretions (e.g., nasal fluid from sneezing or wiping nose, oral secretions from coughing) can transmit to others who contact the objects or surfaces. Disease transmission is greatly reduced when surfaces which people touch are clean, when garbage which can attract insects and rodents is eliminated, and when clean water and soap is available to wash hands and surfaces. However, such mitigation efforts must be continuous and do not counter the principle mode of SARS-CoV-2 transmission, exposure to respiratory droplets carrying infectious virus.[62] When individuals work in close proximity and handle the same materials (e.g., documents, desk

[62] CDC, *SARS o and Surface omite ransmission for Indoor ommunit nvironments*, updated Apr. 5, 2021, https://www.cdc.gov/coronavirus/2019-ncov/more/science-and-research/surface-transmission.html.

space, consoles, equipment, door knobs), it is difficult to keep those materials and areas constantly disinfected.

32. Handwashing also is not enough to replace the effectiveness of vaccines. Germs can spread from other people or surfaces when you: (a) touch your eyes, nose, and mouth with unwashed hands, (b) prepare or eat food and drinks with unwashed hands, (c) touch a contaminated surface or objects, or (d) blow your nose, cough, or sneeze into hands and then touch other people's hands or common objects. Washing hands for 20 seconds, with soap and clean water, is one, very important step for preventing the spread of germs, but is less effective for diseases primarily transmitted via airborne transmission. Handwashing is especially important for people before eating or preparing food, before touching your face, after using the restroom, after leaving a public place, after blowing your nose, coughing, or sneezing, after handling your mask, after changing a diaper, after caring for someone who is sick, and after touching animals or pets.[63]

33. Unlike vaccination, hand washing would not provide continuous protection. To effectively reduce disease, hand washing and sanitation regiments must be rigorously and systematically followed. Individuals frequently touch their face and handle their masks, and individuals can unknowingly touch contaminated objects or surfaces. It is not realistic for the Air Force to put in a system that ensures a member washes their hands for at least 20 seconds any time they touch their face (including when they sneeze or cough) or to sanitize any shared surface after any team member touches it. Finally, even if strict sanitation and hand-washing regiments can eliminate fomites, several studies among animals, in labs, and in human

[63] CDC, *hen and How to ash our Hands* (Aug. 10, 2021), https://www.cdc.gov/handwashing/when-how-handwashing.html.

populations prove the primary mode of transmission for SARS-CoV-2 is airborne transmission.[64, 65, 66] Sanitization is especially less effective in a deployed location where the service member may not have ready access to water or appropriate cleaning and sanitation resources

34. Typical air filtration systems are also ineffective in preventing the spread of illness. While some research has found SARS-CoV-2 virus in a building's heating, ventilation and air conditioning (HVAC) system,[67] the HVAC systems in most non-medical buildings play only a small role in reducing infectious disease transmission. Because the facility where Air Force Officer works is not a medical building, it is unlikely the HVAC systems would provide sufficient protection to eliminate or even greatly reduce COVID-19 transmission in his work area.

Conclusion

35. In summary, none of the measures discussed above are as effective as being fully vaccinated against COVID-19, and relying on them instead of vaccines would hinder the Air Force's mission accomplishment. No medical alternative would reduce a service member's risk of morbidity and mortality associated with COVID-19, to himself and others, as effectively as being vaccinated.

[64] J Port et al. SARS-CoV-2 disease severity and transmission efficiency is increased for airborne compared to fomite exposure in Syrian hamsters. Nature Communications DOI: 10.1038/s41467-021-25156-8 (2021).
[65] Wang, CC, Prather, KA, et al, Airborne transmission of respiratory viruses, SCIENCE, Vol 373, Issue 6558 DOI: 10.1126/science.abd9149 (Aug. 27, 2021) *availa le at* https://www.science.org/doi/10.1126/science.abd9149
[66] National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases, Science Brief: SARS-CoV-2 and Surface (Fomite) Transmission for Indoor Community Environments, updated Apr. 5, 2021, *availa le at* https://www.cdc.gov/coronavirus/2019-ncov/more/science-and-research/surface-transmission.html.
[67] Lednicky, JA, et al., Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients, *International Journal of Infectious isease*, Vol. 100, pages 476–482 (Nov. 2020), *availa le at* https://www.ijidonline.com/article/S1201-9712(20)30739-6/fulltext.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

POEL.JAMES.R.1181237550 Digitally signed by POEL.JAMES.R.1181237550 Date: 2022.03.08 20:14:15 -05'00'

JAMES R. POEL, Col, USAF
Chief, Public Health Branch

Exhibit 17

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
CINCINNATI DIVISION

HUNTER DOSTER, *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	No. 1:22-cv-00084
	)	
FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	
	)	

DECLARATION OF COLONEL ASHLEY HEYEN

I, Ashley Heyen, hereby state and declare as follows:

1. I am a Colonel in the United States Air Force currently assigned as the Director of Assignments at the Department of the Air Force Air Reserve Personnel Center (ARPC). I have been in this position since September 2020. As a part of my duties, I am responsible for liaising with Headquarters Air Force Reserve on military readiness programs. As a force support officer, I serve as the focal point for interpreting and executing both policy and guidance for Air Force Reserve (AFR) military readiness programs.

2. I am generally aware of the allegations set forth in the pleadings filed in this matter. I make this declaration in my official capacity as the Director of Assignments at the Air Reserve Personnel Center and based upon my personal knowledge and upon information that has been provided to me in the course of my official duties.

3. The Air Force Reserve IRR program serves as a resource pool of reservists who, if they meet readiness standards, may be eligible to return to the Selected Reserve in a participating

status (traditional reservists are members of the Selected Reserve). Reassignment to the IRR commences at the unit level, by a member's commander. The reassignment action is then processed by Headquarters Air Reserve Personnel Center and may take a few months. Officers with a military service obligation will remain in the IRR at least until their military service obligation expires and will also remain eligible for promotion. Members who have been reassigned to the IRR are not eligible for Tricare Reserve Select medical insurance benefits, but may be eligible for Tricare dental benefits, a DD Form 2 (green ID card) to access minimal base amenities, and a Montgomery GI Bill or Post 9-11 GI Bill if they have previously qualified for these benefits. Reserve Component members routinely transfer to and from the IRR in order to manage commitments in their personal lives (e.g., following the birth of a baby). The ability to step away from a service obligation to address personal matters is one of the main benefits of being able to transition to and from the IRR. Depending on the timing of the move and how long the member stays in the IRR, a reassignment to the IRR may not adversely affect a member s career.

4. An involuntary reassignment to the IRR allows the Air Force Reserve to transfer a member with remaining military service obligation to the IRR rather than discharging the member out of the Air Force. Members reassigned to the IRR are still able to return to a participating position (provided they meet all of the requirements for their position) with minimal effort and expediency versus having to be re-accessed as a new entry.

5. Air Reserve Personnel Center defines "separation" and "discharge" as follows: a "discharge" is a member being released from their obligation to continue service in the armed forces, and does not have any obligations to return to service. A "separation" is when the member is released from active duty, but still must complete their military reserve obligations.

Reassignment to the IRR is not a separation or discharge. A member in the IRR is still a member of the Air Force.

6. Barring misconduct, individuals that are assigned to the IRR that complete their military service obligation period are honorably discharged.

7. Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

HEYEN.ASHLEY.LEWIS.1095327636

Digitally signed by HEYEN.ASHLEY.LEWIS.1095327636
Date: 2022.03.08 15:01:12 -07'00'

ASHLEY L. HEYEN, Colonel, USAF
Director of Assignments

Exhibit 18

IN THE UNITED STATES DISTRICT COURT FOR THE SOUTHERN DISTRICT OF OHIO CINCINNATI DIVISION

HUNTER DOSTER, *et. al.*	)	
	)	
Plaintiff,	)	
	)	
v.	)	No. 1:22-cv-84
	)	
Hon. FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	
	)	

DECLARATION OF COLONEL RICHARD M. HEASLIP

I, RICHARD M. HEASLIP, hereby state and declare as follows:

1. I am a Colonel in the United States Air Force Reserves currently assigned as the 4th Air Force (4 AF) Director of Staff. I became the Director of Staff on September 16, 2021. 4 AF is located at March Air Reserve Base, California and is responsible for 18 wings and 1 direct report group with a total population of approximately 30,000 military and civilian personnel. As the Director of Staff, I am responsible for managing the 4 AF civilian employees, 4 AF Directors, and 4 AF military members and civilian employees who report directly to the 4th Air Force Commander, Major General Jeffrey T. Pennington, in addition to overseeing 4 AF policies and guidance on behalf of the Commander, Major General Jeffrey T. Pennington. Prior to becoming the Director of Staff, I was the Director of Air, Space, and Operations (A3/5) at Fourth Air Force (4 AF). I was appointed to the Director A3/5 position on November 8, 2020. As the Director for A3/5, I was responsible for directing the operations of the contingency response forces, aircrew training, aircrew evaluations, and classified operational plans. The A3 division focuses on aircraft and aircrew operations for the five major weapons systems within 4 AF. The A5 division focuses on how the 4 AF major weapons systems supports operations plans for the National Defense Strategy.

2. I am aware of the allegations set forth in the pleadings filed in this matter. I make this declaration in my official capacity as the 4 AF Director of Staff and former Director of A3/5 and based upon my personal knowledge and upon information that has been provided to me in the course of my official duties.

3. I was SMSgt Christopher M. Schuldes' immediate director. SMSgt Schuldes is a Traditional Reservist assigned to 4 AF/A3. At a minimum, SMSgt Schuldes performs military duty one weekend per month and two weeks per year. However, because he is assigned to contingency response and flying duties he is required to perform more military duty days than the average traditional reservist. When I arrived at 4 AF as the Director of A3/5, SMSgt Schuldes had gone non-current on all his requirements. SMSgt Schuldes failed to reenlist on time as he hoping that the Air Force would authorize an enlisted aviator bonus. The Air Force did not authorize the bonus at that time and 4 AF began to outprocess SMSgt Schuldes due to his failure to reenlist. Thereafter, he tried to reenlist to avoid outprocessing. Because of failed fitness tests, SMSgt Schuldes was denied reenlistment, which he appealed. The appeal process took approximately 18 months during which time SMSgt Schuldes became non-current on his flying duties. At the time the Secretary of Defense issued the COVID-19 vaccine directive on August 24, 2021, SMSgt Schuldes was still non-current on his flying duties. SMSgt Schuldes appeal was granted, and he was allowed to reenlist in October 2021 at which point he began working to achieve currency on his flying status. Due to the length of his non-concurrency, 4 AF was attempting to determine whether SMSgt Schuldes would need to return to initial qualification training at Altus AFB for the C-17 loadmaster Air Force Specialty Code (AFSC) or whether the 729th Airlift Squadron would be able to provide local requalification training. In addition to being a loadmaster, SMSgt Schuldes is the contingency response program manager in 4 AF/A3.

4. Upon hearing the details of the COVID-19 directive, SMSgt Schuldes informed me he was researching the requirements for a medical exemption from the COVID-19 vaccination. At some

point later, SMSgt Schuldes stated he realized he would not qualify for a medical exemption and changed his focus to requesting a religious accommodation for the COVID-19 vaccination. During the December 2021 Unit Training Assembly (UTA),[1] SMSgt Schuldes informed me that his reservations about taking the vaccine stemmed from his spouse's concern about the shot and not from a concern of his. He went on to say that he would take the NOVAVAX vaccine if it became available in the United States.

5. SMSgt Schuldes' primary duties as a contingency response program manager include providing contingency response guidance and coordinating staff to fulfill worldwide response requirements as dictated by the site or deployed commander. As a contingency response manager for 4 AF, SMSgt Schuldes is responsible for ensuring the training and readiness for 4 AF contingency response airmen. These duties include, but are not limited to, coordinating medical, communication, aerial port, and security capabilities for a contingency response force in the deployed environment. SMSgt Schuldes must also manage contingency response specific in-house training courses that require eyes-on/hands-on presence to complete. In addition to managing the 4 AF training, he provides hands-on training for aeromedical, patient movement, aerial port personnel, security forces movement on and around aircraft, confined places, such as shelter-in-place, and verify that 4 AF contingency response forces meet the deployment requirements.

6. In addition to being the contingency response program manager, SMSgt Schuldes is required to maintain his proficiency as a loadmaster for the C-17 with the 729th Airlift Squadron. Duties required of an aircrew member include simulator and flight training to maintain currency and proficiency and close-quarters flying in crews of three personnel at a minimum. Currently, SMSgt Schuldes is unqualified as a C-17 loadmaster with the 729th Airlift Squadron. He would have to attend requalification training that could last several months. The requalification training

[1] UTAs are defined as a "planned period of training, duty, instructions, or test alert completed by a Reserve Unit." Air Force Manual (AFMAN) 36-2136, *Reserve Personnel Participation*, paragraph 4.1.2, dated September 6, 2019. These are commonly performed one weekend per month and are the primary periods when Traditional Reservists perform their military service.

would consist of several temporary duty missions encompassing five- to seven-day overseas trips to countries requiring COVID-19 vaccination for entry. Each trip would have several stops where SMSgt Schuldes would be required to interact with his own crewmembers, aerial port personnel, ground crew, and possibly base support personnel in the base operations facility. However, he is precluded from traveling for temporary duty assignments based on his unvaccinated status and may be unable to attend these requalification trainings. In an effort to prevent the spread of COVID-19 and to ensure the health and safety of the force, the DoD has limited official travel for unvaccinated service members to only circumstances that are "mission critical" – which is a high bar that requires Secretary or Under Secretary of the Air Force approval. Additionally, because training typically takes place in close proximity to others, many training opportunities require the service member to be vaccinated to attend, separate from travel requirements.

7. As a loadmaster, SMSgt Schuldes would be responsible for maintaining order and safety for over 120 passengers on a single flight due to the cargo and personnel carrying capabilities of the C-17. He could also be tasked with additional duties that are required within a section, such as Operations Security (OPSEC) oversight, mentorship and performance feedback with subordinates, and coordinating other office responsibilities. Although some of this work can be accomplished individually, many of his tasks require him to work in close settings with other service members. Many of the flying duties he would be required to complete involve close personal contact, to include chemical defense systems training and combat survival courses. The physical distance between personnel on an aircraft may range from shoulder-to-shoulder up to separation of at least 6 feet.

8. Many of SMSgt Schuldes' duties require the use of classified materials and systems. Classified materials cannot be viewed and classified systems (e.g., a classified computer network) cannot be accessed outside of a secured facility for security purposes. Generally, aircrew members are not permitted to take classified materials out of the secured facility to work from an unsecured

facility like their homes for training or study. Aircrew members are not permitted to discuss classified materials on unsecured telephones, such as a personal cellular phone or a home phone. Moreover, aircrew members cannot access classified systems from a remote, unsecured facility, like a home residence. SMSgt Schuldes also needs access to secure briefings in the vault in a secured building, such as a Sensitive Compartmentalized Information Facility (SCIF). Because the vault is a secured facility, the outside door must be closed and locked at all times. Due to security protocols, it is not possible to open the outside door to increase ventilation in the secure area. Because vaults and secure areas vary in size, shape and ventilation capabilities there is no way to verify that in any particular situation proper COVID-19 safety mitigation techniques can be assured, much less guaranteed. He must be able to access classified materials and classified systems and must be able to attend classified, in-person meetings and talk to other service members in secured settings about performing his duties, he would be unable to perform his duties remotely or via telework.

9. SMSgt Schuldes works in an office filled with cubicles with less than the required six feet of distance from other A3/5 members. Approximately 14 persons work in SMSgt Schuldes' office, with an additional 11 personnel moving in and out of the office space. Remaining unvaccinated would risk both SMSgt Schuldes' health and the health of the other service members working in close proximity to him.

10. SMSgt Schuldes is a Traditional Reservist and has full-time civilian employment. As a result, the majority of his time in the unit occurs on UTA weekends. He could not perform these duties on non-UTA weekends because the unit is structured to provide all the services and training our service members require one particular weekend a month. The unit does not have the personnel to provide him separate training and events to accomplish on an "off-schedule" UTA to reduce his close contact with others in the vault. It is critical to the unit's mission that SMSgt Schuldes be present for UTA weekends with other Traditional Reservists to accomplish group

tasks and training. Virtually all training SMSgt Schuldes is required to attend on UTA weekends takes place indoors, in conference rooms, auditoriums, and other similar locations in which service members are not able to maintain 6 feet of distance between each other. Furthermore, the purpose of UTAs is to ensure the service members are properly trained and equipped in the event they must mobilize for deployment or backfill their active duty counterparts because of operational necessity. Readiness is essential for someone like SMSgt Schuldes, an aircrew member, who is also responsible for contingency response guidance and staff.

11. In addition, SMSgt Christopher M. Schuldes, like other Air Force service members, must be worldwide deployable at all times. Airmen may need to deploy on a few days' notice. During recent history, some deployments have been voluntary; however, the mission of the military Reserves is to be ready in the event the President or Congress activate that specific Reserve unit (e.g., post September 11, 2001). The service members in 4 AF have the responsibility to stay deployment-ready in the event that not only they get individually tasked with a deployment, but also in the event the entire 4th Numbered Air Force (NAF)[2] gets activated due to current world events. The COVID-19 vaccine is necessary to be fully medically ready for deployment. From the time an individual receives his or her first dose of the FDA-approved COVID-19 vaccine, it takes about one month to become fully vaccinated. Additionally, the symptoms of the COVID-19 virus (e.g., fever, chills, shortness of breath, fatigue, muscle aches, headaches, etc.), the risk that Airmen could get "long COVID," and the possibility that Airmen could get seriously ill, become hospitalized, and die from COVID-19 create an unacceptable risk to personnel and substantially increase the risk of mission failure, both in garrison (i.e., a non-deployed setting) and in a deployed environment.

12. The threat of sickness in a deployed environment is even more serious. Most forward-

[2] A Numbered Air Force is a level of command directly under a MAJCOM with other organizational units, such as Wings, Groups, and Squadrons assigned as subordinate units.

deployed locations do not have extensive medical facilities like we are accustomed to here in the United States. Supplies, beds, and staff are many times at a premium. When deploying, service members typically travel to the deployed location via airplane, such as the C-17, C-5, or C-130. The number of service members deploying can vary and, because necessary equipment is also loaded on the aircraft as cargo, the service members are very likely to be in close proximity to one another during the flight. Depending on the equipment and personnel required for the particular deployment and the aircraft available, the physical distance between deploying personnel on the aircraft may range from shoulder-to-shoulder up to separation of at least 6 feet. Additionally, because deployments can be anywhere in the world, the flight to the deployed location can range from a single-leg flight of 20 minutes to a multiple-leg flight of greater than 15 hours. Furthermore, having a COVID-19 outbreak while deployed, where everyone is in close contact and living within the same area for months at a time, could easily overwhelm that location's medical capacity taking away from treating front-line battle injuries and other illnesses. Deployed personnel and staffing are also, by design, minimally manned. If one service member were to get sick, contract long-COVID, get hospitalized, or die, that section may only have one extra person performing similar duties, leaving little redundancy and backup to support the mission. An outbreak impacting multiple service members could risk support to the mission altogether.

13. In austere, deployed locations, it is common for Airmen to live, eat, and sleep in close quarters for months at a time. This may include working, sleeping, and eating in tents or other temporary structures which would not allow for social distancing. Any disease outbreak, particularly amongst unvaccinated individuals, could easily overwhelm that location's medical capacity, which reduces capacity to treat front-line battle injuries and other illnesses. Further, deployed personnel and staffing are manned minimally with only the service members necessary to accomplish the mission downrange. As such, there is little redundancy in the manning and each casualty due to illness has a significant impact on successful mission accomplishment. An

outbreak impacting multiple service members could cause mission failure.

14. Testing for COVID-19 immediately prior to deployment is not an effective alternative. Due to the nature of deployments, it may not be possible to obtain test results back before SMSgt Schuldes is scheduled to deploy. In addition, if he tested positive immediately prior to deployment, the military would have to quickly modify its operational plans to either find a replacement or risk deploying without his expertise. If he tested negative prior to deployment he would remain unvaccinated and more vulnerable to harm if infected due to limited medical facilities in deployed environments. Depending on the location of the deployment, he may not be eligible for the deployment due to country requirements for entry, resulting in short notice tasking to a vaccinated 4 Air Force member and/or 4 Air Force being unable to fill the deployment requirement. Either scenario threatens to degrade the unit's operational capabilities. Delays – whether caused by having insufficient Airmen on the ground or not being able to deploy on time until a replacement can be found – have real-world impacts on military operations.

15. Giving SMSgt Schuldes an alternate position as an accommodation or placing him in a non-deployable status is not a feasible alternative to vaccination. Reserve units have openings based on the needs of the particular mission and unit. The Air Force places a service member in a non-deployable position when the service member faces a critical medical issue that requires him or her to be within a certain distance of medical facilities. In the case of SMSgt Schuldes, his non-deployable status is controllable and can be resolved with the COVID-19 vaccine. It would not be safe for him, or those around him, for him to deploy without the vaccine. The mission of 4 AF is to ensure that service members of each unit are trained and ready for deployment in support of the National Defense Strategy. The unit cannot afford to place SMSgt Schuldes in a non-deployable status because of the ever-increasing need and dependence on an already short-staffed requirement. Having a member non-deployable places a larger burden on the other service members within the contingency response/loadmaster section and hurts overall unit readiness. Should the AF Reserves

become activated by the President or Congress, SMSgt Schuldes would not be able to deploy with the unit because of his vaccination status. This means that 4 AF would be unable to provide the full support required for the deployment, degrading mission capabilities.

16. Air Force policy requires SMSgt Schuldes to be involuntarily reassigned to the Individual Ready Reserve (IRR). The IRR is not a punishment, but a force management tool, which would allow SMSgt Christopher M Schuldes to remain a part of the Air Force and return to a participating Reserve status should he choose to vaccinate on a future date.

17. On September 8, 2021, Major General Jeffrey T. Pennington, 4 AF Commander, ordered SMSgt Schuldes to receive his first dose of COVID-19 vaccine and provide proof of the same by October 3, 2021. The order also specified that SMSgt Schuldes could alternatively submit a religious accommodation request or proof of a medical exemption by the deadline specified for the first dose of the COVID-19 vaccine. The order also required him to receive his second dose of a COVID-19 vaccine and provide proof of the same by November 7, 2021. These dates are based on the Secretary of Defense's vaccine directive issued on August 24, 2021, and the deadline set by the Secretary of the Air Force in his memorandum issued on September 3, 2021. The Air Force deadline for members of the Reserve to be fully vaccinated was December 2, 2021.

18. On October 2, 2021, SMSgt Schuldes submitted a written request for a religious exemption from the COVID-19 vaccine requirement in accordance with Air Force regulation, Department of the Air Force Instruction (DAFI) 52-201, *Reli ious reedom in the epartment of he Air orce*. He was temporarily exempt from the COVID-19 vaccination requirement while the religious accommodation request was pending resolution. The request was reviewed and routed through the chain of command for endorsements and recommendations pursuant to the procedure set out in DAFI 52-201.

19. On September 30, 2021, I counseled SMSgt Schuldes that noncompliance with immunization requirements may adversely affect readiness for deployment, assignment,

international travel, or result in administrative consequences. SMSgt Schuldes acknowledged receipt of the order and expressed his understanding of this obligation. SMSgt Schuldes also met with a chaplain and medical provider regarding his concerns about receiving the vaccine as part of the exemption request process. On October 25, 2021, SMSgt Schuldes' request for a religious accommodation was disapproved by the Air Force Reserve Command (AFRC) Commander. On October 30, 2021, SMSgt Schuldes appealed that denial to the Air Force Surgeon General.

20. On December 16, 2021, the Air Force Surgeon General denied SMSgt Schuldes' appeal. The Air Force Surgeon General found that SMSgt Schuldes' duties as a loadmaster and contingency response team chief "involves time in and around aircraft and requires frequent contact with other aircrew, CRT team members, aerial port personnel, and passengers." Further, the Surgeon General found that SMSgt Schuldes' duties are "not fully achievable via telework or with adequate distancing." Significantly, the Surgeon General found that SMSgt Schuldes is "in a high ops tempo career field, and short-notice deployment taskings occur frequently, so the delay of vaccination would incur a serious burden on the unit and degrade overall military readiness." On December 16, 2021, SMSgt Schuldes was also presented a subsequent order by the 4 AF Commander to receive his first dose of the COVID-19 vaccine within five calendar days or to refuse the vaccine in writing. On December 21, 2021, SMSgt Schuldes e-mailed me stating that he was unwilling to receive the vaccine as his personal beliefs come before his Air Force career.

21. On January 6, 2022, Major General Jeffrey T. Pennington, 4 AF Commander, issued SMSgt Schuldes a letter of reprimand (LOR) for failing to follow the order to receive the COVID-19 vaccine and placed SMSgt Schuldes in a non-participation status. On February 19, 2022, SMSgt Schuldes responded to the LOR. On February 22, 2022, Major General Jeffrey T. Pennington sustained the LOR and issued a notification of intent to transfer SMSgt Christopher Schuldes to the IRR. SMSgt Schuldes has until March 9, 2022 to respond to the notification of intent to transfer to the IRR.

22. To the best of my knowledge, SMSgt Schuldes has previously met all vaccination requirements for his position as a member of the United States Air Force.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

HEASLIP.RICHARD.MILES.1061822786 Digitally signed by HEASLIP.RICHARD.MILES.1061822786 Date: 2022.03.08 15:18:59 -08'00'

RICHARD M. HEASLIP, Col, USAF
4 AF Director of Staff

Exhibit 19

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
C D

HUNTER DOSTER, *et. al.*	)	
	)	
Plaintiff,	)	
	)	
v.	)	No. 1:22-cv-84
	)	
FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	
	)	

DECLARATION OF COLONEL DONALD F. REN

I, DONALD F. WREN, hereby state and declare as follows:

1. I am a Colonel in the United States Air Force currently assigned as the Commander, 445 Mission Support Group (MSG). As the Group Commander, I am responsible for the agile combat support capability of the 445 Airlift Wing. This effort is comprised of five squadrons and over five-hundred and fifty military and civilian members. These squadrons provide: security, communications, personnel and human resources, logistics, and civil engineering capabilities. The 87 Aerial Port Squadron (APS) falls under my group command. I was appointed to command the 445 MSG on December, 9 2019. The 445 MSG and 87 APS are under the 445 Airlift Wing (AW) at Wright Patterson Air Force Base, Ohio.

2. I am generally aware of the allegations set forth in the pleadings filed in this matter. I make this declaration in my official capacity as the Commander, 445 MSG, and based upon my personal knowledge and upon information that has been provided to me in the course of my official duties.

3. I am Senior Airman (SrA) Joseph Dills' group commander. SrA Dills is a Traditional

Reservist assigned to 87 APS. At the time the Secretary of Defense issued the COVID-19 vaccine directive on August 24, 2021, SrA Dills was assigned to 87 APS.

4. SrA Joseph Dills is a Passenger Representative who is responsible for preparing and processing passengers for transportation on Air Force or contracted carrier aircraft. Although some of this work is accomplished individually, many of his tasks require him to work in close settings with other service members. His immediate work space is the passenger terminal area, where he works with Active Duty Airmen and contractors to process passengers for travel on Air Force or contracted aircraft. This includes: ticketing, security screening, communication, and coordination with aircraft support operations and air crews. SrA Dills' workspace would be at a service counter or security screening station in the common area of the Passenger Terminal. SrA Dills does not have a personal office or separate workspace from others. The common work area is not large enough for service members and passengers to stay 6 feet apart from each other in the terminal common area.

5. On normal UTA weekends,[1] SrA Dills would be in close physical contact with up to 36 other service members during the duty day. The average duty day lasts 8 hours. In addition to working in close physical contact with up to 36 individuals during normal UTA weekends in the open work area, SrA Dills may also be in close physical contact with passengers and other individuals in other areas of the office, such as in a meeting room or the unit breakroom.

6. Remaining unvaccinated would risk both SrA Dills' health and the health of the other service members working in the office. Because his duties include direct contact with passengers, support operations, and air crews, as well as the use of unique cyber information systems, he would be unable to perform his duties remotely or via telework. Since SrA Dills is a

[1] UTAs are defined as a "planned period of training, duty, instruction, or test alert completed by a Reserve Unit." Air Force Manual (AFMAN) 36-2136, *Reserve Personnel Participation*, paragraph 4.1.2, dated September 6, 2019. These are commonly performed one weekend a month and are the primary periods when Traditional Reservists, like SrA Dills, perform their service.

Traditional Reservist, the majority of his time in the unit would occur on UTA weekends. He could not perform these duties on non-UTA weekends because the unit is structured to provide all the services and training service members require on one particular weekend per month. The unit does not have the personnel or resources to provide SrA Dills separate training and events to accomplish on an "off-schedule" UTA to reduce his close contact with others in the office. It is critical to the mission of the unit that SrA Dills be present for UTA weekends with other Traditional Reservists to accomplish group tasks and training. Virtually all training SrA Dills is required to attend takes place indoors, in conference rooms, auditoriums, and other similar locations. Under normal operating conditions, trainings would have well over 50 people attend to maximize the training. Under these conditions, service members are not able to stay 6 feet apart from each other during the training.

7. If SrA Dills attended off-schedule weekends (i.e., non-UTA weekends) or during the week, he would not be able to accomplish all of his required duties, especially those that require him to work with other Reservists who are in the office on UTA weekends. For example, contact with other Reservists would typically be during training, both war skills and On the Job Training, or while performing administrative tasks, such as signing in for accountability and pay purposes, or other formations and meetings. Furthermore, the unit conducts operations during UTA supporting global airlift missions. If SrA Dills came in on off-schedule weekends or during the week, the unit would still run the risk of him interacting with a number of service members who support the full-time mission, as well as passengers.

8. In addition, SrA Dills, like other Air Force members, must be worldwide deployable at all times. Airmen may need to deploy on a few days' notice. The 87 APS is assigned to Reserve Component Period (RCP) 8. RCP deployments are under the authority called out in 10 USC § 12301 and may be involuntary, while other APS deployments may be voluntary. Involuntary deployments are at the authority of the President and Service Secretary. Involuntary

deployments are directive in nature. That is the Reservist is ordered to Active Duty without consent. Voluntary deployments are not compulsive, that is to say, the member must consent to being placed in an Active Duty status. Nevertheless, the mission of the military Reserves is to be ready in the event that specific Reserve unit is activated (e.g., post September 11, 2001). The service members in the 87 APS have the responsibility to stay deployment-ready not only in the event that they get individually tasked with a deployment, but in the event the entire 87 APS is activated due to current world events. The COVID-19 vaccine is necessary to be fully medically ready for deployment. From the time an individual receives his or her first dose of the FDA-approved COVID-19 vaccine, it takes about one month to become fully vaccinated. Additionally, the symptoms of the COVID-19 virus (e.g., fever, chills, shortness of breath, fatigue, muscle aches, headaches, etc.), the risk that Airmen could get "long COVID," and the possibility that Airmen could get seriously ill, become hospitalized, and die from COVID-19 create an unacceptable risk to personnel and substantially increase the risk of mission failure, both in garrison (i.e., a non-deployed setting) and in a deployed environment.

9. The threat of sickness in a deployed environment is even more serious. When deploying, service members typically travel to the deployed location via airplane, such as the C-17, C-5, or C-130. The number of service members deploying can vary and, because necessary equipment is also loaded on the aircraft as cargo, the service members are very likely to be in close proximity to one another during the flight. Depending on the equipment and personnel required for the particular deployment and the aircraft available, the physical distance between deploying personnel on the aircraft may range from shoulder-to-shoulder up to separation of at least 6 feet. Additionally, because deployments can be anywhere in the world, the flight to the deployed location can range from a single-leg flight of 20 minutes to a multiple-leg flight of greater than 15 hours. Most forward-deployed locations do not have extensive medical facilities

like we are accustomed to here in the United States. Supplies, beds, and staff are many times at a premium. Furthermore, having a COVID-19 outbreak while deployed, where everyone is in close contact and living within the same area for months at a time, could easily overwhelm that location's medical capacity taking away from treating front-line battle injuries and other illnesses. Deployed personnel and staffing are also, by design, minimally manned. If one service member were to get sick, contract long-COVID, be hospitalized, or die, that section may only have one extra person performing similar duties, leaving little redundancy and backup to support the mission. An outbreak impacting multiple service members could potentially risk support to the mission altogether.

10. Testing for COVID-19 immediately prior to deployment is not an effective alternative. Due to the nature of deployments, it may not be possible to obtain test results back before SrA Dills is scheduled to deploy. In addition, if he tested positive immediately prior to deployment, the military would have to quickly modify its operational plans to either find a replacement or risk deploying without his expertise. And even if he tested negative prior to deployment he would remain unvaccinated and more vulnerable to harm if infected. Either scenario threatens to degrade the unit's operational capabilities. In a worst-case scenario, the unit's deployment would be delayed until another qualified Airman could be mobilized on extremely short notice to perform relevant duties. These delays – whether caused by having insufficient Airmen on the ground or not being able to deploy on time until a replacement can be found – would have real world impacts on military operations.

11. Giving SrA Dills an alternate position as an accommodation or placing him in a non-deployable status is not a feasible alternative to vaccination. Reserve units fill positions based on the needs of the particular mission and unit. In the case of SrA Dills, his non-deployable status is controllable and can be resolved with the COVID-19 vaccine. It would not be safe for him, or

those around him, for him to deploy without the vaccine. The in-garrison mission of the 87 APS is to train Airmen and prepare for deployment. To afford training for Airmen the 87 APS augments day-to-day operations at Wright Patterson Air Force Base, but service members of the unit are required to be ready to deploy. The unit cannot place SrA Dills in a non-deployable status because all the APS positions are Unit Type Coded as deployable. Having a member non-deployable places a larger burden on the other members within the section, hurts APS' overall unit readiness and degrades its ability to complete the mission. Moreover, the 87 APS is not authorized non-deployable positions therefore, the unit does not have a position in which to assign SrA Dills. Should the 87 APS become activated, SrA Dills would not be able to deploy with the unit because of his vaccination status. This means the 87 APS would be unable to provide the full support required for the deployment, degrading its mission capabilities, or would have to maintain an additional person to backfill his position should it deploy, making his position unnecessarily redundant. The 87 APS overall readiness decreases when certain members are not vaccinated because it cannot count on everyone deploying in a moment's notice should the need arise.

12. On August 24, 2021, the Secretary of Defense mandated that the military services require service members be fully vaccinated against the COVID-19 virus. On September 3, 2021, the Secretary of the Air Force (SECAF) directed that Airmen and Guardians be vaccinated against the virus, and that Reserve members in particular be fully vaccinated by December 2, 2021.

13. The order provided also specified that SrA Dills could submit a religious accommodation request or proof of a medical exemption by the deadline specified for the first dose of the vaccine.

14. The unit commander and a military medical provider counseled SrA Dills on October 3, 2021 that noncompliance with immunization requirements may adversely affect readiness for

deployment, assignment, international travel, or result in administrative consequences.

15. On November 3, 2021 SrA Dills' request for a religious accommodation was disapproved by the Air Force Reserve Command (AFRC) Commander. On November 5, 2021, SrA Dills appealed that denial to the Air Force Surgeon General.

16. On December 17, 2021, SrA Dills was notified that his appeal was denied by the Air Force Surgeon General on December 16, 2021. The Air Force Surgeon General found that SrA Dills' duties require "intermittent to frequent contact with others and is not fully achievable via telework or with adequate distancing." On January 3, 2022, SrA Dills was also presented a subsequent order by 4th Air Force Commander to receive his first dose of the COVID-19 vaccine his first day in a duty status,[2] which was January 3, 2022.

17. On January 3, 2022, when SrA Dills refused to receive the COVID-19 vaccine, Lt Col Michael D. Bennett, 87 APS/CC, served SrA Dills with a Letter of Reprimand. This process was established for all similarly situated service members of the 445 AW and his process was no different than any other service member's.

18. On January 7, 2022, SrA Dills was provided notice of the recommendation that he be transferred to the Individual Ready Reserve (IRR). Air Force policy requires SrA Dills to be involuntarily reassigned to the IRR in this situation. Similar to a discharge, SrA Dills would not be required by the Department of the Air Force to be vaccinated against COVID-19 as a member of the IRR. The IRR, however, is a less significant step than discharge. The IRR is not a punishment, but a force management tool, which would allow SrA Dills to remain a part of the Air Force and return to a participating Reserve status should he choose to vaccinate on a future date.

[2] Unlike Active Duty service members, who are always in a duty status and subject to the Uniform Code of Military Justice, Reservists are only in a duty status when placed on orders, during UTAs, Inactive Duty Training, and other similar situations.

19. To the best of my knowledge, SrA Dills has previously met all vaccination requirements for his position as a member of the United States Air Force.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

WREN.DONALD.F.1077217920
Digitally signed by WREN.DONALD.F.1077217920
Date: 2022.03.08 13:46:49 -05'00'

DONALD F. WREN, Colonel, USAF
Commander, 445th Mission Support Group

Attachment:
Air Force Surgeon General Memorandum to SrA Dills, "Decision on Religious Accommodation Appeal"

Exhibit 20

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO Cincinnati Division

HUNTER DOSTER, *et al*.,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	Case No. 3:21-cv-01211-AW-HTC
	)	
Hon. FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	

DECLARATION OF COLONEL AUL . HARMER
with regard to 2d Lt Hunter Doster

I, Paul K. Harmer, hereby state and declare as follows:

1. I am a Colonel in the United States Air Force currently assigned as the Commander, Air University Detachment 1 (AU Det 1) at the Air Force Institute of Technology (AFIT) on Wright-Patterson AFB, Ohio. I have been in this position since July 2020. As a part of my duties, I am responsible for a broad range of command responsibilities and oversight over active-duty members assigned to AFIT such as the application of all Air Force Policies and Instructions. This includes both in-residence students and students earning degrees at various civilian institutions around the world. Specifically, my authorities include carrying out command responsibilities related to the implementation and enforcement of the Secretary of Defense's vaccine mandate issued on August 24, 2021, and the subsequent deadlines imposed by the Secretary of the Air Force on September 3, 2021.

2. I make this declaration in my official capacity as the Commander, AU Det 1, and based upon my personal knowledge and upon information provided to me in the course of my official duties.

3. I am Second Lieutenant (2d Lt) Hunter Doster's assigned commander. He works in the developmental engineer career field in the United States Air Force. Currently, he is a student attending the Air Force Institute of Technology on Wright-Patterson Air Force Base in Ohio, where he is working towards a Master's degree. He is scheduled to graduate on March 24, 2022, after which he is expected to be assigned to the Air Force Research Laboratory (AFRL), which is also located on Wright-Patterson Air Force Base.

4. As an AFIT student, 2d Lt Doster has completed course requirements and has been conducting thesis research. His primary in-person interactions related to his remaining coursework will likely come mainly from one-on-one interactions with his advisor and his thesis defense committee. At his next assignment, 2d Lt Doster will be assigned to work in a shared cubicle space along with another AFRL employee. Maintaining six feet of separation in this work area is not possible. 2d Lt Doster will be needed to assist with testing of various new technologies in-person, which will require him to be in contact with 2 to 3 people at a time on an intermittent basis. Experiments are conducted in a laboratory, using electronic modules, equipment, cabling and test equipment to conduct RF digital beamforming experiments. 2d Lt Doster will need to be in close contact with other personnel while conducting these experiments. The laboratory is configured with test benches and equipment in a manner to create a collaborative work environment for researchers. Continual six feet distancing cannot be maintained. Remaining unvaccinated would risk both 2d Lt Doster's health and the health of the other service members working in the laboratory. While some of his work can be accomplished via telework, he cannot complete 100% of his duties via telework. He will need to be physically present to help conduct experiments. Additionally, as a junior officer and soon as a new member

of the AFRL team, hands-on supervision and guidance from his leadership will also be crucial to his professional development, and to his ability to lead and mentor subordinates.

5. 2d Lt Doster, like other Air Force service members, must be worldwide deployable at all times to support contingency operations when called upon. The COVID-19 vaccine is necessary to be fully medically ready for deployment. From the time an individual receives his or her first dose of the FDA-approved COVID vaccine, it takes about one month to become fully vaccinated, and Airmen may need to deploy on a few days' notice. Service members have the responsibility to stay deployment-ready in the event that they get individually tasked with a deployment. Additionally, the symptoms of the COVID-19 virus (e.g., fever, chills, shortness of breath, fatigue, muscle aches, headaches, etc.) create an unacceptable risk to personnel and substantially increase the risk of mission failure, both in garrison (i.e., a non-deployed setting) and in a deployed environment.

6. The threat of sickness in a deployed environment is even more serious. Most forward-deployed locations do not have extensive medical facilities like we are accustomed to here in the United States. Supplies, beds, and staff are many times at a minimum. When deploying, service members typically travel to the deployed location via airplane, such as the C-17, C-5, or C-130. The number of service members deploying can vary and, because necessary equipment is also loaded on the aircraft as cargo, the service members are very likely to be in close proximity to one another during the flight. Depending on the equipment and personnel required for the particular deployment and the aircraft available, the physical distance between deploying personnel on the aircraft may range from shoulder-to-shoulder up to separation of at least 6 feet. Additionally, because deployments can be anywhere in the world, the flight to the deployed location can range from a single-leg flight of 20 minutes to a multiple-leg flight of greater than

15 hours. Furthermore, having a COVID-19 outbreak while deployed, where everyone is in close contact and living within the same area for months at a time, could easily overwhelm that location's medical capacity, taking away from treating front-line battle injuries and other illnesses. Deployed personnel and staffing are also, by design, minimally manned. If one service member were to get sick, contract long-COVID, get hospitalized, or die, that section may only have one extra person performing similar duties, leaving little redundancy and backup to support the mission. An outbreak impacting multiple service members could risk support to the mission altogether.

7. In austere, deployed locations, it is common for Airmen to live, eat, and sleep in close quarters for months at a time. This may include working, sleeping, and eating in tents or other temporary structures, which would not allow for social distancing. Any disease outbreak, particularly amongst unvaccinated individuals, could easily overwhelm that location's medical capacity, which reduces capacity to treat front-line battle injuries and other illnesses. Further, deployed personnel and staffing are manned minimally with only those service members necessary to accomplish the mission downrange. As such, there is little redundancy in the manning and each casualty due to illness has a significant impact on successful mission accomplishment. An outbreak impacting multiple service members could cause mission failure.

8. Testing for COVID-19 immediately prior to deployment is not an effective alternative. Due to the nature of deployments, it may not be possible to obtain test results back before 2d Lt Doster is scheduled to deploy. In addition, if he tested positive immediately prior to deployment, the military would have to quickly modify its operational plans to either find a replacement or risk deploying without his expertise. And even if he tested negative prior to deployment he would remain unvaccinated and more vulnerable to harm if infected. Either scenario threatens to

degrade the unit's operational capabilities. In a worst-case scenario, the unit's deployment would be delayed until another qualified officer could be mobilized on extremely short notice. These delays – whether caused by having insufficient officers on the ground or not being able to deploy on time until a replacement can be found – would have real-world impacts on military operations.

9. Giving 2d Lt Doster an alternate position as an accommodation or placing him in a non-deployable status is not a feasible alternative to vaccination. The Air Force places a service member in a non-deployable position when the service member faces a critical medical issue that requires him or her to be within a certain distance of medical facilities. In the case of 2d Lt Doster, his non-deployable status is controllable and can be resolved with the COVID-19 vaccine. It would not be safe for him, or those around him, for him to deploy without the vaccine. The mission of the Air Force is to ensure that service members of each unit are trained and ready for deployment in support of the National Defense Strategy. The unit cannot afford to place 2d Lt Doster in a non-deployable status because of the ever-increasing need and dependence on an already short-staffed requirement. Having a member non-deployable places a larger burden on the other service members within his section and hurts overall unit readiness. Should he be tasked to deploy upon completion of his studies, 2d Lt Doster would not be able to deploy with the unit because of his vaccination status. This means that 2d Lt Doster's unit would be unable to provide the full support required for the deployment, degrading mission capabilities.

10. On September 20, 2021, I provided 2d Lt Doster an order that directed him to receive his first dose of a COVID-19 vaccine and provide proof of the same by September 28, 2021. The order also required him to receive his second dose of a COVID-19 vaccine (if the vaccination series required it) and provide proof of the same by October 19, 2021. These dates are based on

the Secretary of Defense's vaccine mandate issued on August 24, 2021, and the deadline set by the Secretary of the Air Force in his memorandum issued on September 3, 2021. The Air Force deadline for active duty members to be fully vaccinated was November 2, 2021.

11. The order also specified that 2d Lt Doster could alternatively submit a Religious Accommodation Request or proof of a medical exemption by the deadline specified for the first dose of the vaccine.

12. 2d Lt Doster received the order and signed, acknowledging receipt and understanding of the order on September 22, 2021. To the best of my knowledge, 2d Lt Doster has not received any COVID-19 vaccinations.

13. Prior to receiving my written order on September 20, 2021, and in light of guidance from the Secretary of the Air Force directing Airmen to be fully vaccinated against COVID-19 by November 20, 2021, on September 7, 2021, 2d Lt Doster submitted a written request for a religious accommodation to exempt him from the COVID-19 vaccination requirement. As part of the process for the religious accommodation request, 2d Lt Doster received counseling from Lieutenant Colonel Don Salvatore, Section Commander, AU Det 1, on September 13, 2021, regarding the implications and potential challenges related to the request, including potential impacts related to deployment, assignments, and international travel. He then received counseling from the 88th Warrior Operational Medicine Clinic on September 17, 2021. On October 1, 2021, he spoke with a Chaplain from the Wing about his request. Upon completion of the required counseling, as directed in Department of the Air Force Instruction (DAFI) 52-201, *Reli ious reedom in the epartment of he Air* Force, 2d Lt Doster's request was routed through the religious resolution team, the legal office, and the chain of command for recommendations and endorsements pursuant to the procedures set out in DAFI 52-201.

14. On January 6, 2022, 2d Lt Doster's request for a religious accommodation was disapproved by the Air Education and Training Command (AETC) Commander, and 2d Lt Doster received notice of that denial on January 11, 2022. On January 18, 2022, 2d Lt Doster appealed the denial to the Air Force Surgeon General.

15. On February 28, 2022, Lt Col Salvatore notified 2d Lt Doster that his appeal was denied by the Air Force Surgeon General on February 22, 2022. The Air Force Surgeon General found that 2d Lt Doster's duty assignment requires "intermittent to frequent contact with others and is not fully achievable via telework or with adequate distancing." The Air Force Surgeon General also determined that 2d Lt Doster's "health status as a non-immunized individual in this dynamic environment, and aggregated with other non-immunized individuals in steady state operations, would place health and safety, unit cohesion, and readiness at risk." Following notification of his denied appeal, on February 28, 2022, 2d Lt Doster was also presented with an order to receive his first dose of the COVID-19 vaccine within five calendar days. Alternatively, he was informed that he could elect to apply for voluntary separation by the same deadline.

16. Pursuant to DAFI 52-201, 2d Lt Doster was temporarily exempt from the COVID-19 vaccination requirement for the duration of the processing of his religious accommodation request, beginning on September 7, 2021 through February 28, 2022 when he was notified of the denial of his appeal. Should 2d Lt Doster elect to request voluntary separation, he would again be considered temporarily exempt from the vaccination requirement pending a determination of his eligibility for voluntary separation.

17. No administrative or disciplinary action has been taken against 2d Lt Doster for his refusal to begin the COVID-19 vaccination process or for his decision to submit a request for religious accommodation. If he refuses to be vaccinated or to request voluntary separation, 2d Lt

Doster has been notified that he would be subject to administrative and/or punitive action for failing to obey an order, under Article 92, Uniform Code of Military Justice.

18. To the best of my knowledge, 2d Lt Doster previously met all vaccination requirements for his position as a member of the United States Air Force.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

HARMER.PAUL.K.1188115736 Digitally signed by HARMER.PAUL.K.1188115736 Date: 2022.03.08 21:35:11 -05'00'

PAUL K. HARMER, Colonel, USAF, Ph.D.
Commander, Air University Det 1
Air Force Institute of Technology

Exhibit 21

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO

HUNTER DOSTER, *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	No. 1:22-cv-00084
	)	
FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	
	)	

DECLARATION OF COLONEL DEEDRIC L. REESE

I, Deedrick L. Reese, hereby state and declare as follows:

1. I am a Colonel in the United States Air Force currently assigned as the Commander, 1st Special Operations Maintenance Group (1 SOMXG). I was appointed to command the 1 SOMXG on June 11, 2021. The 1 SOMXG is under the 1st Special Operations Wing (1 SOW) at Hurlburt Field, Florida.

2. I am generally aware of the allegations set forth in the pleadings filed in this matter. I make this declaration in my official capacity as the Commander, 1 SOMXG, and based upon my personal knowledge and upon information that has been provided to me in the course of my official duties.

3. I am Airmen 1st Class McKenna Colantonio's Group Commander. A1C Colantonio is an aircraft maintenance fuels technician assigned to the 1st Special Operations Maintenance Squadron (1 SOMXS), which falls under my command in the 1 SOMXG. At the time the Secretary of Defense issued the COVID-19 vaccine directive on August 24, 2021, A1C Colantonio was administratively assigned to the 1 SOMXS under Accessories Flight and is operationally serving a voluntary tour with the Hurlburt Field Base Honor Guard Team.

4. A1C Colantonio enlisted into the Air Force on 10 December 2019. After completing basic training, A1C Colantonio attended technical school, an initial skills training course, before she was able to perform duties as a fuels maintainer in the Air Force.

5. Fuels maintenance training takes approximately two months to complete, during which time the service member is required to complete classroom instruction and testing, in addition to working on mock trainers and training aircraft to learn basic maintenance skills. A1C Colantonio completed her technical skills training on April 2, 2020 and then proceeded to her first duty station at Hurlburt Field, FL.

6. In addition to initial skills training, A1C Colantonio is required to continue with qualification and proficiency on-the-job training in order to pursue her next skill level upgrade. This period takes approximately 12 months to complete to be awarded the 5-skill level. A1C Colantonio completed all her required tasks after 12 months in training and was awarded her 5-skill level on April 7, 2021. In addition to her maintenance skills training, she is also required to complete any personal readiness items, such as taking mandatory annual Air Force trainings and ensuring she is up-to-date on dental and medical requirements. These are secondary duties which all military personnel are expected to perform in addition to their primary duties. A1C Colantonio had completed her annual training and medical requirements which would otherwise qualify her to be in a fully deployment ready status. However, because she has not received the COVID-19 vaccine, she is currently not medically ready and is not in a fully qualified deployment ready status.

7. As a fuels technician, A1C Colantonio's primary duties includes maintaining AFSOC C-130 and CV-22 aircraft fuel systems and ensuring timely and proper completion of associated maintenance tasks. Although some of this work may be able to be accomplished individually,

many of her tasks will require her to work in close settings with other service members. There are currently 91 members in the fuels shop spread across three shifts, in addition to a weekend duty crew. This equates to 21-24 members per shift at any given time, accounting for ten percent of members who may be out on leave, appointments, medical, or for other reasons. Weekend duty would entail 6-8 members on a Friday through Monday schedule.

8. A1C Colantonio is unable to perform her duties via remote work or telework. This is true for all maintainers, but is especially true for someone like A1C Colantonio who is too early in her training and career to be assigned strictly administrative duties. The shop and hangar in which she performs her work consists of administrative offices, a breakroom, training rooms, restrooms and lockers rooms, and a large hangar area for fuel cell maintenance tasks. The office space is reserved for flight leadership, while breakrooms, training rooms, and restrooms are shared space. Depending on the tasks required, A1C Colantonio could be in contact with up to 10 to 20 service members during her duty day with a duty day lasting 8 hours. If A1C Colantonio was assigned to a weekend duty schedule, she could be in contact with 10-20 service members on Fridays and Mondays for a 10 hour duration, and 6-8 service members for a 12 hour duration on Saturdays and Sundays. Aircraft fuels maintenance averages 5 steady jobs that average under 48 hours to complete per week and have had surges of up to 9-10 major jobs. The major jobs can consist of maintenance actions that require depopulation (i.e., removal) of components and access to internal and external fuel tanks. Members may be required to crawl inside a fuel tank for repairs and maintenance actions can take anywhere from 24 to 300 hours of maintenance, depending on the extent of the repair. The unexpected loss of manpower can delay those repairs.

9. A COVID-19 outbreak among the fuels shop where A1C Colantonio is assigned could result in members being ordered to quarantine or isolate, during which time they would be unable to perform aircraft maintenance. If members are in quarantine, they cannot come into the section for a specified period, dependent upon current Health Protection Conditions (HPCON) levels and medical guidance from supporting organizations that dictate quarantine or isolation procedures and timelines. Depending on the severity of an outbreak and loss of manpower due to quarantine, isolation, or physical illness, an outbreak of COVID-19 could risk mission accomplishment, delaying or preventing repairs to operational aircraft. In turn, this could impact the ability to successfully deploy those aircraft in support of special operations throughout the world, degrading Special Operations Command's ability to execute the mission.

10. A1C Colantonio, like other Air Force members, must be worldwide deployable at all times. Because of the unique nature of special operations, airmen in Air Force Special Operations Command (AFSOC) and in the 1 SOMXG may need to deploy within a few days' notice. The service members in the 1 SOMXS have the responsibility to stay deployment-ready in the event that not only they get individually tasked with a deployment, but in the event of a rapid response required due to world events. The COVID-19 vaccine is necessary to be fully medically ready for deployment. From the time an individual receives his or her first dose of a two dose COVID-19 vaccine, it takes about one month to become fully vaccinated. Additionally, the symptoms of the COVID-19 virus (e.g., fever, chills, shortness of breath, fatigue, muscle aches, headaches, etc.), the risk that Airmen could get "long COVID," and the possibility that Airmen could get seriously ill, become hospitalized, and die from COVID-19 create an unacceptable risk to personnel and substantially increase the risk of mission failure, both in garrison (i.e., a non-deployed setting) and in a deployed environment. The threat

of sickness in a deployed environment is even more serious. Most forward-deployed locations do not have extensive medical facilities like we are accustomed to here in the United States. Supplies, beds, and staff are many times at a premium. Furthermore, having a COVID-19 outbreak while deployed, where everyone is in close contact and living within the same area for months at a time, could easily overwhelm that location's medical capacity and take away from the Air Force's ability to treat front-line battle injuries and other illnesses. Deployed personnel and staffing are also, by design, minimally manned. If one service member were to get sick, contract long-COVID, get hospitalized, or die, that section may only have one extra person performing similar duties, leaving little redundancy and backup to support the mission. An outbreak impacting multiple service members could potentially risk support to the mission altogether.

11. I am aware that, in accordance with Air Force regulation, Department of the Air Force Instruction (DAFI) 52-201, *Reli ious reedom in the epartment of he Air orce*, A1C Colantonio requested a religious accommodation and asserted that her request is based on the premise and principle that she has a sincerely held belief in her Catholic convictions, which prevent her from taking this vaccine. Her request was processed in accordance with the procedures set out in DAFI 52-201.

12. A1C Colantonio submitted her request for religious accommodation on September 20, 2021 to her commander of the 1 SOMXS, Major Howard Church. In her memorandum, A1C Colantonio stated, "I respectfully request a religious exemption from the COVID-19 Johnson & Johnson, Pfizer, Moderna vaccination/immunization mandate (to, indefinitely, include and, surely, not exempt any other past, present, or future formulas) set forth by the Secretary of Defense on 24 AUGUST 2021 on the grounds of religious accommodation." She summarized,

"In the end, my arguments are not to contest medical advancement and progression, so long as it is morally derived and experimented; truthfully, I am fighting mandates directly."

13. A1C Colantonio conducted, documented, and signed confirmation of a counseling session with Major Church on September 29, 2021, discussing all the details of the COVID-19 vaccine requirements and options for receiving the vaccine, and the process should she choose to pursue a medical, administrative, or religious exemption waiver. A1C Colantonio met with the Hurlburt Field Chaplain, Captain Mathew Campbell, on September 30, 2021. A1C Colantonio also met with the 1st Special Operations Medical Group to discuss the COVID-19 vaccine and her reservations to the vaccine, as documented in a memorandum dated September 30, 2021.

14. A1C Colantonio's initial religious accommodation request, the signed unit commander counseling memorandum, the chaplain recommendation memorandum, and the medical counseling memorandum were then submitted to the Religious Request Team (RRT) on October 5, 2021; received at the legal office; and was routed to her immediate commander, Major Church, for a commander endorsement memorandum. Each commander in A1C Colantonio's chain of command, including myself, reviewed and provided a recommendation.

15. On December 6, 2021, A1C Colantonio was notified her religious accommodation request was denied by the Approval Authority: the AFSOC commander, Lieutenant General Slife. She was instructed that she had the following options: to appeal this decision to the Air Force Surgeon General (AF/SG), to opt to receive the vaccine, to apply for voluntary separation, or to continue to refuse the vaccine. She was briefed and signed the document indicating she had 5 duty days to make her decision, with a deadline of December 13, 2021.

16. On December 9, 2021, A1C Colantonio submitted her request to appeal to Major Church. On January 6, 2022, Major Church was notified by the 1 SOW that A1C Colantonio's request

was denied by the Air Force Surgeon General. The Air Force Surgeon General found that A1C Colantonio's duty as a fuels technician "requires intermittent to frequent contact with others and is not fully achievable via telework or with adequate distancing." The Air Force Surgeon General also determined that "you are a high ops tempo career field where short-notice deployment taskings occur frequently, so the delay of vaccination would incur a serious burden on the unit and degrade overall military readiness."

17. On January 11, 2022, Major Church met with A1C Colantonio to document and sign notification of her appeal request decision. She was briefed on her options of opting to receive the vaccine; voluntarily submitting for separation, if her remaining enlistment contract met a specified timeline; or continuing to refuse the vaccine. A1C Colantonio was given 5 duty days to make her decision, with a deadline of January 18, 2022. On January 18, 2022, A1C Colantonio signed the memorandum indicating she was refusing the vaccine. She was then instructed that progressive discipline would be issued, beginning with a Letter of Reprimand (LOR) for failure to follow a direct order.

18. On February 23, 2022, Maj Church served A1C Colantonio with an LOR for refusal to follow an order to receive the COVID-19 vaccine following the denial of her religious accommodation request and subsequent denial of her appeal. She was instructed that she has the right to legal counsel with the Area Defense Counsel and may provide a rebuttal within 3 duty days. The rebuttal was provided on February 26, 2022 and follow-on administrative actions are in progress.

19. To the best of my knowledge, A1C Colantonio has previously met all vaccination requirements for her position as a member of the United States Air Force.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

REESE.DEEDRICK.L.1059758990
Digitally signed by REESE.DEEDRICK.L.1059758990
Date: 2022.03.08 15:40:07 -06'00'

DEEDRICK L. REESE, Col, USAF
1 SOMXG/CC

Attachment:
Air Force Surgeon General Memorandum to A1C McKenna Colantonio, "Decision on Religious Accommodation Appeal"

Exhibit 22

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO

HUNTER DOSTER, *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	No. 1:22-cv-00084
	)	
FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	
	)	

DECLARATION OF LIEUTENANT COLONEL NICHOLAS M. ULIRE

I, Nicholas M. Pulire, hereby state and declare as follows:

1. I am a Lieutenant Colonel in the United States Air Force currently assigned as the Commander, 1st Special Operations Command Civil Engineer Squadron (1 SOCES). I was appointed to command the 1 SOCES on July 17, 2021. The 1 SOCES is under the 1st Special Operations Wing at Hurlburt Field, Florida.

2. I am generally aware of the allegations set forth in the pleadings filed in this matter. I make this declaration in my official capacity as the Commander, 1 SOCES, and based upon my personal knowledge and upon information that has been provided to me in the course of my official duties.

3. I am Staff Sergeant (SSgt) Adam Theriault's immediate commander. SSgt Theriault is an Emergency Management Journeyman assigned to 1 SOCES. At the time the Secretary of Defense issued the COVID-19 vaccine directive on August 24, 2021, SSgt Theriault continued to serve as the Non-Commissioned Officer In Charge (NCOIC) of Emergency Management plans where he reviewed wing emergency response plans. Additionally, he continues to serve as an

instructor where he teaches Chemical, Biological, Radiological, and Nuclear classes two to three times a month with class sizes of approximately thirty United States Air Force Personnel.

4. SSgt Theriault is currently assigned as a supervisor to one other Airmen in his flight and works consistently around twelve other flight members daily. SSgt Theriault does not have the capability to complete all his required duties in a telework posture, as most of his responsibilities require his physical presence. Finally, SSgt Theriault is required to be medically and physically ready to deploy. To be medically ready, he is required to be undergo annual physical health assessments, dental examinations, and be current on required vaccines. If he is not current, or has certain medical issues (e.g., needing a root canal), he would not be considered deployable until those issues were addressed. The COVID-19 vaccine is one of several vaccines that members of the armed forces are required to receive in order to be medically ready. Other vaccines include vaccination against tetanus, hepatitis A & B, polio, influenza, and others. Medical readiness requirements, including vaccination, is based on the Department of Defense's assessment as to what is necessary to minimize the health risk of service members in order to maximize lethality and effectiveness.[1] Members are assigned to specific deployment bands however, reclamas, late notifications, and last-minute personnel changes occur at a rate which always requires SSgt Theriault's readiness.

5. Remaining unvaccinated would risk both SSgt Theriault's health and the health of the other service members working in his flight, the unit, and base. The training that SSgt Theriault is responsible for providing contributes to the deployment readiness of all Hurlburt Field personnel, as he is a key instructor for mandatory deployment training requirements. Due to the

[1] Department of Defense Instruction (DODI) 6025.19, *Individual Medical Readiness IMR* , paragraph 3.d. states, in part, "Service members have a responsibility to maintain their health and fitness, meet individual medical readiness requirements, and report medical (including mental health) and health issues that may affect their readiness to deploy or fitness to continue serving in an active status.

current manning posture of this unit, including absences for deployments, personnel and shortage issues, there are a limited number of qualified instructors to manage training requirements. Finally, although personnel qualifications continue, SSgt Theriault is one of only a few Emergency Management personnel that is fully qualified to deploy and possibly lead critical mission support teams.

6. Giving SSgt Theriault an alternate position as an accommodation or placing him in a non-deployable status is not a feasible alternative to vaccination. The Air Force places a service member in a non-deployable position when the member faces a critical medical issue that requires the member to be within a certain distance of certain medical facilities. In the case of SSgt Theriault, his non-deployable status is controllable and can be resolved with the COVID-19 vaccine. It would not be safe for him, or those around him, for him to deploy without the vaccine. The COVID-19 vaccine is necessary to be fully medically ready for deployment. From the time an individual receives his or her first dose of the FDA-approved COVID-19 vaccine, it takes about one month to become fully vaccinated. Additionally, the symptoms of the COVID-19 virus (e.g., fever, chills, shortness of breath, fatigue, muscle aches, headaches, etc.), the risk that Airmen could get "long COVID," and the possibility that Airmen could get seriously ill, become hospitalized, and die from COVID-19 create an unacceptable risk to personnel and substantially increase the risk of mission failure, both in garrison (i.e., a non-deployed setting) and in a deployed environment. The threat of sickness in a deployed environment is even more serious. Most forward-deployed locations do not have extensive medical facilities like we are accustomed to here in the United States. Supplies, beds, and staff are many times at a premium. Furthermore, having a COVID-19 outbreak while deployed, where everyone is in close contact and living within the same area for months at a time, could easily overwhelm that location's

medical capacity taking away from treating front-line battle injuries and other illnesses. Deployed personnel and staffing are also, by design, minimally manned. If one service member were to get sick, contract long-COVID, get hospitalized, or die, that section may only have one extra person performing similar duties, leaving little redundancy and backup to support the mission. An outbreak impacting multiple service members could potentially risk support to the mission altogether.

7. The mission of 1 SOCES is to support day-to-day operations at Hurlburt Field, but members are also required to conduct temporary duty at alternate locations for training and presently SSgt Theriault is not qualified to participate in these events as originally assigned due to his current vaccination status. Having a member non-deployable or unable to be assigned to temporary duty outside of the unit places a larger burden on the other members within the Emergency Management section and hurts our overall unit readiness. This means 1 SOCES would be unable to provide the full support required for the deployments and other mission requirements, degrading our mission capabilities. The 1 SOCES overall readiness decreases when certain members are not vaccinated because it cannot count on everyone deploying in a moment's notice should the need arise.

8. I am aware SSgt Theriault asserts that temporary exemption from the Pfizer, Moderna, and Johnson & Johnson vaccines and honorably discharging him is a less restrictive means of accommodation to his religious accommodation request. If the Letter of Reprimand recently issued to SSgt Theriault is upheld and if he continues to refuse to get vaccinated, Air Force policy requires SSgt Theriault to be involuntarily separated.

9. On August 24, 2021 the Secretary of Defense directed all military departments to begin full vaccination of all members of the Armed Forces under DoD authority on active duty. On

September 3, 2021, Secretary of the Air Force Frank Kendall issued the COVID-19 vaccine implementation guidelines for Department of the Air Force total force military members. On September 9, 2021, I ordered SSgt Theriault to proceed to the Hurlburt Field medical clinic during the 1 SOCES chalk times on the 14th and 15th of September 2021 for vaccination. On September 15, 2021 I received a Religious Accommodation Request from SSgt Theriault which was processed. On November 10, 2021, SSgt Theriault was notified his request was denied by the approving authority. On November 19, 2021 SSgt Theriault submitted an appeal to the approving authority, the United States Air Force Surgeon General. On January 25, 2022 SSgt Theriault was notified his appeal was denied by the United States Air Force Surgeon General. The Surgeon General noted "your deployable position may require you to deploy in a time-frame in which you cannot attain fully immunized status prior to departure. Your instructor role also requires frequent contact and immersion with multiple individuals, which would significantly impact training accomplishment if you or your trainees were exposed or actively infacted."

10. On January 25th I ordered SSgt Theriault to receive an initial dose of a COVID-19 vaccine with full licensure approval from the FDA and provide proof by January 30, 2022. On February 8, 2022, SSgt Theriault was issued a Letter of Reprimand (LOR) for non-compliance with that order. On February 22, 2022, SSgt Theriault met with me to obtain my final determination concerning his LOR and was again ordered to receive the first dose of a COVID-19 vaccine with full licensure approval from the FDA in order to begin his vaccination series and provide proof of said vaccination by February 28, 2022.

11. On February 23, 2022, SSgt Theriault was offered the opportunity to take leave, if he desired, to travel to Canada to take the Novavax COVID-19 vaccine. He had previously indicated a willingness to take the Novavax COVID-19 vaccine. On February 28, 2022, SSgt

Theriault informed us he was unwilling to spend the money or take leave to obtain the Novavax COVID-19 vaccine at the advice of his lawyers.

12. On February 28, 2022, SSgt Theriault submitted a temporary exemption request to me for the period of approximately three months at which time he believed the Novavax vaccination would be available for use within the continental United States. He is temporarily exempt from the immunization requirement while the religious accommodation request is pending.

13. To the best of my knowledge, SSgt Theriault has previously met all vaccination requirements for his position as a member of the United States Air Force.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

PULIRE.NICHOLAS.M.1262677555

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Date: 2022.03.08 15:34:54 -06'00'

NICHOLAS M. PULIRE, Lt Col, USAF
Commander, 1st Spec Ops Civil Engineer Sq

Attachment:
Air Force Surgeon General Memorandum to SSgt Adam P. Theriault, "Decision on Religious Accommodation Appeal"

Exhibit 23

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF FLORIDA

HUNTER DOSTER, *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	No. 1:22-cv-00084
	)	
FRANK KENDALL, *et al.*,	)	
	)	
Defendants.	)	
	)	

DECLARATION OF LIEUTENANT COLONEL JUSTIN L. LON

I, Justin L. Long, hereby state and declare as follows:

1. I am a Lieutenant Colonel in the United States Air Force currently assigned as the Chief, Retirements, Separations, Force Management, and Assignment Policy for Military Personnel (A1P). I have been in this position since approximately June 16, 2021. As a part of my duties, I am responsible for developing and interpreting policy related to military retirements, separations, force management, and assignments, to ensure consistency with Congressional statutes, the Office of the Secretary of Defense and Department of the Air Force instructions.

2. I make this declaration in my official capacity as the Chief, Retirements, Separations, Force Management, and Assignment Policy Branch and based upon my personal knowledge and upon information that has been provided to me in the course of my official duties.

3. On August 24, 2021, the Secretary of Defense (SecDef) issued a mandate for all members of the Armed Forces under the Department of Defense's authority on active duty or in the Ready Reserve to immediately begin full vaccination against Coronavirus Disease 2019 (COVID-19).

Thereafter, on September 3, 2021, the Secretary of the Air Force (SecAF) provided additional mandatory vaccination guidance for Department of the Air Force (DAF) commanders that they take all steps necessary to ensure all uniformed service members receive the COVID-19 vaccine. This guidance directed Commanders to "take action systematically and as expeditiously as possible to ensure prompt and full vaccination of Service members." The guidance further directed all Active Duty Airmen and Guardians, unless exempted, be fully vaccinated by November 2, 2021 (SecAF Memo, September 3, 2021, Mandatory Coronavirus Disease 19 Vaccine of Department of the Air Force Military Members). In addition, the Department of the Air Force developed and promulgated a departmental-wide implementation guide, which included guidance on available administrative and medical exemptions.

4. On December 7, 2021, the SecAF provided a memorandum, "Supplemental Coronavirus Disease 2019 Vaccination Policy." The memo established specific policy and provided guidance applicable to regular Air Force and Space Force members, and Air Force Reserve and Air National Guard members. The memo included supplemental guidance concerning those who requested separation or retirement prior to November 2, 2021, whose request for medical, religious or administrative exemption from the COVID-19 vaccine are denied, and those who refuse to take the COVID-19 vaccine.

5. This memo states the following regarding pending separation or retirement: "unvaccinated regular Airmen and Guardians who submitted a request to retire or separate prior to 2 November 2021, with a retirement or separation date on or before 1 April 2022, may be granted an administrative exemption from the COVID-19 vaccination requirement until their retirement or separation date."

6. Furthermore, the memo states that "unvaccinated regular Airmen or Guardians with a request for medical, religious, or administrative exemption will be temporarily exempt from the COVID-19 vaccination requirement while their exemption request is under review." In addition, the memo states "Service members who receive a denial of their medical, religious, or administrative exemption request have five (5) calendar days to do one of the following:

1) Begin a COVID-19 vaccination regime…;

2) Submit an appeal to the Final Appeal Authority or request a second opinion on a medical exemption . If a final appeal or exemption is denied, the service member will have five (5) calendar days from notice of denial to begin the COVID-19 vaccination regimen; or

3) If able, based upon the absence of or a limited Military Service Obligation, and consistent with opportunities afforded service members prior to November 2, 2021, request to separate or retire on or before April 1, 2022, or no later than the first day of the fifth month following initial or final appeal denial."

7. Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of March 2022.

LONG.JUSTIN.LAMAR.1255594490 Digitally signed by LONG.JUSTIN.LAMAR.1255594490 Date: 2022.03.08 13:40:20 -05'00'

JUSTIN L. LONG, Lt Col, USAF
Chief, Retirement, Separation, Force Management, and Assignment Policy

Exhibit 24

DEPARTMENT OF THE AIR FORCE
1ST SPECIAL OPERATIONS CIVIL ENGINEER SQUADRON
HURLBURT FIELD, FLORIDA

MEMORANDUM FOR AFSOC/CC
1 SOW/CC
1 SOW/JA
1 SOW/RRT
1 SOMSG/CC
1 AFSOC/SG
1 SOCES/CC

FROM SSGT ADAM P. THERIAULT, 1 SOCES, 1506027647, 3E971

SUBJECT: Circumstantial Review- Temporary Religious Accommodation Request for Mandated COVID-19 Vaccination

1.) On 24 August 2021, SecDef published a memorandum pleading for full vaccination amongst the DOD against COVID-19. This request then became a directive by the Secretary of the Air Force on 3 September 2021 for all active-duty Air Force members to obtain a full vaccination on or before 2 November 2021. This order states that only a vaccine that has full FDA approval can be utilized in this effort. On or about 15 September 2021, I submitted a Religious Accommodation Request to AFSOC/CC. On or about 05 November 2021, AFSOC/CC denied the RAR. I appealed the decision on 19 Nov 2021. On or about 21 Jan 2022, the AFSG denied my appeal.

2.) In accordance with Individual readiness requirements and my previous Religious Accommodation Request, and in light of certain changed circumstances, I am seeking a *temporary* religious accommodation for the current FDA approved COVID-19 vaccinations. This is in lieu of recent developments with the named alternative, Novavax, referenced in my RAR.

3.) Novavax filed for Emergency Use Authorization (EUA) for the US market on 31 Jan 2022. Upon approval, Novavax will be made available to citizens of the United States to include members of the DoD.

4.) It is my sincerely held belief that the Novavax vaccine differs from the currently available COVID-19 treatments in the fact that I am aware of no data that directly ties any of its production, manufacture, or testing to the practice of abortion or a derivation of the practice. Additionally, based on my review of information, Novavax the company, does not seemingly participate in, endorse, or produce products relating to abortion. I thus believe, consistent with my religious beliefs, that I can receive this vaccine, which differs from currently available products on the market. Based on past EUA processes with the FDA, it is expected that this product could be available in the United States as soon as May, 2022.

5.) As per my original RAR and its subsequent appeal, I am requesting a temporary exemption: more specifically, for only that period of time that will permit Novavax's EUA to be approved and be made available to the US. In addition to the exemption, I am requesting all disciplinary action relating to this RAR be halted and any disciplinary records purged from my personnel file.

DEPARTMENT OF THE AIR FORCE
1ST SPECIAL OPERATIONS CIVIL ENGINEER SQUADRON
HURLBURT FIELD, FLORIDA

6.) I make this request based on discussions that my attorneys have had with Department of Justice attorneys.

7.) As per Departmental guidance, each Religious Accommodation Request must be individually reviewed and approved or disapproved on a case-by-case basis. What satisfies my sincerely held beliefs may not be appropriate for all members of all faiths.

8.) Please feel free to contact me via DSN -579-7951- or by email -Adam.Theriault@us.af.mil- with any questions you may have.

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Date: 2022.02.28 11:09:55 -06'00'

ADAM P. THERIAULT, SSgt, USAF
Emergency Management

ATTACHMENTS:
1. Religious Exemption Request for Pfizer COVID-19 Vaccination
2. Religious Accommodation Decision
3. Request for Appeal: Religious Accommodation Decision
4. Decision on Religious Accommodation Appeal