Exhibit D

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF NEW YORK
BUFFALO DIVISION

JOSEPH MILLER et al., *Plaintiffs,* -against- **DR. JAMES V. MCDONALD et al.,** *Defendants.*	Civil Action No. 1:23-cv-00484-EAW

EXPERT DECLARATION OF JAMES NEUENSCHWANDER, M.D.

I, Dr. James Neuenschwander, hereby state and declare as follows:

1. I am a licensed physician in the State of Michigan, dually board certified in both Emergency Medicine and Integrative Medicine.

2. I am a graduate of the University of Michigan Medical School. From 1988 until 2018, I practiced emergency medicine in regional hospitals and also started an integrative family practice in 1988 that I now work at full time. I have extensive experience caring for both children and adults though my practice and through my career as an emergency physician. In response to an increase in the number of children with neurodevelopmental delay syndromes presenting to my office, I pursued further training in the biomedical diagnosis and treatment of these neurodevelopmental delay syndromes. I have a private practice in Ann Arbor where I care for chronically ill children and adults, many of whom have been injured by vaccines or report the onset of their symptoms following receipt of one or more vaccines. My practice consists of medically complex adults and children with most of my pediatric patients having issues of

autoimmunity, allergy, gut symptoms, neurological, psychiatric, and/or behavioral issues. My approach is to identify underlying causes of their symptoms and to address the underlying causes.

3. I am the president and am on the executive committee of the Medical Academy of Pediatric Special Needs (MAPS) where I organize a fellowship training program in the biomedical approaches to pediatrics and neurodevelopmental delay. I lecture both nationally and internationally on topics relating to my areas of expertise, including those described above.

4. Because of my work, I have been qualified as an expert on vaccine injuries in multiple jurisdictions in the United States including in the United States Court of Federal Claims, Vaccine Injury Compensation Program.

5. I recognize that in discussing vaccine related issues, anything that is not entirely positive about vaccines must be proven with exacting data or government sources given the assumptions and beliefs that surround these products – especially where the data diverges from the orthodoxy. There are common beliefs about these products and then there is what is reflected in the primary sources and by the evidence. An objective review of the evidence makes plain that the pursuit of public health does not demand prohibiting the Amish from being able to attend their community schools if they cannot receive the vaccines required for school by the State of New York due to their religious beliefs. An objective review also reflects that the Declaration of Debra Blog (**Blog Decl.**) is often misleading or incorrect and otherwise fails to provide necessary context.

6. All exhibits noted below are true and correct copies or excerpts thereof, except that the relevant text in some of the exhibits has been highlighted in yellow.

I. PREVENTING INFECTION & TRANSMISSION

7. I have reviewed the Blog Decl. and Defendants' motion and opposition, and they do not contest that polio, tetanus, diphtheria, pertussis, meningococcal, and hepatitis b vaccines –

four of the six vaccines required to attend school in New York – do not prevent infection or transmission of the target pathogens in school. That is because this is indisputable. The Blog Decl. notes in paragraph 46 that "the level of herd immunity required [] depends on the contagiousness of the disease and the applicable vaccine," but fails to note that it is uncontested that for four of the six vaccines at issue, herd immunity is inapplicable. This misleads one to believe that "herd immunity" is relevant and is affected by each vaccine required by the State to attend school. That is not so.

Polio Vaccine Does Not Prevent Infection & Transmission

8. "Inactivated polio vaccine (IPV) is the only polio vaccine that has been given in the United States since 2000." Attached as **Exhibit 1** is a CDC webpage *Polio Vaccination*, available at https://www.cdc.gov/vaccines/vpd/polio/index.html.

9. "IPV… protects people from polio disease **but does not stop transmission of the virus**." Attached as **Exhibit 2** is a CDC webpage *Polio Disease and Poliovirus Containment*, available at https://www.cdc.gov/orr/polioviruscontainment/diseaseandvirus.htm (page 1 of Ex. 2) which links to CDC, *et al.*, Polio Global Eradication Initiative webpage https://polioeradication.org/polio-today/polio-prevention/the-vaccines/ipv/ (page 2 of Ex. 2) (emphasis added) which further explains: "IPV induces very low levels of immunity in the intestine. As a result, when a person immunized with IPV is infected with wild poliovirus, the virus can still multiply inside the intestines and be shed in the feces … **IPV does not stop transmission of the virus**." (Emphasis added.)

Tetanus & Diphtheria Vaccines Do Not Prevent Infection & Transmission

10. "Tetanus … does not spread from person to person." Attached as **Exhibit 3** is a CDC webpage *About Tetanus*, available at https://www.cdc.gov/tetanus/about/index.html.

Because tetanus is not contagious, any purported benefit of a vaccine is only for the recipient of the vaccine.

11. "Diphtheria toxoid helps prevent symptomatic disease but **does not prevent the carrier state nor stop the spread of infection** … [T]he known importance of carriers in the spread of diphtheria, and the demonstrated failure of toxoid to prevent the carrier state lead us to conclude that the concept of herd immunity is not applicable in the prevention of diphtheria." Attached as **Exhibit 4** is a study by CDC's Epidemiology Program *Diphtheria Immunization*, available at https://www.ncbi.nlm.nih.gov/pubmed/5026197 (emphasis added).

12. Additionally, any benefit provided by tetanus and diphtheria vaccines wanes rapidly requiring a "Td or Tdap booster every 10 years" and in "2019, the proportion of adults aged ≥19 years reporting having received any tetanus toxoid–containing vaccination during the past 10 years was 62.9%, similar to 2018." Attached as **Exhibit 5** is Table 1 of CDC's *Recommended Adult Immunization Schedule* available at https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf and **Exhibit 6** is *CDC's Vaccination Coverage among Adults*, available at https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/pubs-resources/vaccination-coverage-adults-2019-2020.html.

Pertussis Vaccine Does Not Prevent Infection & Transmission

13. In 1999, CDC provided for "exclusive use of acellular pertussis vaccines for all doses of the pertussis vaccine series." Attached as **Exhibit 7** is CDC's *Recommended Childhood Immunization Schedule – United States, 2000*, available at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm4902a4.htm.

14. "Mucosal immunity is essential to prevent colonization and transmission of B. pertussis organisms. Consequently, preventive measures such as aPVs [acellular pertussis vaccine]

that do not induce a valid mucosal response can prevent disease but **cannot avoid infection and transmission**. … aPV pertussis vaccines **do not prevent colonization**. Consequently, they do not reduce the circulation of *B. pertussis* and **do not exert any herd immunity effect**. … Lack of mucosal immune responses after aPV administration favor infection, persistent colonization, and transmission of the pathogen." Attached as **Exhibit 8** is a CDC final response, dated December 30, 2021, which cites https://pubmed.ncbi.nlm.nih.gov/24277828/ and https://pubmed.ncbi.nlm.nih.gov/31333640/ (emphasis added) and relevant pages of the studies.

15. "Many babies who get whooping cough are infected by older siblings, parents, or caregivers who don't know they have it." Attached as **Exhibit 9** is CDC's webpage *Pertussis (Whooping Cough): Causes and How It Spread*, available at https://www.cdc.gov/pertussis/about/causes-transmission.html.

16. These vaccines also wane. "Among adolescents who received … DTaP as children, in a matched case-control study, … vaccine effectiveness against pertussis within one year of Tdap vaccination was 73% (95% CI = 60%–82%), but after 2–4 years, postvaccination vaccine effectiveness decreased to 34% (95% CI = -0.03%–58%). Another study that calculated Tdap vaccine effectiveness among adolescents found that, within the first year after vaccination, effectiveness was 68.8% (95% CI = 59.7%–75.9%); by ≥4 years after vaccination, vaccine effectiveness was 8.9% (95% CI = -30.6%–36.4%)." Attached as **Exhibit 10** are the relevant pages of *Prevention of Pertussis, Tetanus, and Diphtheria with Vaccines in the United States*, available at https://www.cdc.gov/mmwr/volumes/67/rr/rr6702a1.htm.

17. Since acellular pertussis vaccines only potentially reduce symptoms but do not prevent infection and transmission, those vaccinated with this product are less likely to stay home and more likely to continue to attend school while contagious as compared to the unvaccinated.

This also explains why even with widespread use of this vaccine, the amount of circulating pertussis bacteria has not declined and the inter-epidemic intervals have not widened or changed in a significant way. https://pubmed.ncbi.nlm.nih.gov/29180031/ ("That vaccination does not prevent B. pertussis infection in humans, nor the circulation of the organism in human populations in any important manner, comes from the observation that the inter-epidemic intervals have not changed in a major way since the implementation of mass vaccination.")

18. Moreover, those receiving this product develop a defective form of immunity that renders them susceptible to repeated infection with pertussis bacterium. This is because it causes the body to generate immunity to only 5 of the around 3,000 pertussis bacterial antigens. When a vaccinated person is exposed to pertussis bacterium post-vaccination, that person's immune system generates a robust immune response to *only* these five antigens irrespective of how many times he or she is infected, a phenomenon known as linked-epitope suppression; this defective immune response renders those vaccinated susceptible to repeated infection with the pertussis bacterium. In comparison, an unvaccinated person will, after infection, have immunity to all of the approximate 3,000 pertussis antigens which, in turn, prevents reinfection for at least years and often for life upon natural boosting (exposure to pertussis). See studies cited in pertussis discussion above and https://pubmed.ncbi.nlm.nih.gov/30793754/ ("Because of linked-epitope suppression, all children who were primed by DTaP vaccines will be more susceptible to pertussis throughout their lifetimes."); https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2863370/.

Meningococcal Vaccine Does Not Contribute to Herd Immunity

19. "Rates of meningococcal disease have declined in the United States since the 1990s and remain low today. Much of the decline occurred before the routine use of MenACWY vaccines. … [D]ata suggest MenACWY vaccines have **provided protection to those vaccinated, but probably not to the larger, unvaccinated community (population or herd immunity)**." Attached as **Exhibit 11** is the CDC webpage *Meningococcal Vaccination*, available at https://www.cdc.gov/vaccines/vpd/mening/public/index.html (emphasis added).

20. Further, [p]rotection from MenACWY vaccination wanes in most adolescents within 5 years." Attached as **Exhibit 12** is the MenACWY portion of the CDC webpage *Meningococcal Vaccination for Adolescents*, available at https://www.cdc.gov/vaccines/vpd/mening/hcp/adolescent-vaccine.html.

Hepatitis B Not Transmitted in School Setting

21. "A search of our [CDC] records failed to reveal any documents" of "transmission of Hepatitis B in an elementary, middle or high school setting." Attached as **Exhibit 13** is a CDC final response regarding Hep B vaccine. It is also worth noting that "almost all children 6 years and older and adults infected with the hepatitis B virus recover completely and do not develop chronic infection." https://www.cdc.gov/hepatitis/hbv/index.htm.

22. This makes sense since hepatitis B is not transmitted through activities that occur in a school setting.

II. CHICKEN POX VACCINE

23. As for a fifth vaccine required to attend school in New York, the chicken pox vaccine, this product is – unlike the foregoing products – a live virus vaccine. This means there is, albeit modified, live chicken pox virus in each dose. Those vaccinated with this live virus can

infect others with the chicken pox virus for up to six weeks after receipt of the live vaccine. This is why its package insert, approved by FDA, explains "that transmission of varicella vaccine virus (Oka/Merck) resulting in varicella infection including disseminated disease may occur between vaccine recipients (who develop or do not develop a varicella-like rash) and contacts susceptible to varicella including healthy as well as high-risk individuals" and that "[d]ue to concern for transmission of vaccine virus, vaccine recipients should attempt to avoid whenever possible close association with susceptible high-risk individuals for up to six weeks following vaccination" including "[i]mmunocompromised individuals [and] [p]reganant women … [and] [n]ewborn infants of mothers without documented history of varicella." Attached as **Exhibit 14** are pages from the Varivax package insert, available at https://www.fda.gov/media/76008/download.

24. New York, however, does not and needs not exclude children from school for six weeks after getting the chicken pox vaccine. This is because (i) anyone immunocompromised to a degree that chicken pox could seriously harm them is already *not* attending school because if the chicken pox virus can seriously harm them so can the around 1,400 other known pathogens, (ii) pregnant women have virtually all previously been exposed to chicken pox virus and are otherwise tested for chicken pox titers, and (iii) newborns do not attend school. https://wwwnc.cdc.gov/eid/article/11/12/05-0997_article ("literature survey identified 1,407 recognized species of human pathogen"); https://www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states ("Vaccines Licensed for Use"). For this same reason, New York need not exclude unvaccinated (or vaccinated) children as explained further below.

III. SPECIFIC VACCINES DISCUSSED BY BLOG

25. The claims made in the Blog Decl. about each vaccine at issue are addressed below.

Polio Vaccine Claims by Dr. Blog

26. The Blog Decl. discusses polio or the polio vaccine at paragraphs 21, 22, 25, 53, 55, and 56.

27. The Blog Decl., however, fails to mention that the polio vaccine required for school in the United States – the exclusive polio vaccine used in the United States for over two decades – does not, as discussed above, prevent the recipient from becoming infected with and transmitting the polio virus because this product creates antibodies in the blood but not in the intestinal tract where polio proliferates and is then transmitted by fecal-to-oral contamination.

28. The Blog Decl. also fails to mention that in 1966 there were zero cases of polio reported for the entire State of New York (https://stacks.cdc.gov/view/cdc/615, p.8) and I am advised that New York State first required polio vaccination to attend school in 1967. Hence, New York already achieved zero cases of polio absent any state polio vaccine mandate.

29. The Blog Decl. fails to mention these critical facts and instead, in paragraphs 21 and 22, discusses a case of vaccine-derived poliovirus in New York in an adult. As the Blog Decl. admits, this case was not a case of the wild poliovirus but rather was the "weakened live poliovirus contained in oral polio vaccine." Thus, it was an *oral polio vaccine* that was the source of this case of polio. No other case of polio has been reported in New York (or in the US) since this one case (including no cases in this patient's immediate family).

30. Nonetheless, the Blog Decl. attempts to somehow blame the Amish. In footnote 20 the Blog Decl. admits that this case of polio "resulted from an infection of a vaccine-derived poliovirus type 2" but then claims that if this strain is "allowed to circulate in under- or unimmunized populations for long enough, or replicate in an immunodeficient individual, the weakened virus can revert to a form that causes illness and paralysis." But that is equally true for

every single American regardless of whether they are unvaccinated or vaccinated with IPV – the only polio vaccine used in the United States for over two decades. Any unvaccinated Amish students would be just as likely as anyone vaccinated with IPV to hypothetically become infected with and transmit the vaccine strain polio virus (from the oral polio vaccine used outside the United States). In fact, the average IPV vaccinated individual in New York is *more* likely to do so as they are presumably more likely than the Amish to travel outside the United States and be exposed to that vaccine strain.

31. The Blog Decl. also bemoans finding polio vaccine virus in the wastewater of counties with what it calls comparatively "low polio vaccination rates" but fails to advise that New York Department of Health (**DOH**) mainly tested counties it considered as having comparably lower polio vaccination rates. https://health.ny.gov/diseases/communicable/polio/docs/waste_water_surveillance_report.pdf; https://health.ny.gov/diseases/communicable/polio/county_vaccination_rates.htm. Obviously, it can only find something where it looks.

32. Finally, the Blog Decl. claims that "[p]aralytic polio caused by wild-type poliovirus, had been eliminated in the United States in 1979 due to high rates of polio vaccination coverage." The "high" polio vaccination rate in the United States in the 1970s was approximately 60% (it was 59.5% in 1973, 60.0% in 1974, 63.6% in 1975, 61.3% in 1976, 62.6% in 1977, and 59.5% in 1978). Attached as **Exhibit 25** is CDC's Vaccine Coverage Levels – United States, 1962-2009, available at https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/G/coverage.pdf. Thus, the counties of Montgomery and Chautauqua, in which the Amish schools at issue in this case are located, already meet Dr. Blog's criteria of "high rates of polio vaccination coverage" because their polio vaccination rates of 72.7% and 84.8%, respectively, far exceed the approximately 60% polio vaccine coverage the Blog Decl. states reflects a "high rates of polio

vaccination coverage." https://health.ny.gov/diseases/communicable/polio/county_vaccination_rates.htm.

33. Paragraph 52 of the Blog Decl. claims the "2022 reemergence of polio" is a result of lower vaccination rates but this is counter-factual because (i) the 2022 case was a strain of polio vaccine virus, (ii) the polio vaccination rate in the U.S. since 1979 has gone up from around 60 percent to over 90 percent, and (iii) making this claim otherwise requires suspending reason and reality since the polio vaccine exclusively used in the U.S. for over two decades does *not* prevent infection and transmission. If anything, it is the IPV-vaccinated who are more likely to spread polio virus because they are presumably less likely to have symptoms and know to stay home if infected.

34. Paragraph 55 of the Blog Decl. addresses the potential for someone to contract polio outside the United States and return infected to the United States; but this again ignores that New Yorkers vaccinated with IPV are equally capable of being infected with polio virus overseas and presumably on average more likely than the Amish to travel internationally.

35. Paragraph 56 of the Blog Decl. claims that the near eradication of polio can be directly attributed to vaccination despite the fact that polio receded at the same rate in parts of the country with high and low polio vaccine uptake in the 1950s and 1960s. Regardless, it is irrelevant, as the issue is whether a religious exemption would materially impact that goal. The facts reflect it would not because New York reached zero cases of polio without *any* polio vaccine mandate (and the last case of wild polio in the United States occurred in 1979 when the national polio vaccination rate was 59.7%, see Exhibit 25).

36. In all, Dr. Blog's attestations regarding the Amish and polio are misplaced because she knows or should know this vaccine does not prevent infection and transmission of polio.

Tetanus Vaccine Claims by Blog

37. The Blog Decl. specifically discusses tetanus and tetanus vaccine in paragraph 17 stating:

> in 2013 and 2016 there were two tetanus cases that occurred in St. Lawrence County, New York in children from a similar undervaccinated community that happened to be Amish. To put this in context, tetanus cases in the United States are rare, with only 233 cases total reported by the CDC in the eight year period from 2001-2008, and only 264 cases from 2009-2017. Tetanus cases have declined steadily since the 'widespread use of tetanus toxoid-containing vaccines since the late 1940s,' among other contributing factors.

The Blog Decl. fails to mention that, as discussed above, tetanus is not infectious from person-to-person and hence there is a zero percent chance of catching tetanus from an unvaccinated *or* vaccinated person. Stated differently, the risk of an unvaccinated or vaccinated person spreading tetanus to another person is identical: zero percent.

38. The Blog Decl. also fails to mention that among the 233 cases of tetanus it reports occurred from 2001 to 2008, there were no deaths in anyone under 35 years of age and that in the 264 cases it states occurred from 2009 to 2017, there were no deaths in anyone under 55 years of age. (Blog Dec. fn. 17 and 18).

39. The Blog Decl. also leaves the impression that tetanus was once common when the reality is that, even prior to the late 1940s, there were only a few hundred cases per year. (Blog Dec. fn. 17). The Blog Decl. also misleadingly states that, "Tetanus cases have declined steadily since the 'widespread use of tetanus toxoid-containing vaccines since the late 1940s'" when the reality is the decline in tetanus cases had occurred at an even faster rate from 1900 until the late 1940s and that rate simply continued after introduction of the tetanus vaccine. (Blog Decl. fn. 18 at the "Background" section). As for the period after the late 1940s, the Blog Decl. fails to mention

that CDC provides that children need six shots of tetanus vaccine (at 2 months, 4 months, 6 months, 15 months, 4 years, and 11 years of age) and then as adults another shot every ten years for life because any protection provided wanes rapidly, https://www.cdc.gov/vaccines/schedules/index.html; yet tetanus declined from a few hundred cases a year to a dozen or two a year despite the fact that well into the 1980s, only 60% to 70% of children received even three doses of tetanus vaccine (see Exhibit 25), let alone the six recommended by CDC, and the percent among adults is far less (see Exhibit 6).

40. I am advised that New York required tetanus vaccine to attend school for the first time in 2007 for 6th grade and then again in 2011 for kindergarteners. According to the DOH, there were zero cases of tetanus in the preceding years of 2006 and 2010 among school age children in the entire State of New York (and otherwise only one case total in someone over 65 years of age). https://www.health.ny.gov/statistics/diseases/communicable/.

41. Therefore, the Amish's inability to receive tetanus vaccines has not contributed and is not contributing to the spread of tetanus and Dr. Blog knows or should know that tetanus is not transmissible from person to person.

Pertussis Vaccine Claims by Blog

42. The Blog Decl. specifically discusses pertussis and pertussis vaccine in paragraph 17 stating that: "In 2004, 345 cases of pertussis occurred in an undervaccinated community in Delaware that happened to be Amish, affecting primarily preschool-aged children. Of the 123 patients ages 6 months – 5 years residing in households where confirmation interviews occurred, 88 (72%) had no records of receiving a vaccination with diphtheria-tetanus-pertussis (DTP/DTaP)."

43. The Blog Decl. fails to mention that, as discussed above, while the pertussis vaccine may reduce symptoms if the recipient is infected with the pertussis bacteria, it does not prevent the vaccinated person from becoming infected with and transmitting pertussis. (Exhibit 8). In fact, as also discussed above, FDA's study regarding this issue found that those vaccinated carried the pertussis bacteria in their nasopharynx for an even *longer period* on average than the unvaccinated, and CDC warns that asymptomatic individuals can spread pertussis. (Exhibits 8 and 9). That the Amish are more likely to have a "case" of pertussis merely means they are more likely to have a symptomatic case of pertussis; but this fact – that they are more likely to be symptomatic, rather than more likely to be asymptomatic like the vaccinated – makes the unvaccinated Amish *less* likely to spread pertussis. This is because individuals with symptoms stay home from school; the vaccinated who are asymptomatic are more likely to keep going to school which will allow them to transmit. Reflecting this reality, as discussed above, is the fact that the amount of circulating pertussis bacterium has not deceased since introducing the pertussis vaccine.

44. As explained in a consensus study produced by CDC in response to a request for "Documents sufficient to reflect that acellular pertussis vaccines, while reducing symptoms from pertussis, do not prevent infection and transmission":

> Mucosal immunity is essential to prevent colonization and transmission of B. pertussis organisms. Consequently, preventive measures such as aPVs [acellular pertussis vaccine] that do not induce a valid mucosal response can prevent disease but cannot avoid infection and transmission. … aPV pertussis vaccines do not prevent colonization. Consequently, they do not reduce the circulation of *B. pertussis* and do not exert any herd immunity effect. … Lack of mucosal immune responses after aPV administration favor infection, persistent colonization, and transmission of the pathogen.

(Exhibit 8).

45. It is therefore also not surprising that after New York first required pertussis vaccine to attend school in 2007 for 6th grade and in 2011 for kindergarteners, as I am advised, the number of cases of pertussis from 1994 to 2020 (the years available on the DOH website) have had a moderate *increasing* trendline over that period. https://www.health.ny.gov/statistics/diseases/communicable/.

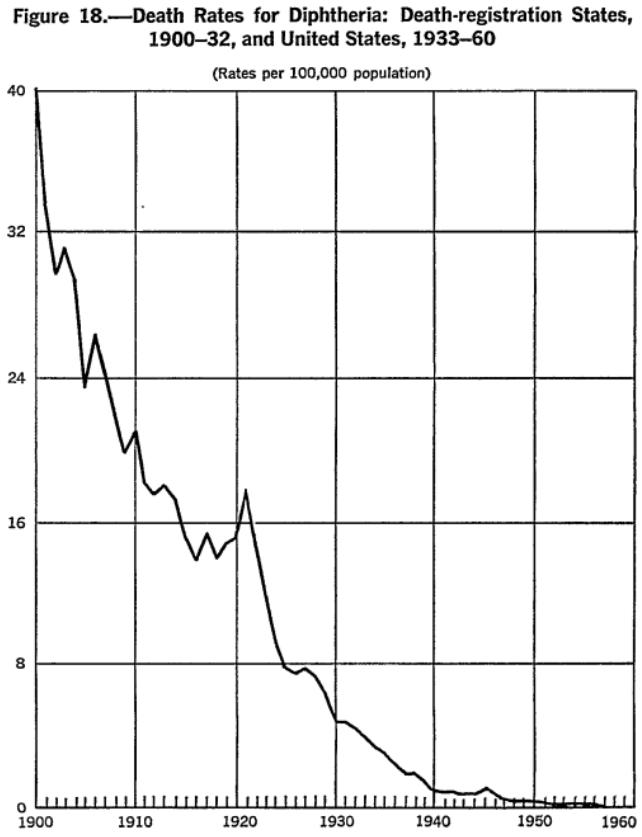
46. The Amish's inability to receive pertussis vaccines is not contributing to the spread of pertussis, and certainly not more so than vaccinated individuals. Dr. Blog knows or should know that the pertussis vaccine does not prevent infection and transmission of pertussis bacterium.

Rubella and Diphtheria Vaccine Claims by Blog

47. The Blog Decl. in paragraph 55 states that "contagious diseases that have been declared eliminated from the United States such as rubella … have … occurred in other countries" and in paragraphs 56 states that "deadly diseases such as diphtheria and rubella are becoming a rarity in the United States as a result of the routine use of vaccination against these and other infectious diseases." No support is cited for either assertion.

48. Dr. Blog's statement implies that deadly cases of rubella were not a rarity prior to the availability of a rubella vaccine. The first rubella vaccine was developed in 1969. In 1968 there were, according to CDC, a total of 24 deaths from rubella in the entire United States, amounting to one death for every approximately 8 million Americans. (Attached as **Exhibit 26** is a CDC chart reflecting annual deaths from certain diseases.) That is less than the number of individuals who die from lightning every year in the United States. https://www.cdc.gov/disasters/lightning/victimdata/infographic.html. Contrary to the claim in the Blog Decl., death from rubella was already "a rarity" before any vaccine for rubella existed.

49. Regarding diphtheria, CDC data reflects that mortality from diphtheria declined by well over 97% *prior* to routine use of the diphtheria vaccine as reflected in the following U.S. government chart:



See **Exhibit 27** and a full copy is available at https://stacks.cdc.gov/view/cdc/6200. In any event, I am advised New York first required diphtheria vaccine to attend school in 1971, and in the year prior, there was one case of diphtheria reported for the entire State of New York. https://stacks.cdc.gov/view/cdc/951, p. 9. Mandating diphtheria vaccination, let alone mandating it without any religious exemption, was not necessary to eliminate diphtheria from New York.

Measles Vaccine Claims by Blog

50. The Blog Decl. focuses primarily on measles. *See* ¶¶ 3-16, 20, 25, 50, and 53.

51. The Blog Decl., in paragraphs 3 through 16, discusses cases of measles in New York from 2018-2019 and references that outbreak in paragraphs 20, 25, 50 and 53.

52. The documentation to which the Blog Decl. cites does not reflect a single case of measles in the Amish community in New York during this period.[1]

53. The Blog Decl. blames the number of measles cases in 2018-2019 on pockets of under-vaccination, but I understand that a major contributor to measles cases in 2018-2019 were "measles parties." [2] Families with religious beliefs contrary to measles vaccine could only send their children back to school with either proof of vaccination or proof of prior infection so, as the state recognized at the time, many opted for the latter.

54. In any event, excluding the Amish from school for not having had a measles vaccine will not, they have advised, change the level of measles vaccination in their community. The Amish families that do not vaccinate have made clear they will not vaccinate.

55. The implications regarding measles and the safety and efficacy of the measles vaccine in the Blog Decl. are also highly misleading.

Safety of the Measles Vaccine

56. Clinical trials relied upon by FDA to license Merck's MMR vaccine in 1978 had a total of 834 children, no control group, and only 42 days of safety review during which, among other adverse events, around a third of the participants developed gastrointestinal issues and a third

[1]The Blog Decl. at footnote 10 explains regarding Yates County that, like the Amish, "[a]t the time of the outbreak, Yates County has the lowest MMR vaccination rate of any county in New York State; however, it is geographically distant from the 2018-2019 outbreak and the unvaccinated community is socially isolated and had not had contact with measles."

[2] *See* https://www.youtube.com/watch?v=ndkoAqcPUg8 at 25:30 (New York State Department of Health expressing concern that families are having measles parties in response to a question about increasing numbers of cases).

developed respiratory issues. Attached as **Exhibit 16** are the relevant pages of the MMR clinical trial reports, full copy available at https://sirillp.com/MMR-clinical-trial. A similar trial was relied upon to license the original MMR vaccine in 1971, see **Exhibit 28** which includes the relevant tables from that trial, full copy available at https://sirillp.com/original-MMR-clinical-trial.

57. By the mid-1980s, there were three routine childhood vaccines (MMR, DTP, and OPV) and numerous sources report that the financial liabilities from these products drove the United States Congress to pass the National Childhood Vaccine Injury Act of 1986 which gave pharmaceutical companies immunity to liability for injuries and deaths caused by these and future childhood vaccines.[3] Attached as **Exhibit 17** is CDC's childhood vaccine schedule from 1983, available at https://www.cdc.gov/vaccines/schedules/images/schedule1983s.jpg. Instead of suing the manufacturers, those who allege they have been injured by a vaccine are required to file their claim against the Secretary of the U.S. Department of Health & Human Services in the Vaccine Injury Compensation Program, part of the U.S. Court of Federal Claims.

58. While the federal health authorities, including CDC and FDA, avoid disclosing harms about vaccines, the CDC "Vaccine Information Statement" does disclose that "after MMR vaccination, a person might experience:" "seizure," "deafness," "long-term seizures, coma, or lowered consciousness," and "brain damage." Attached as **Exhibit 15** is CDC's Vaccine Information Statement for MMR vaccine.

59. After licensure, it is my understanding that federal law (21 C.F.R. 201.57(c)(7)) requires that the package insert for MMR, prepared by Merck and approved by FDA, list

[3] In *Bruesewitz v. Wyeth*, 562 U.S. 223 the Supreme Court said that "by the mid-1980's … the remaining manufacturer … estimated that its potential tort liability exceeded its annual sales by a factor of 200" and "the Vaccine Injury Act pre-empts all design-defect claims against vaccine manufacturers … for injury or death caused by a vaccine side effects."

"*only* those adverse events for which there is some basis to believe there is a *causal relationship* between the drug and the occurrence of the adverse event." Adverse events listed in MMR's package insert include:

> vasculitis, pancreatitis; parotitis; thrombocytopenia; purpura; regional lymphadenopathy; leukocytosis; angioedema (including peripheral or facial edema); bronchial spasm; arthritis; arthralgia; myalgia; encephalitis; encephalopathy; measles inclusion body encephalitis (MIBE) subacute sclerosing panencephalitis (SSPE); Guillain-Barré Syndrome (GBS); acute disseminated encephalomyelitis (ADEM); transverse myelitis; febrile convulsions; afebrile convulsions or seizures; ataxia; polyneuritis; polyneuropathy; ocular palsies; paresthesia; pneumonia; pneumonitis; Stevens-Johnson syndrome; acute hemorrhagic edema of infancy; Henoch-Schönlein purpura; erythema multiforme; nerve deafness; retinitis; optic neuritis; papillitis; epididymitis; orchitis

Attached as **Exhibit 18** is the package insert for the MMR vaccine, available at https://www.fda.gov/media/75191/download.[4]

60. In 2022, GSK obtained licensure of an MMR vaccine (**Priorix** or **MMR-RIT**) based on a clinical trial comparing it to Merck's MMR vaccine (**M-M-R-II**) in which both vaccine groups, within six months of administration, had serious adverse events, emergency room visits, and new onset of chronic diseases (*e.g.*, autoimmune disorders, asthma, type I diabetes, vasculitis, celiac disease, allergies) as summarized by GSK below:

[4] Merck, GSK, and Sanofi make all the vaccines products required to attend school in New York, and these companies disclose in Section 6.2 of the package insert for each numerous serious adverse events they have a basis to believe are casually related to these products. A copy of the FDA's *Vaccines Licensed for Use in the United States* webpage is available at https://www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states.

Supplementary Table 6. Incidence of unsolicited adverse events (Day 0–42), serious adverse events, AEs prompting emergency room visits and NOCDs (Day 0–180) (total vaccinated cohort).

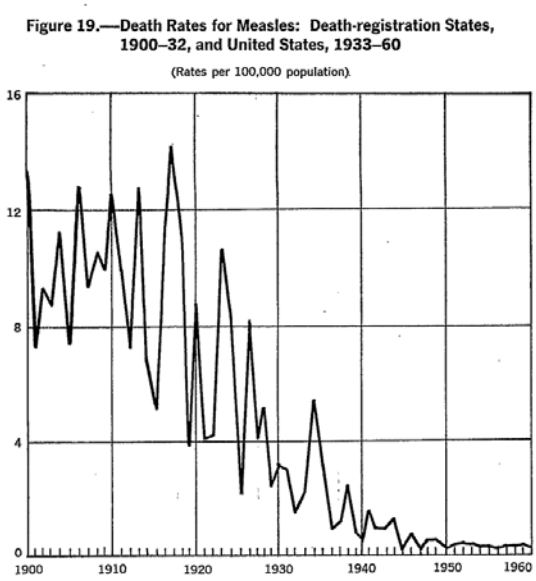
n (%)	MMR-RIT (N=3714)	MMR II (N=1289)
Unsolicited AEs (≥1 symptom)	1857 (50.0)	618 (47.9)
Grade 3	225 (6.1)	85 (6.6)
SAEs (any, ≥1 SAE)	77 (2.1)	25 (1.9)
AEs prompting ER visit	375 (10.1)	134 (10.4)
NOCDs (any, ≥1 NOCD)	128 (3.4)	48 (3.7)

AE, adverse event; ER, emergency room; N, number of children with the documented dose; n (%), number (percentage) of children reporting the AE at least once; NOCDs, new onset chronic diseases (see definition in Patients and methods); SAE, serious AE.
Grade 3 unsolicited AEs were those preventing normal, everyday activities.

Attached as **Exhibit 19** are the relevant pages of the Supplementary Materials for Priorix, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7192400/, summarizing the content of **Exhibit 20** which are the relevant pages of the FDA Clinical Review for Priorix, full version at https://www.fda.gov/media/159591/download; **Exhibit 21** is the FDA webpage *What is a Serious Adverse Event?*, available at https://www.fda.gov/safety/reporting-serious-problems-fda/what-serious-adverse-event.

Efficacy of the Measles Vaccine

61. Measles mortality in the United States declined by over 98% between 1900 and 1963, the year the first measles vaccine was introduced. Attached as **Exhibit 22** are the relevant pages of the U.S. Public Health Service's *Vital Statistics Rates in the United States 1940-1960* (full version at https://www.cdc.gov/nchs/data/vsus/vsrates1940_60.pdf) showing measles mortality in 1900 was 13.3 deaths per 100,000 individuals and in 1960 was 0.2 deaths per 100,000 individuals, a decline of over 98%, and includes the following chart:



Attached as **Exhibit 23** are the relevant pages of the *Vital Statistics Rates in the United States 1962* showing measles mortality in 1961 and 1962 was 0.2 deaths per 100,000 individuals, full version available at https://www.cdc.gov/nchs/data/vsus/VSUS_1962_2A.pdf.

62. The over 98% decline in measles mortality in that period had nothing to do with a measles vaccine since none existed during that period.[5] In countries or areas with limited nutrition, sanitation, acute care, and clean water, deaths from measles can still occur at a higher rate and those conditions still existed in pockets of the United States in the early 1960s.

63. There were approximately 400 deaths per year in the United States in the years before the first measles vaccine in 1963. Exhibit 23, p.3. This amounts to approximately one measles death for every 500,000 Americans at a time when nearly every American had measles.

[5] England and Whales had a similar decline of over 99% in its measles death rate between 1900 and 1968 when the first measles vaccine was introduced there, five years after first being introduced in the U.S. *See* https://webarchive.nationalarchives.gov.uk/ukgwa/20160111174808/http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-215593.

https://www.census.gov/library/publications/1962/compendia/statab/83ed.html providing the total U.S. population in 1962 was approximately 186 million people.

64. Japan tracked over 100,000 of its citizens for over 22 years and found a statistically significant reduction in mortality from cardiovascular disease and stroke among those who *had* measles and mumps as reflected in the following truncated table and chart from the study:

Table 2
Age-adjusted and multivariable hazard ratios (HR) and 95% Confidential Intervals (CI) for Cause-specific mortality according to history of measles or mumps.

History of measles or mumps	Men				Women			
	None	Measles only	Mumps only	Measles and mumps	None	Measles only	Mumps only	Measles and mumps
No. at risk	21,245	14,671	730	7043	24,950	21,202	1256	12,739
Person-years	326,940	236,327	11,802	116,443	411,090	358,358	19,963	209,207
Total stroke, n	946	613	11	159	803	640	31	193
Age-adjusted HR (95% CI)	1.00	0.97 (0.87–1.07)	0.52 (0.29–0.94)	0.83 (0.70–0.98)	1.00	1.07 (0.96–1.18)	1.24 (0.86–1.77)	0.85 (0.73–0.99)
Multivariable HR (95% CI)[a]	1.00	0.95 (0.85–1.06)	0.52 (0.29–0.94)	0.83 (0.70–0.99)	1.00	1.06 (0.95–1.19)	1.27 (0.88–1.82)	0.85 (0.72–0.99)
+ history of CVD[b]	1.00	0.95 (0.85–1.06)	0.52 (0.28–0.94)	0.83 (0.69–0.98)	1.00	1.06 (0.94–1.19)	1.22 (0.87–1.75)	0.84 (0.71–0.99)
Total cardiovascular disease, n	2243	1383	38	365	1913	1378	57	439
Age-adjusted HR (95% CI)	1.00	0.92 (0.86–0.99)	0.76 (0.55–1.04)	0.80 (0.71–0.89)	1.00	0.97 (0.91–1.05)	0.98 (0.75–1.27)	0.83 (0.75–0.92)
Multivariable HR (95% CI)[a]	1.00	0.92 (0.86–0.99)	0.75 (0.55–1.04)	0.81 (0.72–0.91)	1.00	0.98 (0.91–1.06)	1.01 (0.78–1.32)	0.83 (0.75–0.93)
+ history of CVD[b]	1.00	0.92 (0.85–0.99)	0.75 (0.54–1.04)	0.80 (0.71–0.90)	1.00	0.97 (0.90–1.05)	0.97 (0.75–1.27)	0.83 (0.74–0.92)

[a] Adjusted for age, body mass index, history of hypertension, history of diabetes, family history of CVD, alcohol intake, energy intake, smoking status, walking, sports, perceived mental stress and education.
[b] Further adjustment for history of CVD. CVD indicates cardiovascular disease.

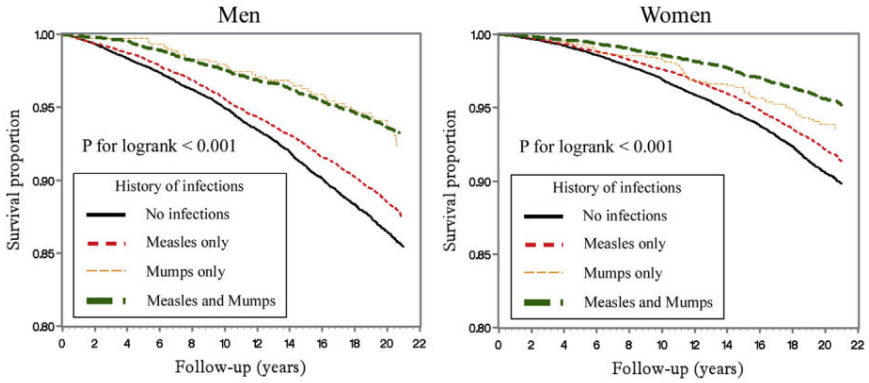


Fig. 1. Kaplan-Meire survival curves of mortality from total cardivascular disease according to the history of infections among men and women.

Attached as **Exhibit 24** is the study *Association of measles and mumps with cardiovascular disease: The Japan Collaborative Cohort (JACC) study*, available at https://pubmed.ncbi.nlm.nih.gov/26122188/. According to CDC, approximately 700,000 individuals in the United States die from cardiovascular disease every year. CDC webpage Heart Disease Facts, available at https://www.cdc.gov/heartdisease/facts.htm. Hence, introducing measles vaccine may have had

the unintended consequence of, while potentially reducing some fraction of the 400 deaths per year from measles, causing far more deaths from cardiovascular disease. [6]

65. Also relevant is that the MMR and chicken pox vaccines involve harvesting live parts of aborted babies and include in each vaccine dose billions of pieces of DNA and cellular material derived from aborted fetuses and the cellular lines created from these fetuses on which the viruses used in these vaccines are grown for vaccine production.

66. The Blog Decl. omits all of the foregoing facts about measles safety and efficacy that place this product and measles into appropriate context. The Amish are already not vaccinated for measles, and I understand will not receive this vaccine. I am also not aware of any support that the

[6] Similar to the finding regarding heart disease, but found in less robust studies, is that having measles appears to confer other health benefits. For example, the International Agency for Research on Cancer found that those who never had measles had a 66% increased rate of Non-Hodgkin Lymphoma and a 233% increased rate of Hodgkin Lymphoma. https://pubmed.ncbi.nlm.nih.gov/16406019/ (See Table 2 and in the Non-Hodgkin's Lymphoma (NHL) column divide the odds ratio 1 (never had measles) with .6 (had measles) which results in a 66% increased risk, and in the Hodgkin's Lymphoma (HL) column divide the odds ratio 1 (never had measles) with .3 (had measles) which results in a 233% increased risk.); https://seer.cancer.gov/statfacts/ (an estimated 21,170 Americans died of these cancers in 2022); https://pubmed.ncbi.nlm.nih.gov/4574047/ (reporting remission of Hodgkin's disease after having measles). Researchers at the Department of Health Care and Epidemiology at the University of British Columbia and the Department of Biology at the University of Victoria found that those who never had measles had a 50% increased rate of ovarian cancer. https://pubmed.ncbi.nlm.nih.gov/16490323/; https://seer.cancer.gov/statfacts/html/ovary.html. (an estimated 12,810 died of this cancer in 2022). Other studies have reached similar conclusions that measles as well as mumps, rubella, pertussis and chickenpox, reduce the rate of various forms of other cancers, including a study from researchers at the University of Berne, Switzerland that specifically reviewed these fever inducing (*i.e.*, febrile) infections and found that the "study consistently revealed a lower cancer risk for patients with a history of FICD [febrile infectious childhood diseases]." https://pubmed.ncbi.nlm.nih.gov/9824838/. Studies have also found that children who have had measles have far less allergies and atopic diseases, such as asthma, and adults who had measles have a reduced risk of Parkinson's Disease. https://pubmed.ncbi.nlm.nih.gov/19255001/; https://pubmed.ncbi.nlm.nih.gov/16854347/ and https://pubmed.ncbi.nlm.nih.gov/4061437/.

status quo in the Amish community in New York has resulted in any harm from measles to anyone in New York State.

Mercurial and/or Nonspecific Claims About Vaccines

67. The foregoing addresses all the claims about specific vaccines made in the Blog Decl. This section addresses the remaining claims that are not directed at any specific vaccine, apparently purposefully, and often without any citation or support.

68. Claims in paragraphs 44 through 50 of the Blog Decl. relate to herd immunity, addressed above.

69. Paragraph 48 of the Blog Decl. claims that "the State's vaccine requirement is rightfully focused on school agreed [sic] children … because they are the most susceptible to the harmful impacts of most contagious diseases." In fact, measles, mumps, rubella and chicken pox are *less* dangerous for school-aged children as compared to adults and newborns. While in the pre-vaccine era, most children had these infections during school age years. That changed in the post-vaccine era due to waning vaccine immunity and lack of robust maternal transfer of vaccine immunity to newborns.

70. The Blog Decl. also claims New York's school vaccine requirements result in "immunized adults" ignoring that New York's school mandate is for only six of the fourteen routine vaccines on CDC's childhood schedule, and even among the six required, most adults in New York were never mandated to receive them as I am advised that New York first required the recombinant HepB vaccine (first licensed in 1986) for school as of 1990, varicella vaccine (first licensed in 1995) as of 2003, pertussis and tetanus vaccines as of 2007, and conjugate meningococcal vaccine (first licensed in 2005) as of 2015.

71. Paragraph 51 of the Blog Decl. states “thousands of children each year, living in the United States, would be expected to die or be left with life-long disabilities as a result of contracting diseases now preventable by vaccination, such as smallpox, poliomyelitis, rubella, measles, diphtheria and pertussis.” First, smallpox is not a required vaccine in New York and, while historically could be deadly, is only contagious after appearance of symptoms (unlike other diseases) and, despite hundreds of years of vaccination, was finally eliminated in 1949 in the United States after the advent of proper quarantine procedures. Second, with regards to the remaining five diseases listed, claiming thousands would die today without the advent of vaccination is belied by the hard cold data and evidence, part of which is described above. For example, measles mortality was at 400 deaths per year pre-vaccine and rapidly declining without introduction of vaccination. Rubella was never lethal, recording a dozen or two deaths annually pre-vaccination and was declining without vaccination. Diphtheria mortality was also declining without vaccination and does not cause mortality today in the United States despite the fact that at least forty percent of Americans do not receive boosters to maintain immunity; this may be explained by studies finding it is only dangerous in individuals with certain nutritional deficiencies most of which have been eliminated in the United States. General statements about vaccines in the Blog Decl., without examining each vaccine, are improper.

72. The Blog Decl. makes claims in paragraph 52 without any support because the claims are nonsensical. First, it is not true that all the diseases for which vaccination is required for school in New York are highly contagious. Most are not. Second, reducing symptomatic cases does not equal reducing circulation of the pathogen for most of the diseases for which vaccination is required in New York as supported by the evidence above. Third, whatever benefit in reducing

symptoms these vaccines afford, the Amish have chosen to accept those risks due to their religious beliefs.

73. Paragraph 53 of the Blog Decl. claims that, "If enough people stop getting vaccinated, outbreaks of now-rare, preventable diseases would return." This is hyperbolic. First, I understand that the entire Amish community in New York is around 20 thousand people, only a fraction of which are school children, while there are over 20 million individuals in New York. Second, I am advised the Amish plaintiffs do not vaccinate and they cannot vaccinate; hence, this is not about whether "enough people stop getting vaccinated" because these Amish do not and cannot vaccinate due to their religious beliefs. In any event, Dr. Blog's claim is unquestionably untrue even for the larger New York population for most of the diseases for which vaccination is required for school as supported by the actual evidence discussed above.

74. Paragraph 54 of the Blog Decl. assumes that Amish children are locked away in closets, have not been attending school for years since the religious exemption was repealed, and do not otherwise congregate regularly in church, barn raisings, and in other social and communal gatherings and events. It also ignores the reality that after 8th grade, which I understand is when the Amish complete their schooling and when there are no vaccine mandates that apply to them, they resume all normal life in the Amish community, including becoming teachers at Amish schools.

75. The claims in paragraph 55 and 56 have been addressed above. The claims in paragraphs 57 and 58 are hyperbolic and reflect purposeful omission or a lack of understanding regarding the products being mandated and the epidemiology and data of the diseases at issue. These claims also ignore that the Amish have been attending school for years unvaccinated, both before and after repeal of the religious exemption in New York.

IV. AMISH CHILDREN ARE HEALTHIER

76. The Blog Decl. insinuates that if they vaccinated their children, the Amish would be healthier. The facts are to the contrary.

77. I am advised that there are 26 families across the three Amish school at issue which have a total of 168 unvaccinated children (meaning they have received no vaccines) and that none of them have any heath issue that arose after birth. In contrast, the following is a list of background rate for just some of the chronic health conditions that now plague American children:

- 5.8% background rate for food allergies (https://www.cdc.gov/healthyschools/foodallergies/index.htm);
- 19% background rate for environmental allergies (https://aafa.org/allergies/allergy-facts/);
- 6.5% background rate for asthma (https://www.cdc.gov/nchs/fastats/asthma.htm);
- 0.5% background rate for seizures (https://www.cdc.gov/epilepsy/data/index.html);
- 1 in 36 children background rate of Autism Spectrum Disorder (https://www.cdc.gov/ncbddd/autism/data.html);
- 9.5% background rate for ADHD (https://www.cdc.gov/ncbddd/adhd/data.html);
- 10.84% background rate for eczema (https://www.cdc.gov/nchs/data/health_policy/eczema_skin_problems_tables.pdf); and
- 22.3 cases per 100,000 Type 1 diabetes background rate and 13.8 cases per 100,000 Type 2 diabetes background rate (https://www.cdc.gov/mmwr/volumes/69/wr/mm6906a3.htm?s_cid=mm6906a3_w).

78. In contrast, among 168 children outside of the Amish community, on average and based on the above background rates in the U.S., one would expect that at least 9 of these 168 Amish children would have food allergies, 31 would have environmental allergies, 10 would have asthma, 4 would have Autism Spectrum Disorder, and 15 would have ADHD.

79. The 168 unvaccinated Amish children in the three schools targeted by New York, in contrast, are not plagued by the chronic health conditions, many of which are immune or immune-mediated conditions, that plague the more vaccinated communities in New York.

80. As another real-world example, the NYS School Health Examination Form, completed by each child's doctor, was collected for every unvaccinated child within four contiguous school districts in Ulster County, NY. By including all the unvaccinated children in these districts, this comparison avoided selection bias and cherry-picking. The accuracy of the information on these forms was also separately confirmed by an MD who interviewed each family. The health of these unvaccinated children (as confirmed by their doctor on a NYS School Health Examination Form prepared by the DOH and completed by NYS licensed doctor, and then double-checked by another MD) was then compared to the background health of children who are mostly vaccinated. The results, as reflected in the following chart, was then sent to the DOH:

Condition	Rate in Unvaccinated Ulster Children	Background Rate
Allergy – Food	2%	8%[2]
Allergy – Environmental	2%	8.4%[3]
Asthma	1%	7.5%[4]
Seizures	0%	0.6%[5]
Diabetes	0%	Type 1: 22.3 per 100,000 Type 2: 13.8 per 100,000[6]
Autism Spectrum Disorder	0%	1 in 54 children[7]
Attention Deficit Hyperactivity Disorder	2%	9.4%[8]
Eczema	1%	12%[9]

Attached as **Exhibit 29** is the letter exchange with the DOH regarding the unvaccinated children in Ulster County, New York.

81. The letter to the DOH also cited studies with similar findings. For example, a study from the School of Public Health at Jackson State University is found that 33% of vaccinated preterm babies had a neurodevelopmental disorder while 0% of the unvaccinated preterm babies

had a neurodevelopmental disorder; and another study by the same group found that vaccinated children, compared to unvaccinated children (receiving no vaccines), had a 50% decreased risk of chicken pox and a 66% decreased risk of pertussis, *but* had an increased risk of 390% for allergies, 420% for ADHD, 420% for autism, 290% for eczema, 520% for learning disabilities, and 370% for any neuro-developmental delay. https://www.oatext.com/pdf/JTS-3-186.pdf; https://www.oatext.com/pdf/JTS-3-187.pdf.

82. In another study aggregating data from three medical practices in the United States, the health outcomes of vaccinated and unvaccinated children born between 2005 and 2015 were compared; this study found that vaccinated children, compared to unvaccinated children, had a statistically significant increased rate of 218% for developmental delay, 449% for asthma and 213% for ear infections. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7268563/.

83. The stated purposes of vaccination are to improve the overall quality of health of Americans and reduce mortality. The letter to DOH pointed out that the increase in the childhood vaccine schedule over the last 30 years from 2 injected vaccines to 13 injected vaccines (plus 2 injected vaccines during pregnancy) has occurred in lockstep with the increase in the rate of autoimmune, developmental, and neurological disorders in children from 12.8% to 54%. It further noted that health authorities have no explanation for why American children today are plagued with an outbreak of chronic disease and disability.

84. The letter concluded by stating that "The Ulster Children are the living proof that unvaccinated children have far better health outcomes than vaccinated children" and therefore requested that "**If you contest these results, please provide the scientific support that reflects that vaccinated children have better long-term health outcomes than the unvaccinated.**" The DOH apparently never provided any such support nor addresses or contested the findings regarding

the Ulster Children nor any of the studies finding similar results. Hence in a follow-up letter, the following was noted:

> The New York State Department of Health has an annual budget of approximately $88.5 billion and a specific focus on promoting vaccines. In fact, a significant portion of your agency's efforts are geared toward promoting vaccines, encouraging the public they are safe, and otherwise increasing vaccination rates. It would therefore be within your interest to share studies which, in fact, support the safety of the childhood vaccine schedule. The fact that you have not done so to date appears a clear and plain admission that you have no such studies.
>
> As public servants, you should be reticent to continue to mandate a liability-free product to children without proper safety studies. Your assumptions regarding these products are akin to beliefs; you believe the assumptions are true without evidence, even in the face of evidence to the contrary. Parents should not have to participate in your beliefs about these products. They prefer to rely on the data, the studies, and their family's experiences regarding these products, which show that their children are healthier than those that participate in your mandated schedule of dozens of injections of these products per child.

No response was ever received from the DOH or any of its agents.

V. MEDICAL EXEMPTIONS

85. In my experience, most students seeking a medical exemption are those who have been previously harmed from a vaccine and need to be exempt from future vaccines. In contrast, the medically exempt child that the Blog Decl. envisions is not real.

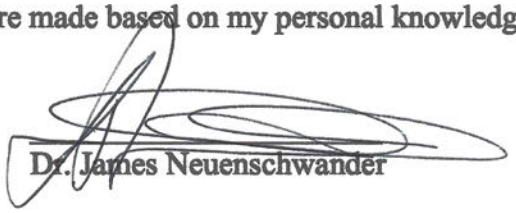
86. There is no such thing as a child in school (or elsewhere) who *is* vulnerable to serious harm from the tiny number of infectious diseases for which vaccines can prevent transmission but who *is not* vulnerable to serious harm from the diseases for which vaccination increases the likelihood of transmission and is also not vulnerable to serious harm from the over 1,400 other known pathogens. The reality is that *if* a child is vulnerable to serious harm from measles, for example, such a child is susceptible to serious harm from any of the diseases for which

vaccines increase the risk of transmission, from diseases for which a vaccine exists but is not mandated (like Covid or influenza), or from the over 1,400 other pathogens for which no vaccine exists. Meaning, a child susceptible to serious harm from an infectious disease is simply not in school because there is no child who is selectively susceptible to serious harm from only the few diseases for which vaccination can prevent transmission and is mandated to attend school. DOH does not even exclude children for six weeks after chicken pox vaccine from school despite FDA's package insert for this vaccine clearly explaining that a vaccinated child can spread the chicken pox virus during this period to the State's hypothetical vulnerable children.

87. In any event, students unvaccinated for religious reasons or medical reasons do not present any different risk of transmission in school of any pathogen for which New York requires vaccination.

Pursuant to 28 U.S.C. §1746, I declare under penalties of perjury under the laws of the United States of America that the foregoing Declaration is true and correct to the best of my knowledge and belief and that such facts are made based on my personal knowledge.

Executed on August 25, 2023



Dr. James Neuenschwander

Exhibit 1

Polio Vaccination

Pronounced [PO-lee-oh]

Polio, or poliomyelitis, is a disabling and potentially deadly disease. It is caused by the poliovirus. The virus spreads from person to person and can infect a person's spinal cord, causing paralysis (can't move parts of the body).

There is no cure for polio, but it can be prevented with safe and effective vaccination. Inactivated polio vaccine (IPV) is the only polio vaccine that has been given in the United States since 2000. It is given by shot in the arm or leg, depending on the person's age. Oral polio vaccine (OPV) is used in other countries.

CDC recommends that children get four doses of polio vaccine. They should get one dose at each of the following ages:

- 2 months
- 4 months
- 6 through 18 months
- 4 through 6 years

Polio Vaccination: What Everyone Should Know

Polio Vaccination: Information for Healthcare Professionals

Page last reviewed: August 11, 2022

Exhibit 2

Centers for Disease Control and Prevention

U.S. National Authority for Containment of Poliovirus

U.S. National Authority for Containment of Poliovirus Home

Polio Disease and Poliovirus Containment

Poliovirus Containment

Poliovirus containment is focused on eradicated polioviruses. Wild poliovirus type 2 (WPV2) and wild poliovirus type 3 (WPV3) were declared eradicated in 2015 and 2019, respectively. Containment measures are in place for laboratories and other facilities that handle or store eradicated polioviruses.

Polio, or poliomyelitis, is a crippling and potentially deadly infectious disease.
Learn more about the symptoms and how the virus is spread from person-to-person.

Polio vaccine provides the best protection against polio disease.Two types of vaccines are used to prevent polio disease– inactivated polio vaccine (IPV) and oral polio vaccine (OPV).

CDC and its international partners have made significant progress towards polio eradication.
Learn more about CDC's polio eradication efforts and the Global Polio Eradication Initiative.

There are three types of wild poliovirus (WPV): type 1, type 2, and type 3. People must protect themselves against all three types of the virus to prevent polio disease. Polio vaccination is the best protection.

Type 2 wild poliovirus was declared eradicated in September 2015. The last detection was in India, 1999. Type 3 wild poliovirus was declared eradicated in October 2019. It was last detected in November 2012. Only type 1 wild poliovirus remains.

There are two vaccines used to protect against polio disease: oral polio vaccine and inactivated poliovirus vaccine. For more information see OPV Cessation – GPEI (polioeradication.org) .

Oral polio vaccine

The oral poliovirus vaccine (OPV) is used in many countries to protect against polio disease. Oral poliovirus vaccine contains attenuated or weakened version of either one (monovalent OPV), two (bivalent OPV), or all three (trivalent OPV) poliovirus types.

After wild poliovirus type 2 was declared eradicated in 2015, the world switched from trivalent OPV to bivalent OPV. Bivalent OPV contains poliovirus type 1 and 3. This switch means that the bOPV used globally no longer protects against WPV2. Countries that use bOPV for routine immunization have added a single dose of IPV to protect against WPV2.

In rare instances, the vaccine-virus may be able to circulate over time and mutate in communities with insufficient immunity or immunocompromised individuals. These mutated OPV strains can cause polio disease. They are called vaccine-derived polioviruses (VDPVs).

For more information on polio vaccination see Polio Vaccination | CDC.

Inactivated poliovirus vaccine

IPV protects people against all three types of poliovirus. IPV does not contain live virus and cannot cause disease. It protects people from polio disease but does not stop transmission of the virus.

OPV can be used to contain a polio outbreak. Use of all OPV will stop when polio is eradicated globally. This will prevent re-establishment of transmission from VDPVs. For more information on polio vaccination see Polio Vaccination | CDC.

Last Reviewed: December 2, 2022, 10:55 AM



IPV

Inactivated poliovirus vaccine



© GAVI

Inactivated polio vaccine (IPV) was developed in 1955 by Dr Jonas Salk. Also called the Salk vaccine IPV consists of inactivated (killed) poliovirus strains of all three poliovirus types. IPV is given by intramuscular or intradermal injection and needs to be administered by a trained health worker. IVP produces antibodies in the blood to all three types of poliovirus. In the event of infection, these antibodies prevent the spread of the virus to the central nervous system and protect against paralysis.

Advantages

- As IPV is not a 'live' vaccine, it carries no risk of VAPP.
- IPV triggers an excellent protective immune response in most people.

Disadvantages

- IPV induces very low levels of immunity in the intestine. As a result, when a person immunized with IPV is infected with wild poliovirus, the virus can still multiply inside the intestines and be shed in the faeces, risking continued circulation.
- IPV is over five times more expensive than OPV. Administering the vaccine requires trained health workers, as well as sterile injection equipment and procedures.

Safety

IPV is one of the safest vaccines in use. No serious systemic adverse reactions have been shown to follow vaccination.

Efficacy

IPV is highly effective in preventing paralytic disease caused by all three types of poliovirus.

Recommended use

An increasing number of industrialized, polio-free countries are using IPV as the vaccine of choice. This is because the risk of paralytic polio associated with continued routine use of OPV is deemed greater than the risk of imported wild virus.

However, as IPV does not stop transmission of the virus, OPV is used wherever a polio outbreak needs to be contained, even in countries which rely exclusively on IPV for their routine immunization programme.
Once polio has been eradicated, use of all OPV will need to be stopped to prevent re-establishment of transmission due to VDPVs.

Related Resources

IPV and routine immunization

Exhibit 3

Centers for Disease Control and Prevention

Tetanus

Tetanus Home

About Tetanus

Tetanus is different from other vaccine-preventable diseases because it does not spread from person to person. The bacteria are usually found in soil, dust, and manure and enter the body through breaks in the skin — usually cuts or puncture wounds caused by contaminated objects.



Causes and How It Spreads



Diagnosis and Treatment



Symptoms and Complications



Prevention

Related Resource

Tetanus Communication and Print Resources

Last Reviewed: August 29, 2022

Exhibit 4

Diphtheria Immunization

Effect Upon Carriers and the Control of Outbreaks

Louis W. Miller, MD; J. Justin Older, MD; James Drake; and Sherwood Zimmerman, Austin, Tex

A diphtheria epidemic in a small central Texas community centered in the elementary school. Epidemiological investigation at the school included throat cultures and immunization histories of 306 of the 310 students and staff. Of these, 104 (34%) had culture-proven diphtheria infections; 15 were symptomatic cases and 89 were carriers. There was no statistical difference in the risk of diphtheria infection among those with full, lapsed, inadequate, or no previous diphtheria immunizations. However, the risk of symptomatic diphtheria was 30 times as great for those with none, and 11.5 times as great for those with inadequate immunizations as for those fully immunized. Diphtheria toxoid helps prevent symptomatic disease but does not prevent the carrier state nor stop the spread of infection. Identifying, isolating, and treating carriers are very important aspects in the control of diphtheria outbreaks.

With the increase in the number of cases of diphtheria in the United States during the past few years, the effect of immunization on the control of outbreaks has become an important question. In the Austin, Tex, diphtheria epidemic of 1967-1969[1] cases continued to occur despite the administration of 155,200 doses of diphtheria toxoid and the concomitant rise in immunization levels of school age children from 68% to 89%. Data from the Austin outbreak suggested that a large reservoir of carriers was important in the continued transmission of *Corynebacterium diphtheriae*. Other diphtheria outbreaks have shown that epidemics occur in populations with high immunization levels.[2-4] A diphtheria outbreak in an elementary school in Elgin, Tex, in the spring of 1970 provided an opportunity to study the effects of immunization on carriers and on the control of an epidemic situation.

Table 1.—Definitions of Immunization Status*

Status	Definition
Full	Primary series (three or more injections), or a primary series plus a booster, completed within ten years.
Lapsed	Primary series, or a primary series plus booster, completed more than ten years ago.
Inadequate	Uncompleted primary series (less than three injections) at any time.
None	No diphtheria toxoid ever received.

* Adapted from the Center for Disease Control.[6]

Materials and Methods

When it became obvious in the Elgin diphtheria epidemic (Older JJ et al, unpublished data) that cases were clustered in the elementary school, a special throat culture and immunization survey was begun there. Throat cultures were obtained from and immunization status was determined for 306 of 310 students and staff. Throat swabs were taken on three separate occasions from each person: April 7, April 17, and May 4. These were streaked on Loeffler blood serum or Pai medium and incubated overnight. Cystine tellurite blood agar and Tinsdale medium were used for isolation, Elek-King agar diffusion plates were used for toxigenicity determination.

Immunization status information was

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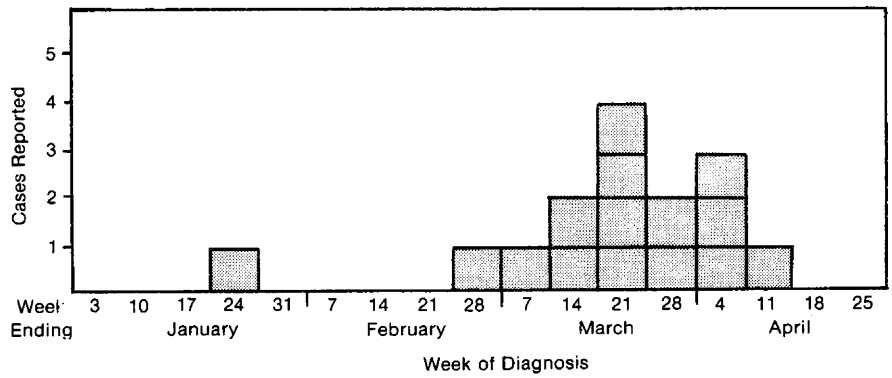
From the Epidemiology Program Center for Disease Control, Atlanta (Drs. Miller, Older, Drake, and Zimmerman); the Communicable Disease Services, Texas State Department of Health, Austin (Drs. Miller, Older, Drake, and Zimmerman); and the Department of Preventive Medicine, University of Maryland School of Medicine, Baltimore (Dr. Miller).

Reprint requests to Epidemiology Program, Center for Disease Control, Atlanta 30333.

obtained by personal interview and review of available school and medical records. The status of each person classified as "adequate," "lapsed," "inadequate," and "none," according to the definitions of the Center for Disease Control[5] (Table 1).

Any person with a sore throat or other symptoms compatible with diphtheria and a positive culture for *C diphtheriae* organisms was classified as a "case." A person without symptoms but who had a positive throat culture for *C diphtheriae* organisms was classified as a "carrier." The term "infection" applied to anyone with a positive culture regardless of his clinical state and, therefore, included both cases and carriers.



Diphtheria cases in Elgin, Tex, elementary school, spring 1970.

Results

When diphtheria was first diagnosed in the elementary school, 67% of the children and staff were already fully immunized, and 97% had had at least one dose of diphtheria toxoid. The first case in the elementary school population was diagnosed in late February 1970, and by April 8, 15 cases had occurred (Figure).

Throat cultures were done on 306 children and staff; toxigenic *C diphtheriae*, gravis type, was isolated from 104 (34%). Fifteen of these (14%) were cases, and 89 (86%) were carriers. There was *no* statistical difference in the risk of diphtheria infection among those with full, lapsed, inadequate, or no previous diphtheria immunization (Table 2). However, the risk of becoming a case was 30 times as great for those with no immunization and 11.5 times as great for those with inadequate immunizations as for those with full diphtheria immunization (Table 3). Among the 104 infected with *C diphtheriae*, the risk of being symptomatic was 13.3 times as great for those inadequately immunized and 37.0 times as great for those with no previous immunizations as for those who were fully immunized (Table 4).

Table 2.—Immunization and Culture Status of Students and Staff, Elgin, Tex, Elementary School, Spring 1970

Immunization Status	Culture Status: Positive	Culture Status: Negative	Culture Status: Total	Diphtheria Infection Attack Rate (per 100)
Full	73	132	205	35.6
Lapsed	0	4	4	0
Inadequate	28	59	87	32.4
None	3	7	10	30.0
Total	104	202	306	34.0

Table 3.—Immunization Status of Diphtheria Cases, Elgin, Tex, Elementary School, Spring 1970

Immunization Status	Cases	No. at Risk	Diphtheria Case Attack Rate (per 100)
Full	2	205	1.0
Lapsed	0	4	0
Inadequate	10	87	11.5
None	3	10	30.0
Total	15	306	4.9

Table 4.—Risk of Symptoms and Immunization Status of Students and Staff With Positive Diphtheria Cultures, Elgin, Tex, Elementary School, Spring 1970

Immunization	Symptomatic Cases	Asymptomatic Carriers	Total Infected	Symptom Attack Rate (per 100 Positive Cultures)	Relative Risk
Full	2	71	73	2.7	. . .
Inadequate	10	18	28	35.8	13.3
None	3	0	3	100.0	37.0
Total	15	89	104	14.4	. . .

Comment

The importance of carriers in the spread of diphtheria was well documented by Doull and Lara[6] in the

early 1920s. In very thorough investigations, only about 20% of diagnosed diphtheria cases could be traced to another suspected case, and the remaining 80% of the cases were attributed to asymptomatic carriers in the population. Recent epidemics in Austin[1] and Elgin,[5] Tex, provided ample evidence that carriers continue to play a very important role in the transmission of diphtheria.

When diphtheria toxoid became available, it was generally believed that it induced immunity that protected individuals from symptomatic illness but not from asymptomatic infection. This was based on the observation that immunity is related to the neutralization of toxin elaborated by *C diphtheriae* and not interference with diphtheria infection.

In 1936, Frost et al[7] alluded to a paucity of observations on record concerning antitoxic immunity and the carrier state. Nonetheless, he stated that the limited data suggested that there is little, if any, difference between those individuals with and those without antitoxic immunity in their risk of becoming infected.

More recently, Tasman and Lansberg[8] put forth the hypothesis that toxoid use reduces the number of carriers. This is based on surveys that showed a steady decline in the prevalence of carriers. Since toxoid immunization does prevent cases and since cases are more contagious than carriers,[6] the decline in carriers could be due to the decrease in contagious cases rather than to the direct effects of immunization.

The findings in Elgin corroborate the assumptions of Frost et al[7] and show that there is no difference in the risk of diphtheria acquisition among those with full, lapsed, inadequate, and no immunizations. However, they also demonstrate the value of immunization in reducing the risk of disease and show that the protection against symptomatic illness afforded those infected with *C diphtheriae* is directly related to their immunization status.

Some authors[9] have estimated that if 70% or 80% of the population were adequately immunized against diphtheria, spread of diphtheria would be prevented. However, diphtheria outbreaks have been described in populations with as much as 94% of the people being previously immunized.[2-4] These outbreaks, the known importance of carriers in the spread of diphtheria, and the demonstrated failure of toxoid to prevent the carrier state lead us to conclude that the concept of herd immunity is not applicable in the prevention of diphtheria. A high level of community immunization will not stop the transmission of diphtheria, but it will limit the number of contagious cases. At the first appearance of a diphtheria case, control activities should be directed toward identifying, isolating, and treating carriers, as well as toward immunizing persons with less than full immunization status. This dual approach will reduce or eliminate the spread of infection by reducing the number of carriers, and it will reduce the number of cases by improving the immunization status of exposed individuals.

Roy Morris, MD, Elgin city health officer, treated the majority of cases and arranged for treatment of carriers; Milton Saxon, Elgin school superintendent, and Eva C. Danklefs, Elgin school nurse helped arrange culture surveys; M.S. Dickerson, MD, coordinated federal, state, and local assistance and support; Will Callihan assisted in culture surveys, interviews, and immunization of patients; Jesse V. Irons, ScD, and Carl D. Heather, DVM, coordinated state laboratory assistance; H.D. Bredthauer and Lucie M. Hickman, Texas State Department of Health, processed bacteriological specimens; and Wallis Jones, PhD, Susan Bickham, Geraldine Wiggins, and Jane McLaughlin, Laboratory Division, Center for Disease Control, Atlanta, processed specimens and performed all typing of *C diphtheriae* organisms. All isolates from the initial throat cultures were typed by the Bacteria Immunology Unit, Center for Disease Control.

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Exhibit 5

Table 1

COVID-19 vaccination recommendations have changed. Find the latest recommendations at www.cdc.gov/covidschedule

Recommended Adult Immunization Schedule for ages 19 years or older, United States, 2023

Vaccine	19–26 years	27–49 years	50–64 years	≥65 years
COVID-19	2- or 3- dose primary series and booster (See Notes)			
Influenza inactivated (IIV4) or **Influenza recombinant** (RIV4)	1 dose annually			
or	or			
Influenza live, attenuated (LAIV4)	1 dose annually			
Tetanus, diphtheria, pertussis (Tdap or Td)	1 dose Tdap each pregnancy; 1 dose Td/Tdap for wound management (see notes)			
	1 dose Tdap, then Td or Tdap booster every 10 years			
Measles, mumps, rubella (MMR)	1 or 2 doses depending on indication (if born in 1957 or later)			For healthcare personnel, see notes
Varicella (VAR)	2 doses (if born in 1980 or later)	2 doses		
Zoster recombinant (RZV)	2 doses for immunocompromising conditions (see notes)		2 doses	
Human papillomavirus (HPV)	2 or 3 doses depending on age at initial vaccination or condition	27 through 45 years		
Pneumococcal (PCV15, PCV20, PPSV23)	1 dose PCV15 followed by PPSV23 OR 1 dose PCV20 (see notes)			See Notes
				See Notes
Hepatitis A (HepA)	2, 3, or 4 doses depending on vaccine			
Hepatitis B (HepB)	2, 3, or 4 doses depending on vaccine or condition			
Meningococcal A, C, W, Y (MenACWY)	1 or 2 doses depending on indication, see notes for booster recommendations			
Meningococcal B (MenB)	2 or 3 doses depending on vaccine and indication, see notes for booster recommendations			
	19 through 23 years			
***Haemophilus influenzae* type b** (Hib)	1 or 3 doses depending on indication			

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended vaccination for adults with an additional risk factor or another indication

Recommended vaccination based on shared clinical decision-making

No recommendation/ Not applicable

Exhibit 6

Centers for Disease Control and Prevention

AdultVaxView

AdultVaxView Home

Vaccination Coverage among Adults in the United States, National Health Interview Survey, 2019–2020

Summary

The Centers for Disease Control and Prevention (CDC) recommends vaccinations for adults based on age, health conditions, prior vaccinations, and other considerations to prevent morbidity and mortality from vaccine-preventable diseases. Updated vaccination recommendations for adults from CDC are published annually, and Healthy People 2030 (HP2030) objectives include increasing the proportion of adults aged 19 years or older who receive recommended age-appropriate vaccines. Still, vaccination coverage among U.S. adults remains low for most vaccines.

To assess vaccination coverage among adults aged ≥19 years, CDC analyzed data from the National Health Interview Survey (NHIS). NHIS is a continuous, cross-sectional national household survey of the noninstitutionalized U.S. civilian population. In a probability sample of households, interviews are conducted over the course of the year and data are compiled and released on an annual basis. For this report, adult receipt of influenza, pneumococcal, herpes zoster, and Td/Tdap vaccines was assessed using data from 2019 and 2020. A composite adult vaccination quality measure (1), which tracks routinely recommended age-appropriate vaccination among adults, was assessed using 2019 data, and trends in adult vaccination were examined during 2010–2020 with a particular focus on vaccination coverage since 2016 to represent recent trends in adult vaccination.

Coverage for the age-appropriate composite adult vaccination measures for 2019 was low (<45%) for both versions of the composite measure among adults aged ≥19 years and among all race/ethnicity groups for adults aged ≥19 (<50%). Coverage for all vaccines differed by race/ethnicity with generally lower coverage among non-White adults compared with White adults. Linear trend tests since 2016 indicated that coverage increased for influenza, herpes zoster and Tdap vaccination and remained stable for pneumococcal and vaccination with any tetanus-containing vaccine.

Substantial improvement in adult vaccination uptake is needed to reduce the burden of vaccine-preventable diseases. Increasing the proportion of adults who receive recommended age-appropriate vaccines and assuring equitable access to and uptake of recommended vaccines is a high-priority public health issue.

Methods

The NHIS is a continuous, cross-sectional national household survey of the noninstitutionalized U.S. civilian population conducted by the U.S. Census Bureau for CDC's National Center for Health Statistics. Due to data collection difficulties posed by the COVID-19 pandemic, the 2020 NHIS shifted from in-person interviewing to all-telephone interviewing starting in late March and continuing through June 2020. From July through December 2020, data collection in select areas was opened for in-person interviewing, however, NHIS data collection remained predominantly by telephone during this period (2). NHIS's objective is to monitor the health of the U.S. population and provide estimates of health indicators, health care use and access, and health-related behaviors (3). Non-institutionalized adults aged ≥19 years with interviews conducted during August 2019–June 2020 (for influenza vaccination), January–December 2020 (for pneumococcal and herpes zoster vaccination), and January–December 2019 (for Td and Tdap vaccination) were included in this analysis. (Information on Td or Tdap vaccination was not collected in the 2020 NHIS.) The total sample of persons aged ≥19 years was 31,633 in 2019 and 31,360 in 2020. The final sample adult core response rate was 59.1% for the 2019 NHIS and 48.9% for the 2020 NHIS. Questions about receipt of vaccinations recommended for adults are asked of one randomly selected adult within each family in the household.

Weighted data were used to produce national vaccination coverage estimates. For non-influenza adult vaccination coverage estimates, the weighted proportion of respondents who reported receiving selected vaccinations was calculated. To better assess influenza vaccination coverage each season, the Kaplan-Meier survival analysis procedure was used. Race/ethnicity was categorized as follows: White, Black, Hispanic, Asian, and Other. In this report, persons categorized as White, Black, Asian, or Other race identified as non-Hispanic. Persons categorized as Hispanic might be of any race. Persons characterized as Other include those who identified as American Indian/Alaska Native and persons who identified multiple races. The five race/ethnicity categories are mutually exclusive.

For the adult vaccination composite measure, data from the 2019 NHIS were analyzed to determine estimates for a composite measure of vaccination coverage for select vaccines routinely recommended for all adults aged ≥19 years (Td, Tdap, and influenza vaccine) or indicated based on age (herpes zoster and pneumococcal vaccines), and for three age groups (19–59 years, 60–64 years, and ≥65 years) based on the vaccines recommended for those age groups. Estimates for composite measures were calculated to include any tetanus-toxoid containing vaccine in the past 10 years, with and without influenza vaccination in the past 12 months. Point estimates and 95% confidence intervals (CIs) were calculated by using SUDAAN software (Research Triangle Institute, Research Triangle Park, NC, version 11.0.1) to account for the complex sample design. T-tests were used for comparisons between data years and for comparisons of each level of each respondent characteristic to a chosen referent level (e.g., for race/ethnicity, White was the reference group). Statistical significance was defined as $p<0.05$. Coverage estimates are not reported for small sample size ($n<30$) or large relative standard errors (standard error/estimate >0.3).

Results

Pneumococcal Vaccination

- Pneumococcal vaccination coverage overall (≥1 dose of PPSV23 or PCV13) among adults aged 19–64 years at increased risk for pneumococcal disease was 23.9% in 2020, similar to the estimate for 2019.
  - Coverage among White adults aged 19–64 years at increased risk was higher (26.3%) compared with Hispanic (16.7%) and Asian (13.8%) adults.
- Coverage among adults aged ≥65 years was 67.5%, similar to the estimate for 2019.
  - Coverage among White adults aged ≥65 years (72.4%) was higher compared with Black (50.8%), Hispanic (48.1%), and Asian (54.9%) adults.

TABLE 1. Estimated proportion of adults aged ≥19 years who ever received pneumococcal vaccination by increased-risk status and race/ethnicity — National Health Interview Survey, United States, 2020

Herpes Zoster Vaccination

- Overall, herpes zoster vaccination coverage among adults aged ≥50 and ≥60 years in 2020 was 29.4% and 39.1%, respectively, higher than estimates for 2019.
  - White adults aged ≥50 and ≥60 years had higher coverage compared with Black, Hispanic, and Other adults.
- Zoster vaccine live (ZVL) coverage in 2020 was 17.8% among adults aged ≥50 years, 4.0% among adults aged 50–59 years, and 25.5% among adults aged ≥60 years, all lower than estimates for 2019.
- Recombinant zoster vaccine (RZV) coverage (≥1 dose) was 14.1% among adults aged ≥50 years, 7.3% among adults aged 50–59 years, and 17.9% among adults aged ≥60 years, all higher than estimates for 2019.
  - RZV coverage (at least 2 doses) was 10.8% among adults aged ≥50 years, 13.9% among adults aged ≥60 years, and 15.1% among adults aged ≥65 years, all higher than estimates for 2019.

TABLE 2. Estimated proportion of adults aged ≥50 years who ever received herpes zoster vaccination, by age and race/ethnicity — National Health Interview Survey, United States, 2020

Tetanus Vaccination Coverage (Td and Tdap)

- In 2019, the proportion of adults aged ≥19 years reporting having received any tetanus toxoid–containing vaccination during the past 10 years was 62.9%, similar to 2018.
    - White adults had higher coverage compared with Black, Hispanic, and Asian adults.
- Among adults aged ≥19 years for whom Tdap vaccination could be assessed specifically, overall coverage was 30.1%, similar to the estimate for 2018.

TABLE 3. Estimated proportion of adults aged ≥19 years who in the past 10 years received any tetanus vaccination and Tdap vaccination, by race/ethnicity and overall by age group — National Health Interview Survey, United States, 2019

Adult Vaccination Composite Measure

- In 2019, few adults aged ≥19 years had received all age-appropriate vaccines (including influenza vaccination) included in the composite measure (21.8%).
- Coverage for the composite adult vaccination quality measure was low in all age groups, ranging from 8.2% among adults aged 50–64 years to 27.6% among adults aged 19–49 years.
    - Low coverage with herpes zoster vaccine was the primary driver of low coverage among adults aged 50–64 years.
- Coverage for the composite adult vaccination quality measure (including influenza vaccination) was lower among Black (15.9%) and Hispanic (17.3%) adults compared with White (23.7%), Asian (23.5%) and Other (25.7%) adults aged ≥19 years.

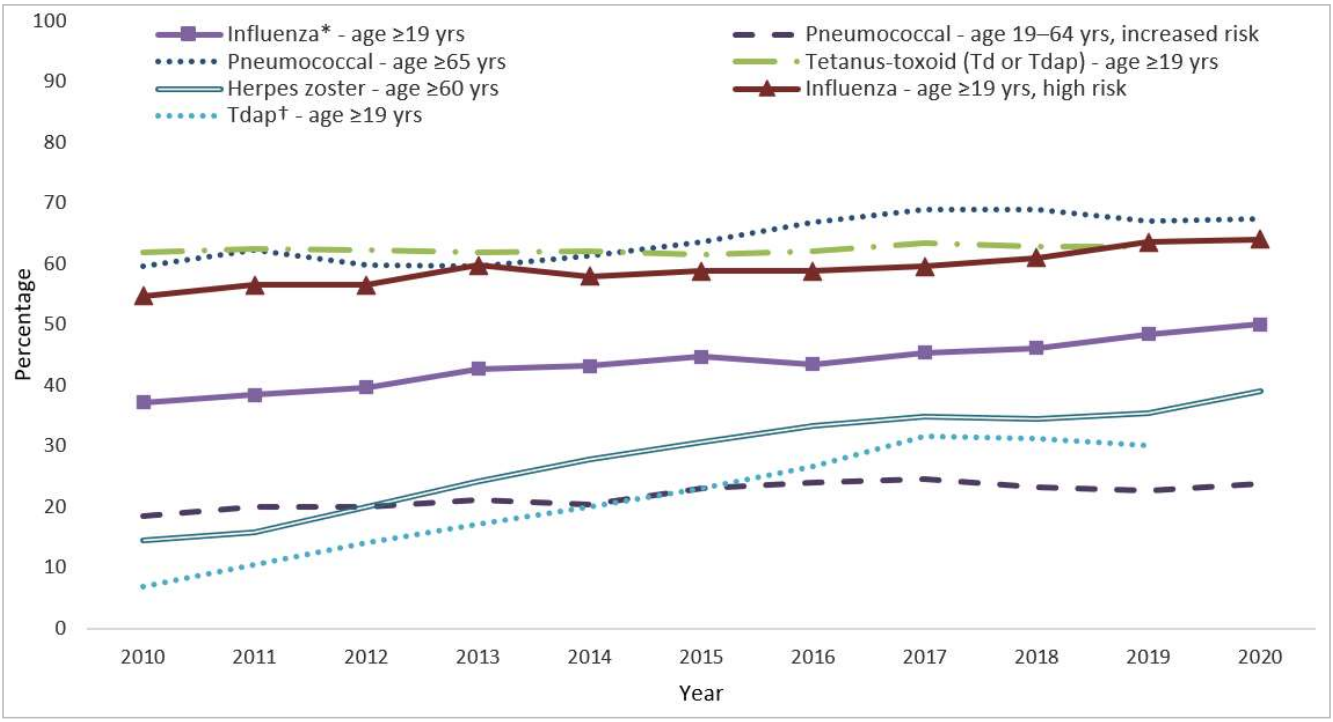
TABLE 4. Vaccination coverage estimates using an age-appropriate composite adult vaccination quality measure and individual component measures, by age group — National Health Interview Survey, United States, 2019

TABLE 4_1. Vaccination coverage estimates using an age-appropriate composite* adult vaccination quality measure and individual component measures, by race/ethnicity† — National Health Interview Survey, United States, 2019

Trends in Adult Vaccination Coverage

- Trends in coverage with select vaccines recommended for adults from 2010–2020 are shown in the Figure.
- While coverage for all vaccines except any tetanus-containing vaccine (Td or Tdap) increased since 2010, coverage for several vaccines has plateaued in recent years.
- From 2016–2020, increases in coverage were observed for influenza vaccination among adults aged ≥19 years (annual average percentage point increase: 1.6%, 95% CI 1.2, 2.0); herpes zoster vaccination among adults aged ≥60 years (annual average percentage point increase: 1.2%, 95% CI 0.8, 1.6); and Tdap vaccination among adults aged ≥19 years (annual average percentage point increase: 1.0%, 95% CI 0.4, 1.5). Coverage for pneumococcal vaccination and for any tetanus-containing vaccine (Td or Tdap) remained stable from 2016–2020.

FIGURE. Estimated proportion of adults aged ≥19 years who received selected vaccines, by age group and risk status — National Health Interview Survey, United States, 2010–2020



Abbreviations: Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.

* Estimates are season-specific. Year 2020 corresponds to the 2019-20 influenza season.

† Tdap vaccination coverage data among adults aged ≥65 years are available beginning in the NHIS 2012 survey.

Discussion

NHIS data from 2019 and 2020 indicate that many adults in the United States remained unprotected against vaccine-preventable diseases. Adult vaccination coverage remained similar to coverage in the year prior for most vaccines, with small increases observed for herpes zoster vaccination. Racial and ethnic differences in vaccination coverage persisted for all vaccinations, with generally lower coverage among non-White and Hispanic adults compared with White adults. Coverage for the age-appropriate composite measures was low in all age groups and in all race/ethnicity groups.

Many changes to Advisory Committee on Immunization Practices (ACIP) recommendations have occurred since 2010 for the vaccines assessed in this report. Since 1997, ACIP has recommended PPSV23 vaccination of all adults aged ≥65 years and younger adults with certain medical conditions (4). In 2012, ACIP recommended PCV13 to adults aged 19–64 years at increased risk and in 2014 recommended PCV13 in series with PPSV23 for all adults aged ≥65 years; the routine recommendation for PCV13 in adults aged ≥65 years was changed in 2019 to a recommendation for administration of PCV13 based on shared clinical decision-making for adults aged ≥65 years who do not have an immunocompromising condition, cerebrospinal fluid lead, or cochlear implant, and who have not previously received PCV13 (5–7). In 2021, ACIP recommended 15-valent or 20-valent PCV for PCV-naïve adults previously eligible for pneumococcal vaccine; when PCV15 is used, it should be followed by a dose of PPSV23 ≥1 year later (8). Despite many changes in recommendations, at least one dose of pneumococcal vaccine has been recommended for eligible adults throughout the period assessed in the report; since 2014, two doses of pneumococcal vaccine have been recommended for certain adults aged ≥65 years. In 2006, ACIP recommended ZVL for adults aged ≥60 years and in 2017, ACIP preferentially recommended RZV for use in immunocompetent adults aged ≥50 years over ZVL due to higher and longer-lasting efficacy (9, 10). In 2021, ACIP recommended two doses of RZV for use in immunodeficient or immunosuppressed adults aged ≥19 years (11). In 2012, ACIP recommended Tdap to all adults aged ≥19 years who have not yet received a dose of Tdap, regardless of interval since the last Td shot (12) and in 2019, updated its recommendations to allow either Td or Tdap to be used for the decennial Td booster, prophylaxis for wound management, and for catch-up doses (13).

The largest average annual changes in vaccination coverage since 2010 have occurred for herpes zoster (2.4%) and Tdap (2.8%) vaccination while smaller increases occurred for influenza and pneumococcal vaccination. Linear trend tests from 2016 indicate increases in coverage for these vaccines have diminished in recent years compared with increases from 2010. Since

the 2010–11 influenza season, ACIP has recommended annual influenza vaccination for all persons aged ≥6 months (14). Though influenza vaccination coverage has continued to increase among all adults since this universal recommendation, coverage remains low with only approximately half of adults vaccinated in the 2019–20 season.

The U.S. Department of Health and Human Services has proposed a developmental HP2030 objective to assess overall adult vaccination performance. This developmental measure targets increasing the proportion of adults aged ≥19 years who receive recommended age-appropriate vaccines. This objective is a high-priority public health issue supported by evidence-based interventions; NHIS data like those presented here are a possible source of the reliable baseline data needed for it to become a core HP2030 objective.

Limitations

The estimates in this report are subject to several limitations. First, all data rely on self-report and were not validated with medical records. However, adult self-reported vaccination status has been shown to be ≥70% sensitive in one or more studies for pneumococcal, tetanus toxoid-containing, herpes zoster, and hepatitis B vaccines and ≥70% specific in one or more studies for all except tetanus and hepatitis B vaccination (15–17). Second, the NHIS response rate was 59.1% in 2019 and 48.9% in 2020. Nonresponse bias can result if respondents and non-respondents differ in their vaccination rates, and if survey weighting does not fully correct for this. Third, NHIS data from 2020 at the start of the COVID-19 pandemic were obtained by telephone rather than in-person interviews and the impact of that change is unknown. While disruptions to certain vaccination services due to COVID-19 have been described (18, 19), vaccination coverage assessed in this report consider cumulative vaccination over time and for 2020 data, any disruptions in health care access or utilization would not be expected to show a substantial impact. Fourth, Tdap estimates are subject to considerable uncertainty and potential for bias. Respondents who reported tetanus vaccination but were unable to say whether Td or Tdap was used (19.1% of respondents reporting tetanus vaccination) were excluded from estimations of Tdap vaccination coverage. Finally, the NHIS sample excludes persons in the military and those residing in institutions, which might result in underestimation or overestimation of vaccination coverage levels.

Conclusion

Despite increases in vaccination coverage among all adults for influenza, herpes zoster and Tdap in recent years, few adults are fully vaccinated according to ACIP recommendations. Disparities in vaccination coverage by race/ethnicity were seen for all vaccines assessed. Increasing the proportion of adults who receive recommended age-appropriate vaccines and assuring equitable access to and uptake of recommended vaccines is a high-priority public health issue.

Authors: Tara C. Jatlaoui, MD, MPH[1]; Mei-Chuan Hung, MPH, PhD[1,2]; Anup Srivastav, B.V.Sc.&A.H., PhD[1,2]; Peng-Jun Lu, MD, PhD[1]; Carla L. Black, PhD[1]; Megan C. Lindley, MPH[1], Ram Koppaka, MD, PhD[1]; James A. Singleton, PhD[1]

[1]Immunization Services Division, National Center for Immunization and Respiratory Diseases, CDC
[2]Leidos, Inc, Atlanta, GA

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Last Reviewed: February 17, 2022

Exhibit 7

MMWR Weekly
January 21, 2000 / 49(02);35-38,47

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Notice to Readers: Recommended Childhood Immunization Schedule -- United States, 2000

Each year, CDC's Advisory Committee on Immunization Practices (ACIP) reviews the recommended childhood immunization schedule to ensure it remains current with changes in manufacturers' vaccine formulations, revisions in recommendations for the use of licensed vaccines, and recommendations for newly licensed vaccines. This report presents the recommended childhood immunization schedule for 2000 (Figure 1) and explains the changes that have occurred since January 1999.

Since the publication of the immunization schedule in January 1999 (1), ACIP, the American Academy of Family Physicians, and the American Academy of Pediatrics have recommended removal of rotavirus vaccine from the schedule, endorsed an all-inactivated poliovirus vaccine (IPV) schedule for polio vaccination, recommended exclusive use of acellular pertussis vaccines for all doses of the pertussis vaccine series, and added hepatitis A vaccine (Hep A) to the schedule to reflect its recommended use in selected geographic areas (2). Detailed recommendations for using vaccines are available from the manufacturers' package inserts, ACIP statements on specific vaccines, and the 1997 Red Book (3). ACIP statements for each recommended childhood vaccine can be viewed, downloaded, and printed at CDC's National Immunization Program World-Wide Web site, http://www.cdc.gov/nip/publications/acip-list.htm.

Removal of Rotavirus Vaccine from the Schedule

On October 22, 1999, ACIP recommended that Rotashield®* (rhesus rotavirus vaccine-tetravalent [RRV-TV]) (Wyeth Laboratories, Inc., Marietta, Pennsylvania), the only U.S. licensed rotavirus vaccine, no longer be used in the United States (4). The decision was based on the results of an expedited review of scientific data presented to ACIP by CDC. Data from the review indicated a strong association between RRV-TV and intussusception among infants 1-2 weeks following vaccination. Vaccine use was suspended in July pending the ACIP data review. Parents should be reassured that children who received the rotavirus vaccine before July are not at increased risk for intussusception now. The manufacturer withdrew the vaccine from the market in October.

Inactivated Poliovirus Vaccine for All Four Doses

As the global eradication of poliomyelitis continues, the risk for importation of wild-type poliovirus into the United States decreases dramatically. To eliminate the risk for vaccine-associated paralytic poliomyelitis (VAPP), an all-IPV schedule is recommended for routine childhood vaccination in the United States (5). All children should receive four doses of IPV: at age 2 months, age 4 months, between ages 6 and 18 months, and between ages 4 and 6 years. Oral poliovirus vaccine (OPV), if available, may be used only for the following special circumstances:

1. Mass vaccination campaigns to control outbreaks of paralytic polio.
2. Unvaccinated children who will be traveling within 4 weeks to areas where polio is endemic or epidemic.
3. Children of parents who do not accept the recommended number of vaccine injections; these children may receive OPV only for the third or fourth dose or both. In this situation, health-care providers should administer OPV only after discussing the risk for VAPP with parents or caregivers.

OPV supplies are expected to be very limited in the United States after inventories are depleted. ACIP reaffirms its support for the global eradication initiative and use of OPV as the vaccine of choice to eradicate polio where it is endemic.

Acellular Pertussis Vaccine

ACIP recommends exclusive use of acellular pertussis vaccines for all doses of the pertussis vaccine series. The fourth dose may be administered as early as age 12 months, provided 6 months have elapsed since the third dose and the child is unlikely to return at 15-18 months.

Hepatitis A

Hepatitis A vaccine (Hep A) is listed on the schedule for the first time because it is recommended for routine use in some states and regions. Its appearance on the schedule alerts providers to consult with their local public health authority to learn the current recommendations for hepatitis A vaccination in their community. Additional information on the use of Hep A can be found in recently published guidelines (2).

Hepatitis B

Special considerations apply in the selection of hepatitis B vaccine products for the dose administered at birth (6).

Vaccine Information Statements

The National Childhood Vaccine Injury Act requires that all health-care providers, whether public or private, give to parents or patients copies of Vaccine Information Statements before administering each dose of the vaccines listed in this schedule (except Hep A). Vaccine Information Statements, developed by CDC, can be obtained from state health departments and CDC's World-Wide Web site, http://www.cdc.gov/nip/publications/VIS. Instructions on use of the Vaccine Information Statements are available from CDC's website or the December 17, 1999, Federal Register (64 FR 70914).

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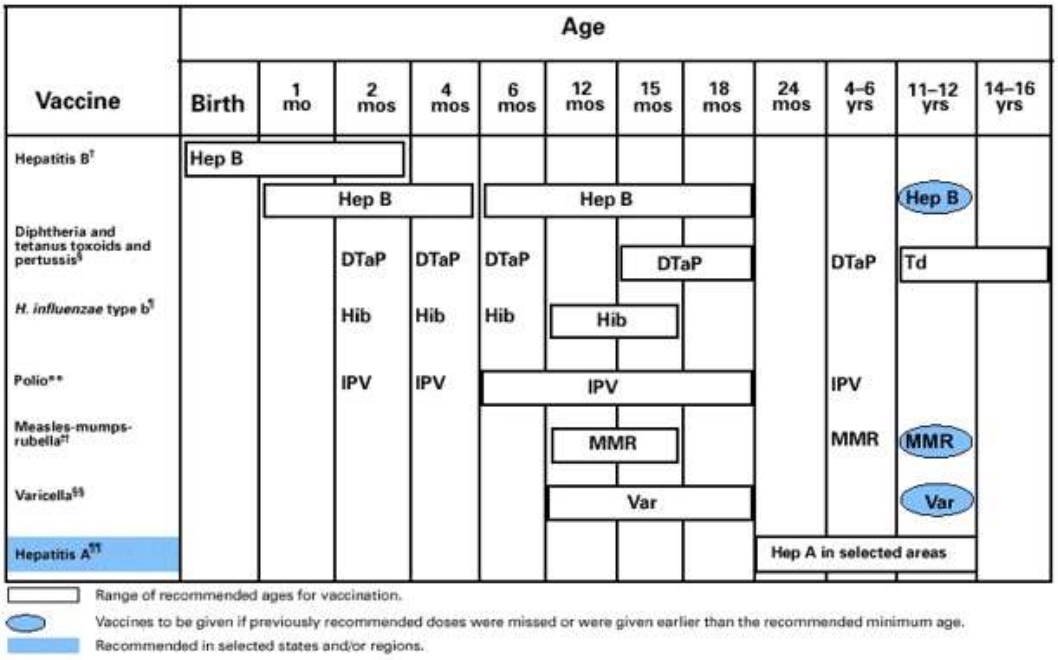
* Use of trade names and commercial sources is for identification only and does not constitute or imply endorsement by CDC or the U.S. Department of Health and Human Services.

Figure 1

FIGURE 1. Recommended childhood immunization schedule* — United States, January–December 2000



On October 22, 1999, the Advisory Committee on Immunization Practices (ACIP) recommended that Rotashield® (rhesus rotavirus vaccine-tetravalent [RRV-TV]), the only U.S.-licensed rotavirus vaccine, no longer be used in the United States (*MMWR*, Vol. 48, No. 43, November 5, 1999). Parents should be reassured that children who received rotavirus vaccine before July 1999 are not now at increased risk for intussusception.

* This schedule indicates the recommended ages for routine administration of licensed childhood vaccines as of November 1, 1999. Any dose not given at the recommended age should be given as a "catch-up" vaccination at any subsequent visit when indicated and feasible. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and the vaccine's other components are not contraindicated. Providers should consult the manufacturers' package inserts for detailed recommendations.

† **Infants born to hepatitis B surface antigen (HBsAg)-negative mothers** should receive the first dose of hepatitis B vaccine (Hep B) by age 2 months. The second dose should be administered at least 1 month after the first dose. The third dose should be administered at least 4 months after the first dose and at least 2 months after the second dose, but not before age 6 months. **Infants born to HBsAg-positive mothers** should receive Hep B and 0.5 mL hepatitis B immune globulin (HBIG) within 12 hours of birth at separate sites. The second dose is recommended at age 1–2 months and the third dose at age 6 months. **Infants born to mothers whose HBsAg status is unknown** should receive Hep B within 12 hours of birth. Maternal blood should be drawn at delivery to determine the mother's HBsAg status; if the HBsAg test is positive, the infant should receive HBIG as soon as possible (no later than age 1 week). **All children and adolescents (through age 18 years)** who have not been vaccinated against hepatitis B may begin the series during any visit. Providers should make special efforts to vaccinate children who were born in or whose parents were born in areas of the world where hepatitis B virus infection is moderately or highly endemic.

§ The fourth dose of diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) can be administered as early as age 12 months, provided 6 months have elapsed since the third dose and the child is unlikely to return at age 15–18 months. Tetanus and diphtheria toxoids (Td) is recommended at age 11–12 years if at least 5 years have elapsed since the last dose of diphtheria and tetanus toxoids and pertussis vaccine (DTP), DTaP, or diphtheria and tetanus toxoids (DT). Subsequent routine Td boosters are recommended every 10 years.

¶ Three *Haemophilus influenzae* type b (Hib) conjugate vaccines are licensed for infant use. If Hib conjugate vaccine (PRP-OMP) (PedvaxHIB® or ComVax® [Merck]) is administered at ages 2 months and 4 months, a dose at age 6 months is not required. Because clinical studies in infants have demonstrated that using some combination products may induce a lower immune response to the Hib vaccine component, DTaP/Hib combination products should not be used for primary vaccination in infants at ages 2, 4, or 6 months unless approved by the Food and Drug Administration for these ages.

** To eliminate the risk for vaccine-associated paralytic poliomyelitis (VAPP), an all-inactivated poliovirus vaccine (IPV) schedule is now recommended for routine childhood polio vaccination in the United States. All children should receive four doses of IPV: at age 2 months, age 4 months, between ages 6 and 18 months, and between ages 4 and 6 years. Oral poliovirus vaccine (OPV) (if available) may be used only for the following special circumstances: 1) mass vaccination campaigns to control outbreaks of paralytic polio; 2) unvaccinated children who will be traveling in <4 weeks to areas where polio is endemic or epidemic; and 3) children of parents who do not accept the recommended number of vaccine injections. Children of parents who do not accept the recommended number of vaccine injections may receive OPV only for the third or fourth dose or both; in this situation, health-care providers should administer OPV only after discussing the risk for VAPP with parents or caregivers. During the transition to an all-IPV schedule, recommendations for the use of remaining OPV supplies in physicians' offices and clinics have been issued by the American Academy of Pediatrics (*Pediatrics*, Vol. 104, No. 6, December 1999).

†† The second dose of measles, mumps, and rubella vaccine (MMR) is recommended routinely at age 4–6 years but may be administered during any visit, provided at least 4 weeks have elapsed since receipt of the first dose and that both doses are administered beginning at or after age 12 months. Those who previously have not received the second dose should complete the schedule no later than the routine visit to a health-care provider at age 11–12 years.

§§ Varicella (Var) vaccine is recommended at any visit on or after the first birthday for susceptible children, i.e., those who lack a reliable history of chickenpox (as judged by a health-care provider) and who have not been vaccinated. Susceptible persons aged ≥13 years should receive two doses given at least 4 weeks apart.

¶¶ Hepatitis A vaccine (Hep A) is recommended for use in selected states and regions. Information is available from local public health authorities and *MMWR*, Vol. 48, No. RR-12, October 1, 1999.

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Source: Advisory Committee on Immunization Practices (ACIP), American Academy of Family Physicians (AAFP), and American Academy of Pediatrics (AAP).

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Exhibit 8

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

December 30, 2021

Elizabeth Brehm
Siri & Glimstad
200 Park Ave, 17th Floor
New York, NY 10166
Via email: foia@sirillp.com

Dear Ms. Brehm:

This letter is our final response to your Centers for Disease Control and Prevention and Agency for Toxic Substances and Disease Registry (CDC/ATSDR) Freedom of Information Act (FOIA) request of September 28, 2020, assigned #20-02418-FOIA, for:

> *"Documents sufficient to reflect that acellular pertussis vaccines, while reducing symptoms from pertussis, do not prevent infection and transmission."*

Published scientific literature was used to inform the sentence in question ("Acellular pertussis vaccines may not prevent colonization (carrying the bacteria in your body without getting sick or spread of the bacteria."). For administrative convenience and to fully respond to your request, program staff have provided examples of literature that support the content of this sentence below.

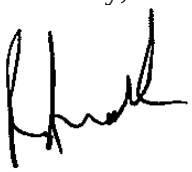
Acellular pertussis vaccines protect against disease but fail to prevent infection and transmission in a nonhuman primate model.
https://pubmed.ncbi.nlm.nih.gov/24277828/

Pertussis Prevention: Reasons for Resurgence, and Differences in the Current Acellular Pertussis Vaccines
https://pubmed.ncbi.nlm.nih.gov/31333640/

Reduced Severity of Pertussis in Persons with Age-Appropriate Pertussis Vaccination-United States, 2010-2012
https://pubmed.ncbi.nlm.nih.gov/29017283/

If you need any further assistance or would like to discuss any aspect of the records provided please contact either our FOIA Requester Service Center at 770-488-6399 or our FOIA Public Liaison at 770-488-6277.

Sincerely,



Roger Andoh
CDC/ATSDR FOIA Officer
Office of the Chief Operating Officer
Phone: (770) 488-6399
Fax: (404) 235-1852

SEE COMMENTARY

Acellular pertussis vaccines protect against disease but fail to prevent infection and transmission in a nonhuman primate model

Jason M. Warfel, Lindsey I. Zimmerman, and Tod J. Merkel[1]

Division of Bacterial, Parasitic and Allergenic Products, Center for Biologics Evaluation and Research, US Food and Drug Administration, Bethesda, MD, 20892

Edited by Rino Rappuoli, Novartis Vaccines and Diagnostics Srl, Siena, Italy, and approved October 22, 2013 (received for review August 5, 2013)

Pertussis is a highly contagious respiratory illness caused by the bacterial pathogen *Bordetella pertussis*. Pertussis rates in the United States have been rising and reached a 50-y high of 42,000 cases in 2012. Although pertussis resurgence is not completely understood, we hypothesize that current acellular pertussis (aP) vaccines fail to prevent colonization and transmission. To test our hypothesis, infant baboons were vaccinated at 2, 4, and 6 mo of age with aP or whole-cell pertussis (wP) vaccines and challenged with *B. pertussis* at 7 mo. Infection was followed by quantifying colonization in nasopharyngeal washes and monitoring leukocytosis and symptoms. Baboons vaccinated with aP were protected from severe pertussis-associated symptoms but not from colonization, did not clear the infection faster than naïve animals, and readily transmitted *B. pertussis* to unvaccinated contacts. Vaccination with wP induced a more rapid clearance compared with naïve and aP-vaccinated animals. By comparison, previously infected animals were not colonized upon secondary infection. Although all vaccinated and previously infected animals had robust serum antibody responses, we found key differences in T-cell immunity. Previously infected animals and wP-vaccinated animals possess strong *B. pertussis*-specific T helper 17 (Th17) memory and Th1 memory, whereas aP vaccination induced a Th1/Th2 response instead. The observation that aP, which induces an immune response mismatched to that induced by natural infection, fails to prevent colonization or transmission provides a plausible explanation for the resurgence of pertussis and suggests that optimal control of pertussis will require the development of improved vaccines.

whooping cough | T-cell memory | animal models | adaptive immunity | IL-17

Pertussis is a highly contagious, acute respiratory illness caused by the bacterial pathogen *Bordetella pertussis* (1, 2). Infection results in a wide spectrum of clinical manifestations ranging from mild respiratory symptoms to a severe cough illness accompanied by marked leukocytosis and the hallmark inspiratory whoop and posttussive emesis (3). Because acellular pertussis vaccines replaced whole-cell vaccines in the 1990s, pertussis has reemerged at a startling rate in the United States despite nationwide vaccine coverage in excess of 95% (4). With a 50-y high of 42,000 reported cases in the United States in 2012, pertussis is the most common of the vaccine-preventable diseases (5). This resurgence is mirrored throughout the industrial world despite similar high rates of vaccination (6–9). Two common hypotheses for the resurgence have been proposed: *i*) current acellular pertussis vaccines (aP) vaccines are less effective than the whole-cell pertussis (wP) vaccines they replaced and *ii*) aP-induced immunity wanes more quickly than anticipated (10–13). However, pertussis resurgence is not completely understood (14, 15).

Hampering our ability to counteract this resurgence is the fact that pertussis pathogenesis and immunity to natural infection have not been well studied in humans because typical pertussis is sporadic given high rates of vaccination in developed countries. Human challenge studies have been proposed but never conducted due to a variety of logistical and ethical problems including the potential for severe disease, the lack of an effective therapeutic for established disease, and the highly contagious nature of pertussis. Although a variety of small-animal models have been used to study pertussis, none of them adequately reproduce the human disease (16). To address this gap, we recently developed a nonhuman primate model of pertussis using baboons (*Papio anubis*) and found the disease is very similar to severe clinical pertussis. Upon challenge, baboons experience 2 wk of heavy respiratory colonization and leukocytosis peaking between 30,000–80,000 cells/mL, similar to the range in pertussis-infected infants (1, 17). In addition, baboons experience a paroxysmal cough illness characterized by repeated fits of 5–10 coughs. The coughing fits last on average >2 wk in the baboon, although this is less than some severely infected children, where the cough can last up to 12 wk (1, 17). We also characterized airborne transmission of *B. pertussis* from infected to naïve animals, which is the route of transmission postulated to occur between humans (18). Because this is the only model of pertussis to reproduce the cough illness and transmission of the human disease, we believe it provides the unique opportunity to test our hypothesis that aP vaccines fail to prevent *B. pertussis* colonization, thus enabling transmission among vaccinated individuals.

Using this model we have confirmed that, as in humans, aP vaccines provide excellent protection against severe disease in baboons. However, aP vaccines do not prevent colonization following direct challenge or infection by transmission. In addition, aP-vaccinated animals are capable of transmitting disease to naïve contacts. By comparison, wP-vaccinated animals cleared infection significantly more quickly than aP-vaccinated or naïve

Significance

Pertussis has reemerged as an important public health concern since current acellular pertussis vaccines (aP) replaced older whole-cell vaccines (wP). In this study, we show nonhuman primates vaccinated with aP were protected from severe symptoms but not infection and readily transmitted *Bordetella pertussis* to contacts. Vaccination with wP and previous infection induced a more rapid clearance compared with naïve and aP-vaccinated animals. While all groups possessed robust antibody responses, key differences in T-cell memory suggest that aP vaccination induces a suboptimal immune response that is unable to prevent infection. These data provide a plausible explanation for pertussis resurgence and suggest that attaining herd immunity will require the development of improved vaccination strategies that prevent *B. pertussis* colonization and transmission.

Author contributions: J.M.W. and T.J.M. designed research; J.M.W., L.I.Z., and T.J.M. performed research; J.M.W. and T.J.M. analyzed data; and J.M.W. and T.J.M. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

See Commentary on page 575.

[1]To whom correspondence should be addressed. E-mail: tod.merkel@fda.hhs.gov.

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animals. We also found that aP vaccination induces T helper 2 (Th2) and T helper 1 (Th1) immune memory responses, whereas infection and—to a lesser extent—wP vaccination induce Th17 and Th1 memory. Our results suggest that in addition to the potential contribution of reduced efficacy and waning immunity of aP, the inability of aP to prevent colonization and transmission provides a plausible explanation for pertussis resurgence.

Results

Acellular Pertussis Vaccines Protect Against Disease but Fail to Prevent Infection. Several observational studies recently concluded that children primed with aP vaccine are at greater risk for pertussis diagnosis compared with wP-primed children (19–22). Although these data suggest aP vaccine is less effective than wP vaccine at preventing colonization, the rate of undiagnosed *B. pertussis* carriage in vaccinated individuals is unknown. To assess the ability of each vaccine to prevent colonization and clinical pertussis symptoms, baboons were vaccinated according to the US schedule at 2, 4, and 6 mo of age with human doses of combination diphtheria, tetanus, and pertussis vaccines containing aP or inactivated wP (Table 1 provides a list of the components of each vaccine). At 7 mo of age, vaccinated, naïve, and previously infected (convalescent) animals were challenged with D420, a *B. pertussis* clinical isolate that causes severe infection in humans and baboons (17). Naïve animals were heavily colonized with peak levels between 10^7–10^8 cfu/mL in nasopharyngeal washes (Fig. 1*A*). After 2 wk, colonization gradually decreased, and the infection cleared after 30 d. Consistent with our previous finding, none of the convalescent animals were colonized (17). Compared with naïve animals, aP-vaccinated animals had slightly reduced colonization for the first 10 d but remained consistently colonized before clearing after 35 d. In wP-vaccinated animals the initial colonization was similar to aP-vaccinated animals but the infection cleared after 18 d, significantly faster than naïve and aP-vaccinated animals (Fig. 1*B*).

To assess the efficacy of the vaccines in preventing the symptoms of severe pertussis, peripheral blood was drawn serially, and complete blood counts were performed to monitor leukocytosis, a significant marker of morbidity in pertussis-infected infants (23). Compared with preinfection levels, naïve animals had a significant increase in circulating white blood cells at each time point, peaking at over 40,000 cells per μL, an eightfold increase over preinfection levels (Fig. 1*C*). In contrast to the colonization data, aP vaccination, wP vaccination, and convalescence all prevented leukocytosis (Fig. 1*C*). In addition, wP-vaccinated, aP-vaccinated, and convalescent animals did not cough and showed no reduction of activity, loss of appetite, or other outward signs of disease.

Acellular Vaccines Fail to Prevent Infection Following Natural Transmission. To assess the ability of vaccination to prevent pertussis infection by transmission, two aP-vaccinated animals and one unvaccinated animal were cohoused with a directly challenged, unvaccinated animal. Similar to our previous findings (18), all animals became colonized 7–10 d after cohousing with the infected animal (Fig. 2). The peak levels and kinetics of colonization were indistinguishable between the naïve and aP-vaccinated animals.

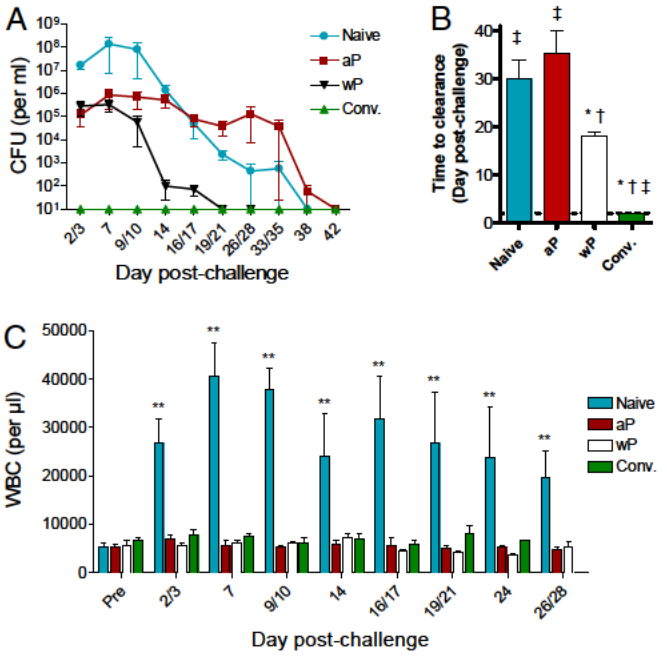

Fig. 1. The effect of vaccination or convalescence on colonization and leukocytosis. Naïve animals, aP-vaccinated animals, wP-vaccinated animals, and previously infected [convalescent conv.)] animals were directly challenged with *B. pertussis* ($n = 3$–4 per group). (*A*) Colonization was monitored by quantifying *B. pertussis* cfu per mL in biweekly nasopharyngeal washes with a limit of detection of 10 cfu per mL. For each animal the time to clearance is defined as the first day that no *B. pertussis* cfu were recovered from nasopharyngeal washes. (*B*) The mean time to clearance is shown for each group ($n = 3$ per group). Because no *B. pertussis* organisms were recovered from the conv. animals, the mean time to clearance was defined as the first day of sampling (day 2, indicated by the dashed line). *$P < 0.05$ vs. Naïve, †$P < 0.05$ vs. aP, ‡$P < 0.05$ vs. wP. (*C*) The mean circulating white blood cell counts before and after challenge are shown for each group of animals ($n = 3$–4 per group). **$P < 0.01$ vs. preinfection from same group.

Acellular-Vaccinated Animals Are Capable of Transmitting *B. pertussis* to Naïve Contacts. Because aP fails to prevent colonization we hypothesized that aP-vaccinated animals can transmit *B. pertussis* infection to contacts. To test this hypothesis, two aP-vaccinated animals were challenged with *B. pertussis* and placed in separate cages. After 24 h, a naïve animal was added to each cage, and all animals were followed for colonization. Both of the naïve animals were infected by transmission from their aP-vaccinated cage mates (Fig. 3).

Vaccination and Previous Infection Induce Robust Antibody Responses. Sera collected before vaccination or primary infection and again at 1 wk before challenge were analyzed for IgG antibodies against heat-killed *B. pertussis* and the vaccine antigens

Table 1. Components of aP and wP vaccines used in this study

Vaccine component	Daptacel	Infanrix	Triple antigen
Diphtheria toxoid	15 Lf	25 Lf	20–30 Lf
Tetanus toxoid	5 Lf	10 Lf	5–25 Lf
Whole-cell *Bordetella pertussis*	—	—	≥4 IU
Inactivated pertussis toxin	10 μg	25 μg	—
Filamentous hemagglutinin	5 μg	25 μg	—
Pertactin	3 μg	8 μg	—
Fimbriae types 2 and 3	5 μg	—	—
Aluminum (from aluminum phosphate)	0.33 mg	≤0.625 mg	≤1.25 mg

IU, international units; Lf, limit of flocculation units.

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Pertussis Prevention: Reasons for Resurgence, and Differences in the Current Acellular Pertussis Vaccines

Susanna Esposito[1], Paola Stefanelli[2], Norman K. Fry[3], Giorgio Fedele[2], Qiushui He[4,5], Pauline Paterson[6], Tina Tan[7], Markus Knuf[8,9], Carlos Rodrigo[10,11], Catherine Weil Olivier[12], Katie L. Flanagan[13,14,15], Ivan Hung[16], Iria Lutsar[17], Kathryn Edwards[18], Miguel O'Ryan[19] and Nicola Principi[20] for the World Association of Infectious Diseases and Immunological Disorders (WAidid) and the Vaccine Study Group of the European Society of Clinical Microbiology and Infectious Diseases (EVASG)*

[1] Department of Surgical and Biomedical Sciences, Paediatric Clinic, Università degli Studi di Perugia, Perugia, Italy, [2] Department of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy, [3] Immunisation and Countermeasures Division, Public Health England–National Infection Service, London, United Kingdom, [4] Institute of Biomedicine, University of Turku, Turku, Finland, [5] Department of Medical Microbiology, Capital Medical University, Beijing, China, [6] Department of Infectious Disease Epidemiology, The Vaccine Confidence Project TM, London School of Hygiene & Tropical Medicine, London, United Kingdom, [7] Division of Pediatric Infectious Diseases, Department of Pediatrics, Northwestern University Feinberg School of Medicine, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, United States, [8] Children's Hospital, Helios HSk, Wiesbaden, Germany, [9] Department of Pediatrics, University Medicine, Mainz, Germany, [10] Department of Pediatrics, Vall d'Hebron University Hospital, Barcelona, Spain, [11] School of Medicine-Germans Trias i Pujol University Hospita, Universidad Autónoma de Barcelona, Barcelona, Spain, [12] Retired, Neuilly-sur-Seine, France, [13] School of Medicine, College of Health and Medicine, University of Tasmania, Hobart, TAS, Australia, [14] School of Health and Biomedical Science, RMIT University, Melbourne, VIC, Australia, [15] Department of Immunology and Pathology, Monash University, Melbourne, VIC, Australia, [16] Department of Medicine, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong, China, [17] Department of Microbiology, Institute of Biomedicine and Translational Medicine, University of Tartu, Tartu, Estonia, [18] Division of Pediatric Infectious Diseases, Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, TN, United States, [19] Microbiology and Mycology Program, Faculty of Medicine, Institute of Immunology and Immunotherapy, University of Chile, Santiago, Chile, [20] Retired, Milan, Italy

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***Correspondence:**
Susanna Esposito
susanna.esposito@unimi.it

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Pertussis is an acute respiratory disease caused by *Bordetella pertussis*. Due to its frequency and severity, prevention of pertussis has been considered an important public health issue for many years. The development of the whole-cell pertussis vaccine (wPV) and its introduction into the pediatric immunization schedule was associated with a marked reduction in pertussis cases in the vaccinated cohort. However, due to the frequency of local and systemic adverse events after immunization with wPV, work on a less reactive vaccine was undertaken based on isolated *B. pertussis* components that induced protective immune responses with fewer local and systemic reactions. These component vaccines were termed acellular vaccines and contained one or more pertussis antigens, including pertussis toxin (PT), filamentous haemagglutinin (FHA), pertactin (PRN), and fimbrial proteins 2 (FIM2) and 3 (FIM3). Preparations containing up to five components were developed, and several efficacy trials clearly demonstrated that the aPVs were able to confer comparable short-term protection than the most effective wPVs with fewer local and systemic reactions. There has been a resurgence of pertussis

were reported in another meta-analysis including studies of aPVs administered according to the USA schedule (46). VE was compared after the childhood series (five doses) and after an adolescent booster dose (sixth dose). Relative VE was defined as VE in the population given prior doses of an aPV and absolute VE was defined as VE in an aPV-naïve population. Absolute VE after the childhood series was 91% (95% CI 87–95%) but declined annually by 9.6% (46). Initial relative VE after adolescent boosting was 70% (95% CI: 54 to 86%) and declined by 45.3% annually. The absolute VE of the full six-dose aPV series was estimated to be 85% (95% CI: 84–86%) in the first year after series completion. However, it declined by 11.7% (95% CI: 11.1 to 12.3%) per year, and at 18 years of age, protection was limited to 28.2% of immunized patients (95% CI: 27 to 29%) (46).

Wang et al. (47) studied 279 children aged 5 to 15 years who presented to primary care with a persistent cough of 2 to 8 weeks duration. Evidence of recent *B. pertussis* infection based on a high oral fluid anti-pertussis toxin IgG titer was demonstrated in 215 children who had been fully vaccinated. Risk was higher in those who had been immunized ≥7 years earlier, but in 12% of these cases, chronic cough was demonstrated in patients given an aPV <7 years before. Further evidence of waning immunity after recent aPV immunization was reported by Principi et al. (48) who documented *B. pertussis* infection in 18.7% (95% CI 11.5–28.0) of children and adolescents with chronic cough who had been immunized with an aPV a few years previously (<2 years in some cases).

Immune Responses to Pertussis Vaccines and Natural Infection

Studies that have compared immune responses after natural *B. pertussis* infection and the administration of both wPVs and aPVs have clearly shown that the immune stimulation evoked by aPVs is different from that due to natural infection and wPVs (49–51). Natural infection evokes both mucosal and systemic immune responses, while aPVs induce only a systemic immune response. As *B.* pertussis is a mucosal pathogen and only exceptionally causes infection outside the respiratory tract, this difference is of particular importance in pertussis control. Mucosal immunity is essential to prevent colonization and transmission of *B. pertussis* organisms. Consequently, preventive measures such as aPVs that do not induce a valid mucosal response can prevent disease but cannot avoid infection and transmission. Animal studies have shown that natural infection is associated with a strong secretory IgA response in both the upper and lower airways and induction of resident memory T cells (TRM) (52, 53). Moreover, it has been recently reported (54) that IL-17 and IFN-γ-secreting CD69+CD4+ TRM cells were expanded in the respiratory tract after *B. pertussis* challenge of mice immunized with wP, but not aP vaccines. However, natural infection was associated with the most persistent protection against nasal colonization and this correlated with potent induction of nasal tissue TRM cells. These animal data suggest that the lack of mucosal immune response after aPV administration might explain its lower efficacy when compared to wPVs and the shorter duration of protection compared to both wPV vaccination and natural infection.

Clear differences between systemic immune response after natural infection and aP and wP vaccines. Natural infection and wPvs induce antibodies of the IgG1, IgG2, and IgG3 subclasses, with marginal production of IgG4 (55), suggesting a strong Th1 response. In contrast, the immune response after aPVs evoke a mixed Th2 and Th17 response (56). APVs evoke the production of IgG1 and IgG4 antibodies, which is consistent with a Th2 response. Furthermore, aPVs evoke CD4+ T-cells that produce high concentrations of IL-4 and IL-5 and low amounts of IFNγ, again consistent with a Th2 response (57).

Since Th1 cytokines play an important role in protection against pertussis (58, 59), this finding can further explain the better protection offered by wPVs and natural infection. Studies carried out in children who have received infant series of either wPV or aPVs have shown children given aPVs exhibited higher pertussis-specific antibody levels and higher memory B- and T-cell responses (5, 60–63). Although no correlates of antibody protection for pertussis have been established (64), the higher IgG levels in aPV-immunized children could lead to the conclusion that better humoral protection was afforded by the aP rather than wP vaccines. However, the antigens measured were only those included in the aPVs and not the additional antigens included in the wPs.

These differences in immune responses persist over time, even after booster aPVs (65, 66). The administration of aPV booster doses at 4 and 9 years of age was associated with an increase in the production of IgG4, regardless of the type of vaccine used for priming, but was significantly higher in aPV-primed children (66). IgG4 antibodies are unable to activate the complement system and lead to a suboptimal inflammatory response with impaired phagocytosis and antimicrobial defense, another potential mechanism for the lower efficacy of aPVs compared to wPVs (67). Moreover, the evidence that production of IgG4 after immunization with aPV increases with each dose seems to indicate that the protection offered by aPVs tends to be as shorter with each subsequent boosters (68, 69). Preadolescent booster vaccination with an aPV was found to induce lower B-cell and Th1 cell responses in aPV-primed compared with wPV-primed children, resulting in significantly lower Th1/Th2 ratios. Confirming this, it has been shown that wPv or aPV primary immunizations in infancy determines adolescent cellular immune profiles, showing a beneficial Th1-dominated response after wP-priming (69). These findings of a preferential Th1 response were also shown in the baboon model, with aPV vaccines preventing disease after natural pertussis challenge, but not preventing transmission of pertussis organisms (70). All these findings indicate that although aPVs are as individually protective as wPVs in the first years after priming, they induce shorter long-term protection than wPVs and a different profile of pertussis-specific immunity.

Finally, aPV pertussis vaccines do not prevent colonization. Consequently, they do not reduce the circulation of *B. pertussis* and do not exert any herd immunity effect.

These findings at least partly explain the resurgence of pertussis.

Genetic Modifications of *Bordetella pertussis*

Circulation of *B. pertussis* strains with modified or absent antigens included in the aPV have been reported in both the pre-vaccine era and the aPV era (71–73). Moreover, strains with polymorphisms of the PT gene resulting in the production of greater amounts of this protein have been detected (74–79). Although it cannot be excluded that this phenomenon might simply be derived from the natural evolutionary course of *B. pertussis*, it has been proposed that it might be a consequence of *B. pertussis* adaptation to aPV use (80).

Genes encoding antigens included in the aPV vaccines have evolved at higher rates than other non-vaccine surface protein-encoding genes soon after the introduction of aPVs into the pediatric immunization schedule (81). The most compelling data have been the evolution of PRN-negative *B. pertussis* strains according to the use of vaccines PRN-containing vaccines. With some exceptions (82–84), studies have demonstrated that the emergence of PRN-deficient strains has resulted as a consequence of aPV-induced selection pressure. The rate of PRN-negative isolates is significantly correlated with aPV use in the USA (85). In Denmark, where an aPV without PRN is used, no PRN-deficient isolates have been detected (86). In Japan where aPVs with PRN were administered for many years (87), consistent rates of PRN-negative strains have been demonstrated over time (2005–2007, 41%; 2008–2010, 35%; and 2011–2013, 25%) (88, 89). However, when these aPV vaccines were replaced with a preparation without PRN in November 2012, a marked reduction of PRN-deleted strains was observed (2014–2016, 8%) (90). The clinical relevance of PRN-deleted strains has not been precisely defined (80), but children infected with these strains do not have more severe pertussis (91, 92), In contrast, *B. pertussis* strains with the enhanced PT promoter allele PTP3, instead of the common PTP2 allele, were found to produce greater amounts of PT (74) and cause more severe disease in younger infants (92).

Interesting, *B. pertussis* strains lacking the *PRN* gene show increased fitness and/or prolonged infection times in animals immunized with ACVs (74, 93, 94). This finding suggests that loss of PRN could lead to a reduced immune response to aPVs and favor pertussis resurgence. However, clinical studies that have evaluated the effectiveness of aPVs containing PRN in the setting of PRN-deficient pertussis have produced conflicting results. One study in the US (80) assessed the VEs of a five-dose DTaP series among 4–10 year-olds and a Tdap booster among 11–19 year-olds in an area where >90% of *B. pertussis* strains were PRN deficient. It was found that overall DTaP VE was 84% (95% CI 58–94%) while that of TdaP was 70% (95% CI 54–81%), which do not substantially differ than rates reported during the circulation of PRN-positive strains. In contrast, a second US study revealed that in vaccinated persons, the likelihood of suffering from pertussis disease was greater if the infecting strain was PRN-negative than if it is PRN-positive (85).

In conclusion, aPV use seems to favor adaptation of *B. pertussis* strains with emergence of mutated strains. However, the role of genetic modification in reducing aPV protection remains unclear with future studies needed.

ROLE OF ANTIGENS INCLUDED IN PRESENTLY AVAILABLE VACCINES IN CONDITIONING PROTECTION

Although pertussis resurgence has been demonstrated to be independent of the type of aPV used, it is theoretically possible that the composition of vaccines and the immunization strategies may have played a role in modifying the pertussis incidence. However, estimates of aPV efficacy and comparisons between different aPVs are very problematic for several reasons. First, the criteria for the diagnosis of pertussis used in the various aPV effectiveness trials have not been uniform. In some cases, significant underestimations of the real pertussis incidence may have limited the reliability of final results. When the WHO's clinical case definition of pertussis as prolonged paroxysmal cough is used, it is highly likely that most of the mild cases are not included. Second, study designs, administration schedules, and duration of follow-up have not been consistent in the effectiveness trials. In many European countries, the primary series includes only two doses of an aPV with a booster dose at ∼1 year. In contrast, in other countries, including the US, the primary series is based on three doses within the first 6 months of life, with a booster dose given after the first birthday. Third, most, but not all, national immunization schedules include a booster before entering school and during adolescence. Fourth, the composition of the administered aPV can vary. Most of these studies have been carried out with vaccines containing three or five antigens, but in earlier studies vaccines with only PT have been included. In addition, the quantity of antigen can differ among the preparations. For example, GSK DTaP vaccines contain 25 μg PT, 25 μg FHA, and 8 μg PRN, while the Sanofi preparation also includes FIM2 and three different amounts of PT, FHA, and PRN for the primary and booster doses. Tdap contains 10 μg PT, 5 μg FHA, and 3 μg PRN when administered alone, but when Tdap is combined with polio, hepatitis B, and *Haemophilus influenzae* type b, the PT and FHA content is increased to 20 μg. In addition, the type of aluminum salt used as an adjuvant and its content vary slightly among between vaccines. Finally, there has been no single study that directly compares all aPV vaccines with different numbers and quantities of included antigens.

Role of the Number of Pertussis Antigens

In those studies that directly compared vaccines using similar vaccine schedules, similar definitions of pertussis disease, and comparable durations of follow-up, it can be concluded that the 3-component aPV (3aPV) and the 5-component aPV (5aPV) have comparable efficacy. Greco et al. evaluated two 3aPVs produced by different pharmaceutical companies (12), and Gustafsson et al. (13) studied a 5aPV, with both studies being conducted in children that had received three doses at ∼2, 4, and

a lack of perceived need for the vaccine, and concerns about its safety and effectiveness (115).

CONCLUSIONS

The resurgence of pertussis observed in recent years seems to be a complex but real phenomenon resulting from a number of cases, including the use of aPV in many locales. Lack of mucosal immune responses after aPV administration favor infection, persistent colonization, and transmission of the pathogen. Moreover, earlier waning of protective immunity and the circulation of *B. pertussis* variants depleted of vaccine-included antigens further favor the increase in pertussis disease. Several different aPVs are available, but it has yet to be determined which of them confers the highest and the most-prolonged protection. Further studies are needed to evaluate the importance of individual antigens included in aPVs in conferring protection against disease, colonization, and transmission. However, present knowledge seems to indicate that PT, particularly if genetically detoxified, represents the main antigen that ensures protection from disease even if not from infection. The contribution of FHA, PRN, and FIM2 and FIM3 in vaccine efficacy and long-lasting protection is still under discussion and needs further study.

The optimal pertussis vaccine would be one that induced both a mucosal and systemic responses similar to those occurring under natural infection, leading to a long-term protection against both disease and infection. Such a vaccine might increase public confidence and result in better vaccine uptake. Meanwhile, the identification of more efficacious vaccination strategies with currently available vaccines reaching high vaccination coverage rates is required, including the vaccination of pregnant women (50).

AUTHOR CONTRIBUTIONS

SE proposed the project, coordinated the Study Group, and wrote the first draft of the study. PS, NF, and GF coordinated the sections of the project on Vaccines, Microbiology, and Immunology, respectively, giving a substantial scientific contribution. QH, PP, TT, MK, CR, CW, KF, IH, IL, KE, and MO gave a substantial scientific contribution. NP co-wrote the first draft of the manuscript and supervised the project. All authors approved the final submitted version of the manuscript.

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Exhibit 9

Causes and How It Spreads

Whooping cough is a very contagious respiratory illness that spreads from person to person.

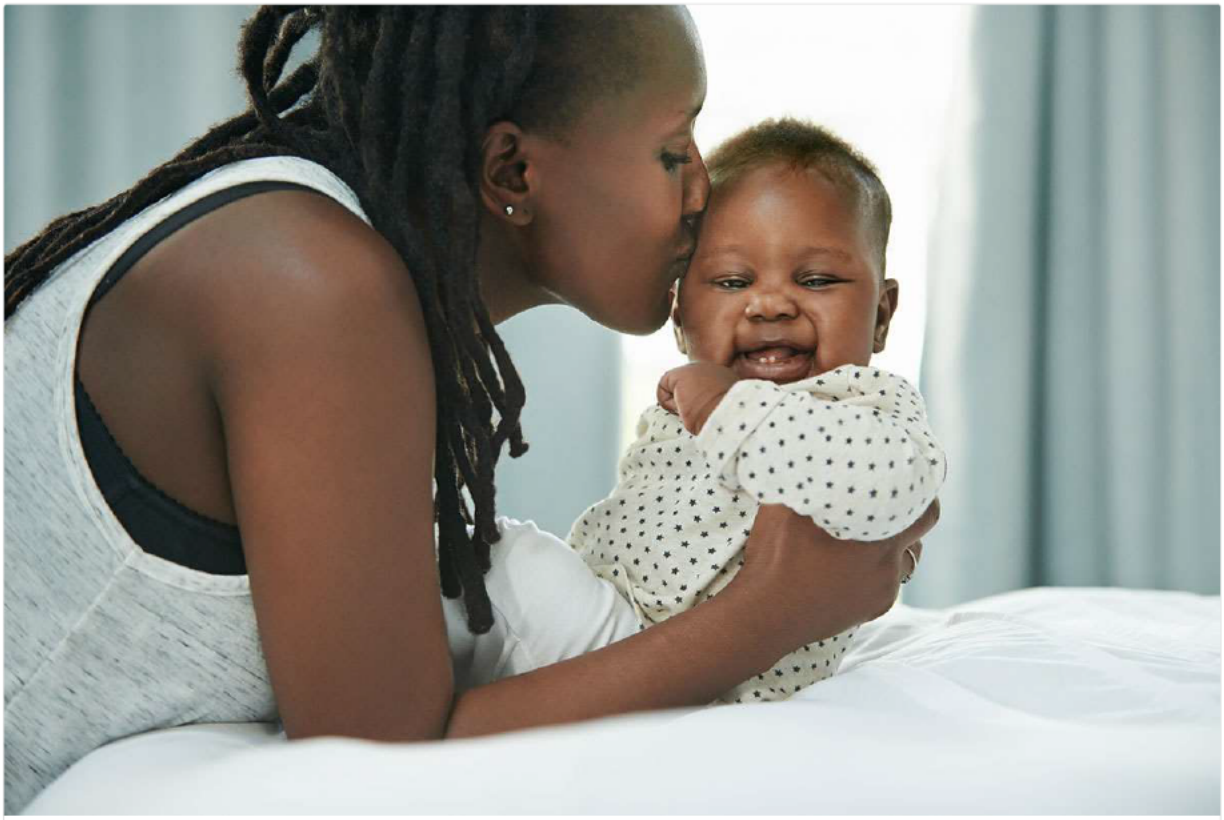
Causes

Whooping cough, also known as pertussis, is a very contagious respiratory illness caused by a type of bacteria called *Bordetella pertussis*. The disease is only found in humans.

Whooping cough bacteria attach to the cilia (tiny, hair-like extensions) that line part of the upper respiratory system. The bacteria release toxins (poisons), which damage the cilia and cause airways to swell.

How it spreads

The bacteria that cause whooping cough spread easily from person to person through the air. When a person who has whooping cough sneezes or coughs, they can release small particles with the bacteria in them. Other people then breathe in the bacteria. It also spreads when people spend a lot of time together or share breathing space, like when you hold a newborn on your chest.



Babies can get whooping cough from family or caregivers who don't know they have it.

People can be contagious for weeks

People can spread the bacteria from the start of the very first symptoms and for at least 2 weeks after coughing begins.

Taking antibiotics early in the illness may shorten the amount of time someone is contagious. Learn more about treatment.

People can spread the disease even if they don't know they have it

Some people have mild symptoms and don't know they have whooping cough, but they can still spread the bacteria to others.

Many babies who get whooping cough are infected by older siblings, parents, or caregivers who don't know they have it. Learn what you can do to protect babies from whooping cough.



Signs and Symptoms



Diagnosis and Treatment



Prevention



Complications

Last Reviewed: August 4, 2022
Source: National Center for Immunization and Respiratory Diseases, Division of Bacterial Diseases

Exhibit 10

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 67 / No. 2
April 27, 2018

Prevention of Pertussis, Tetanus, and Diphtheria with Vaccines in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP)



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Tdap Vaccines

Two Tdap products are licensed for use in adolescents and adults as a single-dose booster vaccination against tetanus, diphtheria, and pertussis: Boostrix (GlaxoSmithKline, Rixensart, Belgium), and Adacel (Sanofi Pasteur, Swiftwater, Pennsylvania). The age indication for approved use differs depending upon the specific Tdap product and licensure (Table 5). Both Tdap products consist of pertussis antigen and diphtheria and tetanus toxoids (Table 5). The pertussis antigen composition and amount differ, as does the amount of diphtheria toxoids between the two Tdap products. Summaries of the data on the immunogenicity and safety of each of these vaccines have been published (*4*,*5*).

Adacel (Sanofi Pasteur) is licensed by FDA as a single dose in persons aged 10–64 years (*141*). Adacel contains the same tetanus toxoid, diphtheria toxoid, and five pertussis antigens (PT, PRN, FHA, and FIM) as those in Daptacel (pediatric DTaP), but is formulated with reduced quantities of the toxoids and antigens (Table 5). Adacel contains no thimerosal or other preservative. Additional information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142764.pdf).

Boostrix (GSK) is licensed by FDA as a single dose in persons aged ≥10 years (*142*). Boostrix contains the same tetanus toxoid, diphtheria toxoid, and three pertussis antigens (PT, PRN, and FHA) as those in Infanrix (pediatric DTaP), but is formulated with reduced quantities of the toxoids and antigens (Table 5). Boostrix contains no thimerosal or other preservative. Additional information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/UCM152842.pdf).

Immunogenicity and Efficacy

Both Tdap products were licensed on the basis of clinical trials demonstrating immunogenicity not inferior to U.S.-licensed Td or pediatric DTaP products and an overall safety profile clinically comparable to U.S.-licensed Td products (*143*,*144*). Determining the efficacy of the tetanus and diphtheria toxoid components for each Tdap product was based on the comparison of the rates of protective immune response to these antigens as compared to U.S.-licensed Td and using established serologic correlates of protection (*45*,*72*). The percentage of persons achieving protective antitetanus and antidiphtheria antibody concentrations (>0.1 IU/mL) and the booster response to each of these antigens 1 month postvaccination were evaluated.

Because no well-accepted serologic or laboratory correlate of protection against pertussis has been established, clinical endpoint efficacy studies of acellular pertussis vaccines among adolescents or adults were not required for Tdap licensure. Instead, the efficacy of the pertussis components of Tdap vaccines was inferred using a serologic bridge to infants vaccinated with DTaP in efficacy trials with clinical endpoints (*145*). The immune response of adolescents and adults to each pertussis vaccine antigen after a single dose of Tdap was compared with the immune responses of infants who received 3 doses of pediatric DTaP that included the same pertussis components as the Tdap being assessed (*141*,*142*). The percentage of persons with an acceptable booster response to pertussis vaccine antigens according to predefined criteria also was evaluated. The predefined lower limit was defined as the lower limit of 95% CI for the GMC ratio of the Tdap/pediatric DTaP. Prelicensure Tdap vaccine efficacy was inferred using a serologic bridge to infants vaccinated with 3 doses of DTaP and ranged from 79% to 89% (*105*,*106*).

Postlicensure Tdap Effectiveness

Following the 2005 Tdap recommendation for adolescents and adults, postlicensure pertussis vaccine effectiveness estimates for Tdap in settings with similar vaccines and recommendation schedules have ranged from 66% to 78% among adolescents who received both DTP and DTaP as children (*146*–*148*). Among adolescents who received only DTaP as children, in a matched case-control study, the overall estimated vaccine effectiveness of Tdap against pertussis was 63.9% (95% CI = 50%–74%) (*29*). Initial vaccine effectiveness against pertussis within one year of Tdap vaccination was 73% (95% CI = 60%–82%), but after 2–4 years, postvaccination vaccine effectiveness decreased to 34% (95% CI = -0.03%–58%) (*29*). Another study that calculated Tdap vaccine effectiveness among adolescents found that, within the first year after vaccination, effectiveness was 68.8% (95% CI = 59.7%–75.9%); by ≥4 years after vaccination, vaccine effectiveness was 8.9% (95% CI = -30.6%–36.4%) (*149*). As observed with DTaP, Tdap vaccine effectiveness declines substantially with increasing time since vaccination (*29*,*149*,*150*). Although there are no studies estimating Tdap vaccine effectiveness in persons who received only DTP as infants, reported rates of pertussis have been observed to be significantly lower among children who had started their vaccination series with DTP than among those who had started with DTaP (*151*,*152*).

Prevention of Transmission: Indirect Protection ("Cocooning")

At the time Tdap was first recommended, it was anticipated that this vaccine would prevent pertussis in adolescents and adults and thereby result in preventing transmission

Exhibit 11

Meningococcal Vaccination: What Everyone Should Know

Key Facts

There are 2 types of meningococcal vaccines used in the United States:

- Meningococcal conjugate or MenACWY vaccines
- Serogroup B meningococcal or MenB vaccines

Who Should Get Meningococcal Vaccines?

CDC recommends meningococcal vaccination for all preteens and teens. In certain situations, CDC also recommends other children and adults get meningococcal vaccines. Below is more information about which meningococcal vaccines, including booster shots, CDC recommends for people by age.

Talk to your or your child's doctor about what is best for your specific situation.

Preteens and Teens

All 11 to 12 year olds should get a MenACWY vaccine, with a booster shot at 16 years old. Teens may also get a MenB vaccine, preferably at 16 through 18 years old.

> Taking a complement inhibitor such as eculizumab (Soliris®) or ravulizumab (Ultomiris®) increases your risk for meningococcal disease. Even if you received meningococcal vaccines, you could still get meningococcal disease.

While any teen may choose to get a MenB vaccine, certain preteens and teens should get it if they:

- Have a rare type of immune disorder called complement component deficiency
- Are taking a type of medicine called a complement inhibitor (for example, Soliris® or Ultomiris®)
- Have a damaged spleen or sickle cell disease, or their spleen has been removed
- Are part of a population identified to be at increased risk because of a serogroup B meningococcal disease outbreak

Get more information about meningococcal vaccine recommendations for teenagers: Meningococcal Vaccination for Preteens and Teens: Information for Parents. Talk to your child's doctor to find out if, and when, they will need MenACWY or MenB booster shots.



Meningococcal Vaccines for Preteens and Teens
This fact sheet answers general questions about meningococcal vaccines for preteens and teens.
English | Spanish

Babies and Children

CDC recommends MenACWY vaccination for children who are between 2 months and 10 years old if they:

- Have a rare type of immune disorder called complement component deficiency

- Are taking a type of medicine called a complement inhibitor (for example, Soliris® or Ultomiris®)
- Have a damaged spleen or sickle cell disease, or their spleen has been removed
- Have HIV
- Are traveling to or residing in countries in which serogroup A, C, W, or Y meningococcal disease is common
- Are part of a population identified to be at increased risk because of a serogroup A, C, W, or Y meningococcal disease outbreak

Helpful Terms

- *Neisseria meningitidis*: The bacteria that cause meningococcal disease.
- Serogroup: A group of bacteria that are closely related. There are 6 serogroups of *Neisseria meningitidis* that cause most meningococcal disease in the world — A, B, C, W, X, and Y.

CDC recommends MenB vaccination for children 10 years or older if they:

- Have a rare type of immune disorder called complement component deficiency
- Are taking a type of medicine called a complement inhibitor (for example, Soliris® or Ultomiris®)
- Have a damaged spleen or sickle cell disease, or their spleen has been removed
- Are part of a population identified to be at increased risk because of a serogroup B meningococcal disease outbreak

Talk to your child's doctor to find out if, and when, they will need MenACWY or MenB booster shots.

Adults

CDC recommends MenACWY vaccination for adults if they:

- Have a rare type of immune disorder called complement component deficiency
- Are taking a type of medicine called a complement inhibitor (for example, Soliris® or Ultomiris®)
- Have a damaged spleen or sickle cell disease, or their spleen has been removed
- Have HIV
- Are a microbiologist who is routinely exposed to *Neisseria meningitidis*
- Are traveling to or residing in countries in which serogroup A, C, W, or Y meningococcal disease is common
- Are part of a population identified to be at increased risk because of a serogroup A, C, W, or Y meningococcal disease outbreak
- Are not up to date with this vaccine and are a first-year college student living in a residence hall
- Are a military recruit

CDC recommends MenB vaccination for adults if they:

- Have a rare type of immune disorder called complement component deficiency
- Are taking a type of medicine called a complement inhibitor (for example, Soliris® or Ultomiris®)
- Have a damaged spleen or sickle cell disease, or their spleen has been removed
- Are a microbiologist who is routinely exposed to *Neisseria meningitidis*
- Are part of a population identified to be at increased risk because of a serogroup B meningococcal disease outbreak

Talk to your doctor to find out if, and when, you will need MenACWY or MenB booster shots.

Who Might Not Be Able to Get These Vaccines?

Because of age or health conditions, some people should not get certain vaccines or should wait before getting them. Read the guidelines below and ask your or your child's doctor for more information.

Tell the person who is giving you or your child a meningococcal vaccine if:

You or your child have had a life-threatening allergic reaction or have a severe allergy.

- If you have ever had a life-threatening allergic reaction after a previous dose of MenACWY or MenB vaccine, do not get another dose of that type of vaccine.
- Do not get a meningococcal vaccine if you have a severe allergy to any part of that vaccine. Your or your child's doctor can tell you about the vaccine's ingredients.

You are pregnant or breastfeeding.

- Pregnant women who are at increased risk for serogroup A, C, W, or Y meningococcal disease may get MenACWY vaccines.
- Pregnant or breastfeeding women who are at increased risk for serogroup B meningococcal disease may get MenB vaccines. However, they should talk with a doctor to decide if the benefits of getting the vaccine outweigh the risks.

You or your child are not feeling well.

- People who have a mild illness, such as a cold, can probably get these vaccines. People who have a moderate or severe illness should probably wait until they recover. Your or your child's doctor can advise you.

What Types of Meningococcal Vaccines Are There?

There are 2 types of meningococcal vaccines available in the United States:

- MenACWY (conjugate) vaccines (Menactra®, Menveo®, and MenQuadfi®)
- MenB (recombinant protein) vaccines (Bexsero® and Trumenba®)

MenACWY Vaccines

- Menactra® , Menveo® , and MenQuadfi® : Vaccine providers give 2 doses to preteens and teens. Vaccine providers also give it to certain people at increased risk of meningococcal disease. It helps protect against 4 types of the bacteria that cause meningococcal disease (serogroups A, C, W, and Y).

Helpful Terms

- **Conjugate:** A type of vaccine that joins a protein to an antigen in order to improve the protection the vaccine provides
- **Recombinant protein:** A type of vaccine that contains protein antigens

MenB Vaccines

- Bexsero® : Vaccine providers give a 2-dose series to people 16 through 23 years old who are not at increased risk of meningococcal disease. Vaccine providers also give a 2-dose series to people 10 years or older at increased risk of meningococcal disease. Bexsero® helps protect against serogroup B meningococcal disease.
- Trumenba® : Vaccine providers give a 2-dose series to people 16 through 23 years old who are not at increased risk of meningococcal disease. Vaccine providers give a 3-dose series to people 10 years or older at increased risk of meningococcal disease. Trumenba® helps protect against serogroup B meningococcal disease.

How Well Do These Vaccines Work?

Summary

Vaccines that help protect against meningococcal disease work well but cannot prevent all cases.

As part of the licensure process, MenACWY and MenB vaccines showed that they produce an immune response. This immune response suggests the vaccines provide protection, but data are limited on how well they work. Since meningococcal disease is uncommon, many people need to get these vaccines in order to measure their effectiveness.

Available data suggest that protection from MenACWY vaccines decreases in many teens within 5 years. Getting the 16-year-old MenACWY booster dose is critical so teens have protection when they are most at risk for meningococcal disease. Available data on MenB vaccines suggest that protective antibodies also decrease quickly (within 1 to 2 years) after vaccination.

In Depth

Rates of meningococcal disease have declined in the United States since the 1990s and remain low today. Much of the decline occurred before the routine use of MenACWY vaccines. In addition, serogroup B meningococcal disease declined even though MenB vaccines were not available until the end of 2014.

CDC first recommended preteens and teens get a MenACWY vaccine in 2005. Since then, rates of meningococcal disease in teens caused by serogroups C, Y, and W have decreased by over 90% (note: serogroup A meningococcal disease continues to be very rare in the United States). Other age groups that CDC does not recommend routine MenACWY vaccination for did not see this large of a percent decline. These

data suggest MenACWY vaccines have provided protection to those vaccinated, but probably not to the larger, unvaccinated community (population or herd immunity). Experts also believe MenB vaccines do not provide protection to unvaccinated people through population immunity.

What Are the Possible Side Effects of Meningococcal Vaccines?

Most people who get a meningococcal vaccine do not have any serious problems with it. With any medicine, including vaccines, there is a chance of side effects. These are usually mild and go away on their own within a few days, but serious reactions are possible.

Mild Problems

MenACWY Vaccines

Mild problems following MenACWY vaccination can include:

- Reactions where the shot was given
  - Redness
  - Soreness
- Muscle pain
- Headache
- Feeling tired

If these problems occur, they usually last for 1 or 2 days.

MenB Vaccines

Mild problems following a MenB vaccination can include:

- Reactions where the shot was given
  - Soreness
  - Redness
  - Swelling
- Feeling tired
- Headache
- Muscle or joint pain
- Fever or chills
- Nausea or diarrhea

If these problems occur, they can last up to 3 to 5 days.

Problems that Could Happen After Getting Any Injected Vaccine

- People sometimes faint after medical procedures, including vaccination. Sitting or lying down for about 15 minutes can help prevent fainting, and injuries caused by a fall. Tell the provider if you or your child feel dizzy, have vision changes, or have ringing in the ears.
- As with any medicine, there is a very remote chance of a vaccine causing a severe allergic reaction, other serious injury, or death.

Where Can I Find These Vaccines?

Your doctor is usually the best place to receive recommended vaccines for you or your child. These vaccines are part of the routine childhood immunization schedule. Therefore, vaccines for children and teens are regularly available at

- Pediatric and family practice offices
- Community health clinics
- Public health departments

If your doctor does not have these vaccines for adults, ask for a referral.

Vaccines may also be available at

- Pharmacies

- Workplaces
- Community health clinics
- Health departments
- Other community locations, such as schools and religious centers

You can also contact your state health department to learn more about where to get vaccines in your community.

When receiving any vaccine, ask the provider to record the vaccine in the state or local vaccine registry, if available. This helps providers at future visits know what vaccines you or your child have already received.

How Can I Get Help Paying for These Vaccines?

People can pay for meningococcal vaccines in several ways:

Private Health Insurance

Most private health insurance plans cover these vaccines. Check with your insurance provider for details on whether there is any cost to you. Ask your insurance provider for a list of in-network vaccine providers.

Vaccines for Children Program

Most health insurance plans cover routine vaccinations. The Vaccines for Children (VFC) program also provides vaccines for children 18 years and younger who are uninsured, underinsured, Medicaid-eligible, American Indian, or Alaska Native.

Related Pages

CDC's Meningococcal Disease Website

Educational Materials on Meningococcal Disease

- Adult Vaccine Assessment Tool: What Vaccines Do You Need?
- Meningococcal Vaccination for Preteens and Teens: Information for Parents

Immunization Schedules

- Recommended Vaccinations for Children (7 through 18 Years Old)
- Recommended Adult Immunization Schedule for Ages 19 Years or Older

Meningococcal Vaccine Information Statements

- MenACWY (English / Other Languages)
- MenB (English / Other Languages)

Vaccine Safety

- CDC's Vaccine Safety Website
- Meningococcal Vaccine Safety Website: A Closer Look at the Safety Data
- Frequently Asked Questions about Vaccine Safety

Meningococcal ACWY State Mandates for Elementary and Secondary Schools
Find out the MenACWY vaccination mandates for elementary and secondary schools in your state

Vaccines for Children Program

Information for the General Public: Cochlear Implants and Vaccination Recommendations

Last Reviewed: October 12, 2021

Exhibit 12

Meningococcal Vaccination for Adolescents: Information for Healthcare Professionals

CDC recommends meningococcal vaccination for all adolescents. Follow the recommended immunization schedule to ensure that your patients get the meningococcal vaccines that they need.

- All 11 to 12 year olds should receive a single dose of meningococcal conjugate (MenACWY) vaccine.
- Since protection wanes, CDC recommends a booster dose at age 16 years. The booster dose provides protection during the ages when adolescents are at highest risk of meningococcal disease.
- Adolescents and young adults (16 through 23 years of age) may also receive a serogroup B meningococcal (MenB) vaccine. The preferred age at which to administer MenB vaccine is 16 through 18 years.
- CDC recommends that certain adolescents and young adults should receive a MenB vaccine. They include those at increased risk because of a serogroup B meningococcal disease outbreak and people with certain medical conditions.

Adolescents are at increased risk for meningococcal disease.

Anyone can get meningococcal disease. However, adolescents and young adults 16 through 23 years of age are at increased risk for meningococcal disease. In addition, college students have a slightly higher risk than other teens and young adults who are not attending college. Meningococcal bacteria can cause severe disease, including meningitis, bacteremia, and septicemia, resulting in permanent disabilities and even death.

Meningococcal Vaccines

Meningococcal conjugate (MenACWY) vaccines

- Menactra®
- Menveo® (one- and two-vial presentations)
- MenQuadfi®

Serogroup B meningococcal (MenB) vaccines

- Bexsero®
- Trumenba®

There are 2 types of meningococcal vaccines available in the United States. Each type helps protect against different serogroups of meningococcal disease.

MenACWY vaccines provide protection against 4 serogroups: A, C, W, and Y. MenB vaccines provide protection against serogroup B. Currently no meningococcal vaccine offers protection in a single shot against these 5 serogroups.

You can administer MenACWY and MenB vaccines at the same time. You can also administer them with other vaccines recommended for adolescents.

Vaccine providers may administer meningococcal and other vaccines during the same visit, but at different injection sites if feasible.

CDC recommends meningococcal vaccination for people identified as being at increased risk during outbreaks.

CDC supports state and local health departments in investigating outbreaks and implementing outbreak control measures. During a serogroup A, C, W, or Y meningococcal disease outbreak, CDC recommends MenACWY vaccination for people at increased risk because of the outbreak. During a serogroup B meningococcal disease outbreak, CDC recommends MenB

vaccination for people at increased risk because of the outbreak. People who have previously received MenACWY or MenB vaccine and become at increased risk because of an outbreak may be recommended to receive a booster dose depending on how long it has been since they previously received the vaccine.

MenACWY Vaccines

Report Adverse Events

Adverse events occurring after administration of any vaccine should be reported to the Vaccine Adverse Event Reporting System (VAERS). Reports can be submitted to VAERS online, by fax, or by mail. Additional information about VAERS is available by telephone (1-800-822-7967) or on the VAERS website .

A MenACWY booster dose helps protect adolescents during the ages they are at highest risk.

Protection from MenACWY vaccination wanes in most adolescents within 5 years. Based on that information, adolescents need a booster dose at age 16 years. The booster dose provides protection during the years when they are at highest risk of meningococcal disease.

MenACWY vaccines are safe.

CDC continually monitors the safety of all vaccines. For information about side effects, see the MenACWY Vaccine Information Statement.

Many colleges require proof of MenACWY vaccination within 5 years before starting school.

CDC recommends that students receive a MenACWY vaccine within 5 years prior to starting college. This vaccination is required to attend many colleges.

The minimum booster dose interval is 8 weeks for MenACWY vaccines.

The minimum interval between doses is 8 weeks. However, healthy adolescents do not need a booster if the initial dose is given at or after age 16 years.

People with certain medical conditions need a 2-dose primary series of MenACWY vaccine and routine booster doses.

Vaccinate people with the following medical conditions with a 2-dose primary series of MenACWY vaccine administered 8 weeks apart:

- Complement component deficiency (e.g., C5-C9, properdin, factor H, factor D, or are taking a complement inhibitor such as Soliris® or Ultomiris®)
- Functional or anatomic asplenia (including sickle cell disease)
- HIV

Administer routine booster doses every 5 years throughout life to people with these medical conditions. Booster doses will help these patients maintain protection against meningococcal disease.

Exhibit 13

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

November 30, 2020

Elizabeth Brehm
Siri & Glimstad
200 Park Ave, 17th Floor
New York, NY 10166
Via email: foia@sirillp.com

Dear Ms. Brehm:

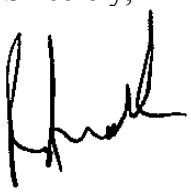
This letter is in response to your Centers for Disease Control and Prevention and Agency for Toxic Substances and Disease Registry (CDC/ATSDR) Freedom of Information Act (FOIA) request of November 9, 2020, for 'documentation sufficient to reflect any case(s) of transmission of Hepatitis B in an elementary, middle, or high school setting.'

A search of our records failed to reveal any documents pertaining to your request.

You may contact our FOIA Public Liaison at 770-488-6277 for any further assistance and to discuss any aspect of your request. Additionally, you may contact the Office of Government Information Services (OGIS) at the National Archives and Records Administration to inquire about the FOIA mediation services they offer. The contact information for OGIS is as follows: Office of Government Information Services, National Archives and Records Administration, 8601 Adelphi Road-OGIS, College Park, Maryland 20740-6001, e-mail at ogis@nara.gov; telephone at 202-741-5770; toll free at 1-877-684-6448; or facsimile at 202-741-5769.

If you are not satisfied with the response to this request, you may administratively appeal by writing to the Deputy Agency Chief FOIA Officer, Office of the Assistant Secretary for Public Affairs, U.S. Department of Health and Human Services, Hubert H. Humphrey Building, 200 Independence Avenue, Suite 729H, Washington, D.C. 20201. You may also transmit your appeal via email to FOIARequest@psc.hhs.gov. Please mark both your appeal letter and envelope "FOIA Appeal." Your appeal must be postmarked or electronically transmitted by February 28, 2021.

Sincerely,



Roger Andoh
CDC/ATSDR FOIA Officer
Office of the Chief Operating Officer
(770) 488-6399
Fax: (404) 235-1852

#21-00200-FOIA

Exhibit 14

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VARIVAX safely and effectively. See full prescribing information for VARIVAX.

VARIVAX®
Varicella Virus Vaccine Live
Suspension for intramuscular or subcutaneous injection
Initial U.S. Approval: 1995

----------RECENT MAJOR CHANGES----------
Dosage and Administration
Dose and Schedule (2.1) ----------02/2023
Reconstitution Instructions (2.2) ----------08/2023
Administration (2.3) ----------02/2023

----------INDICATIONS AND USAGE----------
VARIVAX is a vaccine indicated for active immunization for the prevention of varicella in individuals 12 months of age and older. (1)

---------- DOSAGE AND ADMINISTRATION ----------
For intramuscular or subcutaneous injection only. (2.1, 2.3)
A single dose is approximately 0.5 mL.
Children (12 months to 12 years of age)
- The first dose is administered at 12 to 15 months of age. (2.1)
- The second dose is administered at 4 to 6 years of age. (2.1)
- There should be a minimum interval of 3 months between doses. (2.1)

Adolescents (≥13 years of age) and Adults
- Two doses are administered at a minimum interval of 4 weeks. (2.1)

---------- DOSAGE FORMS AND STRENGTHS ----------
Suspension for injection (approximately 0.5 mL dose) supplied as a lyophilized vaccine to be reconstituted using the accompanying sterile diluent. (2.2, 3, 16)

----------CONTRAINDICATIONS----------
- History of severe allergic reaction to any component of the vaccine (including neomycin and gelatin) or to a previous dose of varicella vaccine. (4.1)
- Immunosuppression. (4.2)
- Moderate or severe febrile illness. (4.3)
- Active untreated tuberculosis. (4.4)
- Pregnancy. (4.5, 8.1, 17)

---------- WARNINGS AND PRECAUTIONS----------
- Evaluate individuals for immune competence prior to administration of VARIVAX if there is a family history of congenital or hereditary immunodeficiency. (5.1)
- Avoid close contact with high-risk individuals susceptible to varicella because of possible transmission of varicella vaccine virus. (5.3)
- Immune Globulins (IG) and other blood products should not be given concomitantly with VARIVAX. (5.4, 7.2)
- Avoid use of salicylates for 6 weeks following administration of VARIVAX to children and adolescents. (5.5, 7.1)

---------- ADVERSE REACTIONS ----------
- Frequently reported (≥10%) adverse reactions in children ages 1 to 12 years include:
  - fever ≥102.0°F (38.9°C) oral: 14.7%
  - injection-site complaints: 19.3% (6.1)
- Frequently reported (≥10%) adverse reactions in adolescents and adults ages 13 years and older include:
  - fever ≥100.0°F (37.8°C) oral: 10.2%
  - injection-site complaints: 24.4% (6.1)
- Other reported adverse reactions in all age groups include:
  - varicella-like rash (injection site)
  - varicella-like rash (generalized) (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Merck Sharp & Dohme LLC at 1-877-888-4231 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov .

----------DRUG INTERACTIONS----------
- Reye syndrome has been reported in children and adolescents following the use of salicylates during wild-type varicella infection. (5.5, 7.1)
- Administration of immune globulins and other blood products concurrently with VARIVAX vaccine may interfere with the expected immune response. (5.4, 7.2)
- VARIVAX vaccination may result in a temporary depression of purified protein derivative (PPD) tuberculin skin sensitivity. (7.3)

---------- USE IN SPECIFIC POPULATIONS ----------
Pregnancy: Do not administer VARIVAX to females who are pregnant. Pregnancy should be avoided for 3 months following vaccination with VARIVAX. (4.5, 8.1, 17)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 08/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Dose and Schedule
2.2 Reconstitution Instructions
2.3 Administration
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
4.1 Severe Allergic Reaction
4.2 Immunosuppression
4.3 Moderate or Severe Febrile Illness
4.4 Active Untreated Tuberculosis
4.5 Pregnancy
5 WARNINGS AND PRECAUTIONS
5.1 Family History of Immunodeficiency
5.2 Use in HIV-Infected Individuals
5.3 Risk of Vaccine Virus Transmission
5.4 Immune Globulins and Transfusions
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6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
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7 DRUG INTERACTIONS
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*Sections or subsections omitted from the full prescribing information are not listed.

Do not freeze reconstituted vaccine.
Do not combine VARIVAX with any other vaccine through reconstitution or mixing.

2.3 Administration

Inject the vaccine intramuscularly or subcutaneously.

3 DOSAGE FORMS AND STRENGTHS

VARIVAX is a suspension for injection supplied as a single-dose vial of lyophilized vaccine to be reconstituted using the accompanying sterile diluent *[see Dosage and Administration (2.2) and How Supplied/Storage and Handling (16)]*. A single dose after reconstitution is approximately 0.5 mL.

4 CONTRAINDICATIONS

4.1 Severe Allergic Reaction

Do not administer VARIVAX to individuals with a history of anaphylactic or severe allergic reaction to any component of the vaccine (including neomycin and gelatin) or to a previous dose of a varicella-containing vaccine.

4.2 Immunosuppression

Do not administer VARIVAX to individuals who are immunodeficient or immunosuppressed due to disease or medical therapy.

Disseminated varicella disease and extensive vaccine-associated rash have been reported in individuals who are immunosuppressed or immunodeficient who were inadvertently vaccinated with a varicella-containing vaccine.

4.3 Moderate or Severe Febrile Illness

Do not administer VARIVAX to individuals with an active febrile illness with fever >101.3°F (>38.5°C).

4.4 Active Untreated Tuberculosis

Do not administer VARIVAX to individuals with active, untreated tuberculosis (TB).

4.5 Pregnancy

Do not administer VARIVAX to individuals who are pregnant or planning on becoming pregnant in the next 3 months. Wild-type varicella is known to cause fetal harm *[see Use in Specific Populations (8.1) and Patient Counseling Information (17)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Family History of Immunodeficiency

Vaccination should be deferred in individuals with a family history of congenital or hereditary immunodeficiency until the individual's immune status has been evaluated and the individual has been found to be immunocompetent.

5.2 Use in HIV-Infected Individuals

The Advisory Committee on Immunization Practices (ACIP) has recommendations on the use of varicella vaccine in HIV-infected individuals.

5.3 Risk of Vaccine Virus Transmission

Post-marketing experience suggests that transmission of varicella vaccine virus (Oka/Merck) resulting in varicella infection including disseminated disease may occur between vaccine recipients (who develop or do not develop a varicella-like rash) and contacts susceptible to varicella including healthy as well as high-risk individuals.

Due to the concern for transmission of vaccine virus, vaccine recipients should attempt to avoid whenever possible close association with susceptible high-risk individuals for up to six weeks following vaccination with VARIVAX. Susceptible high-risk individuals include:

- Immunocompromised individuals;
- Pregnant women without documented history of varicella or laboratory evidence of prior infection;
- Newborn infants of mothers without documented history of varicella or laboratory evidence of prior infection and all newborn infants born at <28 weeks gestation regardless of maternal varicella immunity.

Exhibit 15

MMR (Measles, Mumps, and Rubella) Vaccine: *What You Need to Know*

Many Vaccine Information Statements are available in Spanish and other languages. See www.immunize.org/vis

Hojas de información sobre vacunas están disponibles en español y en muchos otros idiomas. Visite www.immunize.org/vis

1 Why get vaccinated?

Measles, **mumps**, and **rubella** are viral diseases that can have serious consequences. Before vaccines, these diseases were very common in the United States, especially among children. They are still common in many parts of the world.

Measles

- Measles virus causes symptoms that can include fever, cough, runny nose, and red, watery eyes, commonly followed by a rash that covers the whole body.
- Measles can lead to ear infections, diarrhea, and infection of the lungs (pneumonia). Rarely, measles can cause brain damage or death.

Mumps

- Mumps virus causes fever, headache, muscle aches, tiredness, loss of appetite, and swollen and tender salivary glands under the ears on one or both sides.
- Mumps can lead to deafness, swelling of the brain and/or spinal cord covering (encephalitis or meningitis), painful swelling of the testicles or ovaries, and, very rarely, death.

Rubella (also known as German Measles)

- Rubella virus causes fever, sore throat, rash, headache, and eye irritation.
- Rubella can cause arthritis in up to half of teenage and adult women.
- If a woman gets rubella while she is pregnant, she could have a miscarriage or her baby could be born with serious birth defects.

These diseases can easily spread from person to person. Measles doesn't even require personal contact. You can get measles by entering a room that a person with measles left up to 2 hours before.

Vaccines and high rates of vaccination have made these diseases much less common in the United States.

2 MMR vaccine

Children should get 2 doses of MMR vaccine, usually:

- First dose: 12 through 15 months of age
- Second dose: 4 through 6 years of age

Infants who will be traveling outside the United States when they are between 6 and 11 months of age should get a dose of MMR vaccine before travel. This can provide temporary protection from measles infection, but will not give permanent immunity. The child should still get 2 doses at the recommended ages for long-lasting protection.

Adults might also need MMR vaccine. Many adults 18 years of age and older might be susceptible to measles, mumps, and rubella without knowing it.

A third dose of MMR might be recommended in certain mumps outbreak situations.

There are no known risks to getting MMR vaccine at the same time as other vaccines.

There is a combination vaccine called **MMRV** that contains both chickenpox and MMR vaccines. MMRV is an option for some children 12 months through 12 years of age. There is a separate Vaccine Information Statement for MMRV. Your health care provider can give you more information.

3 Some people should not get this vaccine

Tell your vaccine provider if the person getting the vaccine:

- **Has any severe, life-threatening allergies.** A person who has ever had a life-threatening allergic reaction after a dose of MMR vaccine, or has a severe allergy to any part of this vaccine, may be advised not to be vaccinated. Ask your health care provider if you want information about vaccine components.
- **Is pregnant, or thinks she might be pregnant.** Pregnant women should wait to get MMR vaccine until after they are no longer pregnant. Women should avoid getting pregnant for at least 1 month after getting MMR vaccine.
- **Has a weakened immune system** due to disease (such as cancer or HIV/AIDS) or medical treatments (such as radiation, immunotherapy, steroids, or chemotherapy).
- **Has a parent, brother, or sister with a history of immune system problems.**
- **Has ever had a condition that makes them bruise or bleed easily.**
- **Has recently had a blood transfusion or received other blood products**. You might be advised to postpone MMR vaccination for 3 months or more.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

- **Has tuberculosis**.
- **Has gotten any other vaccines in the past 4 weeks**. Live vaccines given too close together might not work as well.
- **Is not feeling well**. A mild illness, such as a cold, is usually not a reason to postpone a vaccination. Someone who is moderately or severely ill should probably wait. Your doctor can advise you.

4 Risks of a vaccine reaction

With any medicine, including vaccines, there is a chance of reactions. These are usually mild and go away on their own, but serious reactions are also possible.

Getting MMR vaccine is much safer than getting measles, mumps, or rubella disease. Most people who get MMR vaccine do not have any problems with it.

After MMR vaccination, a person might experience:

Minor events:

- Sore arm from the injection
- Fever
- Redness or rash at the injection site
- Swelling of glands in the cheeks or neck

If these events happen, they usually begin within 2 weeks after the shot. They occur less often after the second dose.

Moderate events:

- Seizure (jerking or staring) often associated with fever
- Temporary pain and stiffness in the joints, mostly in teenage or adult women
- Temporary low platelet count, which can cause unusual bleeding or bruising
- Rash all over body

Severe events occur very rarely:

- Deafness
- Long-term seizures, coma, or lowered consciousness
- Brain damage

Other things that could happen after this vaccine:

- People sometimes faint after medical procedures, including vaccination. Sitting or lying down for about 15 minutes can help prevent fainting and injuries caused by a fall. Tell your provider if you feel dizzy or have vision changes or ringing in the ears.
- Some people get shoulder pain that can be more severe and longer-lasting than routine soreness that can follow injections. This happens very rarely.
- Any medication can cause a severe allergic reaction. Such reactions to a vaccine are estimated at about 1 in a million doses, and would happen within a few minutes to a few hours after the vaccination.

As with any medicine, there is a very remote chance of a vaccine causing a serious injury or death.

The safety of vaccines is always being monitored. For more information, visit: **www.cdc.gov/vaccinesafety/**

5 What if there is a serious problem?

What should I look for?

- Look for anything that concerns you, such as signs of a severe allergic reaction, very high fever, or unusual behavior.

  Signs of a **severe allergic reaction** can include hives, swelling of the face and throat, difficulty breathing, a fast heartbeat, dizziness, and weakness. These would usually start a few minutes to a few hours after the vaccination.

What should I do?

- If you think it is a **severe allergic reaction** or other emergency that can't wait, call 9-1-1 and get to the nearest hospital. Otherwise, call your health care provider.

  Afterward, the reaction should be reported to the Vaccine Adverse Event Reporting System (VAERS). Your doctor should file this report, or you can do it yourself through the VAERS web site at **www.vaers.hhs.gov**, or by calling **1-800-822-7967**.

VAERS does not give medical advice.

6 The National Vaccine Injury Compensation Program

The National Vaccine Injury Compensation Program (VICP) is a federal program that was created to compensate people who may have been injured by certain vaccines.

Persons who believe they may have been injured by a vaccine can learn about the program and about filing a claim by calling **1-800-338-2382** or visiting the VICP website at **www.hrsa.gov/vaccinecompensation**. There is a time limit to file a claim for compensation.

7 How can I learn more?

- Ask your healthcare provider. He or she can give you the vaccine package insert or suggest other sources of information.
- Call your local or state health department.
- Contact the Centers for Disease Control and Prevention (CDC):
  - Call **1-800-232-4636** (**1-800-CDC-INFO**) or
  - Visit CDC's website at **www.cdc.gov/vaccines**

Vaccine Information Statement

MMR Vaccine

Office use only

2/12/2018

42 U.S.C. § 300aa-26

Exhibit 16



March 27, 2019

Siri & Glimstad LLP
Aaron Siri, Esq.
200 Park Ave
17th Floor
New York, NY 101066

In reply refer to file: **2018-6847**

Dear Mr. Siri,

This is in reply to your Freedom of Information Act (FOIA) request dated August 20, 2018 in which you requested "a copy of the report for each clinical trial relied upon by the FDA when approving M-M-R II in 1978." Your request was received in the Center for Biologics Evaluation and Research (CBER) on August 21, 2018.

Enclosed are the documents responsive to your request.

We have withheld portions of pages under Exemption (b)(4), 5 U.S.C. § 522(b)(4). That exemption permits the withholding of trade secrets and commercial or financial information that was obtained from a person outside the government and that is privileged or confidential. The withholding of such information is permitted if disclosure is likely to cause substantial competitive harm to the person who submitted the information.

In addition, we have withheld portions of pages under Exemption (b)(6), 5 U.S.C. § 522(b)(6). That exemption protects information from disclosure when its release would cause a clearly unwarranted invasion of personal privacy. FOIA Exemption 6 is available to protect information in personnel or medical files and similar files. This requires a balancing of the public's right to disclosure against the individual's right to privacy.

You have the right to appeal this determination. By filing an appeal, you preserve your rights under FOIA and give the agency a chance to review and reconsider your request and the agency's decision.

Your appeal must be mailed within 90 days from the date of this response to:

Ms. Catherine Teti
Deputy Agency Chief FOIA Officer
U.S. Department of Health and Human Services
Office of the Assistant Secretary for Public Affairs
Room 729H
200 Independence Avenue, S.W.
Washington, DC 20201

Please clearly mark both the envelope and your letter "FDA Freedom of Information Act Appeal."

If you would like to discuss our response before filing an appeal to attempt to resolve your dispute without going through the appeals process, please contact:

Beth Brockner-Ryan, Branch Chief
Center for Biologics Evaluation and Research (CBER)
Access Litigation and Freedom of Information Branch
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Building 71, Room 1114
Silver Spring, MD 20993-0002
Email:beth.brocknerryan@fda.hhs.gov
Main Line 240-402-7800
FOI Line 240-402-8008

You also have the right to contact:

FDA FOIA Public Liaison
Office of the Executive Secretariat
5630 Fishers Lane
Room-1050
Rockville, MD 20857
Email: FDAFOIA@fda.hhs.gov

If you are unable to resolve your FOIA dispute through our FOIA Public Liaison, the Office of Government Information Services (OGIS), the Federal FOIA Ombudsman's office, offers mediation services to help resolve disputes between FOIA requesters and Federal agencies. The contact information for OGIS is:

Office of Government Information Services
National Archives and Records Administration
8601 Adelphi Road–OGIS
College Park, MD 20740-6001
Telephone: 202-741-5770
Toll-Free: 1-877-684-6448
E-mail: ogis@nara.gov
Fax: 202-741-5769

If you have any questions or if we can be of further assistance, please let us know by referencing the above file number. You can contact John Hyder by phone at 240-402-8079 or by e-mail at John.Hyder@fda.hhs.gov.

Sincerely,

Beth A. Brockner Ryan -S

Digitally signed by Beth A. Brockner Ryan -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300052489, cn=Beth A. Brockner Ryan -S
Date: 2019.03.27 10:26:33 -04'00'

Beth Brockner Ryan
Chief, Access Litigation and Freedom of Information Branch

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
BETHESDA, MARYLAND 20014

SEP 15 1978

Our Reference Nos. 76-316, 77-303 and 77-304

Alan Gray, Ph.D.
Merck Sharp & Dohme
Division of Merck and Co., Inc.
West Point, Pennsylvania 19486

Dear Dr. Gray:

This is to inform you that the amendments to your product license applications to include the use of the RA27/3 strain rubella virus grown in human diploid cells have been accepted for manufacture of the following products:

Rubella Virus Vaccine, Live
Measles, Mumps and Rubella Virus Vaccine, Live
Measles and Rubella Virus Vaccine, Live

We agree that the results of stability testing of vaccines prepared with the buffered sorbitol-gelatin diluent support your request for a longer dating period. Accordingly, your license applications for the three products are also amended to include the use of the diluent and a dating period of two years at 2°-8°C from date of issue.

Please continue to submit stability data as they become available.

Sincerely yours,

Paul Parkman

for Harry M. Meyer, Jr., M.D.
Director
Bureau of Biologics

Summary of Clinical Tests of Combined Live
Measles-Mumps-Rubella (RA 27/3) Virus Vaccine

Study No.	Investigator	Lot No.	Age		No. Vacc.	Antibody Responses among Triple Seronegatives									Re.
						Measles			Mumps			RA 27/3 Rubella			
			Range	Mean (Yrs.)		No. Conv./ No. Seroneg. (%)		GMT	No. Conv./ No. Seroneg. (%)		GMT	No. Conv./ No. Seroneg. (%)		GMT	
442	Villarejos	621	10m- 7y	3.7	199	23/23	(100)	99	22/23	(96)	7	23/23	(100)	149	1
443	Weibel	621	11m- 8y	1.7	105	65/69	(94)	56	66/69	(96)	8	69/69	(100)	133	2
459	Lerman	60664	14m- 4y	1.6	41	13/14	(93)	62	13/14	(93)	17	14/14	(100)	269	3
467	Weibel	621	11m- 7y	1.9	137	55/58	(95)	71	57/58	(98)	7	58/58	(100)	146	4
473	McCollum	621													5
484	Gershon	621	13m-15y		39										6
511	Villarejos	60664	8m-11y	3.3	50	9/11	(82)	20	10/11	(91)	5	11/11	(100)	226	7
		60665	11m- 7y	3.3	50	4/5	(80)	25	4/5	(80)	11	5/5	(100)	169	
		60666	11m-11y	4.2	50	2/2	(100)	28	2/2	(100)	8	2/2	(100)	256	
513	Weibel	60664	12m- 7y	1.7	53	28/30	(93)	70	29/30	(97)	19	30/30	(100)	256	8
		60665	12m- 4y	1.5	54	33/34	(97)	70	33/34	(97)	23	33/34	(97)	200	
		60666	11m- 4y	1.4	56	32/33	(97)	66	32/33	(97)	26	32/33	(97)	251	
		Totals			834	264/279	(95)	63	268/279	(96)	11	277/279	(99)	178	

4/24/78

Table 10

Clinical Complaints Reported Among Children Who Received Combined Live Measles-Mumps-Rubella (RA 27/3) Virus Vaccine, Lot No. 621/C-D763 (Study #442)

Clinical Complaint	Total Vaccinees (199 Children)						Initially Seronegative to: Measles, Mumps and Rubella (23 Children)					
	Days Post-Vaccination					No. with Complaint	Days Post Vaccination					No. with Complaint
	0-4	5-12	13-18	19-28	29-42		0-4	5-12	13-18	19-28	29-42	
Irritability	32 (16.1%)	9 (4.5)	2 (1.0)	4 (2.1)		39	5 (21.7)			1 (5.0)		5
Malaise	30 (15.1)	14 (7.0)	3 (1.5)	7 (3.6)	1 (0.5)	43	5 (21.7)	1 (4.3)		2 (10.0)		7
Headache		1 (0.5)	2 (1.0)			2						0
Upper Respiratory Illness	9 (4.5)	11 (5.5)	5 (2.5)	8 (4.1)	5 (2.6)	23	1 (4.3)	1 (4.3)	1 (4.3)	2 (10.0)	1 (5.0)	3
Otitis			2 (1.0)	3 (1.5)		3			1 (4.3)	1 (5.0)		1
Ophthalmopathy		1 (0.5)				1						0
Gastrointestinal Illness	13 (6.5)	7 (3.5)	2 (1.0)	5 (2.6)	1 (0.5)	22		1 (4.3)				1
Anorexia	5 (2.5)	3 (1.5)	2 (1.0)	5 (2.6)		13				1 (5.0)		1
Mild Dermatitis		1 (0.5)				1						0
Persons with Complaints:	49 (24.6)	22 (11.1)	11 (5.5)	19 (9.8)	6 (3.1)	73	6 (26.1)	2 (8.7)	1 (4.3)	4 (20.0)	1 (5.0)	10
Persons with No Complaints:	150 (75.4)	177 (88.9)	188 (94.5)	175 (90.2)	187 (96.9)	123	17 (73.9)	21 (91.3)	22 (95.7)	16 (80.0)	19 (95.0)	12
Negative Physician Surveillance				5	6					3	3	

10/3/77

Table 10

Clinical Complaints Reported Among Children Who Received a 0.5 Ml Dose of Combined Live Measles-Mumps-Rubella (RA 27/3) Virus Vaccine, Lot No. 621/C-D763 (Study #443)

Clinical Complaint	Total Vaccinees (102 Children)						Initially Seronegative to: Measles, Mumps and Rubella (68 Children)					
	Days Post-Vaccination					No. with Complaint	Days Post-Vaccination					No. with Complaint
	0-4	5-12	13-18	19-28	29-42		0-4	5-12	13-18	19-28	29-42	
Soreness at Injection Site	4 (4.2%)			1 (1.0)		5	2 (3.0)					2
Lymphadenopathy	2 (2.1)	3 (3.1)		2 (2.1)	2 (2.1)	6	1 (1.5)	1 (1.5)		2 (3.0)	2 (3.0)	3
Measles-Like Rash	1 (1.0)	9 (9.4)	6 (6.2)	1 (1.0)		11	1 (1.5)	7 (10.4)	5 (7.5)	1 (1.5)		9
Arthralgia			1 (1.0)	1 (1.0)		1			1 (1.5)	1 (1.5)		1
Myalgia		1 (1.0)				1		1 (1.5)				1
Irritability	3 (3.0)	3 (3.0)	1 (1.0)	1 (1.0)	1 (1.0)	4	2 (2.9)	2 (2.9)	1 (1.5)	1 (1.5)		3
Headache	2 (2.1)	2 (2.1)				2	2 (3.0)	2 (3.0)				2
Upper Respiratory Illness	38 (39.6)	37 (38.5)	24 (25.0)	35 (36.5)	32 (33.3)	64	28 (41.8)	27 (40.3)	20 (29.8)	25 (37.3)	20 (29.8)	46
Otitis	1 (1.0)	7 (7.3)	2 (2.1)	5 (5.2)	4 (4.2)	14	1 (1.5)	4 (6.0)	2 (3.0)	3 (4.5)	2 (3.0)	9
Ophthalmopathy	2 (2.1)	3 (3.1)	2 (2.1)	4 (4.2)	2 (2.1)	6	2 (3.0)	3 (4.5)	2 (3.0)	4 (6.0)	2 (3.0)	6
Gastrointestinal Illness	18 (18.7)	24 (25.0)	9 (9.4)	17 (17.7)	15 (15.6)	43	14 (20.9)	19 (28.4)	9 (13.4)	14 (20.9)	11 (16.4)	35
Anorexia	13 (13.5)	19 (19.8)	8 (8.3)	10 (10.4)	13 (13.5)	28	10 (14.9)	12 (17.9)	6 (9.0)	9 (13.4)	11 (16.4)	20
Fatigue				1 (1.0)		1				1 (1.5)		1
Rash-Chafing, Diaper, Heat, Herpes	4 (4.2)	4 (4.2)	1 (1.0)	4 (4.2)	5 (5.2)	12	3 (4.5)	4 (6.0)	1 (1.5)	3 (4.5)	3 (4.5)	9
Allergy, Asthma	1 (1.0)	2 (2.1)	3 (3.1)	2 (2.1)	3 (3.1)	6		1 (1.5)	2 (3.0)	1 (1.5)		3
Fever	1 (1.0)	1 (1.0)		2 (2.1)	1 (1.0)	4		1 (1.5)		1 (1.5)		2
Sudoresis	1 (1.0)					1	1 (1.5)					1
Teething	3 (3.0)			1 (1.0)	3 (3.0)	6	3 (4.4)			1 (1.5)	3 (4.4)	6
Persons with Complaints:	50 (52.1)	50 (52.1)	33 (34.4)	43 (44.8)	44 (45.8)	78	38 (56.7)	38 (56.7)	29 (43.3)	32 (47.8)	30 (44.8)	55
Persons with No Complaints:	46 (47.9)	46 (47.9)	63 (65.6)	53 (55.2)	52 (54.2)	18	29 (43.3)	29 (43.3)	38 (56.7)	35 (52.2)	37 (55.2)	9
Negative Physician Surveillance	6	6	6	6	6	6	1	1	1	1	1	1

5/6/77

Table 9

Clinical Complaints Reported Among Children Who Received Combined
Live Measles-Mumps-Rubella (RA 27/3) Virus Vaccine, Lot #60664/C-E810 (Study #459)

Clinical Complaint	Total Vaccinees (41 Children)						Initially Seronegatives (16 Children)					
	Days Post Vaccination					No. with Complaint	Days Post Vaccination					No. with Complaint
	0-4	5-12	13-18	19-28	29-42		0-4	5-12	13-18	19-28	29-42	
Injection Site:												
Soreness	2 (4.9%)					2						0
Systemic:												
Measles-Like Rash		4 (9.8)	2 (4.9)			5			1 (6.3)			1
Irritability	1 (2.4)	3 (7.3)	2 (4.9)		3 (7.5)	6	1 (6.3)				1 (6.7)	2
Anorexia	8 (19.5)	5 (12.2)	8 (19.5)	9 (22.0)	7 (17.5)	20	3 (18.8)	1 (6.3)	2 (12.5)	3 (18.8)	3 (20.0)	6
Disturbed Sleep		1 (2.4)				1		1 (6.3)				1
Upper Respiratory Illness	16 (39.0)	17 (41.5)	10 (24.4)	11 (26.8)	16 (40.0)	28	5 (31.3)	5 (31.3)	2 (12.5)	6 (37.5)	7 (46.7)	10
Otitis		2 (4.9)	1 (2.4)	3 (7.3)	3 (7.5)	8		1 (6.3)	1 (6.3)	2 (12.5)	1 (6.7)	4
Ophthalmopathy	3 (7.3)	1 (2.4)			3 (7.5)	7		1 (6.3)				1
Gastrointestinal Illness	9 (22.0)	9 (22.0)	6 (14.6)	10 (24.4)	9 (22.5)	24	3 (18.8)	1 (6.3)	2 (12.5)	5 (31.3)	3 (20.0)	10
Nonspecific Rash	2 (4.9)	4 (9.8)	2 (4.9)	3 (7.3)	3 (7.5)	5	1 (6.3)	2 (12.5)	2 (12.5)	2 (12.5)	1 (6.7)	3
Varicella				1 (2.4)		1				1 (6.3)		1
Allergy		1 (2.4)				1		1 (6.3)				1
Teething	1 (2.4)	3 (7.3)	1 (2.4)	1 (2.4)	2 (5.0)	4	1 (6.3)	1 (6.3)	1 (6.3)	1 (6.3)	1 (6.7)	1
Herpes-Type Rash	1 (2.4)					1						0
Persons with Complaint:	20 (48.8)	26 (63.4)	18 (43.9)	16 (39.0)	22 (55.0)	34	7 (43.8)	8 (50.0)	6 (37.5)	8 (50.0)	9 (60.0)	14
Persons with No Complaint:	21 (51.2)	15 (36.6)	23 (56.1)	25 (61.0)	18 (45.0)	7	9 (56.3)	8 (50.0)	10 (62.5)	8 (50.0)	6 (40.0)	2
Negative Surveillance					1						1	

4/21/78

Table 11

Clinical Complaints Reported Among Children Who Received a 0.5 ml Dose of Combined Live Measles-Mumps-Rubella (RA 27/3) Virus Vaccine, Lot #621/C-D763 (Study #467)

Clinical Complaint	Total Vaccinees (117 Children)						Initially Seronegatives (61 Children)					
	Days Post Vaccination					No. with Complaint	Days Post Vaccination					No. with Complaint
	0-4	5-12	13-18	19-28	29-42		0-4	5-12	13-18	19-28	29-42	
Soreness at Injection Site	2 (2.2%)	1 (1.1)	1 (1.1)			3	1 (2.1)	1 (2.1)	1 (2.1)			2
Lymphadenopathy		2 (2.2)		1 (1.1)		3		2 (4.3)		1 (2.1)		3
Measles-Like Rash	1 (1.1)	5 (5.6)	3 (3.4)			7	1 (2.1)	4 (8.5)	1 (2.1)			5
Headache		1 (1.1)		1 (1.1)	1 (1.1)	3		1 (2.1)				1
Irritability	4 (4.4)	4 (4.5)		1 (1.1)		8	3 (6.3)	1 (2.1)				4
Fever-Temperature Not Reported	1 (1.1)	1 (1.1)				2		1 (2.1)				1
Anorexia	10 (11.1)	12 (13.5)	6 (6.7)	7 (8.0)	6 (6.8)	23	5 (10.4)	7 (14.9)	4 (8.3)	2 (4.3)	1 (2.1)	11
Flush					1 (1.1)	1						0
Disturbed Sleep	2 (2.2)					2						0
Myalgia	1 (1.1)					1	1 (2.1)					1
Upper Respiratory Illness	15 (16.7)	29 (32.6)	17 (19.1)	20 (22.7)	31 (35.2)	53	6 (12.5)	13 (27.7)	9 (18.8)	9 (19.1)	10 (21.3)	22
Otitis	1 (1.1)	2 (2.2)	2 (2.2)	1 (1.1)	1 (1.1)	2		1 (2.1)	1 (2.1)			1
Ophthalmopathy		5 (5.6)	4 (4.5)	3 (3.4)	4 (4.5)	9		3 (6.4)	3 (6.3)	2 (4.3)	1 (2.1)	4
Gastrointestinal Illness	9 (10.0)	15 (16.9)	10 (11.2)	12 (13.6)	13 (14.8)	31	4 (8.3)	12 (25.5)	6 (12.5)	7 (14.9)	4 (8.5)	16
Nonspecific Rash	1 (1.1)	1 (1.1)	1 (1.1)	1 (1.1)	4 (4.5)	6		1 (2.1)				1
Poison Ivy		1 (1.1)	1 (1.1)			1						0
Allergy		1 (1.1)		1 (1.1)		2		1 (2.1)		1 (2.1)		2
Teething	1 (1.1)	4 (4.5)	4 (4.5)	2 (2.3)	2 (2.3)	10	1 (2.1)	2 (4.3)	2 (4.2)			5
Negative Surveillance	27	28	28	29	29	27	13	14	13	14	14	13
Persons with Complaint:	30 (33.3)	44 (49.4)	28 (31.5)	30 (34.1)	37 (42.0)	56	12 (25.0)	21 (44.7)	14 (29.2)	14 (29.8)	13 (27.7)	25
Persons with No Complaint:	60 (66.7)	45 (50.6)	61 (68.5)	58 (65.9)	51 (58.0)	33	36 (75.0)	26 (55.3)	34 (70.8)	33 (70.2)	34 (72.3)	23

8/24/77

Table 12

Clinical Complaints Reported Among Children Who Received a 1.0 ml Dose of Combined Live Measles-Mumps-Rubella (RA 27/3) Virus Vaccine, Lot #621/C-D763 (Study #467)

Clinical Complaint	Total Vaccinees (20 Children)						Initially Seronegatives (11 Children)					
	Days Post Vaccination					No. with Complaint	Days Post Vaccination					No. with Complaint
	0-4	5-12	13-18	19-28	29-42		0-4	5-12	13-18	19-28	29-42	
Soreness at Injection Site	1 (5.9%)					1	1 (10.0)					1
Lymphadenopathy	1 (5.9)					1	1 (10.0)					1
Arthralgia			1 (5.9)			1						0
Measles-Like Rash			1 (5.9)			1			1 (10.0)			1
Irritability	1 (5.9)	1 (5.9)				1	1 (10.0)	1 (10.0)				1
Fever - Temperature Not Reported				1 (5.9)		1				1 (10.0)		1
Anorexia			1 (5.9)	1 (5.9)		2			1 (10.0)			1
Upper Respiratory Illness	4 (23.5)	5 (29.4)	2 (11.8)	4 (23.5)	1 (5.9)	8	1 (10.0)	1 (10.0)		2 (20.0)		4
Otitis			1 (5.9)	1 (5.9)	1 (5.9)	1			1 (10.0)	1 (10.0)	1 (10.0)	1
Gastrointestinal Illness	3 (17.6)		1 (5.9)	1 (5.9)		4	2 (20.0)		1 (10.0)			2
Impetigo				1 (5.9)		1				1 (10.0)		1
Negative Surveillance	3	3	3	3	3	3	1	1	1	1	1	1
Persons with Complaint:	7 (41.2)	6 (35.3)	5 (29.4)	5 (29.4)	2 (11.8)	9	3 (30.0)	2 (20.0)	2 (20.0)	3 (30.0)	1 (10.0)	5
Persons with No Complaint:	10 (58.8)	11 (64.7)	12 (70.6)	12 (70.6)	15 (88.2)	8	7 (70.0)	8 (80.0)	8 (80.0)	7 (70.0)	9 (90.0)	5

8/24/77

Table 13

Clinical Complaints Reported Among Children Who Received a 0.5 ml Dose of Combined Live Measles-Mumps-Rubella (HPV-77) Virus Vaccine, M-M-R (Study #467)

Clinical Complaint	Total Vaccinees (138 Children)						Initially Seronegatives (70 Children)					
	Days Post Vaccination					No. with Complaint	Days Post Vaccination					No. with Complaint
	0-4	5-12	13-18	19-28	29-42		0-4	5-12	13-18	19-28	29-42	
Injection Site:	7 (6.9%)					7	3 (5.7)					3
Soreness	6					6	2					2
Soreness and Induration	1					1	1					1
Systemic:												
Measles-Like Rash		5 (5.0)	2 (2.0)			5		1 (1.9)				1
Headache	1 (1.0)		1 (1.0)		2 (2.0)	2					1 (1.9)	1
Irritability	3 (3.0)	4 (4.0)	2 (2.0)	3 (3.0)		9	2 (3.8)	1 (1.9)		1 (1.9)		4
Anorexia	11 (10.9)	17 (16.8)	5 (5.0)	6 (5.9)	4 (4.0)	24	6 (11.3)	9 (17.0)	1 (1.9)	3 (5.7)	3 (5.7)	14
Flush	1 (1.0)					1						0
Disturbed Sleep		1 (1.0)				1						0
Myalgia	2 (2.0)					2	1 (1.9)					1
Upper Respiratory Illness	18 (17.8)	19 (18.8)	15 (14.9)	18 (17.8)	24 (23.8)	45	10 (18.9)	9 (17.0)	6 (11.3)	7 (13.2)	8 (15.1)	20
Otitis	1 (1.0)	4 (4.0)	2 (2.0)	1 (1.0)	1 (1.0)	7	1 (1.9)	2 (3.8)				3
Ophthalmopathy	2 (2.0)	3 (3.0)		1 (1.0)	2 (2.0)	6	2 (3.8)	2 (3.8)				4
Gastrointestinal Illness	15 (14.9)	12 (11.9)	5 (5.0)	5 (5.0)	6 (5.9)	27	7 (13.2)	3 (5.7)	3 (5.7)	2 (3.8)	4 (7.5)	11
Rash-Nonspecific	1 (1.0)	3 (3.0)	5 (5.0)	3 (3.0)	4 (4.0)	12	1 (1.9)	1 (1.9)	4 (7.5)	1 (1.9)	1 (1.9)	6
Varicella				1 (1.0)	1 (1.0)	1						0
Other*	1 (1.0)	1 (1.0)				2	1 (1.9)					1
Genitourinary Infection				1 (1.0)	1 (1.0)	1						0
Allergy	2 (2.0)	2 (2.0)		1 (1.0)		3	2 (3.8)	2 (3.8)				2
Teething		2 (2.0)	4 (4.0)	5 (5.0)	2 (2.0)	8		1 (1.9)		1 (1.9)	2 (3.8)	3
Negative Surveillance	37	37	37	37	37	37	17	17	17	17	17	17
Persons with Complaint:	36 (35.6)	41 (40.6)	24 (23.8)	26 (25.7)	30 (29.7)	57	20 (37.7)	18 (34.0)	9 (17.0)	10 (18.9)	12 (22.6)	27
Persons with No Complaints	65 (64.4)	60 (59.4)	77 (76.2)	75 (74.3)	71 (70.3)	44	33 (62.3)	35 (66.0)	44 (83.0)	43 (81.1)	41 (77.4)	26

* Includes ingested lighter fluid and bloody nose.

Table 10

Clinical Complaints Reported Among Children Who Received Combined
Live Measles-Mumps-Rubella (RA 27/3) Virus Vaccine, Lot #60664/C-E810 (Study #511)

Clinical Complaint	Total Vaccinees (50 Children)						Initially Seronegatives (13 Children)					
	Days Post Vaccination					No. with	Days Post Vaccination					No. with
	0-4	5-12	13-18	19-28	29-42	Complaint	0-4	5-12	13-18	19-28	29-42	Complaint
Headache	1 (2.0%)	1 (2.0)	1 (2.0)	1 (2.0)		4						0
Irritability	5 (10.0)	8 (16.0)	6 (12.0)	5 (10.0)		18	2 (15.4)	3 (23.1)	3 (23.1)	1 (7.7)		7
Malaise	7 (14.0)	9 (18.0)	4 (8.0)	4 (8.0)		17	3 (23.1)	3 (23.1)	3 (23.1)	2 (15.4)		7
Anorexia		1 (2.0)		1 (2.0)		2				1 (7.7)		1
Upper Respiratory Illness	2 (4.0)	6 (12.0)	3 (6.0)	1 (2.0)		9			2 (15.4)			2
Lower Respiratory Illness	1 (2.0)	1 (2.0)				1	1 (7.7)	1 (7.7)				1
Gastrointestinal Illness	1 (2.0)	3 (6.0)	1 (2.0)	4 (8.0)	2 (4.0)	7			1 (7.7)	2 (15.4)	1 (7.7)	3
Persons with Complaint:	7 (14.0)	9 (18.0)	7 (14.0)	8 (16.0)	2 (4.0)	21	3 (23.1)	3 (23.1)	4 (30.8)	2 (15.4)	1 (7.7)	8
Persons with No Complaint:	43 (86.0)	41 (82.0)	43 (86.0)	42 (84.0)	48 (96.0)	29	10 (76.9)	10 (76.9)	9 (69.2)	11 (84.6)	12 (92.3)	5

1/31/78

Table 11

Clinical Complaints Reported Among Children Who Received Combined
Live Measles-Mumps-Rubella (RA 27/3) Virus Vaccine, Lot #60665/C-E811 (Study #511)

Clinical Complaint	Total Vaccinees (50 Children)						Initially Seronegatives (6 Children)					
	Days Post Vaccination					No. with Complaint	Days Post Vaccination					No. with Complaint
	0-4	5-12	13-18	19-28	29-42		0-4	5-12	13-18	19-28	29-42	
Headache	2 (4.0%)	1 (2.0)	4 (8.0)	2 (4.0)		8			1 (16.7)			1
Irritability	2 (4.0)	9 (18.0)	4 (8.0)	5 (10.0)	3 (6.1)	18		1 (16.7)		1 (16.7)		2
Malaise	2 (4.0)	7 (14.0)	2 (4.0)	3 (6.0)		12		1 (16.7)		1 (16.7)		2
Anorexia		1 (2.0)				1						0
Upper Respiratory Illness	2 (4.0)	4 (8.0)				4						0
Lower Respiratory Illness		1 (2.0)	1 (2.0)			1						0
Gastrointestinal Illness	1 (2.0)	3 (6.0)	2 (4.0)	1 (2.0)		5						0
Persons with Complaint:	2 (4.0)	11 (22.0)	7 (14.0)	6 (12.0)	3 (6.1)	20	0	1 (16.7)	1 (16.7)	1 (16.7)	0	3
Persons with No Complaint:	48 (96.0)	39 (78.0)	43 (86.0)	44 (88.0)	46 (93.9)	30	6 (100)	5 (83.3)	5 (83.3)	5 (83.3)	5 (100)	3
Negative Surveillance	0	0	0	0	1	0	0	0	0	0	1	0

1/31/78

Table 12

Clinical Complaints Reported Among Children Who Received Combined
Live Measles-Mumps-Rubella (RA 27/3) Virus Vaccine, Lot #60666/C-E812 (Study #511)

Clinical Complaint	Total Vaccinees (50 Children)						Initially Seronegatives (2 Children)					
	Days Post Vaccination					No. with Complaint	Days Post Vaccination					No. with Complaint
	0-4	5-12	13-18	19-28	29-42		0-4	5-12	13-18	19-28	29-42	
Headache		2 (4.0%)	4 (8.0)			6			1 (50.0)			1
Irritability	1 (2.0)	9 (18.0)	3 (6.0)	1 (2.0)	2 (4.0)	12						0
Malaise	2 (4.0)	6 (12.0)	4 (8.0)		3 (6.0)	13			1 (50.0)			1
Anorexia	1 (2.0)	3 (6.0)	1 (2.0)			5						0
Upper Respiratory Illness	1 (2.0)	2 (4.0)				2						0
Lower Respiratory Illness		1 (2.0)				1						0
Otitis	1 (2.0)					1						0
Gastrointestinal Illness	1 (2.0)	1 (2.0)	1 (2.0)			2						0
Persons with Complaint:	2 (4.0)	11 (22.0)	6 (12.0)	1 (2.0)	3 (6.0)	17	0	0	1 (50.0)	0	0	1
Persons with No Complaint:	48 (96.0)	39 (78.0)	44 (88.0)	49 (98.0)	47 (94.0)	33	2 (100)	2 (100)	1 (50.0)	2 (100)	2 (100)	1

1/31/78

Table 10

Clinical Complaints Reported Among Children Who Received Combined
Live Measles-Mumps-Rubella (RA 27/3) Virus Vaccine, Lot #60664/C-E810 (Study #513)

Clinical Complaint	Total Vaccinees (53 Children)						Initially Seronegatives (30 Children)					
	Days Post Vaccination					No. with Complaint	Days Post Vaccination					No. with Complaint
	0-4	5-12	13-18	19-28	29-42		0-4	5-12	13-18	19-28	29-42	
Injection Site:	2 (3.9%)					2	1 (3.3)					1
Soreness	2					2	1					1
Systemic:												
Arthralgia	1 (2.0)	1 (2.0)				1						0
Measles-Like Rash		6 (11.8)	1 (2.0)	1 (2.0)		6		4 (13.3)	1 (3.3)	1 (3.3)		4
Headache		1 (2.0)				1						0
Irritability	4 (7.8)	2 (3.9)	1 (2.0)	2 (3.9)	2 (3.9)	8	4 (13.3)	2 (6.7)	1 (3.3)	2 (6.7)	1 (3.3)	7
Anorexia	4 (7.8)	3 (5.9)	1 (2.0)	2 (3.9)	5 (9.8)	10	2 (6.7)	2 (6.7)		2 (6.7)	3 (10.0)	7
Disturbed Sleep			1 (2.0)		1 (2.0)	1						0
Fatigue		1 (2.0)			1 (2.0)	1		1 (3.3)			1 (3.3)	1
Myalgia	1 (2.0)	1 (2.0)				1						0
Upper Respiratory Illness	9 (17.6)	12 (23.5)	7 (13.7)	12 (23.5)	11 (21.6)	25	4 (13.3)	7 (23.3)	6 (20.0)	7 (23.3)	8 (26.7)	14
Otitis				1 (2.0)		1				1 (3.3)		1
Ophthalmopathy	1 (2.0)	1 (2.0)		1 (2.0)	1 (2.0)	2		1 (3.3)		1 (3.3)	1 (3.3)	1
Gastrointestinal Illness	12 (23.5)	11 (21.6)	2 (3.9)	4 (7.8)	5 (9.8)	18	9 (30.0)	9 (30.0)	1 (3.3)	3 (10.0)	4 (13.3)	15
Nonspecific Rash	5 (9.8)	4 (7.8)	4 (7.8)	6 (11.8)	8 (15.7)	15	2 (6.7)	4 (13.3)	4 (13.3)	5 (16.7)	5 (16.7)	10
Sores on Face		1 (2.0)				1		1 (3.3)				1
Allergy	1 (2.0)		1 (2.0)			2	1 (3.3)		1 (3.3)			2
Teething	2 (3.9)	4 (7.8)	1 (2.0)	2 (3.9)	3 (5.9)	9	1 (3.3)	4 (13.3)	1 (3.3)	2 (6.7)	1 (3.3)	7
Herpes-Type Rash		1 (2.0)		1 (2.0)		2		1 (3.3)		1 (3.3)		2
Persons with Complaint:	24 (47.1)	27 (52.9)	12 (23.5)	18 (35.3)	19 (37.3)	39	14 (46.7)	19 (63.3)	9 (30.0)	12 (40.0)	13 (43.3)	25
Persons with No Complaint:	27 (52.9)	24 (47.1)	39 (76.5)	33 (64.7)	32 (62.7)	12	16 (53.3)	11 (36.7)	21 (70.0)	18 (60.0)	17 (56.7)	5
Negative Surveillance	2	2	2	2	2	2	0	0	0	0	0	0

1/27/78

Table 11

Clinical Complaints Reported Among Children Who Received Combined
Live Measles-Mumps-Rubella (RA 27/3) Virus Vaccine, Lot #60665/C-E811 (Study #513)

Clinical Complaint	Total Vaccinees (54 Children)						Initially Seronegatives (34 Children)					
	Days Post Vaccination					No. with	Days Post Vaccination					No. with
	0-4	5-12	13-18	19-28	29-42	Complaint	0-4	5-12	13-18	19-28	29-42	Complaint
Injection Site:	2 (3.8%)					2	2 (5.9)					2
Soreness	1					1	1					1
Erythema and Soreness	1					1	1					1
Systemic:												
Lymphadenopathy	2 (3.8)	1 (1.9)				3	1 (2.9)	1 (2.9)				2
Measles-Like Rash		5 (9.6)	4 (7.7)	1 (1.9)		7		3 (8.8)	2 (5.9)			4
Irritability	4 (7.7)	6 (11.5)	1 (1.9)	1 (1.9)	2 (3.8)	9	4 (11.8)	4 (11.8)		1 (2.9)	2 (5.9)	7
Malaise	1 (1.9)	1 (1.9)				1	1 (2.9)	1 (2.9)				1
Anorexia	5 (9.6)	5 (9.6)	3 (5.8)	2 (3.8)	4 (7.7)	13	3 (8.8)	4 (11.8)	2 (5.9)	1 (2.9)	3 (8.8)	9
Disturbed Sleep	1 (1.9)	1 (1.9)	1 (1.9)			2	1 (2.9)	1 (2.9)				1
Fatigue	2 (3.8)					2	2 (5.9)					2
Upper Respiratory Illness	10 (19.2)	9 (17.3)	5 (9.6)	10 (19.2)	11 (21.2)	25	4 (11.8)	6 (17.6)	4 (11.8)	6 (17.6)	7 (20.6)	15
Otitis	2 (3.8)	2 (3.8)	2 (3.8)	1 (1.9)	1 (1.9)	4	2 (5.9)	1 (2.9)	1 (2.9)	1 (2.9)	1 (2.9)	2
Ophthalmopathy	1 (1.9)	3 (5.8)		1 (1.9)	1 (1.9)	5	1 (2.9)	2 (5.9)		1 (2.9)	1 (2.9)	4
Gastrointestinal Illness	9 (17.3)	10 (19.2)	5 (9.6)	4 (7.7)	6 (11.5)	18	6 (17.6)	7 (20.6)	3 (8.8)	3 (8.8)	5 (14.7)	11
Nonspecific Rash	4 (7.7)	3 (5.8)		2 (3.8)	2 (3.8)	7	3 (8.8)	3 (8.8)		2 (5.9)	2 (5.9)	6
Allergy	1 (1.9)					1	1 (2.9)					1
Teething	1 (1.9)	1 (1.9)	1 (1.9)	3 (5.8)	3 (5.8)	4	1 (2.9)	1 (2.9)		1 (2.9)	1 (2.9)	2
Persons with Complaint:	24 (46.2)	26 (50.0)	18 (34.6)	21 (40.4)	18 (34.6)	36	16 (47.1)	18 (52.9)	11 (32.4)	13 (38.2)	12 (35.3)	23
Persons with No Complaint:	28 (53.8)	26 (50.0)	34 (65.4)	31 (59.6)	34 (65.4)	16	18 (52.9)	16 (47.1)	23 (67.6)	21 (61.8)	22 (64.7)	11
Negative Surveillance:	2	2	2	2	2	2	0	0	0	0	0	0

1/27/78

Table 12

Clinical Complaints Reported Among Children Who Received Combined
Live Measles-Mumps-Rubella (RA 27/3) Virus Vaccine, Lot #60666/C-E812 (Study #513)

Clinical Complaint	Total Vaccinees (56 Children)						Initially Seronegatives (33 Children)					
	Days Post Vaccination					No. with Complaint	Days Post Vaccination					No. with Complaint
	0-4	5-12	13-18	19-28	29-42		0-4	5-12	13-18	19-28	29-42	
Injection Site:	4 (7.4%)					4	3 (9.1)					3
Soreness	4					4	3					3
Systemic:												
Lymphadenopathy				1 (1.9)		1				1 (3.0)		1
Measles-Like Rash		6 (11.1)	2 (3.7)	1 (1.9)		8		4 (12.1)	2 (6.1)	1 (3.0)		6
Headache	1 (1.9)					1						0
Irritability	4 (7.4)	4 (7.4)	3 (5.6)	3 (5.6)	2 (3.7)	8	2 (6.1)	3 (9.1)	2 (6.1)	3 (9.1)	2 (6.1)	5
Anorexia	6 (11.1)	9 (16.7)	1 (1.9)	2 (3.7)	11 (20.4)	20	4 (12.1)	5 (15.2)			9 (27.3)	13
Disturbed Sleep	1 (1.9)	2 (3.7)				2	1 (3.0)	2 (6.1)				2
Fatigue		1 (1.9)		1 (1.9)		1		1 (3.0)		1 (3.0)		1
Myalgia				1 (1.9)	2 (3.7)	2				1 (3.0)	1 (3.0)	1
Upper Respiratory Illness	13 (24.1)	19 (35.2)	13 (24.1)	14 (25.9)	15 (27.8)	30	10 (30.3)	12 (36.4)	9 (27.3)	11 (33.3)	12 (36.4)	20
Otitis	1 (1.9)	2 (3.7)		2 (3.7)	2 (3.7)	5		1 (3.0)		2 (6.1)	2 (6.1)	3
Ophthalmopathy	2 (3.7)	1 (1.9)		1 (1.9)	1 (1.9)	4	1 (3.0)			1 (3.0)	1 (3.0)	2
Gastrointestinal Illness	6 (11.1)	4 (7.4)	4 (7.4)	5 (9.3)	7 (13.0)	18	4 (12.1)		3 (9.1)	4 (12.1)	3 (9.1)	12
Nonspecific Rash	4 (7.4)	8 (14.8)	6 (11.1)	7 (13.0)	6 (11.1)	19	3 (9.1)	5 (15.2)	4 (12.1)	4 (12.1)	4 (12.1)	13
Sore from Venipuncture	1 (1.9)					1	1 (3.0)					1
Teething		3 (5.6)	2 (3.7)	3 (5.6)	3 (5.6)	5		3 (9.1)	2 (6.1)	3 (9.1)	2 (6.1)	4
Herpes-Type Rash		1 (1.9)				1		1 (3.0)				1
Persons with Complaint:	27 (50.0)	33 (61.1)	22 (40.7)	24 (44.4)	25 (46.3)	41	20 (60.6)	22 (66.7)	16 (48.5)	19 (57.6)	17 (51.5)	27
Persons with No Complaint:	27 (50.0)	21 (38.9)	32 (59.3)	30 (55.6)	29 (53.7)	13	13 (39.4)	11 (33.3)	17 (51.5)	14 (42.4)	16 (48.5)	6
Negative Surveillance	2	2	2	2	2	2	0	0	0	0	0	0

1/27/78

Table 11

Clinical Complaints Reported Among Children Who Received Combined Live Measles-Mumps-Rubella (RA 27/3) Virus Vaccine, Lot No. 621/C-D763 (Study #442)

Clinical Complaint	Total Vaccinees (199 Children)						Initially Seronegative to: Measles, Mumps and Rubella (23 Children)					
	Days Post-Vaccination					No. with Complaint	Days Post Vaccination					No. with Complaint
	0-4	5-12	13-18	19-28	29-42		0-4	5-12	13-18	19-28	29-42	
Irritability	32 (16.1%)	9 (4.5)	2 (1.0)	4 (2.1)		39	5 (21.7)			1 (5.0)		5
Malaise	30 (15.1)	14 (7.0)	3 (1.5)	7 (3.6)	1 (0.5)	43	5 (21.7)	1 (4.3)		2 (10.0)		7
Headache		1 (0.5)	2 (1.0)			2						0
Upper Respiratory Illness	9 (4.5)	11 (5.5)	5 (2.5)	8 (4.1)	5 (2.6)	23	1 (4.3)	1 (4.3)	1 (4.3)	2 (10.0)	1 (5.0)	3
Otitis			2 (1.0)	3 (1.5)		3			1 (4.3)	1 (5.0)		1
Ophthalmopathy		1 (0.5)				1						0
Gastrointestinal Illness	13 (6.5)	7 (3.5)	2 (1.0)	5 (2.6)	1 (0.5)	22		1 (4.3)				1
Anorexia	5 (2.5)	3 (1.5)	2 (1.0)	5 (2.6)		13				1 (5.0)		1
Mild Dermatitis		1 (0.5)				1						0
Persons with Complaints:	49 (24.6)	22 (11.1)	11 (5.5)	19 (9.8)	6 (3.1)	73	6 (26.1)	2 (8.7)	1 (4.3)	4 (20.0)	1 (5.0)	10
Persons with No Complaints:	150 (75.4)	177 (88.9)	188 (94.5)	175 (90.2)	187 (96.9)	123	17 (73.9)	21 (91.3)	22 (95.7)	16 (80.0)	19 (95.0)	12
Negative Physician Surveillance				5	6					3	3	

10/3/77

Exhibit 17

TABLE 1. Recommended schedule for active immunization of normal infants and children (See individual ACIP recommendations for details.)

Recommended age*	Vaccine(s)†	Comments
2 mo.	DTP-1,§ OPV-1¶	Can be given earlier in areas of high endemicity
4 mo.	DTP-2, OPV-2	6-wks-2-mo. interval desired between OPV doses to avoid interference
6 mo.	DTP-3	An additional dose of OPV at this time is optional for use in areas with a high risk of polio exposure
15 mo.**	MMR††	
18 mo.**	DTP-4, OPV-3	Completion of primary series
4-6 yr§§	DTP-5, OPV-4	Preferably at or before school entry
14-16 yr	Td¶¶	Repeat every 10 years throughout life

*These recommended ages should not be construed as absolute, i.e. 2 mos. can be 6-10 weeks, etc.

†For all products used, consult manufacturer's package enclosure for instructions for storage, handling, and administration. Immunobiologics prepared by different manufacturers may vary, and those of the same manufacturer may change from time to time. The package insert should be followed for a specific product.

§DTP—Diphtheria and tetanus toxoids and pertussis vaccine.

¶OPV—Oral, attenuated poliovirus vaccine contains poliovirus types 1, 2, and 3.

**Simultaneous administration of MMR, DTP, and OPV is appropriate for patients whose compliance with medical care recommendations cannot be assured.

††MMR—Live measles, mumps, and rubella viruses in a combined vaccine (see text for discussion of single vaccines versus combination).

§§Up to the seventh birthday.

¶¶Td—Adult tetanus toxoid and diphtheria toxoid in combination, which contains the same dose of tetanus toxoid as DTP or DT and a reduced dose of diphtheria toxoid.

Exhibit 18

Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please call 800-835-4709 or 240-402-8010, extension 1. CBER Consumer Affairs Branch or send an e-mail to: ocod@fda.hhs.gov and include 508 Accommodation and the title of the document in the subject line of your e-mail.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use M-M-R II safely and effectively. See full prescribing information for M-M-R II.

M-M-R® II (Measles, Mumps, and Rubella Virus Vaccine Live)
Suspension for intramuscular or subcutaneous injection
Initial U.S. Approval: 1978

----------RECENT MAJOR CHANGES----------

Dosage and Administration
Dose and Schedule (2.1) ---------- ----------03/2023
Administration (2.2) ---------- ----------03/2023

----------INDICATIONS AND USAGE----------

M-M-R II is a vaccine indicated for active immunization for the prevention of measles, mumps, and rubella in individuals 12 months of age and older. (1)

---------- DOSAGE AND ADMINISTRATION ----------

For intramuscular or subcutaneous injection only. (2.1, 2.2).
A single dose is approximately 0.5 mL.

- The first dose is administered at 12 to 15 months of age. (2.1)
- The second dose is administered at 4 to 6 years of age. (2.1)

---------- DOSAGE FORMS AND STRENGTHS ----------

Suspension for injection (approximately 0.5-mL dose) supplied as a lyophilized vaccine to be reconstituted using accompanying sterile diluent. (3)

----------CONTRAINDICATIONS----------

- Hypersensitivity to any component of the vaccine. (4.1)
- Immunosuppression. (4.2)
- Moderate or severe febrile illness. (4.3)
- Active untreated tuberculosis. (4.4)
- Pregnancy. (4.5, 8.1)

---------- WARNINGS AND PRECAUTIONS----------

- Use caution when administering M-M-R II to individuals with a history of febrile seizures. (5.1)
- Use caution when administering M-M-R II to individuals with anaphylaxis or immediate hypersensitivity following egg ingestion. (5.2)
- Use caution when administering M-M-R II to individuals with a history of thrombocytopenia. (5.3)
- Evaluate individuals for immune competence prior to administration of M-M-R II if there is a family history of congenital or hereditary immunodeficiency. (5.4)
- Immune Globulins (IG) and other blood products should not be given concurrently with M-M-R II. (5.5, 7.2)

---------- ADVERSE REACTIONS ----------

See full prescribing information for adverse reactions occurring during clinical trials or the post-marketing period. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., at 1-877-888-4231 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov .

----------DRUG INTERACTIONS----------

- Administration of immune globulins and other blood products concurrently with M-M-R II vaccine may interfere with the expected immune response. (7.2)
- M-M-R II vaccination may result in a temporary depression of purified protein derivative (PPD) tuberculin skin sensitivity. (7.3)

---------- USE IN SPECIFIC POPULATIONS ----------

- Pregnancy: Do not administer M-M-R II to females who are pregnant. Pregnancy should be avoided for 1 month following vaccination with M-M-R II. (4.5, 8.1, 17)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 03/2023

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

M-M-R II is a vaccine indicated for active immunization for the prevention of measles, mumps, and rubella in individuals 12 months of age and older.

2 DOSAGE AND ADMINISTRATION

Intramuscular or Subcutaneous administration only.

2.1 Dose and Schedule

A single dose of M-M-R II is approximately 0.5 mL.

The first dose is administered at 12 to 15 months of age. A second dose is administered at 4 to 6 years of age.

The second dose may be administered prior to 4 years of age, provided that there is a minimum interval of one month between the doses of measles, mumps and rubella virus vaccine, live {1-2}.

Children who received an initial dose of measles, mumps and rubella vaccine prior to their first birthday should receive additional doses of vaccine at 12-15 months of age and at 4-6 years of age to complete the vaccination series *[see Clinical Studies (14.2)]*.

For post-exposure prophylaxis for measles, administer a dose of M-M-R II vaccine within 72 hours after exposure.

2.2 Administration

Use a sterile syringe free of preservatives, antiseptics, and detergents for each injection and/or reconstitution of the vaccine because these substances may inactivate the live virus vaccine. To reconstitute, use only the diluent supplied with the vaccine since it is free of preservatives or other antiviral substances which might inactivate the vaccine.

Withdraw the entire volume of the supplied diluent from its vial and inject into lyophilized vaccine vial. Agitate to dissolve completely. Discard if the lyophilized vaccine cannot be dissolved.

Withdraw the entire volume of the reconstituted vaccine and inject the vaccine intramuscularly or subcutaneously.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Visually inspect the vaccine before and after reconstitution prior to administration. Before reconstitution, the lyophilized vaccine is a light yellow compact crystalline plug, when reconstituted, is a clear yellow liquid. Discard if particulate matter or discoloration are observed in the reconstituted vaccine.

To minimize loss of potency, administer M-M-R II as soon as possible after reconstitution. If not used immediately, the reconstituted vaccine may be stored between 36°F to 46°F (2°C to 8°C), protected from light, for up to 8 hours. Discard reconstituted vaccine if it is not used within 8 hours.

3 DOSAGE FORMS AND STRENGTHS

M-M-R II vaccine is a suspension for injection supplied as a single dose vial of lyophilized vaccine to be reconstituted using the accompanying sterile diluent *[see Dosage and Administration (2.2) and How Supplied/Storage and Handling (16)]*. A single dose after reconstitution is approximately 0.5 mL.

4 CONTRAINDICATIONS

4.1 Hypersensitivity

Do not administer M-M-R II vaccine to individuals with a history of hypersensitivity to any component of the vaccine (including gelatin) {3} or who have experienced a hypersensitivity reaction following administration of a previous dose of M-M-R II vaccine or any other measles, mumps and rubella-containing vaccine. Do not administer M-M-R II vaccine to individuals with a history of anaphylaxis to neomycin *[see Description (11)].*

4.2 Immunosuppression

Do not administer M-M-R II vaccine to individuals who are immunodeficient or immunosuppressed due to disease or medical therapy. Measles inclusion body encephalitis {4} (MIBE), pneumonitis {5} and death as a direct consequence of disseminated measles vaccine virus infection have been reported in

immunocompromised individuals inadvertently vaccinated with measles-containing vaccine. In this population, disseminated mumps and rubella vaccine virus infection have also been reported.

4.3 Moderate or Severe Febrile Illness

Do not administer M-M-R II vaccine to individuals with an active febrile illness with fever >101.3°F (>38.5°C).

4.4 Active Untreated Tuberculosis

Do not administer M-M-R II vaccine to individuals with active untreated tuberculosis (TB).

4.5 Pregnancy

Do not administer M-M-R II to individuals who are pregnant or who are planning on becoming pregnant within the next month *[see Use in Specific Populations (8.1) and Patient Counseling Information (17)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Febrile Seizure

There is a risk of fever and associated febrile seizure in the first 2 weeks following immunization with M-M-R II vaccine. For children who have experienced a previous febrile seizure (from any cause) and those with a family history of febrile seizures there is a small increase in risk of febrile seizure following receipt of M-M-R II vaccine *[see Adverse Reactions (6)]*.

5.2 Hypersensitivity to Eggs

Individuals with a history of anaphylactic, anaphylactoid, or other immediate reactions (e.g., hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock) subsequent to egg ingestion may be at an enhanced risk of immediate-type hypersensitivity reactions after receiving M-M-R II vaccine. The potential risks and known benefits should be evaluated before considering vaccination in these individuals.

5.3 Thrombocytopenia

Transient thrombocytopenia has been reported within 4-6 weeks following vaccination with measles, mumps and rubella vaccine. Carefully evaluate the potential risk and benefit of vaccination in children with thrombocytopenia or in those who experienced thrombocytopenia after vaccination with a previous dose of measles, mumps, and rubella vaccine {6-8} *[see Adverse Reactions (6)]*.

5.4 Family History of Immunodeficiency

Vaccination should be deferred in individuals with a family history of congenital or hereditary immunodeficiency until the individual's immune status has been evaluated and the individual has been found to be immunocompetent.

5.5 Immune Globulins and Transfusions

Immune Globulins (IG) and other blood products should not be given concurrently with M-M-R II *[see Drug Interactions (7.2)]*. These products may contain antibodies that interfere with vaccine virus replication and decrease the expected immune response.

The Advisory Committee on Immunization Practices (ACIP) has specific recommendations for intervals between administration of antibody containing products and live virus vaccines.

6 ADVERSE REACTIONS

The following adverse reactions include those identified during clinical trials or reported during post-approval use of M-M-R II vaccine or its individual components.

Body as a Whole

Panniculitis; atypical measles; fever; headache; dizziness; malaise; irritability.

Cardiovascular System

Vasculitis.

Digestive System

Pancreatitis; diarrhea; vomiting; parotitis; nausea.

Hematologic and Lymphatic Systems

Thrombocytopenia; purpura; regional lymphadenopathy; leukocytosis.

Immune System

Anaphylaxis, anaphylactoid reactions, angioedema (including peripheral or facial edema) and bronchial spasm.

Musculoskeletal System

Arthritis; arthralgia; myalgia.

Nervous System

Encephalitis; encephalopathy; measles inclusion body encephalitis (MIBE) subacute sclerosing panencephalitis (SSPE); Guillain-Barré Syndrome (GBS); acute disseminated encephalomyelitis (ADEM); transverse myelitis; febrile convulsions; afebrile convulsions or seizures; ataxia; polyneuritis; polyneuropathy; ocular palsies; paresthesia; syncope.

Respiratory System

Pneumonia; pneumonitis; sore throat; cough; rhinitis.

Skin

Stevens-Johnson syndrome; acute hemorrhagic edema of infancy; Henoch-Schönlein purpura; erythema multiforme; urticaria; rash; measles-like rash; pruritus; injection site reactions (pain, erythema, swelling and vesiculation).

Special Senses — Ear

Nerve deafness; otitis media.

Special Senses — Eye

Retinitis; optic neuritis; papillitis; conjunctivitis.

Urogenital System

Epididymitis; orchitis.

In a randomized open-label clinical trial (NCT00432523), conducted in France and Germany, 752 children 12 months through 18 months of age received M-M-R II concomitantly administered with VARIVAX at a separate site, by either the intramuscular (n=374) or subcutaneous (n=378) route. In the overall population, 55.3% were male and the median age was 13.2 months. Local and systemic solicited adverse reactions were recorded by parents or guardians using standardized diary cards. Local solicited reactions were recorded for 4 days after vaccination, and systemic solicited adverse reactions were recorded for 42 days after vaccination. In the event that a participant experienced a rash or a mumps-like illness, parents and/or guardians were instructed to contact the investigator for an examination as soon as possible and no later than 72 hours following onset of symptoms. The nature of any rash was characterized by principal investigator either as a measles-like, rubella-like, varicella-like or "other." Study investigators reviewed the diary card with the participant or participant's legal guardian 42 days vaccination to ensure consistency with protocol definitions. Table 1 below presents the frequency of solicited adverse reactions based on the final assessment by the study investigators.

Table 1: Proportion of Participants Reporting Solicited Adverse Reactions Following Vaccination with M-M-R II, Concomitantly Administered with VARIVAX, by the Intramuscular or Subcutaneous Route

	INTRAMUSCULAR N=374 %	SUBCUTANEOUS N=376 %
Solicited injection-site reactions at MMR injection-site (Days 0 to 4)*		
Erythema†	10.4	16.2
Mild	8.8	13.0
Moderate	0.8	3.2
Severe	0	0
Missing	0.8	0
Pain‡	7.0	7.2
Mild	5.1	5.9
Moderate	1.9	1.3
Severe	0	0

Swelling[†]	1.9	5.3
Mild	1.1	2.9
Moderate	0.5	1.1
Severe	0	0
Missing	0.3	1.3
Solicited systemic reactions (Days 0 to 42)		
Measles-like rash[§]	2.9	2.7
Rubella-like rash[§]	2.7	2.7
Varicella-like rash[§]	0.5	3.2
Mumps-like illness	0	0.3
Fever (temperature ≥38.0°C)[¶, #]	66.5	66.8
38.0-38.5°C	20.4	22.2
>38.5-39.0°C	17.4	16.6
>39.0-39.5°C	14.2	13.4
>39.5-40.0°C	11.8	11.0
>40.0°C	2.7	3.7

N=total number of participants in the group

* During the post vaccination monitoring period (0-42 days), 3 participants experienced a varicella-like injection-site rash at the M-M-R II injection site. All were reported in the subcutaneous group.
† Intensity of injection site reaction: mild or ≤2.5 cm; moderate or >2.5 to ≤5.0 cm; severe or >5.0 cm
‡ Intensity of pain: mild: awareness of symptom but easily tolerated; moderate: definitely acting like something is wrong; severe: extremely distressed or unable to do usual activities.
§ Testing to distinguish between rash caused by wild-type or vaccine virus was not performed. Reports of measles-, rubella- and varicella-like rash included 3 reports of measles, 1 report of rubella, and 1 report of varicella, all with onset within 15 days post-vaccination.
¶ The percentage of fever is defined within the population who had valid temperature measurements. One participant in IM group and two participants in SC group did not have temperature measurements and were excluded from the denominator; resulting in N=373 and N=374, respectively.
# In the IM Group 92.3% of fevers were documented using the rectal route of measurement and 7.7% of fevers were documented only by the axillary route of measurement. In the SC Group 89.6% of fevers were documented using the rectal route of measurement and 10.4% of fevers were documented only by the axillary route of measurement.

Unsolicited adverse events that occurred within 42 days following vaccination were recorded using diary cards supplemented by medical review. Data on unsolicited adverse events were transcribed into the study database during an on-site visit at day 42. The rates and types of reported adverse events (AEs) across groups were similar and included common clinical events that are often reported in the evaluated populations. Serious adverse events occurred at rates of 0.3% and 1% in the intramuscular and subcutaneous groups, respectively. One moderate intensity case of otitis media occurred in a participant in the subcutaneous group was considered related to the study vaccination.

7 DRUG INTERACTIONS

7.1 Corticosteroids and Immunosuppressive Drugs

M-M-R II vaccine should not be administered to individuals receiving immunosuppressive therapy, including high dose corticosteroids. Vaccination with M-M-R II vaccine can result in disseminated disease due to measles vaccine in individuals on immunosuppressive drugs *[see Contraindications (4.2)].*

7.2 Immune Globulins and Transfusions

Administration of immune globulins and other blood products concurrently with M-M-R II vaccine may interfere with the expected immune response {9-11} *[see Warnings and Precautions (5.5)].* The ACIP has specific recommendations for intervals between administration of antibody containing products and live virus vaccines.

7.3 Tuberculin Skin Testing

It has been reported that live attenuated measles, mumps and rubella virus vaccines given individually may result in a temporary depression of tuberculin skin sensitivity. Therefore, if a tuberculin skin test with tuberculin purified protein derivative (PPD) is to be done, it should be administered before, simultaneously with, or at least 4 to 6 weeks after vaccination with M-M-R II vaccine.

7.4 Use with Other Live Viral Vaccines

M-M-R II vaccine can be administered concurrently with other live viral vaccines. If not given concurrently, M-M-R II vaccine should be given one month before or one month after administration of other live viral vaccines to avoid potential for immune interference.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

M-M-R II vaccine is contraindicated for use in pregnant women because infection during pregnancy with the wild-type viruses has been associated with maternal and fetal adverse outcomes.

Increased rates of spontaneous abortion, stillbirth, premature delivery and congenital defects have been observed following infection with wild-type measles during pregnancy. {12,13} Wild-type mumps infection during the first trimester of pregnancy may increase the rate of spontaneous abortion.

Infection with wild-type rubella during pregnancy can lead to miscarriage or stillbirth. If rubella infection occurs during the first trimester of pregnancy, it can result in severe congenital defects, Congenital Rubella Syndrome (CRS). Congenital Rubella Syndrome in the infant includes but is not limited to eye manifestations (cataracts, glaucoma, retinitis), congenital heart defects, hearing loss, microcephaly, and intellectual disabilities. M-M-R II vaccine contains live attenuated measles, mumps and rubella viruses. It is not known whether M-M-R II vaccine can cause fetal harm when administered to pregnant woman. There are no adequate and well-controlled studies of M-M-R II vaccine administration to pregnant women.

All pregnancies have a risk of birth defect, loss or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Available data suggest the rates of major birth defects and miscarriage in women who received M-M-R II vaccine within 30 days prior to pregnancy or during pregnancy are consistent with estimated background rates *(see Data)*.

Data

Human Data

A cumulative assessment of post-marketing reports for M-M-R II vaccine from licensure 01 April 1978 through 31 December 2018, identified 796 reports of inadvertent administration of M-M-R II vaccine occurring 30 days before or at any time during pregnancy with known pregnancy outcomes. Of the prospectively followed pregnancies for whom the timing of M-M-R II vaccination was known, 425 women received M-M-R II vaccine during the 30 days prior to conception through the second trimester. The outcomes for these 425 prospectively followed pregnancies included 16 infants with major birth defects, 4 cases of fetal death and 50 cases of miscarriage. No abnormalities compatible with congenital rubella syndrome have been identified in patients who received M-M-R II vaccine. Rubella vaccine virus can cross the placenta, leading to asymptomatic infection of the fetus. Mumps vaccine virus has also been shown to infect the placenta {14}, but there is no evidence that it causes congenital malformations or disease in the fetus or infant.

The CDC established the Vaccine in Pregnancy registry (1971-1989) of women who had received rubella vaccines within 3 months before or after conception. Data on 1221 inadvertently vaccinated pregnant women demonstrated no evidence of an increase in fetal abnormalities or cases of Congenital Rubella Syndrome (CRS) in the enrolled women {15}.

8.2 Lactation

Risk Summary

It is not known whether measles or mumps vaccine virus is secreted in human milk. Studies have shown that lactating postpartum women vaccinated with live attenuated rubella vaccine may secrete the virus in breast milk and transmit it to breast-fed infants. {16,17} In the breast-fed infants with serological evidence of rubella virus vaccine strain antibodies, none exhibited severe disease; however, one exhibited mild clinical illness typical of acquired rubella. {18,19}

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for M-M-R II, and any potential adverse effects on the breastfed child from M-M-R II or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

M-M-R II vaccine is not approved for individuals less than 12 months of age. Safety and effectiveness of measles vaccine in infants below the age of 6 months have not been established *[see Clinical Studies (14)]*. Safety and effectiveness of mumps and rubella vaccine in infants less than 12 months of age have not been established.

8.5 Geriatric Use

Clinical studies of M-M-R II did not include sufficient numbers of seronegative subjects aged 65 and over to determine whether they respond differently from younger subjects.

11 DESCRIPTION

M-M-R II vaccine is a sterile lyophilized preparation of (1) Measles Virus Vaccine Live, an attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture; (2) Mumps Virus Vaccine Live, the Jeryl Lynn™ (B level) strain of mumps virus propagated in chick embryo cell culture; and (3) Rubella Virus Vaccine Live, the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts. {20,21} The cells, virus pools, recombinant human serum albumin and fetal bovine serum used in manufacturing are tested and determined to be free of adventitious agents.

After reconstitution, each approximately 0.5 mL dose contains not less than 3.0 $\log_{10}$ $TCID_{50}$ (tissue culture infectious doses) of measles virus; 4.1 $\log_{10}$ $TCID_{50}$ of mumps virus; and 3.0 $\log_{10}$ $TCID_{50}$ of rubella virus.

Each dose is calculated to contain sorbitol (14.5 mg), sucrose (1.9 mg), hydrolyzed gelatin (14.5 mg), recombinant human albumin (≤0.3 mg), fetal bovine serum (<1 ppm), approximately 25 mcg of neomycin and other buffer and media ingredients. The product contains no preservative.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

M-M-R II vaccination induces antibodies to measles, mumps, and rubella associated with protection which can be measured by neutralization assays, hemagglutination-inhibition (HI) assays, or enzyme linked immunosorbent assay (ELISA) tests. Results from efficacy studies or effectiveness studies that were previously conducted for the component vaccines of M-M-R II were used to define levels of serum antibodies that correlated with protection against measles, mumps, and rubella *[see Clinical Studies (14)].*

12.4 Persistence of Antibody Responses After Vaccination

Neutralizing and ELISA antibodies to measles, mumps, and rubella viruses are still detectable in 95-100%, 74-91%, and 90-100% of individuals respectively, 11 to 13 years after primary vaccination. {22-28}

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

M-M-R II vaccine has not been evaluated for carcinogenic or mutagenic potential or impairment of fertility.

14 CLINICAL STUDIES

14.1 Clinical Efficacy

Efficacy of measles, mumps, and rubella vaccines was established in a series of double-blind controlled trials. {29-34} These studies also established that seroconversion in response to vaccination against measles, mumps and rubella paralleled protection. {35-38}

14.2 Immunogenicity

Clinical studies enrolling 284 triple seronegative children, 11 months to 7 years of age, demonstrated that subcutaneously administered M-M-R II vaccine is immunogenic. In these studies, a single subcutaneous injection of the vaccine induced measles HI antibodies in 95%, mumps neutralizing antibodies in 96%, and rubella HI antibodies in 99% of susceptible individuals.

A study of 6-month-old and 15-month-old infants born to mothers vaccinated with a measles vaccine in childhood, demonstrated that, following infant and toddler vaccination subcutaneously with Measles Virus Vaccine, Live (previously US-licensed, manufactured by Merck), 74% of the 6-month-old infants developed detectable neutralizing antibody titers while 100% of the 15-month-old infants vaccinated with Measles Virus Vaccine, Live or M-M-R II vaccine developed neutralizing antibodies {39}. When the 6-month-old infants of immunized mothers were revaccinated at 15 months with M-M-R II vaccine, they developed antibody titers similar to those of toddlers who were vaccinated previously at 15-months of age.

In an open label clinical trial (NCT00432523) 752 children 12 through 18 months of age received M-M-R II either intramuscularly (n=374) or subcutaneously (n=378), concomitantly with VARIVAX. Antibody responses to measles, mumps, and rubella viruses were measured by ELISAs using sera obtained 6 weeks postvaccination. For anti-measles virus, anti-mumps virus and anti-rubella virus, seroresponse rates were defined as the percentage of children seronegative at baseline who achieved antibody titers above the respective seroresponse threshold for each assay 6 weeks post vaccination. Seroresponse thresholds were defined as 255 mIU/mL, 10 EU/mL, and 10 IU/mL for anti-measles virus, anti-mumps virus, and anti-rubella virus antibodies, respectively. For each vaccine antigen at least 89% of enrolled children were seronegative at baseline. In a post hoc analysis, seroresponse rates to mumps and rubella viruses were noninferior for the intramuscular group compared to the subcutaneous group (the lower bound of the 95% confidence interval for the difference in seroresponse rates [intramuscular group minus subcutaneous group] ≥-5%). While the seroresponse rate to measles virus narrowly missed meeting the post hoc criterion of -5% for noninferiority (lower bound of the 95% CI for the difference in seroresponse rate -5.28%), it met the pre-specified criterion using a -10% noninferiority margin. For measles, mumps and rubella antigens the lower bound of the 95% CI of the seroresponse rates was >90% after intramuscular administration. The point estimates of the proportions of children achieving antibody titers above the seroresponse thresholds for measles, mumps, and rubella viruses were as follows: 94.3%, 97.7%, and 98.1%, respectively, in the intramuscular group and 96.1%, 98.1%, and 98.1%, respectively, in the subcutaneous group.

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16 HOW SUPPLIED/STORAGE AND HANDLING

No. 4681 — M-M-R II vaccine is supplied as follows:
(1) a box of 10 single-dose vials of lyophilized vaccine (package A), NDC 0006-4681-00
(2) a box of 10 vials of diluent (package B)
Exposure to light may inactivate the vaccine viruses.

To maintain potency, M-M-R II must be stored between -58°F and +46°F (-50°C to +8°C). Use of dry ice may subject M-M-R II to temperatures colder than -58°F (-50°C).

Before reconstitution, refrigerate the lyophilized vaccine at 36°F to 46°F (2°C to 8°C).

Store accompanying diluent in the refrigerator (36°F to 46°F, 2°C to 8°C) or at room temperature (68°F to 77°F, 20°C to 25°C). **Do not freeze the diluent**.

Administer M-M-R II vaccine as soon as possible after reconstitution. If not administered immediately, reconstituted vaccine may be stored between 36°F to 46°F (2°C to 8°C), protected from light, for up to 8 hours. Discard reconstituted vaccine if it is not used within 8 hours.

For information regarding the product or questions regarding storage conditions, call 1-800-MERCK-90 (1-800-637-2590).

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Package Insert).

Discuss the following with the patient:

- Provide the required vaccine information to the patient, parent, or guardian.
- Inform the patient, parent, or guardian of the benefits and risks associated with vaccination.
- Question the patient, parent, or guardian about reactions to a previous dose of M-M-R II vaccine or other measles-, mumps-, or rubella-containing vaccines.
- Question females of reproductive potential regarding the possibility of pregnancy. Inform female patients to avoid pregnancy for 1 month following vaccination *[see Contraindications (4.5) and Use in Specific Populations (8.1)]*.
- Inform the patient, parent, or guardian that vaccination with M-M-R II may not offer 100% protection from measles, mumps, and rubella infection.
- Instruct patients, parents, or guardians to report any adverse reactions to their health-care provider. The U.S. Department of Health and Human Services has established a Vaccine Adverse Event Reporting System (VAERS) to accept all reports of suspected adverse events after the administration of any vaccine, including but not limited to the reporting of events required by the National Childhood Vaccine Injury Act of 1986. For information or a copy of the vaccine reporting form, call the VAERS toll-free number at 1-800-822-7967, or report online at **https://www.vaers.hhs.gov** .

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Exhibit 19

Immunogenicity and safety of a measles-mumps-rubella vaccine administered as a first dose to children 12–15 months of age: a phase III, randomized, non-inferiority, lot-to-lot consistency study

Authors: Nicola P Klein et al.

Running title: Immunogenicity and safety of MMR vaccine

Corresponding author:

Nicola P Klein

Kaiser Permanente Vaccine Study Center
1 Kaiser Plaza, 16th Floor
Oakland, CA 94612 USA
e-mail: nicola.klein@kp.org

Supplementary Material

Supplementary Methods

This study is registered in ClinicalTrials.gov (NCT01702428) and a summary of the study protocol is available at https://www.gsk-clinicalstudyregister.com/study/115648?search=study&study_ids=115648#ps.

Other eligibility criteria

We only enrolled children who were in stable health, as established by medical history and clinical exam, and for whom the investigator believed that their parent(s)/legally acceptable representative(s) could comply with protocol requirements. In the United States (US), we only included children who had previously received a 3-dose primary series of a 13-valent pneumococcal conjugate vaccine (PCV13) with the last dose ≥60 days prior to study entry, and we excluded any child who had previously received a dose of 7-valent pneumococcal conjugate vaccine (*Prevnar/Prevenar*, Pfizer) or a fourth dose of any other pneumococcal conjugate vaccine.

Supplementary Table 6. Incidence of unsolicited adverse events (Day 0–42), serious adverse events, AEs prompting emergency room visits and NOCDs (Day 0–180) (total vaccinated cohort).

n (%)	MMR-RIT (N=3714)	MMR II (N=1289)
Unsolicited AEs (≥1 symptom)	1857 (50.0)	618 (47.9)
Grade 3	225 (6.1)	85 (6.6)
SAEs (any, ≥1 SAE)	77 (2.1)	25 (1.9)
AEs prompting ER visit	375 (10.1)	134 (10.4)
NOCDs (any, ≥1 NOCD)	128 (3.4)	48 (3.7)

AE, adverse event; ER, emergency room; N, number of children with the documented dose; n (%), number (percentage) of children reporting the AE at least once; NOCDs, new onset chronic diseases (see definition in Patients and methods); SAE, serious AE.
Grade 3 unsolicited AEs were those preventing normal, everyday activities.

Exhibit 20

BLA Clinical Review Memorandum

Application Type	Biologics License Application
STN	125748/0
CBER Received Date	June 4, 2021
PDUFA Goal Date	June 4, 2022
Division / Office	DVRPA/OVRR
Priority Review (Yes/No)	No
Reviewer Name(s)	Robin Wisch, MD, Nadine Peart Akindele, MD
Review Completion Date / Stamped Date	June 3, 2022
Supervisory Concurrence	Anuja Rastogi, MD, MHS 1st Level Supervisory Review Clinical Review Staff, Immediate Office of Director DVRPA, OVRR, CBER Douglas Pratt, MD, MPH 2nd Level Supervisory Review Associate Director, Medical Affairs DVRPA, OVRR, CBER
Applicant	GlaxoSmithKline Biologicals, SA
Established Name	Combined Measles, Mumps, and Rubella (MMR) Live (Attenuated) Viral Vaccine
(Proposed) Trade Name	PRIORIX
Pharmacologic Class	Vaccine
Formulation(s), including Adjuvants	Each dose (approximately 0.5 mL) contains not less than 3.4 log10 Cell Culture Infective Dose 50% (CCID50) of measles virus, 4.2 log10 CCID50 of mumps virus, and 3.3 log10 CCID50 of rubella virus. Each dose also contains 32 mg of anhydrous lactose, 9 mg of sorbitol, 9 mg of amino acids, and 8 mg of mannitol. Each dose may also contain residual amounts of neomycin sulphate (≤25 µg) from the manufacturing process.
Dosage Form(s) and Route(s) of Administration	Dosage form: Suspension Route of Administration: Subcutaneous
Dosing Regimen	The first dose is administered at 12 through 15 months of age. The second dose is administered at 4 through 6 years of age. If PRIORIX is not administered according to this schedule and 2 doses of measles-, mumps- and rubella-virus vaccine are recommended for an individual, there should be a minimum of 4 weeks between the first and second dose. PRIORIX may be administered as a second dose to individuals who have received a first dose of another measles, mumps and rubella virus-containing vaccine.
Indication(s) and Intended Population(s)	Active immunization for the prevention of measles, mumps, and rubella in individuals 12 months of age and older.
Orphan Designated (Yes/No)	No

5.3 Table of Studies/Clinical Trials

Table 3: Clinical Trials Submitted in Support of Safety and Efficacy

Study Number	Region	Description	Population (Schedule)	Study Groups: # Enrolled (# Exposed)
Trial # 1: MMR-160 Lot Consistency Immunogenicity Safety (NCT01702428)	US (including Puerto Rico) Estonia Finland Mexico Spain	Phase 3, observer-blind, randomized, controlled, consistency and non-inferiority study to evaluate the immunogenicity and safety of PRIORIX vs. MMR-II, as a first dose	Healthy children 12 through 15 months (1 dose at Day 0 with VV and HAV, and PCV13 in US only)	PRIORIX: 3,719 (3,714) Lot 1: 1,239 (1,239) Lot 2: 1,234 (1,232) Lot 3: 1,246 (1,243) M-M-R II: 1,291 (1,289)
Trial # 2: MMR-158 Immunogenicity Safety (NCT01621802)	US Republic of Korea Taiwan	Phase 3, observer-blind, randomized, controlled study to evaluate non-inferiority PRIORIX as a second dose vs. M-M-R II as a second dose	Healthy children 4 through 6 years (1 dose at Day 0 with VV and DTaP-IPV in a US-only sub-cohort)	PRIORIX: 2,918 (2,917) Sub-cohort 1: 802 (802) Sub-cohort 2: 796 (796) Sub-cohort 3: 1,320 (1,319) M-M-R II: 1,091 (1,090) Sub-cohort 1: 299 (298) Sub-cohort 2: 303 (303) Sub-cohort 3: 489 (489)
Trial # 3: MMR-161 Immunogenicity Safety (NCT01681992)	US (including Puerto Rico) Czech Republic Finland Malaysia Spain Thailand	Phase 3, observer-blind, randomized, controlled study to evaluate the immunogenicity and safety of PRIORIX at an end of shelf-life potency (established for each antigen) vs. MMR-II	Healthy children 12 through 15 months (2 doses: 1 at Day 0 with VV and HAV, and PCV13 in US only and 1 at Day 42)	PRIORIX: 2998 (2990) Min: 1497 (1493) Med: 1501 (1497) M-M-R II: 1530 (1526)
Trial # 4: MMR-162 Safety Immunogenicity (NCT02184572)	US (including Puerto Rico) Estonia Finland Taiwan	Phase 3, observer-blind, randomized, controlled study to evaluate the safety and immunogenicity of PRIORIX (at a potency used to define maximum release limits) vs. MMR-II, as a first dose	Healthy children 12 through 15 months (1 dose at Day 0 with VV and HAV, and PCV13 in US only)	PRIORIX: 1165 (1164) M-M-R II: 575 (572)
Trial # 5: MMR-159 Immunogenicity Safety (NCT02058563)	US Estonia Slovakia	Phase 3, observer-blind, randomized, controlled study to evaluate non-inferiority of PRIORIX as a second dose vs. M-M-R II as a second dose	Healthy children, adolescents, and adults ≥ 7 years primed with at least 1 dose of an MMR vaccine (1 dose at Day 0)	PRIORIX: 497 (454) M-M-R II: 497 (457)

mIU/mL and White: 2831.4 mIU/mL). Otherwise, the immune responses by country, gender, and race were similar to those reported in the primary immunogenicity analyses.

6.1.11.4 Dropouts and/or Discontinuations

Approximately 95% of enrolled participants completed the study. Missing or non-evaluable immunogenicity measurements were not replaced. Immunogenicity analyses therefore excluded participants with missing or non-evaluable measurements. See Section 6.1.10.1.2.

6.1.11.5 Exploratory and Post Hoc Analyses

Not applicable.

6.1.12 Safety Analyses

6.1.12.1 Methods

Safety data surveillance is described in Section 6.1.7 above and shown in Table 16. Participant compliance with returning symptom sheets for collection of local and systemic solicited AEs following administered vaccines was ≥95.4%.

6.1.12.2 Overview of Adverse Events

Safety Overview
Safety data were collected for PRIORIX groups (by lot and pooled) and the M-M-R II group (pooled lots). Safety data were overall similar between individual lots and pooled lots for PRIORIX groups. Table 16 provides an overview of the rates of adverse events in the pooled PRIORIX lots compared to the pooled M-M-R II lots during the study period.

Table 16. Proportion of Participants Reporting at Least One Adverse Event Following MMR Vaccination, TVC, Study MMR-160

AE Type: Monitoring Period[a]	PRIORIX % (n/N)	M-M-R II % (n/N)
Immediate AE: 30 minutes	0.1% (3/3714)	0.2% (3/1289)
Solicited local at injection site[b]: 0-3 days	39.8% (1416/3555)	41.5% (515/1242)
Solicited systemic[c]: 0-14 days	71.8% (2560/3566)	74.7% (929/1243)
Fever (temperature ≥38.0 ºC): 0-42 days	34.7% (1239/3566)	33.1% (411/1243)
Rash: 0-42 days	29.2% (1043/3566)	30.4% (378/1243)
varicella-like rash	7.0% (250/3566)	6.8% (85/1243)
Measles/rubella-like rash	6.6% (235/3566)	6.2% (77/1243)
Other rash	19.0% (679/3566)	20.8% (259/1243)
Parotid/salivary gland swelling: 0-42 days	0	0
Meningism[d]: 0-42 days	0.3% (10/3566)	0.2% (3/1243)
Unsolicited: 0-42 days	50.0% (1857/3714)	47.9% (618/1289)
AEs leading to study w/d: Entire study period	<0.01% (2/3714)	0
SAEs: Entire study period	2.1% (77/3714)	1.9% (25/1289)

AE Type: Monitoring Period[a]	PRIORIX % (n/N)	M-M-R II % (n/N)
AEs of specific interest[e]: Entire study period	12.9% (478/3714)	13.1% (169/1289)
Deaths: Entire study period	0	0

Source: Adapted from STN 125748/0, MMR-160 Clinical Study Report Amendment 2, Section 8.2.1, Table 23, Table 24, Tables 47-50, Table 8.44, and MMR (RIT) Analysis #16 Table 6
Abbreviations: AE=adverse event; N=number of participants in population; n=number of participants who experienced the event; SAE=serious adverse event; TVC=Total Vaccinated Cohort was used as the analyses set for safety; w/d=withdrawal
Temperature 38.0 C =100.4 F
Note: For unsolicited events, the N is the number of participants in the TVC; For solicited local events, the N is the number of participants from the TVC with documented local events; For solicited systemic events, the N is the number of participants from the TVC with documented systemic events.
Two different lots of M-M-R II were used during this study. Data from both lots were pooled for this summary.
Data from the three PRIORIX lots were pooled for this summary.
a. Monitoring Period: time interval that the relevant type of AE was monitored for post-vaccination
b. Solicited local included pain, redness, and swelling at injection site
c. Solicited systemic included any systemic symptom including drowsiness, loss of appetite, or irritability
d. Signs or symptoms indicative of meningism (i.e., neck stiffness with or without light intolerance [photophobia] and headache; or convulsion/seizure) and included febrile convulsions
e. AEs of specific interest included new onset chronic disease (NOCD, e.g., autoimmune disorders, asthma, type I diabetes, vasculitis, celiac disease, conditions associated with sub-acute or chronic thrombocytopenia and allergies) and AEs prompting emergency room (ER) visit

The rates for any reported AE, including local and systemic solicited reactions, unsolicited AEs, and SAEs, were similar between the PRIORIX and M-M-R II pooled groups. Overall, 87.1% and 88.3% of participants, respectively, reported at least one solicited or unsolicited symptom during the 43-day post-vaccination period. There were two AEs in the PRIORIX group that led to study withdrawal and no deaths throughout the entire study period for either group.

Subpopulation Analyses

Descriptive summary safety data were reported by country, gender, and race if there were at least 50 participants per treatment group. In general, findings were similar to those reported in the safety analyses for the overall group. No clinically meaningful differences between vaccine groups in incidence of solicited local or systemic symptoms were observed in females and males or in any race group.

Solicited Adverse Reactions

Table 17 includes the percentages of PRIORIX and M-M-R II participants who reported any solicited adverse reactions, which are stratified by grade.

Table 17. Proportion of Participants With Solicited Reactions Post-Vaccination, TVC, Study MMR-160

Solicited Adverse Reaction	PRIORIX N=3555-3566	M-M-R II N=1242-1243
Local (injection site)	--	--
Pain[a], % (n/N)	--	--
Any	25.9% (919/3555)	28.1% (349/1242)
Grade 0	0.1% (2/3555)	0.0% (0/1242)
Grade 1	19.6% (697/3555)	20.9% (260/1242)
Grade 2	5.5% (196/3555)	6.2% (77/1242)
Grade 3	0.7% (24/3555)	1% (12/1242)
Erythema, % (n/N)	--	--
Any	24.5% (870/3555)	25.2% (313/1242)
Grade 0 (none)	0.1% (2/3555)	0.0% (0/1242)
Grade 1 (>0 to ≤5 mm)	20.5% (728/3555)	21.9% (272/1242)
Grade 2 (>5 to ≤20 mm)	3.5% (126/3555)	2.7% (33/1242)
Grade 3 (>20 mm)	0.4% (14/3555)	0.6% (8/1242)

Table 29. Proportion of Participants Reporting at Least One Adverse Event Following MMR Vaccination, TVC, Study MMR-158

AE Type: Monitoring Period[a], % (n/N)	PRIORIX Sub-cohort 1	M-M-R II Sub-cohort 1	PRIORIX Sub-cohort 2	M-M-R II Sub-cohort 2	PRIORIX Sub-cohort 3	M-M-R II Sub-cohort 3
Immediate AE: 30 minutes	0	0	0	0	0	0
Solicited local at injection site[b]: 0-3 days	48.3% (351/727)	48.7% (130/267)	29.8% (228/766)	30.4% (88/289)	33.0% (426/1289)	36.9% (177/480)
Solicited systemic[c]: 0-3 days	33.5% (245/731)	33.2% (89/268)	NA	NA	NA	NA
Fever (Any): 0-42 days	24.2% (177/731)	25.0% (67/268)	19.0% (146/767)	19.9% (58/291)	19.9% (257/1291)	20.0% (96/481)
Rash: 0-42 days	--	--	--	--	--	--
Any rash	8.3% (61/731)	10.4% (28/268)	4.8% (37/767)	4.1% (12/291)	4.3% (56/1291)	4.8% (23/481)
varicella-like rash[d]	0.5% (4/731)	1.1% (3/268)	NA	NA	NA	NA
Measles/rubella-like rash	1.9% (14/731)	1.9% (5/268)	0.4% (3/767)	0.7% (2/291)	0.3% (4/1291)	0.4% (2/481)
Other rash (not measles/rubella-like)	6.2% (45/731)	7.5% (20/268)	4.4% (34/767)	3.4% (10/291)	4.0% (52/1291)	4.4% (21/481)
Parotid/salivary gland swelling: 0-42 days	0	0	0	0.3% (1/291)	0.1% (1/1291)	0.2% (1/481)
Meningism[e]: 0-42 days	0	0.7% (2/268)	0.1% (1/767)	0	0	0
Unsolicited: 0-42 days	34.4% (276/802)	30.2% (90/298)	39.4% (314/796)	37.0% (112/303)	38.5% (508/1319)	38.0% (186/489)
AEs leading to study w/d: Entire study period	0	0	0	0	0	0
SAEs: Entire study period	0.5% (4/802)	0	1.8% (14/796)	0.3% (1/303)	1.9% (25/1319)	1.8% (9/489)

AE Type: Monitoring Period[a], % (n/N)	PRIORIX Sub-cohort 1	M-M-R II Sub-cohort 1	PRIORIX Sub-cohort 2	M-M-R II Sub-cohort 2	PRIORIX Sub-cohort 3	M-M-R II Sub-cohort 3
AEs of specific interest[f]: Entire study period	8.5% (68/802)	10.7% (32/298)	8.5% (68/796)	7.3% (22/303)	8.4% (111/1319)	7.8% (38/489)
Deaths: Entire study period	0	0	0	0	0	0

Source: Adapted from STN 125748/0, MMR-158 Clinical Study Report Amendment 2 Section 8.2.1 and Tables 24, 25, 26, 27, 28, 29, 69, 70, 71, 72, 73, 74, 75, 85, 8.67, 8.71, 8.72, 8.73, 8.77, 8.78, and 8.79; MMR (RIT) Analysis #16 Tables 1, 2, and 3.
Abbreviations: AE=adverse event; N=number of participants in cohort; n=number of participants who experienced the event; SAE=serious adverse event; TVC=Total Vaccinated Cohort was used as the analyses set for safety; w/d=withdrawal
Temperature 38.0 C =100.4 F
Note: For unsolicited events, the N is the number of participants in the TVC; For solicited local events, the N is the number of participants from the TVC with documented local events; For solicited systemic events, the N is the number of participants from the TVC with documented systemic events.
Note: Sub-cohort 1 (co-administration) = GSK PRIORIX or Merck M-M-R II concomitantly administered with varicella vaccine and DTaP-IPV and analyzed for immunogenicity and safety.
Sub-cohort 2 (immunogenicity) = GSK PRIORIX or Merck M-M-R II alone and analyzed for immunogenicity and safety.
Sub-cohort 3 (safety) = GSK PRIORIX or Merck M-M-R II alone and analyzed for safety only.
a. Monitoring Period: time interval that the relevant type of AE was monitored for post-vaccination
b. Solicited local includes pain, redness, and swelling at injection site
c. Drowsiness and loss of appetite are standard solicited symptoms in clinical trials evaluating DTaP-IPV vaccine recipients
d. Only collected for participants who received varicella vaccine
e. Signs or symptoms indicative of meningism (i.e., neck stiffness with or without light intolerance [photophobia] and headache; or convulsion/seizure) and includes febrile convulsions
f. AEs of specific interest includes new onset chronic disease (NOCD, e.g., autoimmune disorders, asthma, type I diabetes, vasculitis, celiac disease, conditions associated with sub-acute or chronic thrombocytopenia and allergies) and AEs prompting emergency room (ER) visit

Table 40. Proportion of Participants Reporting at Least One Adverse Event Following MMR Vaccination, TVC, Study MMR-161

AE Type: Monitoring Period[a], % (n/N)	Medium Potency PRIORIX Post-Dose 1	M-M-R II Post-Dose 1	Medium Potency PRIORIX Post-Dose 2	M-M-R II Post-Dose 2
Immediate AE: 30 minutes	0.1% (1/1497)	0	0	0
Solicited local at injection site[b]: 0-3 days after each dose	28.6% (419/1464)	31.2% (462/1482)	21.1% (304/1440)	22.7% (330/1456)
Solicited systemic[c]: 0-14 days after dose 1	64.7% (948/1466)	62.4% (927/1486)	NA	NA
Fever (temperature ≥38.0 ºC): 0-42 days after each dose	42.0% (616/1466)	41.5% (616/1486)	32.5% (469/1443)	34.3% (499/1455)
Rash: 0-42 days after each dose	22.0% (322/1466)	22.4% (333/1486)	10.4% (150/1443)	9.7% (141/1455)
Varicella-like rash	3.6% (53/1466)	3.0% (45/1486)	0	0.1% (1/1455)
Measles/rubella-like rash	4.2% (61/1466)	4.6% (68/1486)	1.0% (14/1443)	1.0% (14/1455)
Other rash	15.7% (230/1466)	16.6% (247/1486)	9.6% (138/1443)	8.7% (127/1455)
Parotid/salivary gland swelling: 0-42 days after each dose	0.1% (2/1466)	0.2% (3/1486)	0.1% (2/1443)	0
Meningism[d]: 0-42 days after each dose	0.3% (4/1466)	0.2% (3/1486)	0.4% (6/1443)	0.3% (4/1455)
Unsolicited: 0-42 days	53.0% (794/1497)	50.9% (777/1526)	48.0% (703/1464)	46.5% (690/1483)
AEs leading to study w/d: Entire study period	NA	NA	0.1% (2/1497)	0.2% (3/1526)
SAEs: Entire study period	NA	NA	6.8% (102/1497)	6.0% (92/1526)
AEs of specific interest[e]: Entire study period	NA	NA	25.7% (384/1497)	24.2% (370/1526)
Deaths: Entire study period	NA	NA	0.06% (1/1497)	0.06% (1/1526)

Source: Adapted from STN 125748/0, MMR-161 Clinical Study Report Amendment 2, Section 8.2.1, Table 22, Tables 44-46, Table 8.2, and MMR (RIT) Analysis #16 Tables 7-12
Abbreviations: AE=adverse event; N=number of participants in cohort; n=number of participants who experienced the event; SAE=serious adverse event; TVC=Total Vaccinated Cohort was used as the analyses set for safety; w/d=withdrawal
Temperature 38.0 C =100.4 F
Note: For unsolicited events, the N is the number of participants in the TVC
Note: For solicited local events, the N is the number of participants from the TVC with documented local events
Note: For solicited systemic events, the N is the number of participants from the TVC with documented systemic events
a. Monitoring Period: time interval that the relevant type of AE was monitored for post-vaccination
b. Solicited local includes pain, redness, and swelling at injection site
c. Solicited systemic includes any systemic symptom including drowsiness, loss of appetite, or irritability
d. Signs or symptoms indicative of meningism (i.e., neck stiffness with or without light intolerance [photophobia] and headache; or convulsion/seizure) and includes febrile convulsions
e. AEs of specific interest includes new onset chronic disease (NOCD, e.g., autoimmune disorders, asthma, type I diabetes, vasculitis, celiac disease, conditions associated with sub-acute or chronic thrombocytopenia and allergies) and AEs prompting emergency room (ER) visit

Overall, for any solicited or unsolicited symptom, the rates were similar across groups. Post-dose 1, the rate was 85.1% in the minimum potency PRIORIX group, 86.3% in the medium potency PRIORIX group, and 84.8% in the M-M-R II group. Rates were also similar across groups post-dose 2, and lower than following the first dose, at 63.9%, 67.4%, and 67.0%, respectively. There were 4 AEs (2 in the min potency PRIORIX group and 1 each in the med potency PRIORIX and M-M-R II groups), 1 nonfatal SAE (M-M-R II group), and 3 fatal events (1 each in the min potency PRIORIX group, med potency PRIORIX group, and M-M-R II group) that led to premature discontinuation from the study. None of these events were considered by the investigator to be related to the study vaccination.

6.4.12.2 Overview of Adverse Events

Co-Primary objectives: Rates of Fever

The comparability of observed rates of fever between groups was determined if the upper limit of the 95% CI for the difference [PRIORIX minus M-M-R II] in fever rates was <5% when fever was defined as >39.0°C (Primary Objective #1) and was <10% when fever was defined as ≥38.0°C (Primary Objective 2). The co-primary objectives of Fever >39.0°C and Fever ≥38.0°C were ***met*** as shown in Table 46.

Table 46. Percentage Difference in Participants Reporting Fever, Days 5 Through 12 Post-Vaccination, TVC, Study MMR-162

Axillary Temperature	PRIORIX N=1,126 n (%)	M-M-R II N=555 n (%)	PRIORIX-M-M-R II Difference Percentage (95% CI)
All	250 (22.2%)	123 (22.2%)	0.04% (-4.28, 4.17)
≥38.0°C	205 (18.2%)	95 (17.1%)	1.09% (-2.89, 4.85)
>39.0°C	47 (4.2%)	17 (3.1%)	1.11% (-0.93, 2.89)

Source: Adapted from STN 125748/0, Study MMR-162 Amendment 2, Table 22
Abbreviations: CI=confidence interval; N=number of participants in TVC; n=number of participants fulfilling the item followed by (%); TVC=Total Vaccinated Cohort was used as the analyses set for safety
Note: Two different lots of M-M-R II were used during this study. Data from both lots were pooled for this summary.

Safety Overview

Safety data were presented for the PRIORIX group and the M-M-R II groups (pooled lots). Table 47 provides an overview of the rates of adverse events in the PRIORIX lot compared to the pooled M-M-R II lots during the study period.

Table 47. Proportion of Participants Reporting at Least One Adverse Event Following MMR Vaccination, TVC, Study MMR-162

AE Type: Monitoring Period[a]	PRIORIX % (n/N)	M-M-R II % (n/N)
Immediate AE: 30 minutes	0.1% (1/1164)	0
Solicited local at injection site[b]: 0-3 days	40.2% (451/1123)	38.5% (213/553)
Solicited systemic[c]: 0-14 days	71.3% (803/1126)	70.1% (389/555)
Measles-like illness[d]: 5-12 days	1.5% (18/1164)	0.9% (5/572)
Temperature ≥38.0ºC: 0-42 days	31.1% (350/11260)	32.3% (179/555)
Rash: 0-42 days	24.4% (275/1126)	27.4% (152/555)
Parotid gland swelling: 0-42 days	0	0
Meningism[e]: 0-42 days	0.2% (2/1126)	0
Unsolicited AE: 0-42 days	51.4% (598/1164)	48.4% (277/572)
AEs leading to study withdrawal: Entire study period	0	0
SAEs: Entire study period	2.1% (24/1164)	1.6% (9/572)

AE Type: Monitoring Period[a]	PRIORIX % (n/N)	M-M-R II % (n/N)
AEs of specific interest[f]: Entire study period	16.4% (191/1164)	11.0% (63/572)
Deaths: Entire study period	0	0

Source: Adapted from STN 125748/0, Study MMR-162, Clinical Study Report Amendment 2, Section 7.2.1, Table 17, Table 18, Tables 26-29, Table 33, and MMR (RIT) Analysis #16 Table 13
TVC: Total Vaccinated Cohort was used as the analyses set for safety. n: #participants who experienced the event; C: degrees Celsius. AE: adverse event; AEs leading to w/d: adverse events leading to study withdrawal; SAEs: serious adverse events.
Temperature 38.0 C =100.4 F
Note: For unsolicited events, the N is the number of participants in the TVC (see Table B); For solicited local events, the N is the number of participants from the TVC with documented local events; For solicited systemic events, the N is the number of participants from the TVC with documented systemic events.
a. Monitoring Period: time interval that the relevant type of AE was monitored for post-vaccination
b. Solicited local includes pain, redness, and swelling at injection site
c. Solicited systemic includes any systemic symptom including drowsiness, loss of appetite, or irritability
d. Measles-like illness is defined as the occurrence of the following signs and symptoms in the absence of another confirmed diagnosis: maculopapular rash and fever (≥38 C), and at least one symptom of cough, coryza, conjunctivitis, or diarrhea, with fever or rash occurring between Day 5 and Day 12 inclusive.
e. Signs or symptoms indicative of meningism (i e., neck stiffness with or without light intolerance [photophobia] and headache; or convulsion/seizure) and included febrile convulsions
f. AEs of specific interest included new onset chronic disease (NOCD, e.g., autoimmune disorders, asthma, type I diabetes, vasculitis, celiac disease, conditions associated with sub-acute or chronic thrombocytopenia and allergies) and AEs prompting emergency room (ER) visit

The rates for any reported AE including local and systemic solicited reactions, unsolicited AEs and SAEs were comparable between groups. Overall, 51.4% and 48.8% of participants in the PRIORIX and M-M-R II groups, respectively, reported at least one solicited or unsolicited symptom during the 43-day post-vaccination period. There were no AEs that lead to study withdrawal and no deaths throughout the entire study period for either group.

Subpopulation Analyses

Descriptive summary safety data were reported by country, gender, and race (geographic ancestry). In general, findings were similar to those reported in the safety analyses for the overall group. Number and percentages of those compliant in returning symptom information and incidence and nature of symptoms reported (local and systemic reactions) were similar when evaluated as sub-groups. No clinically meaningful differences between vaccine groups in incidence of solicited local or general symptoms were observed in females and males or in any race group.

Solicited Adverse Reactions

Table 48 includes the percentages of PRIORIX and M-M-R II participants who reported any solicited adverse reactions, which are stratified by grade.

Table 48. Proportion of Participants With Solicited Reactions Post-Vaccination, TVC, Study MMR-162

Solicited Adverse Reaction	PRIORIX N=1123-1126	M-M-R II N=553-555
Local (injection site)	--	--
Pain[a], % (n/N)	--	--
Any	27.8% (312/1123)	23.7% (131/553)
Grade 1	21.5% (242/1123)	18.6% (103/553)
Grade 2	5.7% (64/1123)	4.7% (26/553)
Grade 3	0.5% (6/1123)	0.4% (2/553)
Erythema, % (n/N)	--	--
Any	23.2% (260/1123)	24.8% (137/553)
Grade 1 (>0 to ≤5 mm)	18.1% (203/1123)	19.9% (110/553)
Grade 2 (>5 to ≤20 mm)	4.4% (49/1123)	3.6% (20/553)
Grade 3 (>20 mm)	0.7% (8/1123)	1.3% (7/553)

Safety data were presented for PRIORIX and M-M-R II groups. Table 55 provides an overview of the rates of adverse events in the PRIORIX compared to the M-M-R II groups during the study period.

Table 55. Proportion of Participants Reporting at Least One Adverse Event Following MMR Vaccination, TVC, Study MMR-159

AE Type: Monitoring Period[a]	PRIORIX % (n/N)	M-M-R II % (n/N)
Immediate AE: 30 minutes	0.4% (2/454)	1.1% (5/457)
Solicited local at vaccine site[b]: 0-3 days	19.4% (84/433)	19.3% (86/445)
Solicited systemic[c]:	NA	NA
Temperature ≥38.0 ºC: 0-42 days	3.0% (13/431)	5.2% (23/445)
Rash: 0-42 days	2.1% (9/431)	1.1% (5/445)
Parotid gland swelling: 0-42 days	0.2% (1/431)	0.2% (1/445)
Arthralgia/Joint pain	1.9% (8/431)	0.9% (4/445)
Meningism[d]: 0-42 days	0.2% (1/431)	0.2% (1/445)
Unsolicited AE: 0-42 days	20.9% (95/454)	17.9% (82/457)
AEs leading to study withdrawal: Entire study period	0	0
SAEs: Entire study period	0	0
AEs of specific interest[e]: Entire study period	3.5% (16/454)	2.2% (10/457)
Deaths: Entire study period	0	0

Source: Adapted from STN 125748/0, MMR-159, Clinical Study Report Amendment 1, Table 14, Table 15, Tables 24-30, and MMR (RIT) Analysis #16 Table 4
Abbreviations: AE=adverse event; N=number of participants in cohort; n=number of participants who experienced the solicited event; SAE=serious adverse event; TVC=Total Vaccinated Cohort was used as the analyses set for safety
Temperature 38.0 C=100.4 F
Note: For unsolicited events, the N is the number of participants in the TVC; For solicited local events, the N is the number of participants from the TVC with documented local events; For solicited systemic events, the N is the number of participants from the TVC with documented systemic events
a. Monitoring Period: time interval that the relevant type of AE was monitored for post-vaccination.
b. Solicited local includes pain, redness, and swelling at injection site.
c. Due to ages of the participants, the following solicited systemic reactions were not collected in this study: drowsiness, loss of appetite, or irritability/fussiness.
d. Signs or symptoms indicative of meningism (i.e., neck stiffness with or without light intolerance [photophobia] and headache; or convulsion/seizure) and included febrile convulsions.
e. AEs of specific interest included new onset chronic disease (NOCD, e.g., autoimmune disorders, asthma, type I diabetes, vasculitis, celiac disease, conditions associated with sub-acute or chronic thrombocytopenia and allergies) and AEs prompting emergency room (ER) visit

Within 43 days post-vaccination, the rates for any reported AE, including local and systemic, solicited reactions, unsolicited AEs, and SAEs were generally similar between the PRIORIX and M-M-R II groups. Overall, 35.7% and 33.9% of participants, respectively reported at least one solicited or unsolicited symptom during the 43-day post-vaccination period. There were no AEs in the PRIORIX group that let to study withdrawal and no deaths throughout the entire study period for either group.

Subpopulation Analyses

Descriptive summary safety data were reported by country, gender, and age. In general, findings were similar to those reported in the safety analyses for the overall group. No clinically meaningful differences between vaccine groups in incidence of solicited local or general symptoms were observed in females and males or in any age group.

Solicited Adverse Reactions

Table 56 includes the percentages of PRIORIX and M-M-R II participants who reported any solicited adverse reactions, which are stratified by grade.

Exhibit 21

An official website of the United States government Here's how you know

What is a Serious Adverse Event?

Subscribe to Email Updates

Share Tweet LinkedIn Email Print

Reporting Serious Problems to FDA

- What is a Serious Adverse Event?
- Product Problems
- Reporte problemas serios a la FDA
- ¿Qué es una reacción adversa grave?
- Problemas con los productos

Content current as of:
05/18/2023

An adverse event is any undesirable experience associated with the use of a medical product in a patient. The event is serious and should be reported to FDA when the patient outcome is:

Death

Report if you suspect that the death was an outcome of the adverse event, and include the date if known.

Life-threatening

Report if suspected that the patient was at substantial risk of dying at the time of the adverse event, or use or continued use of the device or other medical product might have resulted in the death of the patient.

Hospitalization (initial or prolonged)

Report if admission to the hospital or prolongation of hospitalization was a result of the adverse event.

Emergency room visits that do not result in admission to the hospital should be evaluated for one of the other serious outcomes (e.g., life-threatening; required intervention to prevent permanent impairment or damage; other serious medically important event).

Disability or Permanent Damage

Report if the adverse event resulted in a substantial disruption of a person's ability to conduct normal life functions, i.e., the adverse event resulted in a significant, persistent or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities and/or quality of life.

Congenital Anomaly/Birth Defect

Report if you suspect that exposure to a medical product prior to conception or during pregnancy may have resulted in an adverse outcome in the child.

Required Intervention to Prevent Permanent Impairment or Damage (Devices)

Report if you believe that medical or surgical intervention was necessary to preclude permanent impairment of a body function, or prevent permanent damage to a body structure, either situation suspected to be due to the use of a medical product.

Other Serious (Important Medical Events)

Report when the event does not fit the other outcomes, but the event may jeopardize the patient and may require medical or surgical intervention (treatment) to prevent one of the other outcomes. Examples include allergic brochospasm (a serious problem with breathing) requiring treatment in an emergency room, serious blood dyscrasias (blood disorders) or seizures/convulsions that do not result in hospitalization. The development of drug dependence or drug abuse would also be examples of important medical events.

Resources For You

- Report a Serious Medical Product Problem Online
- Report Dietary Supplements and Tobacco Product Problems Online
- Form FDA 3500 - Voluntary Reporting

MedWatch safety alerts delivered to you
Clinically important and timely information about the drugs and devices you use, prescribe, or dispense every day, delivered to your email from the FDA.

Email Address Subscribe

Exhibit 22

VITAL STATISTICS RATES IN THE UNITED STATES 1940–1960

By
Robert D. Grove, Ph. D.
and
Alice M. Hetzel

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
Washington, D.C. 1968
National Center for Health Statistics

For sale by the Superintendent of Documents, U.S. Government Printing Office
Washington, D.C. 20402 - Price $5.25

NATIONAL CENTER FOR HEALTH STATISTICS

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ARNE B. NELSON, M.A., *Chief, Vital Records Survey Branch*
MICHAEL J. ZUGZDA, *Acting Chief, Statistical Resources Section*

Public Health Service Publication No. 1677

Figure 19.—Death Rates for Measles: Death-registration States, 1900–32, and United States, 1933–60

(Rates per 100,000 population)

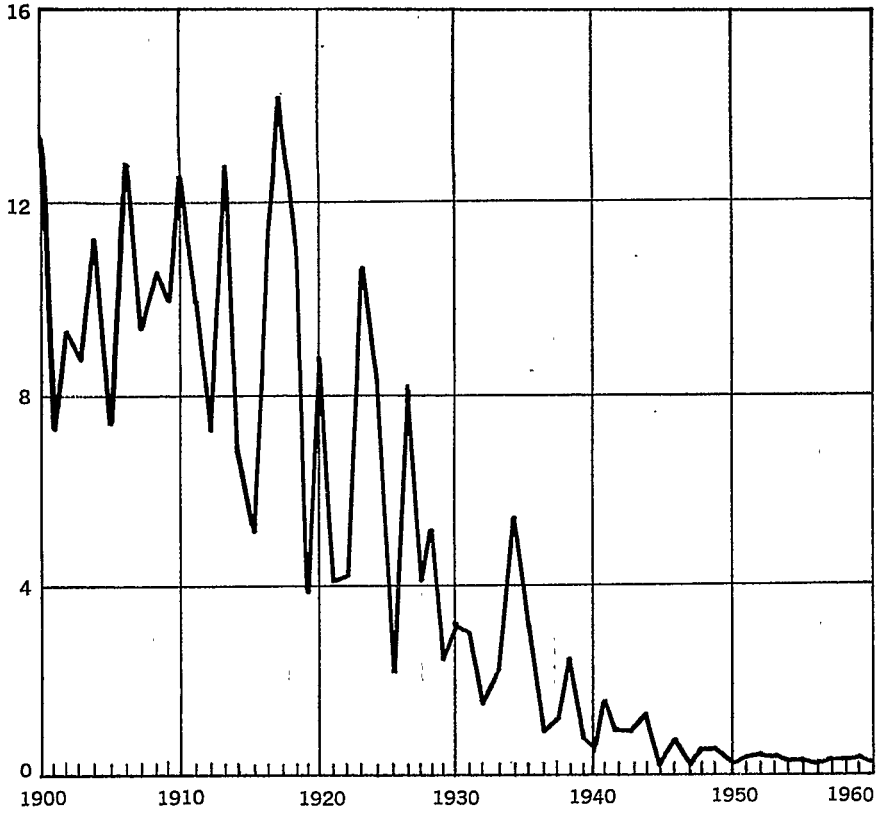

TABLE 65.—*Death rates for detailed causes: Death-registration States, 1900–1932, and United States, 1933–60*

Section A, 1900–1909

[Rates are deaths per 100,000 population. Numbers before causes of death are category numbers of First Revision of the International Lists]

Int. List No.	Cause of death	1900	1901	1902	1903	1904	1905	1906	1907	1908	1909
	All causes	1,719.1	1,641.5	1,548.1	1,562.8	1,640.0	1,588.9	1,571.8	1,592.5	1,468.2	1,424.7
	I.—General diseases	466.5	456.0	412.2	421.4	430.1	408.3	412.6	416.3	391.5	372.3
1	Typhoid fever (abdominal typhus)	31.3	27.6	26.4	24.6	23.9	22.4	30.9	28.2	23.4	20.2
2	Exanthematic typhus	0.0	—	0.0	—	0.0	0.0	—	0.0	—	0.0
3	Relapsing fever	0.0	0.0	0.0	0.0	0.0	—	0.0	—	0.0	—
4	Intermittent fever and malarial cachexia	6.2	5.0	4.0	3.0	2.9	2.5	2.3	1.8	1.3	1.4
5	Smallpox	0.3	3.6	6.5	1.5	0.8	0.6	0.2	0.1	0.2	0.1
6	Measles	13.3	7.4	9.3	8.8	11.3	7.4	12.9	9.6	10.6	10.0
7	Scarlet fever	9.6	13.6	11.9	12.3	11.6	6.8	7.3	9.3	12.4	11.1
8	Whooping cough	12.2	8.7	12.4	14.3	5.8	8.9	16.1	11.3	10.7	10.0
9	Diphtheria and croup	40.3	33.5	29.8	31.1	29.3	23.5	26.3	24.2	21.9	19.9
10	Influenza	26.7	36.5	10.4	19.2	21.8	20.5	10.2	25.0	21.1	13.3
11	Miliary fever	—	—	0.0	0.0	0.0	—	—	—	0.0	—
12	Asiatic cholera	—	—	—	—	—	—	—	—	—	—
13	Cholera nostras	2.8	1.8	1.4	1.2	1.2	1.4	1.4	1.0	1.1	0.8
14	Dysentery	12.0	11.1	10.1	7.3	8.1	8.3	8.0	6.1	6.1	5.4
15	Bubonic plague	—	0.0	—	—	—	—	—	0.2	0.0	0.0
16	Yellow fever	0.0	0.0	0.0	—	—	0.0	—	—	—	—
17	Leprosy	—	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
18	Erysipelas	5.4	4.5	4.1	4.0	5.1	4.7	4.3	4.4	3.8	3.9
19	Other epidemic diseases	0.2	0.1	0.2	0.2	0.2	0.2	0.4	0.3	0.3	0.3
20	Purulent infection and septicemia	7.2	5.9	5.9	4.7	4.9	4.4	3.8	3.7	3.2	2.9
21	Glanders and farcy	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
22	Malignant pustule	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.0	0.0
23	Rabies	0.1	0.1	0.1	0.1	0.0	0.1	0.2	0.2	0.2	0.1
24	Actinomycosis, trichinosis, etc.	0.0	0.0	0.0	0.0	0.1	0.1	0.0	0.0	0.1	0.1
25	Pellagra	0.0	—	—	0.0	—	—	—	—	—	0.0
	Tuberculosis (all forms)	194.4	189.9	174.2	177.2	188.1	179.9	175.8	174.2	162.1	156.3
26	Tuberculosis of the larynx	1.2	1.6	1.6	1.5	1.6	1.6	1.5	1.6	1.5	1.6
27	Tuberculosis of the lungs	173.3	167.9	152.8	154.2	164.2	155.5	151.8	150.4	138.6	133.3
28	Tuberculosis of the meninges	9.4	9.1	9.2	9.6	9.8	9.9	9.8	9.8	9.4	9.1
29	Abdominal tuberculosis	4.9	5.4	5.1	5.2	5.8	5.8	6.0	5.8	5.7	5.9
30	Pott's disease	1.5	1.4	1.4	1.5	1.6	1.6	1.5	1.4	1.6	1.4
31	Cold abscess, abscess by congestion	0.1	0.1	0.1	0.2	0.2	0.2	0.1	0.2	0.2	0.1
32	White swelling	0.6	0.6	0.6	0.6	0.7	0.8	0.8	0.6	0.8	0.7
33	Tuberculosis of other organs	1.0	1.2	1.1	1.4	1.6	1.5	1.6	1.6	1.7	1.7
34	General tuberculosis	2.3	2.7	2.4	3.0	2.7	3.0	2.6	2.8	2.8	2.3

TABLE 65.—*Death rates for detailed causes: Death-registration States, 1900–1932, and United States, 1933–60*—Continued
Section F, 1949–1960—Continued

Cause of death	1949	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960
I.—Infective and parasitic diseases—Continued												
Syphilis and its sequelae—Continued												
Other syphilis of central nervous system 026	0.6	0.5	0.5	0.4	0.3	0.3	0.3	0.2	0.2	0.2	0.2	0.1
All other syphilis 027–029	0.2	0.2	0.2	0.1	0.1	0.1	0.1	0.1	0.0	0.0	0.0	0.0
Gonococcal infection 030–035	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Typhoid fever 040	0.1	0.1	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Paratyphoid fever and other Salmonella infections 041, 042	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Cholera 043	—	—	—	—	—	—	—	—	—	—	—	—
Brucellosis (undulant fever) 044	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Dysentery, all forms 045–048	1.0	0.6	0.7	0.6	0.6	0.4	0.3	0.3	0.3	0.2	0.2	0.2
Food poisoning (infection and intoxication) 049	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.0	0.0	0.0	0.0	0.0
Scarlet fever 050	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Streptococcal sore throat 051	0.3	0.2	0.2	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Erysipelas 052	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Septicemia and pyemia 053	0.4	0.4	0.4	0.5	0.5	0.6	0.6	0.7	0.8	1.0	1.0	1.1
Diphtheria 055	0.4	0.3	0.2	0.1	0.1	0.1	0.1	0.1	0.0	0.0	0.0	0.0
Whooping cough 056	0.5	0.7	0.6	0.3	0.2	0.2	0.3	0.2	0.1	0.1	0.2	0.1
Meningococcal infections 057	0.6	0.6	0.7	0.9	0.8	0.6	0.6	0.5	0.5	0.4	0.4	0.4
Plague 058	0.0	0.0	—	—	—	—	—	0.0	—	—	0.0	—
Leprosy 060	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Tetanus 061	0.3	0.2	0.3	0.2	0.2	0.2	0.2	0.1	0.2	0.2	0.2	0.1
Anthrax 062	—	0.0	0.0	0.0	—	—	—	—	0.0	0.0	—	—
Acute poliomyelitis 080	1.8	1.3	1.0	2.0	0.9	0.8	0.6	0.3	0.1	0.1	0.3	0.1
Late effects of acute poliomyelitis 081	0.0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Acute infectious encephalitis 082	0.3	0.3	0.3	0.3	0.2	0.3	0.2	0.3	0.3	0.3	0.3	0.3
Late effects of acute infectious encephalitis 083	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.0
Smallpox 084	0.0	0.0	0.0	—	0.0	—	—	—	—	—	—	—
Measles 085	0.6	0.3	0.4	0.4	0.3	0.3	0.2	0.3	0.2	0.3	0.2	0.2
Yellow fever 091	—	—	—	—	—	—	—	—	—	—	—	—
Infectious hepatitis 092	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Rabies 094	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Tick-borne typhus 104	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Typhus, other and unspecified, and other rickettsial diseases 100–103, 105–108	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	—
Malaria 110–117	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Schistosomiasis 123	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Hydatid disease 125	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Filariasis 127	0.0	0.0	—	0.0	—	—	—	—	—	—	—	—
Ancylostomiasis 129	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	—	0.0	0.0	—
Other diseases due to helminths 124, 126, 128, 130	0.1	0.1	0.1	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
All other infective and parasitic diseases 036–039, 054, 059, 063–074, 086–090, 093, 095, 096, 120–122, 131–138	0.7	0.7	0.8	0.8	0.8	0.7	0.7	0.8	0.7	0.7	0.8	0.8

Exhibit 23

VITAL STATISTICS OF THE UNITED STATES

1962

VOLUME II—MORTALITY

PART A

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE

ANTHONY J. CELEBREZZE, SECRETARY

PUBLIC HEALTH SERVICE

LUTHER L. TERRY, SURGEON GENERAL

WASHINGTON: 1964

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Table 1-8. Death Rates for 60 Selected Causes: United States, 1953-62

(Data refer only to deaths occurring within the United States Alaska included beginning 1959, and Hawaii, 1960. Excludes fetal deaths. Rates per 100,000 population residing in area, enumerated as of April 1 for 1960 and estimated as of July 1 for all other years Numbers after causes of death are category numbers of the Seventh Revision of the International Lists, 1955. Deaths are classfied according to the Sixth Revision for 1953-57 and according to the Seventh Revision for 1958-62)

CAUSE OF DEATH	1962	1961	1960	1959	1958	1957	1956	1955	1954	1953
ALL CAUSES	945.4	929.6	954.7	938.6	950.7	958.5	935.1	930.4	919.0	959.0
Tuberculosis, all forms---001-019	5.1	5.4	6.1	6.5	7.1	7.8	8.4	9.1	10.2	12.4
Tuberculosis of respiratory system---001-008	4.7	5.0	5.6	6.0	6.6	7.3	7.8	8.3	9.3	11.3
Tuberculosis, other forms---010-019	0.4	0.4	0.4	0.5	0.5	0.6	0.6	0.8	0.8	1.1
Syphilis and its sequelae---020-029	1.5	1.6	1.6	1.7	2.0	2.2	2.3	2.3	3.0	3.3
Dysentery, all forms---045-048	0.2	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.4	0.6
Scarlet fever and streptococcal sore throat---050,051	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2
Diphtheria---055	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1
Whooping cough---056	0.0	0.0	0.1	0.2	0.1	0.1	0.2	0.3	0.2	0.2
Meningococcal infections---057	0.3	0.3	0.4	0.4	0.4	0.5	0.5	0.6	0.6	0.8
Acute poliomyelitis---080	0.0	0.0	0.1	0.3	0.1	0.1	0.3	0.6	0.8	0.9
Measles---085	0.2	0.2	0.2	0.2	0.3	0.2	0.3	0.2	0.3	0.3
Other infective and parasitic diseases---030-044,049,052-054,058-074,081-084,086-139	3.1	3.1	3.2	3.1	3.2	2.8	2.7	2.6	2.7	2.7
Malignant neoplasms, including neoplasms of lymphatic and hematopoietic tissues---140-205	148.9	149.4	149.2	147.3	146.8	148.6	147.8	146.5	145.6	144.8
Malignant neoplasm of buccal cavity and pharynx---140-148	3.5	3.5	3.4	3.4	3.3	3.4	3.3	3.4	3.3	3.2
Malignant neoplasm of digestive organs and peritoneum, not specified as secondary---150-159A,157-159	49.5	50.1	50.8	50.7	50.9	51.7	52.4	52.3	53.0	53.4
Malignant neoplasm of respiratory system, not specified as secondary---160-164	24.0	23.1	22.2	21.2	20.4	19.9	19.2	18.2	17.1	16.7
Malignant neoplasm of breast---170	13.4	13.4	13.4	13.1	13.1	13.3	13.3	13.4	13.0	13.0
Malignant neoplasm of genital organs---171-179	21.3	21.4	21.6	21.6	22.1	22.6	22.6	22.8	22.9	22.9
Malignant neoplasm of urinary organs---180,181	7.2	7.1	7.1	7.1	7.0	7.1	7.0	7.0	6.9	6.9
Malignant neoplasm of other and unspecified sites---156B,165,190-199	16.6	16.4	16.5	16.2	16.1	16.7	16.3	16.4	16.5	16.3
Leukemia and aleukemia---204	7.0	7.0	7.1	7.0	6.9	6.9	6.8	6.6	6.5	6.3
Lymphosarcoma and other neoplasms of lymphatic and hematopoietic tissues---200-203,205	7.4	7.4	7.2	7.1	6.9	7.0	6.8	6.5	6.3	6.1
Benign neoplasms and neoplasms of unspecified nature---210-239	3.6	3.5	2.7	2.6	2.9	3.0	2.9	3.1	3.2	3.3
Asthma---241	3.6	2.7	3.0	2.8	2.9	3.9	3.6	3.8	3.8	4.3
Diabetes mellitus---260	16.8	16.4	16.7	15.9	15.9	16.0	15.6	15.5	15.6	16.3
Anemias---290-293	1.8	1.8	1.9	1.8	1.8	1.8	1.9	1.9	2.0	2.3
Meningitis, except meningococcal and tuberculous---340	1.2	1.2	1.3	1.3	1.3	1.2	1.2	1.1	1.1	1.3
Major cardiovascular-renal diseases---330-334,400-468,592-594	521.4	511.5	521.8	515.9	523.5	523.4	510.5	506.0	495.2	514.8
Diseases of cardiovascular system---330-334,400-466	515.2	505.1	515.1	508.9	515.5	514.6	501.4	496.3	484.6	503.0
Vascular lesions affecting central nervous system---330-334	106.3	108.4	109.0	108.4	110.1	110.2	108.3	106.0	104.1	107.3
Diseases of heart---400-402,410-443	370.3	362.4	369.0	363.2	367.6	369.4	361.0	356.5	348.3	361.4
Rheumatic fever and chronic rheumatic heart disease---400-402,410-416	9.6	9.8	10.3	10.4	10.8	11.8	12.0	12.0	12.1	13.3
Arteriosclerotic heart disease, including coronary disease---420	283.9	274.4	275.6	268.6	266.2	265.6	255.5	247.0	235.7	236.1
Nonrheumatic chronic endocarditis and other myocardial degeneration---421,422	29.4	29.8	31.0	31.8	33.8	36.9	37.7	39.9	41.0	46.3
Other diseases of heart---430-443	13.9	15.8	14.5	13.8	14.2	12.8	12.6	12.6	13.0	14.3
Hypertensive heart disease---440-443	33.5	34.6	37.9	38.6	42.7	42.5	43.3	45.0	46.6	51.3
Other hypertensive disease---444-447	6.7	6.7	7.1	7.4	8.0	8.5	8.5	8.8	7.1	7.8
General arteriosclerosis---450	19.8	19.3	20.0	19.6	19.9	19.5	19.1	19.8	18.9	20.4
Other diseases of circulatory system---451-469	12.2	11.3	11.0	10.3	9.9	9.0	8.4	7.3	6.4	6.0
Chronic and unspecified nephritis and other renal sclerosis---592-594	6.1	6.3	6.7	7.0	8.0	8.8	9.1	9.6	10.6	11.9
Influenza and pneumonia, except pneumonia of newborn---480-493	32.3	30.1	37.3	31.2	33.1	35.8	28.2	27.1	25.4	33.0
Influenza---480-483	1.8	1.2	4.4	1.6	2.6	4.4	1.4	1.7	1.7	6.0
Pneumonia, except pneumonia of newborn---490-493	30.4	29.0	32.9	29.6	30.6	31.4	26.8	25.4	23.8	27.0
Bronchitis---500-502	2.5	2.2	2.4	2.2	2.3	2.1	1.9	1.9	1.8	1.8
Other bronchopulmonic diseases---525-527	10.6	9.7	9.6	8.5	8.2	8.1	7.0	6.1	5.4	5.1
Ulcer of stomach and duodenum---540,541	6.6	6.3	6.3	6.0	6.2	6.1	6.0	5.9	5.8	5.8
Appendicitis---550-553	1.0	1.0	1.0	1.0	1.1	1.2	1.3	1.4	1.4	1.5
Hernia and intestinal obstruction---560,561,570	5.2	5.0	5.1	5.2	5.1	5.0	5.1	5.3	5.3	5.5
Gastritis, duodenitis, enteritis, and colitis, except diarrhea of newborn---543,571,572	4.4	4.3	4.4	4.4	4.5	4.7	4.5	4.7	4.9	5.4
Cirrhosis of liver---581	11.7	11.3	11.3	10.9	10.8	11.3	10.7	10.2	10.1	10.4
Cholelithiasis, cholecystitis, and cholangitis---534,585	2.6	2.6	2.6	2.5	2.7	2.9	3.1	3.6	3.5	3.5
Acute nephritis, and nephritis with edema including nephrosis---590,591	0.8	0.9	0.9	1.0	1.3	1.3	1.4	1.5	1.6	1.8
Infections of kidney---600	4.7	4.4	4.3	3.9	4.0	3.7	3.4	3.0	2.7	[illegible]
Hyperplasia of prostate---610	2.2	2.3	2.5	2.6	2.7	3.0	3.2	3.7	3.8	3.9
Deliveries and complications of pregnancy, childbirth, and the puerperium---640-689	0.8	0.9	0.9	0.9	0.9	1.0	1.0	1.2	1.3	1.5
Abortion---650-652	0.2	0.2	0.2	0.2	0.1	0.2	0.1	0.2	0.2	0.2
Other complications of pregnancy, childbirth, and the puerperium---640-649,660-689	0.6	0.7	0.7	0.7	0.8	0.9	0.9	1.0	1.1	1.3
Congenital malformations---750-759	11.4	12.0	12.2	12.5	12.4	12.8	12.6	12.[illegible]	12.5	12.6
Certain diseases of early infancy---760-776	34.6	35.9	37.4	38.5	39.8	39.1	38.6	39.0	39.4	40.1
Birth injuries, postnatal asphyxia, and atelectasis---760-762	15.2	15.6	16.6	17.1	18.2	17.8	17.7	17.8	17.8	17.9
Infections of newborn---763-769	2.4	3.6	2.7	2.9	3.2	3.0	2.8	2.6	2.7	2.6
Other diseases peculiar to early infancy, and immaturity unqualified---769-776	16.9	17.5	18.2	18.5	18.4	18.3	18.1	18.6	18.9	19.8
Symptoms, senility, and ill-defined conditions---780-795	10.6	10.4	11.4	10.8	11.4	11.2	11.3	12.1	12.5	13.7
All other diseases---Residual	28.1	28.2	29.0	28.8	28.4	26.9	25.9	25.7	25.7	27.1
Accidents---E800-E962	52.3	50.4	52.3	52.2	52.3	55.9	56.6	56.9	55.9	60.1
Motor vehicle accidents---E810-E835	22.0	20.8	21.3	21.5	21.3	22.7	23.7	23.4	22.1	24.0
Other accidents---E800-E802,E840-E962	30.3	29.6	31.0	30.7	30.9	33.2	33.0	33.5	33.8	36.1
Suicide---E963,E970-E979	10.9	10.4	10.6	10.6	10.7	9.8	10.0	10.2	10.1	10.1
Homicide---E964,E980-E985	4.9	4.7	4.7	4.6	4.5	4.5	4.6	4.5	4.8	4.8

11 times footnote

Table 1-24. Deaths From 258 Selected Causes, by Color

(By place of residence. Data refer only to deaths occurring within the United States. Excludes fetal deaths. Numbers after causes of death are category numbers of the Seventh Revi- did not require reporting of the

CAUSE OF DEATH	UNITED STATES						
	Total			White		Nonwhite	
	Both sexes	Male	Female	Male	Female	Male	Female
ALL CAUSES	1,756,720	994,789	761,931	846,458	641,655	114,262	92,321
I. INFECTIVE AND PARASITIC DISEASES	19,774	12,838	6,936	9,355	4,910	3,082	1,809
TUBERCULOSIS, ALL FORMS..001-019	9,506	6,942	2,564	5,028	1,704	1,660	767
TUBERCULOSIS OF RESPIRATORY SYSTEM..001-008	8,792	6,531	2,261	4,792	1,552	1,504	635
TUBERCULOSIS OF MENINGES AND CENTRAL NERVOUS SYSTEM..010	225	119	106	71	53	43	47
TUBERCULOSIS OF INTESTINES, PERITONEUM, AND MESENTERIC GLANDS..011	51	32	19	16	7	16	12
TUBERCULOSIS OF BONES AND JOINTS..012,013	80	39	41	25	35	13	6
TUBERCULOSIS OF OTHER ORGANS AND SYSTEMS..014-018	143	83	60	62	37	16	17
DISSEMINATED TUBERCULOSIS..019	215	138	77	62	20	68	50
SYPHILIS AND ITS SEQUELAE..020-029	2,811	1,998	813	1,391	527	564	264
CONGENITAL SYPHILIS..020	50	32	18	14	11	16	7
EARLY SYPHILIS..021	1	1	-	-	-	1	-
ANEURYSM OF AORTA..022	1,440	1,019	421	811	315	181	93
OTHER CARDIOVASCULAR SYPHILIS..023	836	589	247	316	119	263	120
TABES DORSALIS..024	59	49	10	42	8	6	2
GENERAL PARALYSIS OF INSANE..025	145	107	38	79	25	28	13
OTHER SYPHILIS OF CENTRAL NERVOUS SYSTEM..026	222	167	55	110	32	55	23
ALL OTHER SYPHILIS..027-029	58	34	24	19	17	14	6
GONOCOCCAL INFECTION..030-035	23	20	3	9	-	11	3
TYPHOID FEVER..040	15	11	4	5	3	6	1
PARATYPHOID FEVER AND OTHER SALMONELLA INFECTIONS..041,042	62	36	26	25	18	11	8
CHOLERA..043	-	-	-	-	-	-	-
BRUCELLOSIS..044	12	9	3	7	3	2	-
DYSENTERY, ALL FORMS..045-048	323	183	140	114	79	68	61
FOOD POISONING, INFECTION AND INTOXICATION..049	39	18	21	13	13	4	8
SCARLET FEVER..050	10	4	6	3	5	1	1
STREPTOCOCCAL SORE THROAT..051	92	47	45	35	32	10	12
ERYSIPELAS..052	25	11	14	11	12	-	1
SEPTICEMIA AND PYEMIA..053	2,084	1,126	958	847	730	251	198
DIPHTHERIA..055	41	23	18	11	11	12	6
WHOOPING COUGH..056	83	45	38	21	13	24	25
MENINGOCOCCAL INFECTIONS..057	649	366	283	294	232	57	36
PLAGUE..058	-	-	-	-	-	-	-
LEPROSY..060	8	5	3	3	1	2	2
TETANUS..061	215	123	92	66	44	57	48
ANTHRAX..062	-	-	-	-	-	-	-
ACUTE POLIOMYELITIS..080	60	37	23	29	17	7	5
LATE EFFECTS OF ACUTE POLIOMYELITIS..081	123	57	66	51	60	4	6
ACUTE INFECTIOUS ENCEPHALITIS..082	582	283	299	235	238	38	48
LATE EFFECTS OF ACUTE INFECTIOUS ENCEPHALITIS..083	80	52	28	45	26	4	-
SMALLPOX..084	-	-	-	-	-	-	-
MEASLES..085	408	180	228	126	153	51	69
YELLOW FEVER..091	-	-	-	-	-	-	-
INFECTIOUS HEPATITIS..092	911	386	525	317	436	52	69
RABIES..094	1	1	-	1	-	-	-
TICK-BORNE TYPHUS..104	12	7	5	5	4	2	-
ALL OTHER RICKETTSIAL DISEASES..100-103,105-108	4	3	1	3	1	-	-
MALARIA..110-117	12	10	2	6	1	4	1
SCHISTOSOMIASIS..123	2	1	1	1	1	-	-
HYDATID DISEASE..125	7	4	3	3	3	1	-
FILARIASIS..127	1	1	-	1	-	-	-
ANCYLOSTOMIASIS..129	6	3	3	2	3	1	-
OTHER DISEASES DUE TO HELMINTHS..124,126,128,130	60	24	36	6	9	17	27
ALL OTHER INFECTIVE AND PARASITIC DISEASES..RESIDUAL	1,507	822	685	641	531	161	143
II. NEOPLASMS	283,243	152,146	131,097	131,866	113,500	14,137	12,265
MALIGNANT NEOPLASMS, INCLUDING NEOPLASMS OF LYMPHATIC AND HEMATOPOIETIC TISSUES..140-205	278,562	150,009	128,553	130,050	111,449	13,884	11,856
MALIGNANT NEOPLASM OF BUCCAL CAVITY AND PHARYNX..140-148	6,481	4,920	1,561	4,253	1,350	455	145
OF LIP..140	219	199	20	189	17	5	1
OF TONGUE..141	1,552	1,181	371	1,015	329	91	25
OF OTHER AND UNSPEC. PARTS OF BUCCAL CAVITY..142-144	2,092	1,443	649	1,268	560	125	64
OF PHARYNX..145-148	2,618	2,097	521	1,781	444	234	55
MALIGNANT NEOPLASM OF DIGESTIVE ORGANS AND PERITONEUM, NOT SPECIFIED AS SECONDARY..150-156A,157-159	92,047	49,936	42,111	42,709	36,729	5,026	3,519
OF ESOPHAGUS..150	5,088	3,973	1,115	3,028	871	755	191
OF STOMACH..151	19,378	11,947	7,431	9,840	6,301	1,603	821
OF SMALL INTESTINE, INCLUDING DUODENUM..152	745	388	357	330	317	37	28
OF LARGE INTESTINE, EXCEPT RECTUM..153	29,837	13,561	16,276	12,019	14,501	884	1,030
CECUM, APPENDIX, AND ASCENDING COLON..153.0	4,264	1,812	2,452	1,609	2,205	97	141
TRANSVERSE COLON..153.1	1,608	745	863	661	763	45	44
DESCENDING COLON..153.2	1,256	533	723	467	652	42	41
SIGMOID COLON..153.3	6,188	3,000	3,188	2,677	2,863	161	156
MULTIPLE PARTS OF LARGE INTESTINE..153.7	74	37	37	32	36	1	-
LARGE INTESTINE, PART UNSPECIFIED..153.8	14,929	6,823	8,106	6,039	7,179	490	591
INTESTINAL TRACT, PART UNSPECIFIED..153.9	1,518	611	907	534	803	48	57
OF RECTUM..154	10,853	6,131	4,722	5,460	4,101	370	369
OF BILIARY PASSAGES AND OF LIVER, PRIMARY SITE..155	6,423	2,822	3,601	2,406	3,253	308	216
LIVER..155.0	2,145	1,384	761	1,119	656	215	82
OT. & MULT. SITES OF BILIARY PASSAGES..155.1,155.8	4,278	1,438	2,840	1,287	2,597	93	134
OF LIVER NOT STATED WHETHER PRIMARY OR SECONDARY..156A	2,958	1,533	1,425	1,283	1,205	190	153
OF PANCREAS..157	15,019	8,725	6,294	7,660	5,447	753	594
OF PERITONEUM AND OF UNSPEC. DIGESTIVE ORGANS..158,159	1,746	856	890	683	733	126	117

Table 1-24. Deaths From 258 Selected Causes, by Color

(By place of residence. Data refer only to deaths occurring within the United States. Excludes fetal deaths. Numbers after causes of death are category numbers of the Seventh Revi- did not require reporting of the

CAUSE OF DEATH	WEST VIRGINIA					WISCONSIN				
	Total	White		Nonwhite		Total	White		Nonwhite	
		Male	Female	Male	Female		Male	Female	Male	Female
ALL CAUSES	18,684	10,371	7,153	717	443	38,380	21,494	16,218	376	292
I. INFECTIVE AND PARASITIC DISEASES	247	146	68	25	8	256	142	99	9	6
TUBERCULOSIS, ALL FORMS 001-019	145	89	38	14	4	103	65	29	7	2
TUBERCULOSIS OF RESPIRATORY SYSTEM 001-008	138	86	35	13	4	87	57	24	5	1
TUBERCULOSIS OF MENINGES AND CENTRAL NERVOUS SYSTEM 010	6	2	3	1	-	2	-	-	2	-
TUBERCULOSIS OF INTESTINES, PERITONEUM, AND MESENTERIC GLANDS 011	-	-	-	-	-	1	1	-	-	-
TUBERCULOSIS OF BONES AND JOINTS 012,013	-	-	-	-	-	3	1	2	-	-
TUBERCULOSIS OF OTHER ORGANS AND SYSTEMS 014-018	-	-	-	-	-	7	4	3	-	-
DISSEMINATED TUBERCULOSIS 019	1	1	-	-	-	3	2	-	-	1
SYPHILIS AND ITS SEQUELAE 020-029	39	22	9	7	1	33	23	9	-	1
CONGENITAL SYPHILIS 020	-	-	-	-	-	-	-	-	-	-
EARLY SYPHILIS 021	-	-	-	-	-	-	-	-	-	-
ANEURYSM OF AORTA 022	22	15	6	1	-	16	12	4	-	-
OTHER CARDIOVASCULAR SYPHILIS 023	9	5	2	2	-	8	4	3	-	1
TABES DORSALIS 024	-	-	-	-	-	3	3	-	-	-
GENERAL PARALYSIS OF INSANE 025	2	-	-	2	-	3	2	1	-	-
OTHER SYPHILIS OF CENTRAL NERVOUS SYSTEM 026	4	2	-	1	1	3	2	1	-	-
ALL OTHER SYPHILIS 027-029	2	-	1	1	-	-	-	-	-	-
GONOCOCCAL INFECTION 030-035	1	-	-	1	-	1	-	-	-	1
TYPHOID FEVER 040	-	-	-	-	-	1	-	1	-	-
PARATYPHOID FEVER AND OTHER SALMONELLA INFECTIONS 041,042	-	-	-	-	-	-	-	-	-	-
CHOLERA 043	-	-	-	-	-	-	-	-	-	-
BRUCELLOSIS 044	-	-	-	-	-	1	1	-	-	-
DYSENTERY, ALL FORMS 045-048	1	1	-	-	-	-	-	-	-	-
FOOD POISONING, INFECTION AND INTOXICATION 049	1	1	-	-	-	-	-	-	-	-
SCARLET FEVER 050	1	-	1	-	-	-	-	-	-	-
STREPTOCOCCAL SORE THROAT 051	1	-	1	-	-	2	1	1	-	-
ERYSIPELAS 052	-	-	-	-	-	3	1	2	-	-
SEPTICEMIA AND PYEMIA 053	16	11	3	1	1	37	14	23	-	-
DIPHTHERIA 055	-	-	-	-	-	-	-	-	-	-
WHOOPING COUGH 056	-	-	-	-	-	3	1	1	1	-
MENINGOCOCCAL INFECTIONS 057	4	3	-	1	-	10	5	5	-	-
PLAGUE 058	-	-	-	-	-	-	-	-	-	-
LEPROSY 060	-	-	-	-	-	-	-	-	-	-
TETANUS 061	2	1	1	-	-	3	2	1	-	-
ANTHRAX 062	-	-	-	-	-	-	-	-	-	-
ACUTE POLIOMYELITIS 080	1	1	-	-	-	1	1	-	-	-
LATE EFFECTS OF ACUTE POLIOMYELITIS 081	-	-	-	-	-	3	1	2	-	-
ACUTE INFECTIOUS ENCEPHALITIS 082	7	2	3	1	1	16	7	9	-	-
LATE EFFECTS OF ACUTE INFECTIOUS ENCEPHALITIS 082	-	-	-	-	-	1	-	1	-	-
SMALLPOX 084	-	-	-	-	-	-	-	-	-	-
MEASLES 085	3	2	1	-	-	2	2	-	-	-
YELLOW FEVER 091	-	-	-	-	-	-	-	-	-	-
INFECTIOUS HEPATITIS 092	10	3	6	-	1	10	4	6	-	-
RABIES 094	-	-	-	-	-	-	-	-	-	-
TICK-BORNE TYPHUS 104	-	-	-	-	-	-	-	-	-	-
ALL OTHER RICKETTSIAL DISEASES 100-103,105-108	-	-	-	-	-	-	-	-	-	-
MALARIA 110-117	-	-	-	-	-	-	-	-	-	-
SCHISTOSOMIASIS 123	-	-	-	-	-	-	-	-	-	-
HYDATID DISEASE 125	-	-	-	-	-	1	-	1	-	-
FILARIASIS 127	-	-	-	-	-	-	-	-	-	-
ANCYLOSTOMIASIS 129	-	-	-	-	-	-	-	-	-	-
OTHER DISEASES DUE TO HELMINTHS 124,126,128,130	1	1	-	-	-	-	-	-	-	-
ALL OTHER INFECTIVE AND PARASITIC DISEASES RESIDUAL	14	9	5	-	-	25	14	8	1	2
II. NEOPLASMS	2,799	1,430	1,205	109	55	6,407	3,388	2,937	44	38
MALIGNANT NEOPLASMS, INCLUDING NEOPLASMS OF LYMPHATIC AND HEMATOPOIETIC TISSUES 140-205	2,749	1,412	1,176	108	53	6,319	3,350	2,891	42	36
MALIGNANT NEOPLASM OF BUCCAL CAVITY AND PHARYNX 140-148	47	27	15	4	1	139	114	24	1	-
OF LIP 140	2	2	-	-	-	8	7	1	-	-
OF TONGUE 141	8	6	2	-	-	36	32	4	-	-
OF OTHER AND UNSPEC. PARTS OF BUCCAL CAVITY 142-144	18	8	8	1	1	35	20	15	-	-
OF PHARYNX 145-148	19	11	5	3	-	60	55	4	1	-
MALIGNANT NEOPLASM OF DIGESTIVE ORGANS AND PERITONEUM, NOT SPECIFIED AS SECONDARY 150-156A,157-159	865	413	404	32	16	2,289	1,271	998	14	6
OF ESOPHAGUS 150	32	14	14	4	-	119	95	17	6	1
OF STOMACH 151	179	95	73	9	2	529	322	205	2	-
OF SMALL INTESTINE, INCLUDING DUODENUM 152	2	2	-	-	-	15	6	9	-	-
OF LARGE INTESTINE, EXCEPT RECTUM 153	253	104	138	6	5	770	386	380	3	1
CECUM, APPENDIX, AND ASCENDING COLON 153.0	31	14	17	-	-	116	53	63	-	-
TRANSVERSE COLON 153.1	13	5	8	-	-	38	23	14	1	-
DESCENDING COLON 153.2	11	6	5	-	-	36	14	22	-	-
SIGMOID COLON 153.3	37	12	24	1	-	195	100	95	-	-
MULTIPLE PARTS OF LARGE INTESTINE 153.7	-	-	-	-	-	1	1	-	-	-
LARGE INTESTINE, PART UNSPECIFIED 153.8	142	60	72	5	5	341	175	163	2	1
INTESTINAL TRACT, PART UNSPECIFIED 153.9	19	7	12	-	-	43	20	23	-	-
OF RECTUM 154	90	45	41	2	2	274	173	100	1	-
OF BILIARY PASSAGES AND OF LIVER, PRIMARY SITE 155	59	23	34	1	1	168	68	96	1	3
LIVER 155.0	13	6	6	-	1	48	29	17	1	1
OT. & MULT. SITES OF BILIARY PASSAGES 155.1,155.8	46	17	28	1	-	120	39	79	-	2
OF LIVER NOT STATED WHETHER PRIMARY OR SECONDARY 156A	68	25	38	2	3	68	25	41	1	1
OF PANCREAS 157	160	91	58	8	3	313	180	133	-	-
OF PERITONEUM AND OF UNSPEC. DIGESTIVE ORGANS 158,159	22	14	8	-	-	33	16	17	-	-

Exhibit 24

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Association of measles and mumps with cardiovascular disease: The Japan Collaborative Cohort (JACC) study

Yasuhiko Kubota [a], Hiroyasu Iso [a, *], Akiko Tamakoshi [b], the JACC Study Group

[a] Public Health, Department of Social Medicine, Osaka University Graduate School of Medicine, Osaka, Japan
[b] Department of Public Health, Hokkaido University Graduate School of Medicine, Hokkaido, Japan

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ABSTRACT

Objective: Although it has been suggested that exposure to infections during childhood could decrease risk of atherosclerotic cardiovascular disease (CVD), the evidence is scarce. We investigated the association of measles and mumps with CVD.
Methods: 43,689 men and 60,147 women aged 40–79 years at baseline (1988–1990) completed a lifestyle questionnaire, including their history of measles and mumps, and were followed until 2009. Histories of infections were categorized as having no infection (reference), measles only, mumps only, or both infections. Hazard ratios (HR) for mortality from CVD across histories of infections were calculated.
Results: Men with measles only had multivariable HR (95% confidence interval) of 0.92 (0.85–0.99) for total CVD, those with mumps only had 0.52 (0.28–0.94) for total stroke and 0.21 (0.05–0.86) for hemorrhagic stroke, and those with both infections had 0.80 (0.71–0.90) for total CVD, 0.71 (0.53–0.93) for myocardial infarction, and 0.83 (0.69–0.98) for total stroke. Women with both infections had 0.83 (0.74–0.92) for total CVD and 0.84 (0.71–0.99) for total stroke. We also compared subjects with measles only or mumps only (reference) and those with both infections. Men with both infections had 0.88 (0.78–0.99) for total CVD. Women with both infections had 0.85 (0.76–0.94) for total CVD, 0.79 (0.67–0.93) for total stroke, 0.78 (0.62–0.98) for ischemic stroke and 0.78 (0.62–0.98) for hemorrhagic stroke.
Conclusions: Measles and mumps, especially in case of both infections, were associated with lower risks of mortality from atherosclerotic CVD.

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1. Introduction

It has been suggested that infection can impact atherosclerotic cardiovascular disease (CVD) either deleteriously or positively [1]. The former proposes that inflammation caused by chronic infections with pathogens such as *Chlamydia pneumonia* and herpes simplex virus type I can accelerate atherosclerosis [1–6]. The latter suggests that infections suffered during childhood can protect from atherosclerosis [1]. The 'hygiene hypothesis' is a possible mechanism underlying this effect [1,7,8]. Improved hygiene decreases the opportunities for infections, which are necessary for normal development of the immune system. Weakened immune systems lead to decreased production, as well as inactivation, of regulatory T cells, which control the balance of T helper cell types, Th1 and Th2. As a result, inflammation at the arterial wall is not well controlled, leading to the development of atherosclerosis. Therefore, people with a history of infections may have a lower risk of CVD, especially atherosclerotic diseases such as stroke and myocardial infarction, compared to those without previous infections. However, to the best of our knowledge, only one previous study, which used a retrospective design and had a small number of participants, has suggested that viral or bacterial infections could protect against CVD [1].

To confirm the protective effect of infections against CVD, this study prospectively examined whether a history of measles and mumps, diseases typically seen in children, alters the risk of mortality from CVD before the era of measles, mumps, and rubella (MMR) vaccination [1,9].

* Corresponding author. Public Health, Department of Social Medicine, Osaka University Graduate School of Medicine, 565-0871, 2-2, Yamadaoka, Suita, Osaka, Japan.
E-mail address: iso@pbhel.med.osaka-u.ac.jp (H. Iso).

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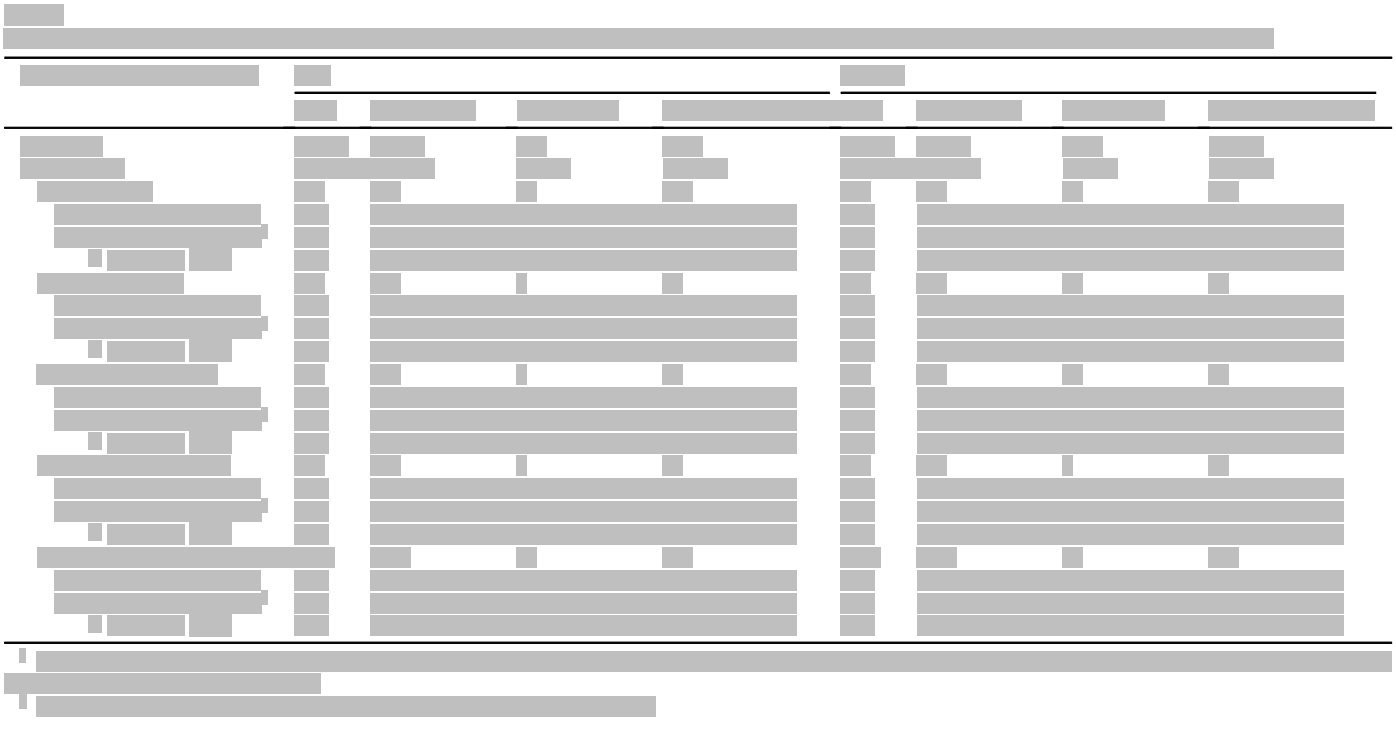



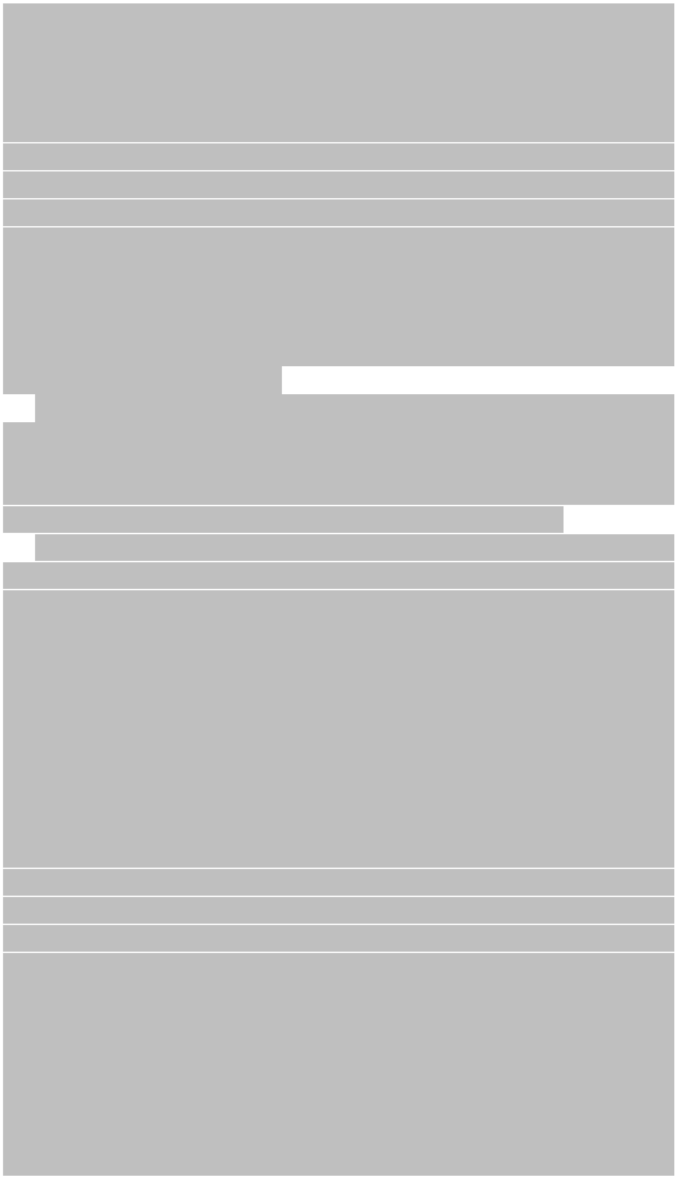

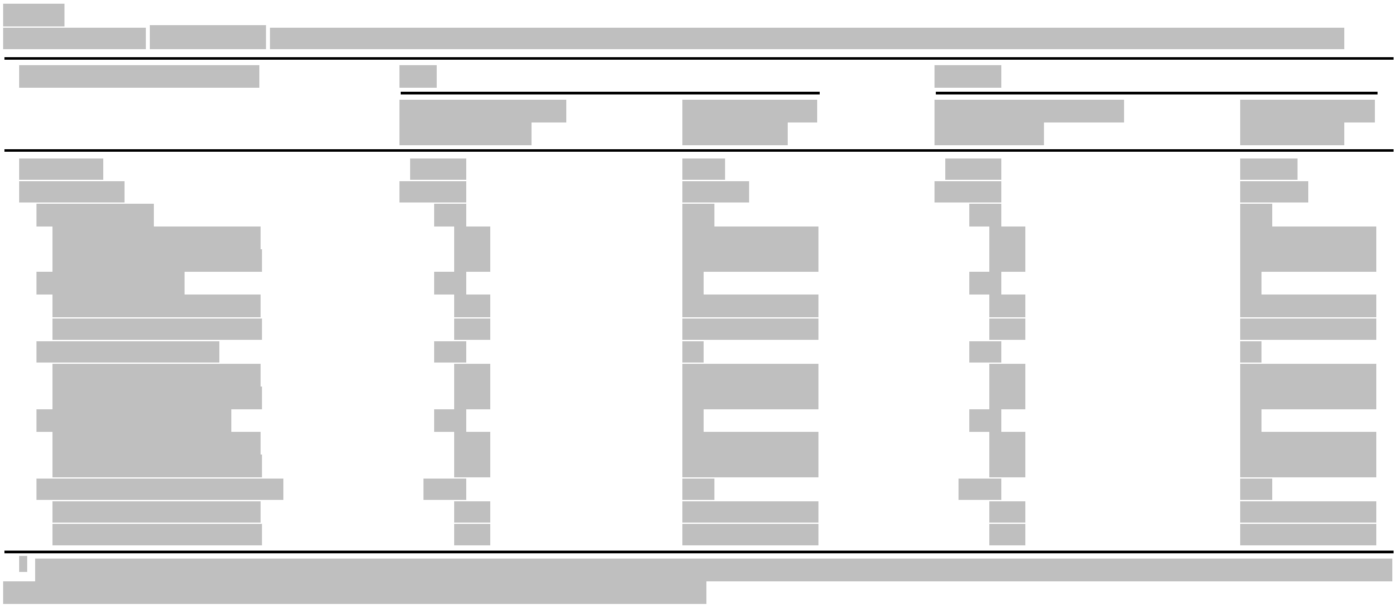

Exhibit 25

Vaccine Coverage Levels – United States, 1962-2009

Year	DTP 3+	DTP4+	Polio 3+	MMR*	Hib3+	Var	PCV3+	HepB3+	Combined 4-3-1	Combined 4-3-1-3
1962	67.3									
1963	71.4									
1964	74.6									
1965	72.7									
1966	74.0									
1967	77.9			60.0						
1968	76.8			61.5						
1969	77.4			61.4						
1970	76.4			58.4						
1971	77.8			62.2						
1972	74.1			62.8						
1973	71.7		59.5	61.0						
1974	72.4		60.0	63.4						
1975	73.2		63.6	65.5						
1976	72.7		61.3	66.3						
1977	69.6		62.6	65.0						
1978	66.6		59.5	63.6						
1979	64.4		59.7	66.5						
1080	66.0		58.9	66.6						
1981	68.1		59.2	66.8						
1982	67.1		57.0	67.6						
1983	65.4		56.9	66.3						
1984	65.0		53.2	65.8						
1985	63.6		53.6	61.2						
1986†										
1987†										
1988†										
1989†										
1990†										
1991	68.8		53.2	82.0						
1992	83.0	59.0	72.4	82.5	28.2			8.0	68.7	55.3
1993	88.2	72.1	78.9	84.1	55.0			16.3	67.1	
1994	93.0	77.7	83.0	89.0	86.0			37.0	75.0	
1995	94.7	78.5	87.9	87.6	91.7			68.0	76.2	74.2
1996	95.0	81.1	91.1	90.7	91.7	16.0		81.8	78.4	76.5
1997	95.5	81.5	90.8	90.5	92.7	25.9		83.7	77.9	76.2
1998	95.6	83.9	90.8	92.0	93.4	43.2		87.0	80.6	79.2
1999	95.9	83.3	89.6	91.5	93.5	57.5		88.1	79.9	78.4
2000	94.1	81.7	89.5	90.5	93.4	67.8		90.3	77.6	76.2
2001	94.3	82.1	89.4	91.4	93.0	76.3		88.9	78.6	77.2
2002	94.9	81.6	90.2	91.6	93.1	80.6	40.8	88.9	78.5	77.5
2003	96.0	84.8	91.6	93.0	93.9	84.8	68.1	92.4	82.2	81.3
2004	95.9	85.5	91.6	93.0	93.5	87.5	73.2	92.4	83.5	82.5
2005	96.1	85.7	91.7	91.5	93.9	87.9	82.8	92.9	83.1	82.4
2006	95.8	85.2	92.9	92.4	93.4	89.3	87.0	93.4	83.2	82.3
2007	95.5	84.5	92.6	92.3	92.6	90.0	90.0	92.7	82.8	81.1
2008		84.6	93.6	92.1	90.9	90.7	80.1§	93.5		
2009	94.0	83.9	92.8	90.0	92.1	89.6	92.6	92.4	81.5	

*Previously reported as measles-containing vaccine (MCV)
†No national coverage data were collected from 1986 through 1990.
§In 2008, data are for PCV4+.

Combined 4-3-1: Four or more doses of DTP/DTaP/DT, three or more doses of poliovirus vaccine, and one or more doses of any measles-containing vaccine.

Combined 4-3-1-3: Four or more doses of DTP/DTaP/DT, three or more doses of poliovirus vaccine, one or more doses of any measles-containing vaccine, and three or more doses of *Haemophilus influenzae* type b vaccine.

Data prior to 1993 were collected by the National Health Interview Survey and represent 2-year-old children. Data from 1993 forward are from the National Immunization Survey and represent 19-35 month-old children. Different methods were used for the two surveys.

Data are available for combinations of vaccines not reflected on this table. For more information about annual coverage figures from 1994 to the present, see http://www.cdc.gov/vaccines/stats-surv/nis/default.htm.

Exhibit 26

	Measles		Mumps		Rubella		CRS
Year	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases
1950	319,124	468	NR		NR		NR
1951	530,118	683	NR		NR		NR
1952	683,077	618	NR		NR		NR
1953	449,146	462	NR		NR		NR
1954	682,720	518	NR		NR		NR
1955	555,156	345	NR		NR		NR
1956	611,936	530	NR		NR		NR
1957	486,799	389	NR		NR		NR
1958	763,094	552	NR		NR		NR
1959	406,162	385	NR		NR		NR
1960	441,703	380	NR	42	NR	12	NR
1961	423,919	434	NR	53	NR	14	NR
1962	481,530	408	NR	43	NR	8	NR
1963	385,156	364	NR	48	NR	16	NR
1964	458,083	421	NR	50	NR	53	NR
1965	261,904	276	NR	31	NR	16	NR
1966	204,136	261	NR	43	46,975	12	NR
1967	62,705	81	NR	37	46,888	16	NR
1968	22,231	24	152,209	25	49,371	24	NR
1969	25,826	41	90,918	22	57,686	29	62
1970	47,351	89	104,953	16	56,552	31	67
1971	75,290	90	124,939	22	45,086	20	44
1972	32,275	24	74,215	16	25,507	14	32
1973	26,690	23	69,612	12	27,804	16	30
1974	22,094	20	59,128	6	11,917	15	22
1975	24,374	20	59,647	8	16,652	21	32
1976	41,126	12	38,492	8	12,491	12	22
1977	57,345	15	21,436	5	20,395	17	29
1978	26,871	11	16,817	3	18,269	10	30
1979	13,597	6	14,255	2	11,795	1	57
1980	13,506	11	8,576	2	3,904	1	14
1981	3,124	2	4,941	1	2,077	5	10

Exhibit 27

VITAL STATISTICS RATES IN THE UNITED STATES 1940–1960

By
Robert D. Grove, Ph. D.
and
Alice M. Hetzel

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
Washington, D.C. 1968
National Center for Health Statistics

For sale by the Superintendent of Documents, U.S. Government Printing Office
Washington, D.C. 20402 - Price $5.25

Figure 18.—Death Rates for Diphtheria: Death-registration States, 1900–32, and United States, 1933–60

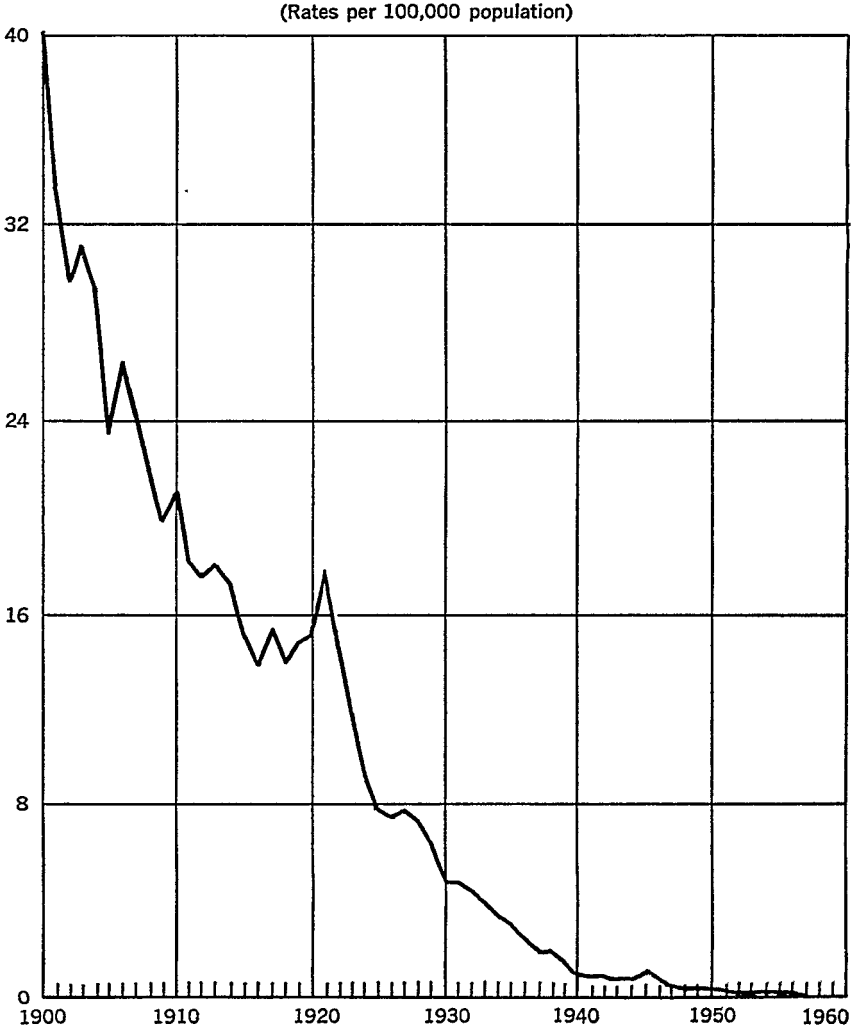

Exhibit 28

PRODUCT LICENSE APPLICATION

PLA-0002-XXX-CY04 Vol 2

MERCK & CO., INC.
Measles, Mumps and Rubella Virus Vaccine Live

DCC Volume Sequence No. 157802

F

Table 4: Clinical Complaints for Children Vaccinated with Combined Measles-Mumps-Rubella Vaccine Lot 310 at Lankenau Hospital Outpatient Clinic from 9/26/68 to 10/10/68 (Study #212)

Clinical Complaint	Total Vaccinees				Children Initially Seronegative to Measles, Mumps and Rubella			
	Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness	10 (25.6%)	9 (23.1%)	5 (12.8%)	5 (12.8%)	8 (26.7%)	9 (30.0%)	5 (16.7%)	3 (10.0%)
Otitis				1 (2.6%)				1 (3.3%)
Lymphadenopathy		1 (2.6%)						
Gastrointestinal	1 (2.6%)	3 (7.7%)			1 (3.3%)	2 (6.7%)		
Rash (not measles)	1 (2.6%)	3 (7.7%)	2 (5.1%)	1 (2.6%)	1 (3.3%)	2 (6.7%)	2 (6.7%)	1 (3.3%)
Irritability	2 (5.1%)	5 (12.8%)	2 (5.1%)		2 (6.7%)	3 (10.0%)	2 (6.7%)	
Malaise	1 (2.6%)							
Irrelevant		2 (5.1%)	1 (2.6%)	1 (2.6%)		2 (6.7%)	1 (3.3%)	
No Complaint	25 (64.1%)	21 (53.8%)	30 (76.9%)	32 (82.0%)	19 (63.3%)	15 (50.0%)	21 (70.0%)	25 (83.3%)
Total Subjects	39	39	39	39	30	30	30	30

Table 5: Clinical Complaints Recorded for Children Vaccinated with Combined Measles-Mumps-Rubella Vaccine Lot 92126 and for Their Unvaccinated Contact Controls (Study 232)

Clinical Complaints	Contact Control Children				Total Vaccinees				Initially Seronegative to Measles-Mumps-Rubella			
	Days Observed				Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness		2 (6.4%)	3 (9.7%)	2 (6.4%)	15 (15.0%)	20 (20.0%)	12 (12.0%)	14 (14.0%)	13 (15.8%)	16 (19.5%)	10 (12.2%)	9 (11.0%)
Otitis					1 (1.0%)	1 (1.0%)		2 (2.0%)	1 (1.2%)	1 (1.2%)		1 (1.2%)
Swollen Glands						1 (1.0%)				1 (1.2%)		
Conjunctivitis						1 (1.0%)				1 (1.2%)		
Gastrointestinal					11 (11.0%)	11 (11.0%)	6 (6.0%)	6 (6.0%)	9 (11.0%)	10 (12.2%)	6 (7.3%)	5 (6.1%)
Rash	1 (3.2%)	1 (3.2%)			3 (3.0%)	3 (3.0%)	2 (2.0%)	3 (3.0%)	3 (3.6%)	3 (3.6%)	2 (2.4%)	3 (3.6%)
Irritability					4 (4.0%)	6 (6.0%)	4 (4.0%)	4 (4.0%)	4 (4.9%)	5 (6.1%)	4 (4.9%)	4 (4.9%)
Malaise					1 (1.0%)				1 (1.2%)			
Irrelevant								1 (1.0%)				1 (1.2%)
Anorexia					2 (2.0%)	2 (2.0%)	1 (1.0%)	1 (1.0%)	2 (2.4%)	2 (2.4%)	1 (1.2%)	1 (1.2%)
Swelling of Face						1 (1.0%)	1 (1.0%)			1 (1.2%)	1 (1.2%)	
Flush							1 (1.0%)				1 (1.2%)	
Viral Infection								2 (2.0%)				2 (2.4%)
Measles-like Rash						4 (4.0%)	1 (1.0%)			4 (4.9%)	1 (1.2%)	
Fatigue					2 (2.0%)	1 (1.0%)	1 (1.0%)	1 (1.0%)	1 (1.2%)			
Teething					4 (4.0%)	2 (2.0%)	1 (1.0%)	1 (1.0%)	3 (3.6%)	1 (1.2%)	1 (1.2%)	1 (1.2%)
No Complaints	30 (96.8%)	28 (90.3%)	28 (90.3%)	29 (93.5%)	70 (70.0%)	64 (64.0%)	76 (76.0%)	71 (71.0%)	57 (69.5%)	52 (63.4%)	61 (74.4%)	60 (73.2%)
Physician's Surveillance Negative	1	1	1	1	1	1	1	1				
Total Subjects	32	32	32	32	101	101	101	101	82	82	82	82

Table 5: Clinical Complaints Recorded for Children Vaccinated with Combined Measles-Mumps-Rubella Vaccine Lot 92127 and for Their Unvaccinated Contact Controls (Study 232)

Clinical Complaints	Contact Control Children				Total Vaccinees				Initially Seronegative to Measles-Mumps-Rubella			
	Days Observed				Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness	5 (16.1%)	8 (25.8%)	3 (9.7%)	3 (9.7%)	20 (20.6%)	30 (30.9%)	14 (14.4%)	16 (16.5%)	15 (20.0%)	24 (32.0%)	10 (13.3%)	14 (18.7%)
Otitis			1 (3.2%)		2 (2.1%)	3 (3.1%)	1 (1.0%)	3 (3.1%)	2 (2.7%)	3 (4.0%)	1 (1.3%)	3 (4.0%)
Swollen Glands			1 (3.2%)			1 (1.0%)						
Gastrointestinal	1 (3.2%)	2 (6.4%)			9 (9.3%)	6 (6.2%)	3 (3.1%)	2 (2.1%)	6 (8.0%)	4 (5.3%)	3 (4.0%)	1 (1.3%)
Headache				1 (3.2%)								
Viral Infection				1 (3.2%)				1 (1.0%)				
Conjunctivitis							1 (1.0%)	1 (1.0%)				
Rash					5 (5.2%)	3 (3.1%)		1 (1.0%)	5 (6.7%)	2 (2.7%)		1 (1.3%)
Irritability					7 (7.2%)	7 (7.2%)	3 (3.1%)	2 (2.1%)	6 (8.0%)	5 (6.7%)	1 (1.3%)	1 (1.3%)
Chicken pox								1 (1.0%)				1 (1.3%)
Irrelevant							1 (1.0%)	3 (3.1%)				1 (1.3%)
Fever						1 (1.0%)	1 (1.0%)			1 (1.3%)	1 (1.3%)	
Anorexia					1 (1.0%)	1 (1.0%)			1 (1.3%)	1 (1.3%)		
Genitourinary Infection							1 (1.0%)					
Flush						1 (1.0%)				1 (1.3%)		
Scarlatina							1 (1.0%)				1 (1.3%)	
Allergy							1 (1.0%)				1 (1.3%)	
Measles-like Rash						3 (3.1%)	1 (1.0%)			3 (4.0%)	1 (1.3)	
Teething					3 (3.1%)	3 (3.1%)	4 (4.1%)	1 (1.0%)	3 (4.0%)	2 (2.7%)	2 (2.7%)	1 (1.3%)
No Complaints	25 (80.6%)	22 (71.0%)	27 (87.1%)	27 (87.1%)	62 (63.9%)	57 (58.8%)	72 (74.2%)	71 (73.2%)	47 (62.7%)	43 (57.3%)	59 (78.7%)	55 (73.3%)
Negative Physician's Surveillance	3	3	3	3	4	4	4	4	1	1	1	1
Total Subjects	34	34	34	34	101	101	101	101	76	76	76	76

Table 5: Clinical Complaints Recorded for Children Vaccinated with Combined Measles-Mumps-Rubella Vaccine Lot 96400 and for Their Unvaccinated Contact Controls (Study 232)

Clinical Complaints	Contact Control Children				Total Vaccinees				Initially Seronegative to Measles-Mumps-Rubella			
	Days Observed				Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness	4 (10.5%)	7 (18.4%)	5 (13.2%)	6 (15.8%)	15 (15.2%)	22 (22.2%)	10 (10.1%)	13 (13.1%)	13 (18.6%)	16 (22.8%)	8 (11.4%)	10 (14.3%)
Otitis				1 (2.6%)		2 (2.0%)	2 (2.0%)	4 (4.0%)		1 (1.4%)	2 (2.8%)	3 (4.3%)
Gastrointestinal	2 (5.3%)		1 (2.6%)		1 (1.0%)	4 (4.0%)	3 (3.0%)	3 (3.0%)		4 (5.7%)	2 (2.8%)	1 (1.4%)
Rash	1 (2.6%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	2 (2.0%)	1 (1.0%)	3 (3.0%)	1 (1.0%)	2 (2.8%)	1 (1.4%)	2 (2.8%)	
Headache	1 (2.6%)					1 (1.0%)		1 (1.0%)				1 (1.4%)
Irritability	2 (5.3%)				7 (7.1%)	8 (8.1%)	1 (1.0%)	1 (1.0%)	5 (7.1%)	7 (10.0%)	1 (1.4%)	
Anorexia	1 (2.6%)				1 (1.0%)	2 (2.0%)		1 (1.0%)	1 (1.4%)	2 (2.8%)		1 (1.4%)
Viral Infection			1 (2.6%)					2 (2.0%)				2 (2.8%)
Fatigue		1 (2.6%)										
Teething		1 (2.6%)			1 (1.0%)	5 (5.0%)	3 (3.0%)	5 (5.0%)	1 (1.4%)	5 (7.1%)	2 (2.8%)	4 (5.7%)
Local Reaction - Injection Site					2 (2.0%)				1 (1.4%)			
Malaise						1 (1.0%)				1 (1.4%)		
Chicken Pox					1 (1.0%)				1 (1.4%)			
Irrelevant					1 (1.0%)			2 (2.0%)	1 (1.4%)			2 (2.8%)
Flush						1 (1.0%)				1 (1.4%)		
Pain							1 (1.0%)				1 (1.4%)	
Measles-like Rash						2 (2.0%)				2 (2.8%)		
Whooping Cough					1 (1.0%)				1 (1.4%)			
Swollen Glands						2 (2.0%)				2 (2.8%)		
No Complaints	27 (71.0%)	29 (76.3%)	30 (78.9%)	30 (78.9%)	71 (71.7%)	62 (62.6%)	81 (81.8%)	69 (69.7%)	47 (67.1%)	40 (57.1%)	56 (80.0%)	48 (68.6%)
Physician's Surveillance Negative	2	2	2	2	2	2	2	2				
Total Subjects	40	40	40	40	101	101	101	101	70	70	70	70

Table 4: Clinical Complaints Recorded for Children Vaccinated with Combined Measles-Mumps-Rubella Vaccine Lot 92127 and for Their Unvaccinated Contact Controls (Study 220-220B)

Clinical Complaints	Adult Contact Controls				Contact Control Children				Total Vacciness				Initially Seronegative to Measles, Mumps, & Rubella			
	Days Observed				Days Observed				Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness	3 (1.8%)	13 (7.7%)	5 (3.0%)	5 (3.0%)	2 (5.6%)	9 (25.0%)	6 (16.7%)	4 (11.1%)	52 (14.2%)	74 (20.3%)	48 (13.2%)	34 (9.3%)	10 (12.2%)	16 (19.5%)	9 (11.0%)	8 (9.8%)
Otitis	1 (0.6%)	6 (3.6%)	4 (2.4%)	1 (0.6%)		1 (2.8%)			1 (0.3%)	6 (1.6%)		1 (0.3%)		3 (3.7%)		
Swollen Glands	1 (0.6%)	4 (2.4%)	3 (1.8%)			2 (5.6%)				3 (0.8%)	2 (0.5%)			1 (1.2%)		
Conjunctivitis	2 (1.2%)	2 (1.2%)			1 (2.8%)	1 (2.8%)	1 (2.8%)	1 (2.8%)	3 (0.8%)	11 (3.0%)	4 (1.1%)	2 (0.5%)		1 (1.2%)	1 (1.2%)	1 (1.2%)
Gastrointestinal	5 (3.0%)	13 (7.7%)	5 (3.0%)	4 (2.4%)	2 (5.6%)	10 (27.8%)	7 (19.4%)	5 (13.9%)	41 (11.2%)	82 (22.5%)	34 (9.3%)	31 (8.5%)	7 (8.5%)	22 (26.8%)	9 (11.0%)	8 (9.8%)
Rash											1 (0.3%)	1 (0.3%)				
Headache	33 (19.6%)	48 (28.6%)	16 (9.5%)	9 (5.4%)	1 (2.8%)	2 (5.6%)			12 (3.3%)	14 (3.8%)	5 (1.4%)	2 (0.5%)	1 (1.2%)	4 (4.9%)		1 (1.2%)
Irritability	5 (3.0%)	9 (5.4%)	2 (1.2%)	1 (0.6%)	2 (5.6%)	8 (22.2%)	5 (13.9%)	6 (16.7%)	23 (6.3%)	81 (22.2%)	40 (11.0%)	21 (5.8%)	8 (9.8%)	27 (32.9%)	13 (15.9%)	8 (9.8%)
Malaise	23 (13.7%)	34 (20.2%)	13 (7.7%)	6 (3.6%)	3 (8.3%)	6 (16.7%)	5 (13.9%)	4 (11.1%)	52 (14.2%)	72 (19.7%)	33 (9.0%)	20 (5.5%)	16 (19.5%)	20 (24.4%)	8 (9.8%)	3 (3.7%)
Irrelevant	1 (0.6%)															
Fever	2 (1.2%)	6 (3.6%)	1 (0.6%)	1 (0.6%)	1 (2.8%)	5 (13.9%)	3 (8.3%)	2 (5.6%)	18 (4.9%)	54 (14.8%)	19 (5.2%)	4 (1.1%)	3 (3.7%)	11 (13.4%)	5 (6.1%)	
Anorexia	14 (8.3%)	20 (11.9%)	8 (4.8%)	5 (3.0%)	4 (11.1%)	9 (25.0%)	4 (11.1%)	2 (5.6%)	33 (9.0%)	70 (19.2%)	30 (8.2%)	19 (5.2%)	10 (12.2%)	18 (22.0%)	9 (11.0%)	6 (7.3%)
Exanthema						1 (2.8%)	1 (2.8%)		1 (0.3%)	3 (0.8%)	3 (0.8%)	4 (1.1%)		1 (1.2%)	1 (1.2%)	2 (2.4%)
Rubella-like Rash										1 (0.3%)	1 (0.3%)					
Aggravated Infection Injection Site	-											1 (0.3%)				
Measles-like Rash												1 (0.3%)				
No Complaints	113 (67.3%)	103 (61.3%)	131 (78.0%)	148 (88.1%)	27 (75.0%)	17 (47.2%)	22 (61.1%)	25 (69.4%)	231 (62.9%)	165 (45.2%)	251 (68.8%)	282 (77.3%)	52 (63.4%)	37 (45.1%)	55 (67.1%)	62 (75.6%)
Physician's Surveillance Negative	15	15	15	15						2	2	2				
Total Subjects	183	183	183	183	36	36	36	36	367	367	367	367	82	82	82	82

Table 4: Clinical Complaints Recorded for Children Vaccinated with Combined Measles-Mumps-Rubella Vaccine Lot 92126 and for their Unvaccinated Contact Controls (Study 220 and 220B)

Clinical Complaint	Adult Contact Controls				Contact Control Children				Total Vaccinees				Initially Seronegative to Measles-Mumps-Rubella			
	Days Observed				Days Observed				Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness	6 (3.8%)	9 (5.7%)	5 (3.1%)	2 (1.2%)	3 (9.7%)	4 (12.9%)	1 (3.2%)	2 (6.4%)	24 (7.7%)	49 (15.6%)	32 (10.2%)	24 (7.7%)	2 (4.0%)	9 (18.0%)	6 (12.0%)	3 (6.0%)
Otitis	2 (1.2%)	2 (1.2%)		1 (0.6%)				1 (3.2%)	6 (1.9%)	5 (1.6%)	3 (1.0%)	1 (0.3%)	2 (4.0%)	1 (2.0%)		
Swollen Glands					1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	4 (1.3%)	17 (5.4%)	2 (0.6%)	3 (1.0%)		6 (12.0%)		1 (2.0%)
Conjunctivitis		1 (0.6%)							6 (1.9%)	4 (1.3%)	2 (0.6%)	5 (1.6%)				
Gastrointestinal	9 (5.7%)	9 (5.7%)	2 (1.2%)	3 (1.9%)	3 (9.7%)	5 (16.1%)	5 (16.1%)	8 (25.8%)	27 (8.6%)	48 (15.3%)	29 (9.3%)	47 (15.0%)	2 (4.0%)	12 (24.0%)	11 (22.0%)	9 (18.0%)
Local Reaction												1 (0.3%)				
Headache	13 (8.2%)	19 (11.9%)	13 (8.2%)	6 (3.8%)	3 (9.7%)	2 (6.4%)		1 (3.2%)	5 (1.6%)	9 (2.9%)	2 (0.6%)	2 (0.6%)		2 (4.0%)	1 (2.0%)	
Irritability	2 (1.2%)	1 (0.6%)	2 (1.2%)	1 (0.6%)	4 (12.9%)	1 (3.2%)			22 (7.0%)	34 (10.9%)	12 (3.8%)	10 (3.2%)		5 (10.0%)	3 (6.0%)	2 (4.0%)
Malaise	10 (6.3%)	21 (13.2%)	15 (9.4%)	6 (3.8%)	2 (6.4%)	2 (6.4%)	2 (6.4%)	1 (3.2%)	23 (7.3%)	34 (10.9%)	13 (4.2%)	11 (3.5%)	2 (4.0%)	7 (14.0%)	3 (6.0%)	2 (4.0%)
Fever		2 (1.2%)	1 (0.6%)	1 (0.6%)	2 (6.4%)	6 (19.4%)	4 (12.9%)	8 (25.8%)	21 (6.7%)	79 (25.2%)	41 (13.1%)	27 (8.6%)	4 (8.0%)	22 (44.0%)	10 (20.0%)	2 (4.0%)
Anorexia	6 (3.8%)	10 (6.3%)	10 (6.3%)	8 (5.0%)	3 (9.7%)	2 (6.4%)	5 (16.1%)	5 (16.1%)	21 (6.7%)	33 (10.5%)	24 (7.7%)	29 (9.3%)	1 (2.0%)	11 (22.0%)	7 (14.0%)	5 (10.0%)
Exanthema								1 (3.2%)		1 (0.3%)	4 (1.3%)	4 (1.3%)				
Rubella-like Rash										2 (0.6%)						
No Complaints	137 (86.2%)	124 (78.0%)	136 (85.5%)	146 (91.8%)	21 (67.7%)	18 (58.1%)	21 (67.7%)	15 (48.4%)	234 (74.8%)	152 (48.6%)	210 (67.1%)	204 (65.2%)	41 (82.0%)	16 (32.0%)	27 (54.0%)	33 (66.0%)
Physician's Surveillance Negative	10	10	10	10												
Total Subjects	169	169	169	169	31	31	31	31	313	313	313	313	50	50	50	50

Table 4: Clinical Complaints Recorded for Children Vaccinated with Combined Measles-Mumps-Rubella Vaccine Lot 96400 and for Their Unvaccinated Contact Controls (Study 220B)

Clinical Complaint	Contact Control Children				Total Vaccinees				Initially Seronegative to Measles-Mumps-Rubella			
	Days Observed				Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness	10 (22.7%)	6 (14.0%)	4 (9.3%)	4 (9.3%)	83 (30.4%)	92 (34.3%)	42 (15.7%)	51 (19.0%)	24 (36.4%)	29 (43.9%)	12 (18.2%)	13 (19.7%)
Swollen Glands								2 (0.7%)				
Conjunctivitis	3 (6.8%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	8 (2.9%)	6 (2.2%)	1 (0.4%)	1 (0.4%)	1 (1.5%)			1 (1.5%)
Gastrointestinal	4 (9.1%)	6 (14.0%)	1 (2.3%)	5 (11.6%)	62 (22.7%)	49 (18.3%)	27 (10.1%)	48 (17.9%)	18 (27.3%)	16 (24.2%)	9 (13.6%)	16 (24.2%)
Arthralgia	1 (2.3%)	1 (2.3%)										
Headache	1 (2.3%)	1 (2.3%)		1 (2.3%)	9 (3.3%)	9 (3.4%)	1 (0.4%)	5 (1.9%)	3 (4.5%)	2 (3.0%)		
Irritability	3 (6.8%)	4 (9.3%)			21 (7.7%)	29 (10.8%)	7 (2.6%)	6 (2.2%)	7 (10.6%)	6 (9.1%)		1 (1.5%)
Malaise	1 (2.3%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	18 (6.6%)	17 (6.3%)	2 (0.7%)	3 (1.1%)	4 (6.1%)	5 (7.6%)		1 (1.5%)
Rubella								1 (0.4%)				
Irrelevant						1 (0.4%)				1 (1.5%)		
Fever	5 (11.4%)	6 (14.0%)	4 (9.3%)	1 (2.3%)	61 (22.3%)	58 (21.6%)	24 (9.0%)	19 (7.1%)	14 (21.2%)	19 (28.8%)	9 (13.6%)	7 (10.6%)
Anorexia	1 (2.3%)	1 (2.3%)	1 (2.3%)		4 (1.5%)	13 (4.8%)	6 (2.2%)	4 (1.5%)	1 (1.5%)	6 (9.1%)	1 (1.5%)	
Musculoskeletal							1 (0.4%)	1 (0.4%)				
Allergy						1 (0.4%)	1 (0.4%)	1 (0.4%)				
Exanthema								1 (0.4%)				
Rubella-like Rash	2 (4.5%)	2 (4.6%)			3 (1.1%)	5 (1.9%)	3 (1.1%)	10 (3.7%)	2 (3.0%)	3 (4.5%)	1 (1.5%)	2 (3.0%)
Measles-like Rash						1 (0.4%)	1 (0.4%)			1 (1.5%)	1 (1.5%)	
Aggravated Infection at Injection Site								2 (0.7%)				1 (1.5%)
No Complaints	25 (56.8%)	28 (65.1%)	32 (74.4%)	34 (79.1%)	127 (46.5%)	121 (45.1%)	184 (68.7%)	168 (62.7%)	27 (40.9%)	18 (27.3%)	43 (65.2%)	32 (48.5%)
Physician's Surveillance Negative		1	1	1	14	19	19	19				
Total Subjects	44	44	44	44	287	287	287	287	66	66	66	66

Table 4: Clinical Complaints Recorded for Children Vaccinated with Measles-Mumps-Rubella Vaccine Lot 92126 and for Their Unvaccinated Controls (Study 220C)

Clinical Complaint	Contact Control Children				Total Vaccinees				Initially Seronegative to Measles-Mumps-Rubella			
	Days Observed				Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness	2 (7.1%)	4 (14.3%)	2 (7.1%)	4 (14.3%)	18 (7.9%)	44 (19.3%)	46 (20.2%)	32 (14.0%)	8 (7.8%)	21 (20.4%)	25 (24.3%)	15 (14.6%)
Otitis	1 (3.6%)	1 (3.6%)	1 (3.6%)		2 (0.9%)	6 (2.6%)	3 (1.3%)	2 (0.9%)	1 (1.0%)	2 (1.9%)	1 (1.0%)	1 (1.0%)
Lymphadenopathy				1 (3.6%)	1 (0.4%)	2 (0.9%)	4 (1.8%)	5 (2.2%)			3 (2.9%)	5 (4.9%)
Conjunctivitis					3 (1.3%)	8 (3.5%)	7 (3.1%)	1 (0.4%)		2 (1.9%)	1 (1.0%)	1 (1.0%)
Gastrointestinal		1 (3.6%)	3 (10.7%)	2 (7.1%)	14 (6.1%)	28 (12.3%)	16 (7.0%)	13 (5.7%)	5 (4.9%)	12 (11.6%)	5 (4.9%)	3 (2.9%)
Rash						1 (0.4%)	1 (0.4%)	1 (0.4%)		1 (1.0%)	1 (1.0%)	1 (1.0%)
Headache		1 (3.6%)	1 (3.6%)			3 (1.3%)	2 (0.9%)			1 (1.0%)		
Irritability		2 (7.1%)	1 (3.6%)	1 (3.6%)	11 (4.8%)	33 (14.5%)	18 (7.9%)	11 (4.8%)	6 (5.8%)	15 (14.6%)	8 (7.8%)	4 (3.9%)
Malaise		2 (7.1%)	1 (3.6%)	1 (3.6%)	13 (5.7%)	32 (14.0%)	20 (8.8%)	10 (4.4%)	6 (5.8%)	13 (12.6%)	7 (6.8%)	5 (4.9%)
Measles	1 (3.6%)				1 (0.4%)	5 (2.2%)						
Fever	2 (7.1%)	2 (7.1%)	2 (7.1%)	3 (10.7%)	3 (1.3%)	22 (9.6%)	15 (6.6%)	14 (6.1%)	2 (1.9%)	11 (10.7%)	7 (6.8%)	7 (6.8%)
Anorexia		2 (7.1%)	1 (3.6%)	1 (3.6%)	7 (3.1%)	27 (11.8%)	18 (7.9%)	8 (3.5%)	1 (1.0%)	10 (9.7%)	6 (5.8%)	4 (3.9%)
Allergy		2 (7.1%)	2 (7.1%)		1 (0.4%)	3 (1.3%)	1 (0.4%)	2 (0.9%)	1 (1.0%)	2 (1.9%)		1 (1.0%)
Exanthema					1 (0.4%)	4 (1.8%)	4 (1.8%)		1 (1.0%)	2 (1.9%)	2 (1.9%)	
Measles-like Rash	1 (3.6%)	1 (3.6%)	1 (3.6%)		1 (0.4%)	6 (2.6%)	5 (2.2%)	1 (0.4%)				
Whooping Cough			1 (3.6%)			1 (0.4%)		1 (0.4%)		1 (1.0%)		1 (1.0%)
No Complaint	25 (89.3%)	19 (67.9%)	20 (71.4%)	20 (71.4%)	187 (82.0%)	132 (57.9%)	147 (64.5%)	174 (76.3%)	86 (83.5%)	55 (53.4%)	59 (57.3%)	73 (70.9%)
Physician's Surveillance Negative					7	7	7	7	2	2	2	2
Total Subjects	28	28	28	28	235	235	235	235	105	105	105	105

Table 4: Clinical Complaints Recorded for Children Vaccinated with Measles-Mumps-Rubella Vaccine Lot 92127 and for Their Unvaccinated Controls (Study 220C)

Clinical Complaint	Contact Control Children				Total Vaccinees				Initially Seronegative to Measles-Mumps-Rubella			
	Days Observed				Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness		6 (54.5%)	5 (45.5%)	2 (18.2%)	8 (6.2%)	57 (44.5%)	48 (37.5%)	28 (21.9%)	4 (6.3%)	33 (52.4%)	29 (46.0%)	16 (25.4%)
Otitis		1 (9.1%)				4 (3.1%)	2 (1.6%)	3 (2.3%)		2 (3.2%)	1 (1.6%)	2 (3.2%)
Lymphadenopathy			1 (9.1%)			10 (7.8%)	11 (8.6%)	7 (5.5%)		5 (7.9%)	5 (7.9%)	5 (7.9%)
Conjunctivitis		1 (9.1%)	1 (9.1%)		3 (2.3%)	21 (16.4%)	10 (7.8%)	6 (4.7%)	3 (4.8%)	10 (15.9%)	6 (9.5%)	4 (6.3%)
Gastrointestinal	1 (9.1%)	1 (9.1%)	1 (9.1%)	2 (18.2%)	5 (3.9%)	13 (10.2%)	9 (7.0%)	8 (6.2%)	2 (3.2%)	6 (9.5%)	6 (9.5%)	3 (4.8%)
Headache					2 (1.6%)	4 (3.1%)		1 (0.8%)	1 (1.6%)	2 (3.2%)		1 (1.6%)
Irritability	2 (18.2%)	3 (27.3%)	1 (9.1%)	2 (18.2%)	9 (7.0%)	39 (30.5%)	23 (18.0%)	8 (6.2%)	4 (6.3%)	26 (41.3%)	17 (27.0%)	4 (6.3%)
Malaise	3 (27.3%)	3 (27.3%)	1 (9.1%)	1 (9.1%)	12 (9.4%)	27 (21.1%)	6 (4.7%)	5 (3.9%)	7 (11.1%)	16 (25.4%)	6 (9.5%)	5 (7.9%)
Fever	1 (9.1%)	1 (9.1%)	3 (27.3%)	3 (27.3%)	4 (3.1%)	21 (16.4%)	16 (12.5%)	18 (14.1%)	3 (4.8%)	16 (25.4%)	8 (12.7%)	8 (12.7%)
Anorexia	1 (9.1%)	1 (9.1%)	1 (9.1%)		5 (3.9%)	14 (10.9%)	7 (5.5%)	5 (3.9%)	4 (6.3%)	10 (15.9%)	6 (9.5%)	5 (7.9%)
Allergy					2 (1.6%)	7 (5.5%)	7 (5.5%)	2 (1.6%)	2 (3.2%)	6 (9.5%)	5 (7.9%)	1 (1.6%)
Exanthema						1 (0.8%)	2 (1.6%)	3 (2.3%)		1 (1.6%)		1 (1.6%)
No Complaint	7 (63.6%)	4 (36.4%)	4 (36.4%)	6 (54.5%)	103 (80.5%)	39 (30.5%)	54 (42.2%)	65 (50.8%)	49 (77.8%)	12 (19.0%)	19 (30.2%)	28 (44.4%)
Total Subjects	11	11	11	11	128	128	128	128	63	63	63	63

Table 4: Clinical Complaints Recorded for Children Vaccinated with Measles-Mumps-Rubella Vaccine Lot 96400 and for Their Unvaccinated Controls (Study 220C)

Clinical Complaint	Contact Control Children				Total Vaccinees				Initially Seronegative to Measles-Mumps-Rubella			
	Days Observed				Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness	1 (4.0%)	3 (12.0%)	1 (4.0%)	3 (12.0%)	15 (6.7%)	19 (8.5%)	14 (6.2%)	19 (8.5%)	4 (4.4%)	5 (5.5%)	3 (3.3%)	8 (8.8%)
Otitis	1 (4.0%)				1 (0.4%)		1 (0.4%)	1 (0.4%)				
Parotitis					1 (0.4%)							
Lymphadenopathy				1 (4.0%)	1 (0.4%)	4 (1.8%)	3 (1.3%)	2 (0.9%)				
Conjunctivitis	1 (4.0%)	1 (4.0%)			4 (1.8%)	6 (2.7%)		1 (0.4%)	1 (1.1%)	2 (2.2%)		1 (1.1%)
Gastrointestinal	1 (4.0%)	1 (4.0%)	1 (4.0%)	2 (8.0%)	20 (8.9%)	38 (17.0%)	17 (7.6%)	10 (4.5%)	13 (14.3%)	20 (22.0%)	9 (9.9%)	7 (7.7%)
Headache					5 (2.2%)	9 (4.0%)	6 (2.7%)	2 (0.9%)	2 (2.2%)	4 (4.4%)	2 (2.2%)	1 (1.1%)
Irritability	1 (4.0%)	1 (4.0%)		1 (4.0%)	6 (2.7%)	14 (6.2%)	2 (0.9%)	3 (1.3%)	3 (3.3%)	6 (6.6%)	1 (1.1%)	1 (1.1%)
Malaise		1 (4.0%)	1 (4.0%)	1 (4.0%)	6 (2.7%)	11 (4.9%)	4 (1.8%)	6 (2.7%)	4 (4.4%)	7 (7.7%)	2 (2.2%)	5 (5.5%)
Measles		1 (4.0%)				1 (0.4%)						
Fever	1 (4.0%)	3 (12.0%)	2 (8.0%)	5 (20.0%)	12 (5.3%)	49 (21.9%)	19 (8.5%)	32 (14.3%)	8 (8.8%)	23 (25.3%)	6 (6.6%)	13 (14.3%)
Anorexia		1 (4.0%)			11 (4.9%)	19 (8.5%)	7 (3.1%)	4 (1.8%)	6 (6.6%)	12 (13.2%)	6 (6.6%)	2 (2.2%)
Allergy					1 (0.4%)	1 (0.4%)		1 (0.4%)				1 (1.1%)
Exanthema					1 (0.4%)	1 (0.4%)	1 (0.4%)	2 (0.9%)				1 (1.1%)
Measles-like Rash		1 (4.0%)	1 (4.0%)			1 (0.4%)	1 (0.4%)					
No Complaint	22 (88.0%)	19 (76.0%)	21 (84.0%)	14 (56.0%)	166 (74.1%)	120 (53.6%)	172 (76.8%)	164 (73.2%)	61 (67.0%)	43 (47.3%)	71 (78.0%)	64 (70.3%)
Physician's Surveillance Negative					2	2	2	2				
Total Subjects	25	25	25	25	226	226	226	226	91	91	91	91

TABLE 6.--Miscellaneous Clinical Complaints Among Triple Seronegative Children Given Trivalent Vaccine Compared with Unvaccinated Controls (Suburban Philadelphia).

Complaint	Vaccinated Children (228)				Contact Controls (106)			
	Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Conjunctivitis		1 (0.4)						
Otitis	3 (1.3%)	5 (2.2)	3 (1.3)	7 (3.1)			1 (0.9)	1 (0.9)
Upper respiratory illness	41 (18.0)	56 (24.6)	28 (12.3)	33 (14.5)	9 (8.5)	17 (16.0)	11 (10.4)	11 (10.4)
Lymphadenopathy		3 (1.3)					1 (0.9)	
Gastroenteritis	15 (6.6)	18 (7.9)	11 (4.8)	7 (3.1)	3 (2.8)	2 (1.9)	1 (0.9)	
Rash (non-measles)	10 (4.4)	6 (2.6)	4 (1.8)	4 (1.8)	2 (1.9)	2 (1.9)	1 (0.9)	1 (0.9)
Local reaction - inj. site	1 (0.4)							
Headache				1 (0.4)	1 (0.9)			1 (0.9)
Irritability	15 (6.6)	17 (7.5)	6 (2.6)	5 (2.2)	2 (1.9)			
Malaise	1 (0.4)	1 (0.4)						
Anorexia	4 (1.8)	5 (2.2)	1 (0.4)	2 (0.9)	1 (0.9)			
Measles-like rash		9 (3.9)	2 (0.9)					
Fatigue	1 (0.4)					1 (0.9)		
Unrelated illness	10 (4.4)	12 (5.3)	11 (4.8)	15 (6.6)		1 (0.9)	1 (0.9)	1 (0.9)
No complaints	152 (66.7)	136 (59.6)	177 (77.6)	164 (71.9)	88 (83.0)	85 (80.2)	91 (85.8)	92 (86.8)

TABLE 7.--Miscellaneous Clinical Complaints Among Triple Seronegative Children Given Trivalent Vaccine Compared with Unvaccinated Controls (Costa Rica-San Salvador).

Complaint	Vaccinated Children (457)				Contact Controls (175)			
	Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Conjunctivitis	5 (1.1%)	15 (3.3)	8 (1.8)	8 (1.8)	5 (2.9)	4 (2.3)	3 (1.7)	2 (1.1)
Otitis	3 (0.7)	8 (1.8)	2 (0.4)	3 (0.7)	2 (1.1)	3 (1.7)	1 (0.6)	1 (0.6)
Upper respiratory illness	52 (11.4)	113 (24.7)	84 (18.4)	63 (13.8)	18 (10.3)	32 (18.3)	19 (10.9)	19 (10.9)
Lymphadenopathy		12 (2.6)	8 (1.8)	11 (2.4)	1 (0.6)	3 (1.7)	2 (1.1)	3 (1.7)
Gastroenteritis	47 (10.3)	88 (19.3)	49 (10.7)	46 (10.1)	11 (6.3)	24 (13.7)	18 (10.3)	24 (13.7)
Natural measles					1 (0.6)	1 (0.6)		
Fever	24 (5.3)	102 (22.3)	45 (9.8)	37 (8.1)	12 (6.9)	23 (13.1)	18 (10.3)	22 (12.6)
Headache	7 (1.5)	15 (3.3)	3 (0.7)	3 (0.7)	5 (2.9)	6 (3.4)	1 (0.6)	2 (1.1)
Irritability	28 (6.1)	85 (18.6)	42 (9.2)	20 (4.4)	12 (6.9)	19 (10.9)	7 (4.0)	10 (5.7)
Malaise	39 (8.5)	68 (14.9)	26 (5.7)	21 (4.6)	9 (5.1)	15 (8.6)	11 (6.3)	9 (5.1)
Anorexia	23 (5.0)	67 (14.7)	35 (7.7)	22 (4.8)	9 (5.1)	16 (9.1)	12 (6.9)	8 (4.6)
Measles-like rash		1 (0.2)	1 (0.2)		1 (0.6)	2 (1.1)	2 (1.1)	
Exanthema	1 (0.2)	4 (0.9)	3 (0.7)	4 (0.9)		1 (0.6)	1 (0.6)	1 (0.6)
Rubella-like rash	2 (0.4)	3 (0.7)	1 (0.2)	2 (0.4)	2 (1.1)	2 (1.1)		
Arthralgia					1 (0.6)	1 (0.6)		
Unrelated illness	3 (0.7)	11 (2.4)	6 (1.3)	6 (1.3)		2 (1.1)	3 (1.7)	
No complaints	318 (69.6)	183 (40.0)	276 (60.4)	294 (64.3)	127 (72.6)	106 (60.6)	121 (69.1)	115 (65.7)

Table 3

Clinical Complaints Recorded for Children Vaccinated with Combined Measles-Mumps-Rubella Vaccine Lot 12238 (Study #253)

Clinical Complaint	Total Vaccinees				Initially Seronegative to Measles-Mumps-Rubella			
	Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness		4 (3.4%)	2 (1.7%)	3 (2.6%)		3 (5.1%)	1 (1.7%)	3 (5.1%)
Otitis	1 (0.9%)	5 (4.3%)			1 (1.7%)	1 (1.7%)		
Swollen Glands		1 (0.9%)						
Conjunctivitis	1 (0.9%)	1 (0.9%)						
Gastrointestinal	2 (1.7%)	7 (6.0%)	3 (2.6%)	2 (1.7%)	1 (1.7%)	5 (8.5%)	3 (5.1%)	2 (3.4%)
Headache		1 (0.9%)				1 (1.7%)		
Irritability	4 (3.4%)	23 (19.7%)	4 (3.4%)	10 (8.5%)	4 (6.8%)	16 (27.1%)	3 (5.1%)	6 (10.2%)
Malaise	4 (3.4%)	23 (19.7%)	4 (3.4%)	10 (8.5%)	4 (6.8%)	16 (27.1%)	3 (5.1%)	6 (10.2%)
Irrelevant		1 (0.9%)				1 (1.7%)		
Fever	3 (2.6%)	20 (17.1%)	3 (2.6%)	6 (5.1%)	3 (5.1%)	13 (22.0%)	2 (3.4%)	4 (6.8%)
Anorexia	6 (5.1%)	22 (18.8%)	4 (3.4%)	8 (6.8%)	5 (8.5%)	16 (27.1%)	3 (5.1%)	5 (8.5%)
Allergy		2 (1.7%)	2 (1.7%)			2 (3.4%)	2 (3.4%)	
No Complaints	108 (92.3%)	83 (70.9%)	110 (94.0%)	106 (90.6%)	53 (89.8%)	39 (66.1%)	53 (89.8%)	52 (88.1%)
Total Subjects	117	117	117	117	59	59	59	59

Table 4

Clinical Complaints Recorded for Children Vaccinated with Combined Measles-Mumps-Rubella Vaccine Lot 92127 and for Their Unvaccinated Contact Controls (Study 246)

Clinical Complaints	Contact Control Children				Total Vaccinees				Initially Seronegative to Measles-Mumps-Rubella			
	Days Observed				Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness	2 (33.3%)	2 (33.3%)			36 (32.7%)	48 (43.6%)	18 (16.4%)	13 (11.8%)	21 (32.8%)	29 (45.3%)	9 (14.1%)	8 (12.5%)
Conjunctivitis					2 (1.8%)	3 (2.7%)	2 (1.8%)		1 (1.6%)	2 (3.1%)	1 (1.6%)	
Gastrointestinal					4 (3.6%)	6 (5.5%)			4 (6.2%)	4 (6.2%)		
Headache					5 (4.5%)	2 (1.8%)			1 (1.6%)	1 (1.6%)		
Irritability					11 (10.0%)	9 (8.2%)	1 (0.9%)	1 (0.9%)	7 (10.9%)	6 (9.4%)		
Malaise					10 (9.1%)	3 (2.7%)	2 (1.8%)	1 (0.9%)	4 (6.2%)	2 (3.1%)	1 (1.6%)	
Measles						1 (0.9%)						
Anorexia					10 (9.1%)	12 (10.9%)	5 (4.5%)	3 (2.7%)	6 (9.4%)	6 (9.4%)	3 (4.7%)	2 (3.1%)
Exanthema					1 (0.9%)	2 (1.8%)	1 (0.9%)		1 (1.6%)	1 (1.6%)		
No Complaints	4 (66.7%)	4 (66.7%)	6 (100%)	6 (100%)	62 (56.4%)	55 (50.0%)	87 (79.1%)	94 (85.5%)	36 (56.2%)	32 (50.0%)	51 (79.7%)	53 (82.8%)
Total Subjects	6	6	6	6	110	110	110	110	64	64	64	64

Table

Clinical Complaints Recorded for Children Vaccinated with Combined Measles-Mumps-Rubella Vaccine Lot 96400 and for Their Unvaccinated Contact Controls (Study 246)

Clinical Complaints	Contact Control Children				Total Vaccinees				Initially Seronegative to Measles-Mumps-Rubella			
	Days Observed				Days Post-Vaccination				Days Post-Vaccination			
	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28	1-4	5-12	13-18	19-28
Upper Respiratory Illness	1 (33.3%)	1 (33.3%)	1 (33.3%)		31 (39.7%)	32 (41.0%)	7 (9.0%)	5 (6.4%)	12 (32.4%)	16 (43.2%)	6 (16.2%)	2 (5.4%)
Otitis						1 (1.3%)						
Swollen Glands					1 (1.3%)	1 (1.3%)						
Conjunctivitis	1 (33.3%)	1 (33.3%)										
Gastrointestinal						2 (2.6%)	1 (1.3%)	3 (3.8%)		2 (5.4%)	1 (2.7%)	2 (5.4%)
Headache					3 (3.8%)	1 (1.3%)						
Irritability	1 (33.3%)	1 (33.3%)			5 (6.4%)	3 (3.8%)			1 (2.7%)	1 (2.7%)		
Malaise	2 (66.7%)	2 (66.7%)			8 (10.3%)	3 (3.8%)			2 (5.4%)	1 (2.7%)		
Anorexia					1 (1.3%)	5 (6.4%)	1 (1.3%)	1 (1.3%)		2 (5.4%)	1 (2.7%)	1 (2.7%)
Exanthema					1 (1.3%)	1 (1.3%)			1 (2.7%)	1 (2.7%)		
No Complaints	1 (33.3%)	1 (33.3%)	2 (66.7%)	3 (100%)	46 (59.0%)	44 (56.4%)	70 (89.7%)	71 (91.0%)	25 (67.6%)	20 (54.1%)	30 (81.1%)	33 (89.2%)
Total Subjects	3	3	3	3	78	78	78	78	37	37	37	37

Exhibit 29

Siri | Glimstad

200 Park Avenue, Seventeenth Floor, New York, NY 10166
sirillp.com | P: (212) 532-1091 | F: (646) 417-5967

May 21, 2021

VIA EMAIL AND FEDEX

Dr. Howard A. Zucker
Commissioner,
New York State Department of Health
Corning Tower
Empire State Plaza
Albany, NY 12237
howard.zucker@health.ny.gov

Dr. Betty A. Rosa
Commissioner of Education
New York State Education Department
89 Washington Avenue
Albany, New York 12234
Commissioner@nysed.gov

Re: *Vaccinated vs. unvaccinated health outcomes in Ulster children*

Dear Dr. Zucker and Dr. Rosa:

We represent a group comprising all of the families of unvaccinated children[1] (the "**Ulster Children**") in the following four contiguous school districts: Kingston City, New Paltz, Rondout Valley, and Wallkill (collectively, the "**School Districts**").

Like almost all parents, these families seek to safeguard the long-term health of their children. Unlike most parents, they have concluded that avoiding vaccines confers an overall health benefit for their children. While there is an abundance of evidence to support this conclusion, the most compelling evidence are the health outcomes of their children as compared with the health outcomes of the vaccinated children in their school districts.

What makes the difference in these health outcomes particularly compelling is that these unvaccinated children are all of the known unvaccinated children in grades K through 12 in these School Districts. They comprise 56 families with a total of 99 unvaccinated children. By including all unvaccinated children within the School Districts, there is no selection bias or cherry picking. While the better health outcome of any one of these children could be, and typically is, discarded by health authorities as anecdotal, collectively, their health outcomes are not anecdotal.

To assess any health issues among the Ulster Children, the most recent completed NYS School Health Examination Form, which is completed by each child's pediatrician, was collected for each child. These forms include check boxes for whether the child has, among other things,

[1] "Unvaccinated child" means a child who has not received any vaccines.

allergies, asthma, seizures, or diabetes, as well as any cardiovascular, neurological, speech, social emotional, etc., issues. Additionally, an MD interviewed each family to assure that there were no other diagnosed medical conditions not reflected on these forms.

The result was as follows:

Condition	Rate in Unvaccinated Ulster Children	Background Rate
Allergy – Food	2%	8%[2]
Allergy – Environmental	2%	8.4%[3]
Asthma	1%	7.5%[4]
Seizures	0%	0.6%[5]
Diabetes	0%	Type 1: 22.3 per 100,000 Type 2: 13.8 per 100,000[6]
Autism Spectrum Disorder	0%	1 in 54 children[7]
Attention Deficit Hyperactivity Disorder	2%	9.4%[8]
Eczema	1%	12%[9]

The above finding is consistent with the handful of studies that assessed health outcomes between those who have received vaccines and those who have not received any vaccines. For example, Dr. Peter Aaby is renowned for studying and promoting vaccines in Africa and has published over 300 peer-reviewed articles and studies regarding vaccination.[10] In 2017, he and co-authors published a study finding that infants were 10 times more likely to die by 6 months of age following their DTP vaccination than those that did not receive any vaccines during the first 6 months of life.[11] Children vaccinated with DTP were dying from causes never associated with this vaccine, such as respiratory infections, diarrhea, and malaria.[12] This indicated that while DTP's

[2] *See* https://www.cdc.gov/healthyschools/foodallergies/index.htm.

[3] *See* https://www.aafa.org/allergy-facts/.

[4] *See* https://www.cdc.gov/nchs/fastats/asthma.htm.

[5] *See* https://www.cdc.gov/epilepsy/data/index.html.

[6] *See* https://www.cdc.gov/mmwr/volumes/69/wr/mm6906a3.htm?s_cid=mm6906a3_w.

[7] *See* https://www.cdc.gov/ncbddd/autism/data.html.

[8] *See* https://www.cdc.gov/ncbddd/adhd/data.html.

[9] *See* https://www.cdc.gov/nchs/data/health_policy/eczema_skin_problems_tables.pdf.

[10] *See* https://www.ncbi.nlm.nih.gov/pubmed/?term=PETER+AABY%5BAuthor+-+Full%5D.

[11] *See* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360569/.

[12] *See* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360569/.

purpose is to reduce the incidence of diphtheria, tetanus, and pertussis, it actually increased mortality from other infections.[13] The study therefore concludes:

> All currently available evidence suggests that DTP vaccine may kill more children from other causes than it saves from diphtheria, tetanus or pertussis.[14]

In a related finding, a study out of the University of Hong Kong, Queen Mary Hospital, and Centre for Influenza Research compared children receiving the influenza vaccine with those receiving a saline injection in a prospective randomized double-blind study.[15] Both groups had a statistically similar rate of influenza, but the group receiving the influenza vaccine had a statistically significant 440% increase in the rate of non-influenza infections.[16] Thus, the influenza vaccine increased children's susceptibility to other respiratory viral infections, just as DTP vaccine increased susceptibility to other infections which, in turn, increased mortality.

Similarly instructive is that measles vaccination appears to have significantly increased – not decreased – overall mortality related to measles in the United States. The first vaccine for measles was licensed in the United States in 1963 and, according to the CDC, the mortality rate from measles declined by over 98% between 1900 and 1962.[17] In the years leading up to 1963 (when no measles vaccine existed), the CDC reported a total of approximately 400 deaths from measles per year in the United States during a time when virtually every American had measles, reflecting an annual death rate from measles of 1 in 500,000 Americans prior to the introduction of the measles vaccine.[18] On the other hand, eliminating measles has demonstrably and measurably increased certain cancer rates, the risk of heart disease, and other serious medical conditions. For example, the International Agency for Research on Cancer found that those who have never had measles had a 66% increased rate of Non-Hodgkin Lymphoma and a 233% increased rate of Hodgkin Lymphoma.[19] These two cancers killed **20,960** Americans in 2018. *Id*. Likewise, researchers at the University of British Columbia and the University of Victoria have confirmed that those who never had measles had a 50% increased rate of ovarian cancer, which killed **14,070** Americans in 2018.[20] The nation of Japan concluded, after tracking over 100,000 of its citizens for more than 22 years, that having measles

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[13] *See* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360569/.

[14] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360569/.

[15] *See* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404712/.

[16] *See* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404712/.

[17] *See* https://physiciansforinformedconsent.org/measles/dis/; *see also* https://www.cdc.gov/nchs/data/vsus/vsrates1940_60.pdf.

[18] *See* https://www.cdc.gov/nchs/data/vsus/vsrates1940_60.pdf; and https://www.census.gov/library/publications/1961/dec/pc-s1-10.html. Medical care for acute viral infections has also made significant advances since 1962.

[19] *See* https://pubmed.ncbi.nlm.nih.gov/16406019/; *see also* https://pubmed.ncbi.nlm.nih.gov/9824838/; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1589969/?page=1; https://seer.cancer.gov/statfacts/html/nhl.html; and https://seer.cancer.gov/statfacts/html/hodg.html.

[20] *See* https://www.sciencedirect.com/science/article/abs/pii/S0361090X06000043; https://seer.cancer.gov/statfacts/html/ovary.html.

and mumps was "associated with lower risks of mortality from heart disease," which killed **610,000** Americans in 2018.[21] Additionally, peer reviewed studies reflect that children who have had measles suffer from far less allergies and atopic diseases, such as asthma, and adults who have had measles have a reduced risk of Parkinson's Disease.[22] Hence, as with the DTP vaccine, the body of science regarding the measles vaccine reflects that eliminating measles has caused far more deaths annually in the United States from cancer and heart disease than the potentially few hundred lives saved from eliminating measles.[23]

Perhaps most concerning with regard to the DTP study is that it was based on data from the 1980s that had been collecting dust for over 30 years.[24] This begs the question: what other serious vaccine injuries and non-specific adverse effects are being missed by our health authorities?

One indication of what is being missed is the following finding from the School of Public Health at Jackson State University: 33% of vaccinated preterm babies had a neurodevelopmental disorder while 0% of the unvaccinated preterm babies had a neurodevelopmental disorder; and another pilot study by the same group found that vaccinated children, compared to unvaccinated children (receiving no vaccines), had a statistically significant increased rate of 390% for allergies, 420% for ADHD, 420% for autism, 290% for eczema, 520% for learning disabilities, and 370% for any neuro-developmental delay.[25]

In another recent study, aggregating data from three medical practices in the United States, the health outcomes of vaccinated and unvaccinated children born between 2005 and 2015 were compared; this study found that vaccinated children, compared to unvaccinated children, had a statistically significant increased rate of 218% for developmental delay, 449% for asthma and 213% for ear infections. [26] Another similar study, looking at the medical records of 3,324 children from a single pediatric practice over a ten year period, found that the vaccinated, as compared to the unvaccinated, had a statistically significant increased rate of, among other things, 648% for allergic rhinitis, 633% for anemia, 476% for eczema, and 313% for behavioral issues.[27] One particularly standout observation among many was that zero of the 516 unvaccinated children in

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[21] https://pubmed.ncbi.nlm.nih.gov/26122188/; https://www.cdc.gov/heartdisease/facts.htm.

[22] *See* https://pubmed.ncbi.nlm.nih.gov/19255001/; *see also* https://pubmed.ncbi.nlm.nih.gov/16854347/; and https://academic.oup.com/aje/article-abstract/122/6/1017/72271?redirectedFrom=fulltext.

[23] Stated differently: until the introduction of the vaccine, measles was considered a mild childhood infection, like the chickenpox; the ecological relationship humans developed with measles through millennia did not eliminate measles; and the evidence supports that having measles conferred benefits for survival that exceeded its negative effects.

[24] *See* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360569/; *see also* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404712/.

[25] *See* http://www.oatext.com/pdf/JTS-3-186.pdf; http://www.oatext.com/pdf/JTS-3-187.pdf.

[26] *See* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7268563/.

[27] *See* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7709050/.

the study had attention deficit hyperactivity disorder (ADHD) compared to 5.3% of the partially or fully vaccinated children.[28]

Consider that there are over 420 disorders listed on package inserts of infant vaccines – a large portion of which are immune and nervous system disorders – which are *only* listed there because its manufacturer has a basis to believe there is a causal relationship between the vaccine and the occurrence of the adverse event.[29] Federal law is clear that the package insert should include "*only* those adverse events for which there is some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event."[30]

The greatest vaccine safety signal may be the ever-growing percentage of Americans refusing to vaccinate their children. According to the CDC, between 2001 and 2017 the number of completely unvaccinated two-year-old children in America has increased by 433%.[31] One in 77 two-year old American children are now completely unvaccinated and 1 in 2 children skip one or more vaccines on CDC's childhood vaccine schedule.[32] This growth has occurred despite stricter vaccination laws and access to free vaccinations for lower income populations.

Parents declining one or more recommended vaccines for their children often have concerns about vaccine safety because they themselves, their children, or someone else close to them has had a personal experience with a life-altering adverse event following vaccination.[33] Parents who make this informed choice, as CDC admits, are typically well-educated, and do so in the face of social stigma and exclusion; hence, they often never make this decision lightly, but rather after careful research or a personal experience with vaccine injury.[34]

Doctors have long been trained to listen to their patients, and studies have repeatedly shown that parents are the best source of information about their children and provide highly accurate information for detecting symptoms of and addressing developmental and behavioral problems.[35] The New York State Department of Health ("**NYSDOH**") and the New York State Education Department ("**NYSED**") should take heed of this age-old wisdom and listen to the growing number of parents who, as the vaccine schedule has expanded, have reported that they observed their children regress into poor health after vaccination, including losing previously met cognitive and physical milestones and suffering changes in personality and behavior. If the NYSDOH and NYSED want to prove them wrong, they need to produce real science showing the actual safety

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[28] *See* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7709050/.

[29] *See* 21 C.F.R. 201.57; https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm093833.htm.

[30] 21 C.F.R. 201.57.

[31] *See* https://www.cdc.gov/mmwr/volumes/67/wr/mm6740a4.htm.

[32] *See* https://www.cdc.gov/mmwr/volumes/67/wr/mm6740a4.htm; https://stacks.cdc.gov/view/cdc/59415.

[33] *See* https://www.ncbi.nlm.nih.gov/pubmed/25200366.

[34] *See* https://www.ncbi.nlm.nih.gov/pubmed/18816357; *see also* https://www.ncbi.nlm.nih.gov/pubmed/28578210; and https://www.cnn.com/2015/02/03/health/the-unvaccinated/index.html.

[35] *See* https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1440-1754.1999.00342.x.

of the childhood vaccine schedule. That science demands, at the very least, a properly sized and controlled study comparing health outcomes in vaccinated and completely unvaccinated children.

The stated purposes of vaccination are to improve the overall quality of health of Americans and reduce mortality. Yet, the increase in the childhood vaccine schedule over the last 30 years from 2 injected vaccines[36] to 13 injected vaccines[37] (plus 2 injected vaccines during pregnancy[38]) has occurred in lockstep with the increase in the rate of autoimmune, developmental, and neurological disorders in children from 12.8% to 54%.[39] Health authorities have no explanation for why U.S. children today are plagued with a chronic disease and disability epidemic.

This as yet unexplained explosion in chronic disease and disability among American children, which coincides with the rapid increase in the numbers of vaccinations given to infants and children in the first six years of life, is a serious vaccine safety signal that demands methodologically sound studies to rule out vaccines or the childhood vaccine schedule as a contributing cause. It is accepted science that adverse responses to vaccination can lead to certain chronic disorders, including autoimmune, developmental, and neurological disorders – it is only the rate at which this occurs that is either disputed or admittedly unknown.[40]

The Ulster Children are the living proof that unvaccinated children have far better health outcomes than vaccinated children. **If you contest these results, please provide the scientific support that reflects that vaccinated children have better long-term health outcomes than the unvaccinated.** Please also provide evidence that the growing rate and list of chronic diseases and disabilities affecting children are not caused by vaccination.

If the NYSDOH or the NYSED do not have such evidence, then they cannot assess whether the childhood vaccine schedule it promotes and enforces is causing more harm than good, and its

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[36] *See* https://www.cdc.gov/vaccines/schedules/images/schedule1983s.jpg (OPV is given orally).

[37] *See* https://www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html#schedule (Rotavirus is given orally. Assumes 4-dose Hib series, 3-dose HPV series, and no combination vaccines; but even with combination vaccines still have a total of 40 injections.)

[38] *See* https://www.cdc.gov/vaccines/pregnancy/downloads/immunizations-preg-chart.pdf.

[39] Compare https://www.cdc.gov/vaccines/schedules/images/schedule1983s.jpg with https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf.

[40] Among other sources: https://www.hrsa.gov/sites/default/files/vaccinecompensation/vaccineinjurytable.pdf; https://www.nap.edu/read/1815/chapter/2#7; https://www.nap.edu/read/2138/chapter/2#11; https://www.nap.edu/read/13164/chapter/2#2; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360569/; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404712/; children must "prove that the vaccine was the cause" for all off-Table vaccine injuries, https://www.ncbi.nlm.nih.gov/nlmcatalog/101633437, 98% of vaccine injury claims are off-Table, http://www.gao.gov/assets/670/667136.pdf, and partial database of off-Table vaccine injury awards, https://www.uscfc.uscourts.gov/aggregator/sources/7; see studies compiled in this white paper: http://icandecide.org/white-papers/ICAN-AluminumAdjuvant-Autism.pdf; conditions listed in Appendix B are reported in one or more pediatric vaccine package inserts, https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm093833.htm, because, as required by federal law, there is a "basis to believe there is a causal relationship between the drug and the occurrence of the adverse event," 21 C.F.R. 201.57.

vaccination requirements not only fail to meet strict scrutiny, but they lack a rational basis. If you fail to timely provide this evidence, we have been authorized to commence an action challenging the constitutionality of the school immunization requirements for kindergarten through the twelfth grade.

Our client looks forward to receiving the scientific support requested.

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Very truly yours,



Aaron Siri, Esq.
Elizabeth A. Brehm, Esq.
Jessica Wallace, Esq.

Aaron Siri

From: doh.sm.DLAHouse <dlahouse@health.ny.gov>
Sent: Wednesday, June 16, 2021 8:00 AM
To: Elizabeth Brehm; Aaron Siri
Subject: Vaccinated vs. unvaccinated health outcomes in Ulster children

Dear Elizabeth Brehm and Aaron Siri,

Thank you for your recent correspondence to Commissioner Zucker requesting information about childhood vaccinations and school vaccination requirements.

Detailed information concerning the efficacy and safety of childhood vaccinations is widely available to the public, including on the websites of the Department of Health (https://www.health.ny.gov/prevention/immunization/) and the federal Centers for Disease Control and Prevention (https://www.cdc.gov/vaccinesafety/index.html), as well as in decades of scientific literature.

In addition, the State's authority to mandate vaccinations in schools and other settings, as an essential tool to protect the public health, has been clearly established by both federal and state courts dating back well over a century (See, e.g., *Jacobson v. Massachusetts*, 197 U.S. 11 (1905)).

Vaccinations are one of the most important methods available to protect children from serious and sometimes deadly diseases, and the Department of Health will continue to support childhood vaccinations and the enforcement of Public Health Law mandates for vaccinating school-age children.

Sincerely,

Richard Thomas
Deputy Director, Bureau of Program Counsel
Division of Legal Affairs

New York State Department of Health
ESP Corning Tower, Albany, NY 12237
health.ny.gov

Siri | Glimstad

NEW YORK | LOS ANGELES | MIAMI
PHOENIX | DETROIT

200 Park Avenue, 17th Floor, New York, NY 10166
sirillp.com | P: (212) 532-1091 | F: (646) 417-5967

August 11, 2021

VIA EMAIL AND FEDEX

Dr. Howard A. Zucker
Commissioner,
New York State Department of Health
Corning Tower
Empire State Plaza
Albany, NY 12237
howard.zucker@health.ny.gov

Dr. Betty A. Rosa
Commissioner of Education
New York State Education Department
89 Washington Avenue
Albany, New York 12234
Commissioner@nysed.gov

Richard Thomas
Deputy Director, Bureau of Program Counsel
Division of Legal Affairs
New York State Department of Health
Corning Tower
Empire State Plaza
Albany, NY 12237
dlahouse@health.ny.gov

Re: *Vaccinated vs. unvaccinated health outcomes in Ulster children*

Dear Dr. Zucker, Dr. Rosa, and Mr. Thomas:

We represent a group comprising all of the families of unvaccinated children[1] (the "**Ulster Children**") in the following four contiguous school districts: Kingston City, New Paltz, Rondout Valley, and Wallkill (collectively, the "**School Districts**"). We previously wrote to Dr. Zucker and Dr. Rosa on May 21, 2021 (that letter is appended here for convenience) with the results of an assessment of health outcomes in vaccinated versus unvaccinated children within the School Districts which showed living proof that unvaccinated children have far better health outcomes than vaccinated children.

On June 16, 2021, we received a response from Mr. Thomas (also appended here) which directed us to two webpages, one from the New York State Department of Health, the other from the Centers for Disease Control and Prevention. We were further directed to "detailed information" in "decades of scientific literature" without any citations to same.

The request, plainly stated in our original letter, was as follows:

[1] "Unvaccinated child" means a child who has not received any vaccines.

> The Ulster Children are the living proof that unvaccinated children have far better health outcomes than vaccinated children. If you contest these results, please provide the *scientific support that reflects that vaccinated children have better long-term health outcomes than the unvaccinated*. Please also provide *evidence that the growing rate and list of chronic diseases and disabilities affecting children are not caused by vaccination*.

We note that neither link provides evidence that the growing rate and list of chronic diseases and disabilities affecting children are not caused by vaccination. Absent receipt of this proof, we have been directed to commence an action challenging the constitutionality of the school immunization requirements for kindergarten through the twelfth grade.

Our client looks forward to receiving the scientific support requested.

All rights reserved.

Very truly yours,



Aaron Siri, Esq.
Elizabeth A. Brehm, Esq.
Jessica Wallace, Esq.

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PHOENIX | DETROIT | DENVER | AUSTIN

200 Park Avenue, 17th Floor, New York, NY 10166
sirillp.com | P: (212) 532-1091 | F: (646) 417-5967

November 11, 2021

VIA EMAIL AND FEDEX

Dr. Howard A. Zucker
Commissioner, New York State Department of Health
Corning Tower Empire State Plaza
Albany, NY 12237
Howard.zucker@health.ny.gov

Dr. Betty A. Rosa
Commissioner of Education
New York State Education Department
89 Washington Avenue
Albany, NY 12234
Commissioner@nysed.gov

Mr. Richard Thomas
Deputy Director, Bureau of Legal Affairs
New York State Department of Health
Corning Tower Empire State Plaza
Albany, NY 12237
dlahouse@health.ny.gov

Re: *Vaccinated vs. unvaccinated health outcomes in Ulster children*

Dear Dr. Zucker, Dr. Rosa, and Mr. Thomas:

We write to follow-up on our prior communications of May 21, 2021, June 16, 2021, and August 11, 2021, attached hereto.

The New York State Department of Health has an annual budget of approximately $88.5 billion and a specific focus on promoting vaccines. In fact, a significant portion of your agency's efforts are geared toward promoting vaccines, encouraging the public they are safe, and otherwise increasing vaccination rates. It would therefore be within your interest to share studies which, in fact, support the safety of the childhood vaccine schedule. The fact that you have not done so to date appears a clear and plain admission that you have no such studies.

As public servants, you should be reticent to continue to mandate a liability-free product to children without proper safety studies. Your assumptions regarding these products are akin to beliefs; you believe the assumptions are true without evidence, even in the face of evidence to the contrary. Parents should not have to participate in your beliefs about these products. They prefer to rely on the data, the studies, and their family's experiences regarding these products, which

show that their children are healthier than those that participate in your mandated schedule of dozens of injections of these products per child.

As there is no longer any excuse that you have not had sufficient time to gather appropriate studies, unless we receive same by November 30, 2021, we will be taking formal legal action.

Govern yourselves accordingly.

Best regards,



Aaron Siri, Esq.
Elizabeth A. Brehm, Esq.

Siri | Glimstad

NEW YORK | LOS ANGELES | MIAMI
PHOENIX | DETROIT | DENVER | AUSTIN

200 Park Avenue, 17th Floor, New York, NY 10166
sirillp.com | P: (212) 532-1091 | F: (646) 417-5967

December 27, 2021

SENT VIA EMAIL AND FEDEX
Dr. Mary Bassett
Acting Commissioner, New York State Department of Health
Corning Tower Empire State Plaza
Albany, NY 12237
Mary.Bassett@health.ny.gov

Re: *Vaccinated vs. unvaccinated health outcomes in Ulster children*

Dear Acting Commissioner Bassett:

We write on behalf of a group we represent, comprising all of the families of unvaccinated children in the four contiguous school districts of Kingston City, New Paltz, Rondout Valley, and Wallkill, and we welcome to your recent appointment as Acting Director of the New York State Department of Health.

Attached is correspondence with the former Commissioner, Dr. Zucker, spanning a six-month time period earlier this year. We share this exchange with you with the hope that you will provide a more substantial response to the important issues and concerns raised forthwith, prior to our legal filing.

Best regards,

Aaron Siri, Esq.
Elizabeth A. Brehm, Esq.

Siri | Glimstad

NEW YORK | LOS ANGELES | MIAMI
PHOENIX | DETROIT | DENVER | AUSTIN

200 Park Avenue, 17th Floor, New York, NY 10166
sirillp.com | P: (212) 532-1091 | F: (646) 417-5967

March 24, 2022

SENT VIA EMAIL AND FEDEX
Mary Bassett, MD, MPH
Acting Commissioner, New York State Department of Health
Corning Tower Empire State Plaza
Albany, NY 12237
Mary.Bassett@health.ny.gov

Re: *Follow-up on Vaccinated vs. Unvaccinated Health Outcomes in Ulster Children*

Dear Acting Commissioner Bassett:

We write to follow up on our December 27, 2021 letter to you on behalf of a group we represent comprised of all of the families of unvaccinated children in the four contiguous school districts of Kingston City, New Paltz, Rondout Valley, and Wallkill.

Attached is our December 27, 2021 letter, which includes correspondence with the former Commissioner, Dr. Zucker, in 2021.

In order to avoid litigation, we do sincerely hope that you will respond to these important issues and concerns raised forthwith.

Best regards,

Aaron Siri, Esq.
Elizabeth A. Brehm, Esq.

Enclosure