The following documents were submitted by members of the public prior to, and at the October 1, 2019 Marathon County Board of Health meeting.

13 Reasons Why You Should Question Vaccines:

#1. Untested with normal scientific methods.

Vaccines are untested by scientific methods that are the accepted methods in all other areas of science. The studies have not been done against unvaccinated populations, but only testing results between people getting one vaccine and people getting another. Accepted scientific research is done with double blind studies comparing those who do use a drug and those who do not.

#2. Studies Done by Those who Profit from Vaccines

Vaccines are tested and studied by the corporations that stand to profit from the vaccines. The profits are going to be billions of dollars at this time. This is like having the fox guard the hen house holding his knife and fork. Testing has never been done outside of these corporations that has been considered when giving approval. So why should we trust it?

#3. Conflict of Interest in Studies Done

Those who do studies in corporations about specific ingredients whether it's pharmaceuticals or Monsanto or any other corporate giant, are given jobs in the alphabet agencies (CDC, FDA, EPA and USDA) and given the job to approve the very thing they did the study on. Can you spell conflict of interest? The last head of the FDA was an exec from Monsanto and the current head of the FDA is from the pharmaceutical companies. Julie Gerberding, the former head of the CDC when the fraud was committed about the MMR, left the CDC for a cushy job at Merck in the vaccine division. How safe does that make you feel about your food and your drugs and vaccines? There should be rules forbidding anyone from moving from a company to the alphabet agency or back again, ever, but at least for 10 years or some large number. The woman at Monsanto who did a study on the growth hormone given to cows rBgH, went to the FDA and got a job and is the one who approved it as safe. Where was the independent testing? None done and there is none done in the pharmaceutical and vaccine industry either.

#4. No long term studies or studies on the vaccine schedule ever

There has been no long term study done ever on vaccines and the ingredients in them, or the large number of vaccines given. It took 50 years and scientific advancements in DNA testing to know that the retroviruses in the Polio vaccine had changed the human genome and were causing havoc.

#5. Foreign DNA and Cell Fragments in Vaccines

There have been no studies done on the insertion of foreign DNA in vaccines. Monkey, pig, insect, dog, bird and human DNA are all ingredients. Dr Paul Offit, the darling of the vaccine industry owned a patent on Rotateq which is a vaccine for Rotavirus. He made a profit of $40 million dollars on its sale. A 2010 study published in *Journal of Virology* revealed that his multi-million dollar grossing patent on the Rotateq vaccine contains a

live simian retrovirus (with a 96% match of certainty) that has likely infected millions of children over the past few years with a virus that causes great harm. Retrovirus infections are permanent, and can carry on indefinitely into future generations. In other words, once they are inserted into the human genome they cannot be removed. Foreign DNA is changing the human genome. Corporations are playing god for profit. This is definitely not ok. Here is Dr Teresa Deisher, a world renowned geneticist on the subject.
https://www.youtube.com/watch?v=H4A-vEfaPKI&t=1432s

What is Coming through the needle- Contamination in foreign DNA
http://www.rense.com/general32/thrur.htm
Deep Sequencing Reveals Viral Vaccine Contaminants http://www.virology.ws/2010/03/29/deep-sequencing-reveals-viral-vaccine-contaminants/
http://www.greenmedinfo.com/sites/default/files/pdf/ML-Hewitson_2014_Advances_in_Virology.pdf

#6. Ingredients or Adjuvants
The things in vaccines are deadly and there is lots of information on those adjuvants or in another word ingredients, online everywhere from published journals, to Wikipedia, to OSHA and a host of other places. Thank God this is the information age. Some possible adjuvants are: aluminum (considered a neurotoxin), formaldehyde (embalming fluid. Remember biology class and the jars on the shelf with little pigs and frogs being preserved?), Thimerosal (mercury and it has been removed from some vaccines but is still in the flu and HIB and in trace amounts in almost all vaccines), Polysorbate 80 (linked to sterility), Phenoxyethanol (apreservative used in the cosmetic industry), Glutaraldehyde (acleaning fluid used to clean oil and gas pipelines and hospital equipment), and the list goes on.

Look up the ingredients on the CDC Website :
http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/excipient-table-2.pdf
A Glimpse Into the World of Vaccine Adjuvants
http://vaccinechoicecanada.com/vacc...

#7. Vaccines are being pedaled to pregnant women.
There have been NO studies done on fetal development and vaccines. The package inserts of all these vaccines say that specifically. In fact there are a few studies that show a rise of fetal deaths through spontaneous abortion: 16.7% with the DTaP, and in a 3 year period of the flu season, there was a 4000% rise due to vaccinations. We warn women to eat a clean diet and then want to inject them with neuro toxins and foreign DNA which crosses the placenta into their precious babies.

Dr. Suzanne Humphries talks about what is wrong with the study about flu shots for pregnant women.
http://www.vaccinationcouncil.org/2012/02/29/3013/
DTaP causes 16.7% miscarriage rate
http://www.ncbi.nlm.nih.gov/pubmed/22727350
Fluvaccine and 4000% increase in miscarriage http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3888271/

#8 The vaccine companies cannot be sued for injuries or deaths. The National Childhood Vaccine Injury Act of 1986 was passed by congress after the vaccine manufacturers: Merck, Wyeth, Lederle, and Connaught threatened to stop making vaccines altogether in the United States. So the law was passed that they can't be sued. Instead a Vaccine Injury Court was set up and a portion from each vaccine (which you pay for), goes to pay for payouts through that court for injuries and deaths. Only about 10% of injuries make it there. Until there is liability, like there is in every other drug on the market, then all the vaccines are suspect. The vaccine court has paid out over$3 billion in damages. It is also holding on to much money that should go to families. It is interesting to note that there are 290 or more new vaccines in the works, including those for acne, high blood pressure, cholesterol, cancer and more. Manufacturers are moving away from drugs and to vaccines because they cannot be sued. Imagine the long lines for the blood pressure vaccine and people start to realize they have developed an autoimmune disorder or asthma or GBS. Imagine when they find out there is no liability. No more bad drug ads. It's a win win for the Pharmaceutical companies and a bad thing for the rest of us.

Childhood Injury Act of 1986
http://www.nvic.org/injury-compensa...

#9. Doctors receive bonuses at the end of the year from the pharmaceutical companies for the number of patients they have who are vaccinated. This does not stop with bonuses. If a certain number are not vaccinated the insurance company can drop a doctor.

A Pediatrician Lays Out the Dollars for you
https://www.facebook.com/knowthevax...

#10. Whistleblower at the CDC
has come forward and given as many as 10,000 documents to congress from the CDC about the link that was suppressed between the MMR and autism.This is just the tip of the iceberg. The lead developer of Gardasil has come forward to say that the vaccine is unnecessary. How many more just haven't spoken out? Corruption, lying, deception being practiced all in the name of profit. The pro vaccine crowd and your doctor's office will say this is debunked, but 100,000 documents say otherwise.

We Destroyed Documents Showing the MMR Caused Autism
https://sharylattkisson.com/cdc-sci…
Congressman Bill Posey addressing the congress- August 2015
https://www.youtube.com/watch?v=jGRjn_gIJw0

#11.The CDC owns the patents to vaccines.
The CDC owns patents to Ebola, some Influenza strains, and who knows what else. They make a profit on the disease. If there is a pandemic they can make billions. Why should the government make a profit on sickness? That is just suspect and another reason not to trust what they are doing.

CDC List of Patents Owned
https://steemit.com/vaccines/@canadian-coconut/patents-that-cdc-owns-for-vaccines-conflict-of-interest-biased-towards-profit-and-not-public-health

#12. Doctors and Nurses are not educated on what is in vaccine or reactions.
It is apparent that most doctors and nurses giving vaccinations don't read the package inserts, don't study what is in the vaccines and really are not well read about them. They have not read the toxicology of the adjuvants in the vaccines (the extra stuff in them like chemicals and foreign DNA). They tell a pregnant women not to eat too much fish because of mercury, yet try to get her to take a flu shot which has mercury in it. Those we should be able to trust are not trustworthy. When parents call after their child receives a vaccine, because the child is having seizures or has other problems, they are told it's normal. Encephalitis is not normal. it is a very, very, dangerous condition. Seizures, breathing difficulties, rashes, paralysis, coma and death are listed in various package inserts, yet when parents call, experiencing any of these things they are often told not to worry about it. WORRY! Get to the ER immediately if your child experiences anything you aren't comfortable with. Your doctor can't be sued any more than the vaccine companies and is protected against liability. In every prescription drug commercial on TV, a rash is listed as a serious allergic sign and to stop immediately. Why not so with vaccines? Just ask your doctor if he has read the inserts?

Package Inserts by Manufacturer and Vaccine http://www.immunize.org/packageinserts/

#13. Religious Objections
This one is personal. Take it or leave it as you see fit. As a Christian, I believe that God created us the way we are supposed to be. The use of fetal cell tissue that has its origins with aborted babies is abhorrent to me, and I believe to God, who is the creator of life. The use of foreign DNA from monkeys, pigs, dogs, sheep or insects is, I

believe,against the laws of God. I believe that this is scientists playing god for profit. You might be surprised to know that more than 23 vaccines contain cells, cellular debris, protein, and DNA from aborted babies,including: Adenovirus, Polio, Dtap/Polio/HiB Combo, Hep A, Hep A/Hep B Combo, MMR, MMRV Pro Quad, Rabies, Varicella, and the Shingles vaccines.

§ PERC6 came from a healthy 18 week-old baby who was aborted for social reasons.This tumorogenic strain is being used to develop Adenovirus, Ebola, influenza, malaria, tuberculosis, and HIV vaccines. Developers call it a “human designer cell” but what they really mean is “aborted baby cells.”

§ TheHEK293 cellline is derived from the kidneys of a healthy aborted fetus and is being used to develop new influenza vaccines.

§ WI-38 (RA27/3) was a 16-week-old female baby (20 cm long) who was aborted in Sweden because the parents felt they had too many children.The baby was packed on ice and sent to the United States (speculation suggests without consent –which was common) where it was dissected. The use of WI-38 cells is a lucrative money making business.

§ WI-1 through WI-25 cell strains were derived from the lung, skin, muscle, kidney,heart, thyroid, thymus, and liver of 21 separate elective (and some speculate illegal) abortions.

§ WI-27 was the fetus from which researchers extracted the live virus used in the rubella vaccine.

§ WI-44 was derived from the lung of a three-month old surgically aborted fetus.

§ MCR-5 cell line was derived from the lung tissue of a 14-week-old male(Britain).

§ Eighty elective abortions (recorded) were involved in the research andfinal production of the current rubella vaccine: 21 from the original WI-1through WI-26 fetal cell lines that failed, plus WI-38 itself, plus 67 from the attempts to isolate the rubella virus.

§ There are studies linking foreign DNA to autism and cancer. These studies are only a few available
The Connection between fetal DNA fragments in vaccines and autism
https://www.ncbi.nlm.nih.gov/pubmed/26103708/

Impact of Environmental Factors on the Prevalence of Autistic Disorders after 1979
Full Length paper studies fetal and retroviral contaminants which are DNA
http://www.academicjournals.org/journal/JPHE/article-abstract/C98151247042

§ http://www.cbsnews.com/8301-31727_162-20049118-10391695.html

As I said...this one is personal. Thank you to Living Whole for this information given so completely. When we play god there are repercussions. Some of these things are changing the human genome permanently, and that is another thing that has huge consequences. The use of animal DNA is not often discussed in the Religious objection category.

Animal cells have been used in vaccines since the early days. Why would we object as a religious reason? If we believe that God created man in his own image (Genesis 1:27) or that He formed our inward parts and that we are fearfully and wonderfully made (Ps 139: 13,14), or perhaps that we are God's handiwork (Eph 2:10), then we have to believe that our genome was created by Him as well.Vaccines have animal DNA: monkey, pig, dog, birds, guinea pig, army worm and perhaps more that we have no idea about. These foreign animal cells are contaminated by retroviruses that are particular to these animals. The polio shots given in the late 1950s and early 1960s were contaminated by 2 viruses. SV40 which is a simian (monkey) cancer virus, and Simian Coryza Virus (recently renamed RSV or Respiratory Syncytial Virus). You might have heard of RSV which can be a very serious respiratory virus in babies. SV40 has been found in the tumors of children with cancer today even though the vaccine has not been used for 40 years or so. How is this possible? It means that these viruses have changed the human genome. Animal DNA has changed our own genes that God created and made them something else. Have a look at these articles on cell contamination from animal cells. Keep in mind it has taken 50 years for them to realize that these viruses are here and that they are causing sickness and cancer now. How long will it take to realize that the current contaminated vaccines have infected the human race. We are no longer created in His image,but now we have been changed. For any true believer, that is blasphemy of the highest order.

SV40monkey cancervirus in polio vaccines http://www.sv40foundation.org/cpv-link.html http://vaccinechoicecanada.com/in-the-news/sv-40-contamination-of-polio-virus-vaccines/

Contaminate mouse cells cause leukemia
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3109487/

And a more recent video from Dr Judy Mikovitz, PhD who discovered retroviruses in vaccines and was told to burn her research. She refused and was sent to prison for 4 years, and a gag order was put on her. It recently was lifted and she is talking. Well worth listening to and it will cause your head to want to explode. Read her book Plague. https://vimeo.com/146831570

Finally on the subject of DNA and religious objections to the injecting of foreign dna fragments into our bodies, a comprehensive look at why we might object for this reason https://docs.google.com/document/d/1jb4tncNLpNfyURLV3jPyvPzlA4Ny0JBNtLB4kPBSNVo/edit?usp=sharing

In conclusion, there are many reasons to question the validity and safety of vaccines. We question everything else. We question the alphabet agencies in regards to their stand on prescription drugs, on food, on supplements on organics. We don't trust congress, or our government. Why do we swallow blindly the stuff they are feeding us here? Let's be wise. Let's research. The information is out there and there is a lot. We can look at the same studies the doctors look at. Don't believe everything you are told without checking it out first. Please feel free to copy and paste any or all of this note onto your own notes, and onto Word.

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

FLUARIX QUADRIVALENT (Influenza Vaccine) injectable suspension, for intramuscular use
2019-2020 Formula
Initial U.S. Approval: 2012

---------- **INDICATIONS AND USAGE**----------
FLUARIX QUADRIVALENT is a vaccine indicated for active immunization for the prevention of disease caused by influenza A subtype viruses and type B viruses contained in the vaccine. FLUARIX QUADRIVALENT is approved for use in persons aged 6 months and older. (1)

----------**DOSAGE AND ADMINISTRATION**----------
For intramuscular injection only. (2)

Age	Vaccination Status	Dose and Schedule
6 months through 8 years	Not previously vaccinated with influenza vaccine	Two doses (0.5-mL each) at least 4 weeks apart (2.1)
	Vaccinated with influenza vaccine in a previous season	One or 2 doses[a] (0.5-mL each) (2.1)
9 years and older	Not applicable	One 0.5-mL dose (2.1)

[a] One dose or 2 doses (0.5-mL each) depending on vaccination history as per the annual Advisory Committee on Immunization Practices (ACIP) recommendation on prevention and control of influenza with vaccines. If 2 doses, administer each 0.5-mL dose at least 4 weeks apart. (2.1)

---------- **DOSAGE FORMS AND STRENGTHS**----------
Suspension for injection supplied in 0.5-mL single-dose prefilled syringes. (3)

---------- **CONTRAINDICATIONS** ----------
History of severe allergic reactions (e.g., anaphylaxis) to any component of the vaccine, including egg protein, or following a previous dose of any influenza vaccine. (4, 11)

---------- **WARNINGS AND PRECAUTIONS**----------
- If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give FLUARIX QUADRIVALENT should be based on careful consideration of potential benefits and risks. (5.1)
- Syncope (fainting) can occur in association with administration of injectable vaccines, including FLUARIX QUADRIVALENT. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope. (5.2)

---------- **ADVERSE REACTIONS** ----------
- In adults, the most common (≥10%) solicited local adverse reaction was pain (36%); the most common systemic adverse reactions were muscle aches (16%), headache (16%), and fatigue (16%). (6.1)
- In children aged 6 through 35 months, the most common (≥10%) solicited local adverse reactions were pain (17%) and redness (13%); the most common systemic adverse reactions were irritability (16%), loss of appetite (14%), and drowsiness (13%). (6.1)
- In children aged 3 through 17 years, the solicited local adverse reactions were pain (44%), redness (23%), and swelling (19%). (6.1)
- In children aged 3 through 5 years, the most common (≥10%) systemic adverse reactions were drowsiness (17%), irritability (17%), and loss of appetite (16%); in children aged 6 through 17 years, the most common systemic adverse reactions were fatigue (20%), muscle aches (18%), headache (16%), arthralgia (10%), and gastrointestinal symptoms (10%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

---------- **USE IN SPECIFIC POPULATIONS** ----------
Geriatric Use: Antibody responses were lower in geriatric subjects who received FLUARIX QUADRIVALENT than in younger subjects. (8.5)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 07/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

***Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

FLUARIX QUADRIVALENT is indicated for active immunization for the prevention of disease caused by influenza A subtype viruses and type B viruses contained in the vaccine *[see Description (11)]*. FLUARIX QUADRIVALENT is approved for use in persons aged 6 months and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Dosage and Schedule

The dose and schedule for FLUARIX QUADRIVALENT are presented in Table 1.

Table 1. FLUARIX QUADRIVALENT: Dosing

Age	Vaccination Status	Dose and Schedule
6 months through 8 years	Not previously vaccinated with influenza vaccine	Two doses (0.5-mL each) at least 4 weeks apart
	Vaccinated with influenza vaccine in a previous season	One or 2 doses[a] (0.5-mL each)
9 years and older	Not applicable	One 0.5-mL dose

[a] One dose or 2 doses (0.5-mL each) depending on vaccination history as per the annual Advisory Committee on Immunization Practices (ACIP) recommendation on prevention and control of influenza with vaccines. If 2 doses, administer each 0.5-mL dose at least 4 weeks apart.

2.2 Administration Instructions

Shake well before administration. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exists, the vaccine should not be administered.

Attach a sterile needle to the prefilled syringe and administer intramuscularly.

The preferred sites for intramuscular injection are the anterolateral thigh for children aged 6 through 11 months and the deltoid muscle of the upper arm for persons aged 12 months and older if muscle mass is adequate. Do not inject in the gluteal area or areas where there may be a major nerve trunk.

Do not administer this product intravenously, intradermally, or subcutaneously.

3 DOSAGE FORMS AND STRENGTHS

FLUARIX QUADRIVALENT is a suspension for injection. Each 0.5-mL dose is supplied in single-dose prefilled TIP-LOK syringes.

4 CONTRAINDICATIONS

Do not administer FLUARIX QUADRIVALENT to anyone with a history of severe allergic reactions (e.g., anaphylaxis) to any component of the vaccine, including egg protein, or following a previous administration of any influenza vaccine *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Guillain-Barré Syndrome

If Guillain-Barré syndrome (GBS) has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give FLUARIX QUADRIVALENT should be based on careful consideration of the potential benefits and risks.

The 1976 swine influenza vaccine was associated with an increased frequency of GBS. Evidence for a causal relation of GBS with subsequent vaccines prepared from other influenza viruses is inconclusive. If

influenza vaccine does pose a risk, it is probably slightly more than 1 additional case/1 million persons vaccinated.

5.2 Syncope

Syncope (fainting) can occur in association with administration of injectable vaccines, including FLUARIX QUADRIVALENT. Syncope can be accompanied by transient neurological signs such as visual disturbance, paresthesia, and tonic-clonic limb movements. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope.

5.3 Preventing and Managing Allergic Vaccine Reactions

Prior to administration, the healthcare provider should review the immunization history for possible vaccine sensitivity and previous vaccination-related adverse reactions. Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of FLUARIX QUADRIVALENT.

5.4 Altered Immunocompetence

If FLUARIX QUADRIVALENT is administered to immunosuppressed persons, including individuals receiving immunosuppressive therapy, the immune response may be lower than in immunocompetent persons.

5.5 Limitations of Vaccine Effectiveness

Vaccination with FLUARIX QUADRIVALENT may not protect all susceptible individuals.

5.6 Persons at Risk of Bleeding

As with other intramuscular injections, FLUARIX QUADRIVALENT should be given with caution in individuals with bleeding disorders, such as hemophilia or on anticoagulant therapy, to avoid the risk of hematoma following the injection.

6 ADVERSE REACTIONS

The safety experience with FLUARIX (trivalent influenza vaccine) is relevant to FLUARIX QUADRIVALENT because both vaccines are manufactured using the same process and have overlapping compositions *[see Description (11)]*.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared with rates in the clinical trials of another vaccine and may not reflect the rates observed in practice. There is the possibility that broad use of FLUARIX QUADRIVALENT could reveal adverse reactions not observed in clinical trials.

In adults who received FLUARIX QUADRIVALENT, the most common (≥10%) solicited local adverse reaction was pain (36%). The most common (≥10%) systemic adverse reactions were muscle aches (16%), headache (16%), and fatigue (16%).

In children aged 6 through 35 months who received FLUARIX QUADRIVALENT, the most common (≥10%) solicited local adverse reactions were pain (17%) and redness (13%). The most common (≥10%) systemic adverse reactions were irritability (16%), loss of appetite (14%), and drowsiness (13%). In children aged 3 through 17 years who received FLUARIX QUADRIVALENT, solicited local adverse reactions were pain (44%), redness (23%), and swelling (19%). In children aged 3 through 5 years, the

most common (≥10%) systemic adverse reactions were drowsiness (17%), irritability (17%), and loss of appetite (16%); in children aged 6 through 17 years, the most common systemic adverse reactions were fatigue (20%), muscle aches (18%), headache (16%), arthralgia (10%), and gastrointestinal symptoms (10%).

FLUARIX QUADRIVALENT in Adults

Trial 1 (NCT01204671) was a randomized, double-blind (2 arms) and open-label (one arm), active-controlled, safety, and immunogenicity trial. In this trial, subjects received FLUARIX QUADRIVALENT (n = 3,036) or one of 2 formulations of comparator trivalent influenza vaccine (FLUARIX; TIV-1, n = 1,010; or TIV-2, n = 610), each containing an influenza type B virus that corresponded to one of the 2 type B viruses in FLUARIX QUADRIVALENT (a type B virus of the Victoria lineage or a type B virus of the Yamagata lineage). The population was aged 18 years and older (mean age: 58 years) and 57% were female; 69% were white, 27% were Asian, and 4% were of other racial/ethnic groups. Solicited events were collected for 7 days (day of vaccination and the next 6 days). The frequencies of solicited adverse reactions are shown in Table 2.

Table 2. FLUARIX QUADRIVALENT: Incidence of Solicited Local Adverse Reactions and Systemic Adverse Reactions within 7 Days[a] of Vaccination in Adults[b] (Total Vaccinated Cohort)

	FLUARIX QUADRIVALENT[c] n = 3,011-3,015 %		Trivalent Influenza Vaccine (TIV)			
			TIV-1 (B Victoria)[d] n = 1,003 %		TIV-2 (B Yamagata)[e] n = 607 %	
Adverse Reaction	**Any**	**Grade 3[f]**	**Any**	**Grade 3[f]**	**Any**	**Grade 3[f]**
Local						
Pain	36.4	0.8	36.8	1.2	31.3	0.5
Redness	1.9	0	1.7	0	2.0	0
Swelling	2.1	0	2.1	0	1.3	0
Systemic						
Muscle aches	16.4	0.5	19.4	0.8	16.1	0.5
Headache	15.9	0.9	16.4	0.8	13.2	0.7
Fatigue	15.8	0.7	18.4	0.6	14.8	0.5
Arthralgia	8.4	0.5	10.4	0.7	9.4	0.3
Gastrointestinal symptoms[g]	6.5	0.4	6.5	0.2	5.9	0.3
Shivering	4.2	0.4	5.0	0.3	4.3	0.2
Fever[h]	1.6	0	1.2	0	1.5	0

Total vaccinated cohort for safety included all vaccinated subjects for whom safety data were available.
n = Number of subjects with diary card completed.

[a] Seven days included day of vaccination and the subsequent 6 days.

[b] Trial 1: NCT01204671.

[c] Contained the same composition as FLUARIX (trivalent formulation) manufactured for the 2010-2011 season and an additional influenza type B virus of Yamagata lineage.

[d] Contained the same composition as FLUARIX manufactured for the 2010-2011 season (2 influenza A subtype viruses and an influenza type B virus of Victoria lineage).

[e] Contained the same 2 influenza A subtype viruses as FLUARIX manufactured for the 2010-2011 season and an influenza type B virus of Yamagata lineage.

[f] Grade 3 pain: Defined as significant pain at rest; prevented normal everyday activities.
Grade 3 redness, swelling: Defined as >100 mm.
Grade 3 muscle aches, headache, fatigue, arthralgia, gastrointestinal symptoms, shivering: Defined as prevented normal activity.
Grade 3 fever: Defined as >102.2°F (39.0°C).

[g] Gastrointestinal symptoms included nausea, vomiting, diarrhea, and/or abdominal pain.

[h] Fever: Defined as ≥99.5°F (37.5°C).

Unsolicited events occurring within 21 days of vaccination (Day 0 to 20) were reported in 13%, 14%, and 15% of subjects who received FLUARIX QUADRIVALENT, TIV-1, or TIV-2, respectively. The unsolicited adverse reactions that occurred most frequently (≥0.1% for FLUARIX QUADRIVALENT) included dizziness, injection site hematoma, injection site pruritus, and rash. Serious adverse events occurring within 21 days of vaccination were reported in 0.5%, 0.6%, and 0.2% of subjects who received FLUARIX QUADRIVALENT, TIV-1, or TIV-2, respectively.

FLUARIX QUADRIVALENT in Children

Trial 7 (NCT01439360) was a randomized, observer-blind, non-influenza vaccine-controlled trial evaluating the efficacy of FLUARIX QUADRIVALENT. In this trial, subjects aged 6 through 35 months received FLUARIX QUADRIVALENT (n = 6,006) or a control vaccine (n = 6,012). The comparator was pneumococcal 13-valent conjugate vaccine [Diphtheria CRM197 Protein] (Wyeth Pharmaceuticals, Inc.) in children younger than 12 months, HAVRIX (Hepatitis A Vaccine) in children 12 months and older with a history of influenza vaccination, or HAVRIX (Dose 1) and a varicella vaccine (U.S. Licensed Manufactured by Merck & Co., Inc. or Non-U.S. Licensed Manufactured by GlaxoSmithKline Biologicals) (Dose 2) in those with no history of influenza vaccination. Subjects were aged 6 through 35 months, and one child aged 43 months (mean age: 22 months); 51% were male; 27% were white, 45% were Asian, and 28% were of other racial/ethnic groups. Children aged 12 months and older with no history of influenza vaccination and children younger than 12 months received 2 doses of FLUARIX QUADRIVALENT or the control vaccine approximately 28 days apart. Children aged 12 months and older with a history of influenza vaccination received one dose. Solicited local adverse reactions and systemic adverse events were collected using diary cards for 7 days (day of vaccination and the next 6 days). The incidences of solicited adverse reactions are shown in Table 3.

Table 3. FLUARIX QUADRIVALENT: Incidence of Solicited Local Adverse Reactions and Systemic Adverse Reactions within 7 Days[a] after First Vaccination in Children Aged 6 through 35 Months[b] (Total Vaccinated Cohort)

Adverse Reaction	FLUARIX QUADRIVALENT %		Non-Influenza Active Comparator[c,d] %	
	Any	Grade 3[e]	Any	Grade 3[e]
Local	**n = 5,899**		**n = 5,896**	
Pain	17.2	0.4	17.8	0.5
Redness	13.1	0	14.1	0
Swelling	7.9	0	8.8	0
Systemic	**n = 5,898**		**n = 5,896**	
Irritability	16.2	0.7	17.5	1.1
Loss of appetite	14.4	1.2	14.8	1.0
Drowsiness	12.5	0.7	14.1	0.9
Fever[f]	6.3	1.3	7.2	1.3

Total vaccinated cohort for safety included all vaccinated subjects for whom safety data were available.
n = Number of subjects with diary card completed.

[a] Seven days included day of vaccination and the subsequent 6 days.

[b] Trial 7: NCT01439360.

[c] Children younger than 12 months: pneumococcal 13-valent conjugate vaccine [Diphtheria CRM197 Protein] (Wyeth Pharmaceuticals, Inc.).

[d] Children 12 months and older: HAVRIX (Hepatitis A Vaccine) for those with a history of influenza vaccination; or HAVRIX (Dose 1) and a varicella vaccine (U.S. Licensed Manufactured by Merck & Co., Inc. or Non-U.S. Licensed Manufactured by GlaxoSmithKline Biologicals) (Dose 2) for those with no history of influenza vaccination.

[e] Grade 3 pain: Defined as cried when limb was moved/spontaneously painful.
Grade 3 swelling, redness: Defined as >50 mm.
Grade 3 irritability: Defined as crying that could not be comforted/prevented normal activity.
Grade 3 loss of appetite: Defined as not eating at all.
Grade 3 drowsiness: Defined as prevented normal activity.
Grade 3 fever: Defined as >102.2°F (39.0°C).

[f] Fever: Defined as ≥100.4°F (38.0°C).

In children who received a second dose of FLUARIX QUADRIVALENT or the Non-Influenza Active Comparator vaccine, the incidences of solicited adverse reactions following the second dose were generally lower than those observed after the first dose.

Unsolicited adverse events occurring within 28 days of vaccination were reported in 44% and 45% of subjects who received FLUARIX QUADRIVALENT (n = 6,006) and the comparator vaccine (n = 6,012), respectively. Serious adverse events (SAEs) occurring during the study period (6 to 8 months) were reported in 3.6% of subjects who received FLUARIX QUADRIVALENT and in 3.3% of subjects who received the comparator vaccine.

Trial 2 (NCT01196988) was a randomized, double-blind, active-controlled, safety, and immunogenicity trial. In this trial, subjects received FLUARIX QUADRIVALENT (n = 915) or one of 2 formulations of comparator trivalent influenza vaccine (FLUARIX; TIV-1, n = 912; or TIV-2, n = 911), each containing

an influenza type B virus that corresponded to one of the 2 type B viruses in FLUARIX QUADRIVALENT (a type B virus of the Victoria lineage or a type B virus of the Yamagata lineage). Subjects were aged 3 through 17 years and 52% were male; 56% were white, 29% were Asian, 12% were black, and 3% were of other racial/ethnic groups. Children aged 3 through 8 years with no history of influenza vaccination received 2 doses approximately 28 days apart. Children aged 3 through 8 years with a history of influenza vaccination and children aged 9 years and older received one dose. Solicited local adverse reactions and systemic adverse events were collected using diary cards for 7 days (day of vaccination and the next 6 days). The frequencies of solicited adverse reactions are shown in Table 4.

Table 4. FLUARIX QUADRIVALENT: Incidence of Solicited Local Adverse Reactions and Systemic Adverse Reactions within 7 Days[a] after First Vaccination in Children Aged 3 through 17 Years[b] (Total Vaccinated Cohort)

	FLUARIX QUADRIVALENT[c] %		Trivalent Influenza Vaccine (TIV)			
			TIV-1 (B Victoria)[d] %		TIV-2 (B Yamagata)[e] %	
	Any	Grade 3[f]	Any	Grade 3[f]	Any	Grade 3[f]
Adverse Reaction	**Aged 3 through 17 Years**					
Local	**n = 903**		**n = 901**		**n = 905**	
Pain[g]	43.7	1.6	42.4	1.8	40.3	0.8
Redness	23.0	1.0	21.3	0.2	20.9	0.7
Swelling	18.5	0.8	17.2	1.1	14.9	0.2
	Aged 3 through 5 Years					
Systemic	**n = 291**		**n = 314**		**n = 279**	
Drowsiness	17.2	1.0	12.4	0.3	13.6	0.7
Irritability	16.8	0.7	13.4	0.3	14.3	0.7
Loss of appetite	15.5	0.3	8.0	0	10.4	0.7
Fever[h]	8.9	0.3	8.9	0.3	8.2	1.1
	Aged 6 through 17 Years					
Systemic	**n = 613**		**n = 588**		**n = 626**	
Fatigue	19.7	1.5	18.5	1.4	15.5	0.5
Muscle aches	17.5	0.7	16.0	1.4	15.8	0.5
Headache	16.3	1.3	19.2	0.7	15.2	0.6
Arthralgia	9.8	0.3	9.4	0.7	7.3	0.2
Gastrointestinal symptoms[i]	9.8	1.0	9.5	0.7	7.2	0.3
Shivering	6.4	0.5	4.4	0.5	5.0	0
Fever[h]	6.0	1.1	8.5	0.5	6.1	0.3

Total vaccinated cohort for safety included all vaccinated subjects for whom safety data were available.
n = Number of subjects with diary card completed.

[a] Seven days included day of vaccination and the subsequent 6 days.

[b] Trial 2: NCT01196988.

[c] Contained the same composition as FLUARIX (trivalent formulation) manufactured for the 2010-2011 season and an additional influenza type B virus of Yamagata lineage.

[d] Contained the same composition as FLUARIX manufactured for the 2010-2011 season (2 influenza A subtype viruses and an influenza type B virus of Victoria lineage).

[e] Contained the same 2 influenza A subtype viruses as FLUARIX manufactured for the 2010-2011 season and an influenza type B virus of Yamagata lineage.

[f] Grade 3 pain: Defined as cried when limb was moved/spontaneously painful (children <6 years), or significant pain at rest, prevented normal everyday activities (children ≥6 years).
Grade 3 redness, swelling: Defined as >50 mm.
Grade 3 drowsiness: Defined as prevented normal activity.
Grade 3 irritability: Defined as crying that could not be comforted/prevented normal activity.
Grade 3 loss of appetite: Defined as not eating at all.

Grade 3 fever: Defined as >102.2°F (39.0°C).
Grade 3 fatigue, muscle aches, headache, arthralgia, gastrointestinal symptoms, shivering: Defined as prevented normal activity.

[g] Percentage of subjects with any pain by age subgroup: 39%, 38%, and 37% for FLUARIX QUADRIVALENT, TIV-1, and TIV-2, respectively, in children aged 3 through 8 years and 52%, 50%, and 46% for FLUARIX QUADRIVALENT, TIV-1, and TIV-2, respectively, in children aged 9 through 17 years.

[h] Fever: Defined as ≥99.5°F (37.5°C).

[i] Gastrointestinal symptoms included nausea, vomiting, diarrhea, and/or abdominal pain.

In children who received a second dose of FLUARIX QUADRIVALENT, TIV-1, or TIV-2, the incidences of adverse reactions following the second dose were generally lower than those observed after the first dose.

Unsolicited adverse events occurring within 28 days of any vaccination were reported in 31%, 33%, and 34% of subjects who received FLUARIX QUADRIVALENT, TIV-1, or TIV-2, respectively. The unsolicited adverse reactions that occurred most frequently (≥0.1% for FLUARIX QUADRIVALENT) included injection site pruritus and rash. Serious adverse events occurring within 28 days of any vaccination were reported in 0.1%, 0.1%, and 0.1% of subjects who received FLUARIX QUADRIVALENT, TIV-1, or TIV-2, respectively.

FLUARIX (Trivalent Formulation)

FLUARIX has been administered to 10,317 adults aged 18 through 64 years, 606 subjects aged 65 years and older, and 2,115 children aged 6 months through 17 years in clinical trials. The incidence of solicited adverse reactions in each age-group is shown in Tables 5 and 6.

Table 5. FLUARIX (Trivalent Formulation): Incidence of Solicited Local Adverse Reactions and Systemic Adverse Reactions within 4 Days[a] of Vaccination in Adults (Total Vaccinated Cohort)

Adverse Reaction	Trial 3[b]				Trial 4[c]			
	Aged 18 through 64 Years				Aged 65 Years and Older			
	FLUARIX n = 760 %		Placebo n = 192 %		FLUARIX n = 601-602 %		Comparator n = 596 %	
	Any	Grade 3[d]	Any	Grade 3[d]	Any	Grade 3[d]	Any	Grade 3[d]
Local								
Pain	54.7	0.1	12.0	0	19.1	0	17.6	0
Redness	17.5	0	10.4	0	10.6	0.2	13.1	0.7
Swelling	9.3	0.1	5.7	0	6.0	0	8.9	0.7
Systemic								
Muscle aches	23.0	0.4	12.0	0.5	7.0	0.3	6.5	0
Fatigue	19.7	0.4	17.7	1.0	9.0	0.3	9.6	0.7
Headache	19.3	0.1	21.4	1.0	7.5	0.3	7.9	0.3
Arthralgia	6.4	0.1	6.3	0.5	5.5	0.5	5.0	0.2
Shivering	3.3	0.1	2.6	0	1.7	0.2	2.2	0
Fever[e]	1.7	0	1.6	0	1.7	0	0.5	0

Total vaccinated cohort for safety included all vaccinated subjects for whom safety data were available.
n = Number of subjects with diary card completed.

[a] Four days included day of vaccination and the subsequent 3 days.

[b] Trial 3 was a randomized, double-blind, placebo-controlled, safety, and immunogenicity trial (NCT00100399).

[c] Trial 4 was a randomized, single-blind, active-controlled, safety, and immunogenicity trial (NCT00197288). The active control was FLUZONE, a U.S.-licensed trivalent, inactivated influenza vaccine (Sanofi Pasteur Inc.).

[d] Grade 3 pain, muscle aches, fatigue, headache, arthralgia, shivering: Defined as prevented normal activity.
Grade 3 redness, swelling: Defined as >50 mm.
Grade 3 fever: Defined as >102.2°F (39.0°C).

[e] Fever: Defined as ≥100.4°F (38.0°C) in Trial 3, and ≥99.5°F (37.5°C) in Trial 4.

Table 6. FLUARIX (Trivalent Formulation): Incidence of Solicited Local Adverse Reactions and Systemic Adverse Reactions within 4 Days[a] of First Vaccination in Children Aged 3 through 17 Years[b] (Total Vaccinated Cohort)

Adverse Reaction	Aged 3 through 4 Years				Aged 5 through 17 Years			
	FLUARIX n = 350 %		Comparator n = 341 %		FLUARIX n = 1,348 %		Comparator n = 451 %	
	Any	Grade 3[c]	Any	Grade 3[c]	Any	Grade 3[c]	Any	Grade 3[c]
Local								
Pain	34.9	1.7	38.4	1.2	56.2	0.8	56.1	0.7
Redness	22.6	0.3	19.9	0	17.7	1.0	16.4	0.7
Swelling	13.7	0	13.2	0	13.9	1.5	13.3	0.7
Systemic								
Irritability	20.9	0.9	22.0	0	–	–	–	–
Loss of appetite	13.4	0.9	15.0	0.9	–	–	–	–
Drowsiness	13.1	0.6	19.6	0.9	–	–	–	–
Fever[d]	6.6	1.4	7.6	1.5	4.2	0.3	3.3	0.2
Muscle aches	–	–	–	–	28.8	0.4	28.8	0.4
Fatigue	–	–	–	–	19.9	1.0	18.8	1.1
Headache	–	–	–	–	15.1	0.5	16.4	0.9
Arthralgia	–	–	–	–	5.6	0.1	6.2	0.2
Shivering	–	–	–	–	3.1	0.1	3.5	0.2

Total vaccinated cohort for safety included all vaccinated subjects for whom safety data were available.
n = Number of subjects with diary card completed.

[a] Four days included day of vaccination and the subsequent 3 days.

[b] Trial 6 was a single-blind, active-controlled, safety, and immunogenicity U.S. trial (NCT00383123). The active control was FLUZONE, a U.S.-licensed trivalent, inactivated influenza vaccine (Sanofi Pasteur Inc.).

[c] Grade 3 pain, irritability, loss of appetite, drowsiness, muscle aches, fatigue, headache, arthralgia, shivering: Defined as prevented normal activity.
Grade 3 swelling, redness: Defined as >50 mm.
Grade 3 fever: Defined as >102.2°F (39.0°C).

[d] Fever: Defined as ≥99.5°F (37.5°C).

In children who received a second dose of FLUARIX or the comparator vaccine, the incidences of adverse reactions following the second dose were similar to those observed after the first dose.

Serious Adverse Reactions: In the 4 clinical trials in adults (N = 10,923), there was a single case of anaphylaxis within one day following administration of FLUARIX (<0.01%).

6.2 Postmarketing Experience

Beyond those events reported above in the clinical trials for FLUARIX QUADRIVALENT or FLUARIX, the following adverse reactions have been identified during postapproval use of FLUARIX QUADRIVALENT or FLUARIX (trivalent influenza vaccine). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to the vaccine.

Blood and Lymphatic System Disorders

Lymphadenopathy.

Cardiac Disorders

Tachycardia.

Ear and Labyrinth Disorders

Vertigo.

Eye Disorders

Conjunctivitis, eye irritation, eye pain, eye redness, eye swelling, eyelid swelling.

Gastrointestinal Disorders

Abdominal pain or discomfort, swelling of the mouth, throat, and/or tongue.

General Disorders and Administration Site Conditions

Asthenia, chest pain, influenza-like illness, feeling hot, injection site mass, injection site reaction, injection site warmth, body aches.

Immune System Disorders

Anaphylactic reaction including shock, anaphylactoid reaction, hypersensitivity, serum sickness.

Infections and Infestations

Injection site abscess, injection site cellulitis, pharyngitis, rhinitis, tonsillitis.

Nervous System Disorders

Convulsion, encephalomyelitis, facial palsy, facial paresis, Guillain-Barré syndrome, hypoesthesia, myelitis, neuritis, neuropathy, paresthesia, syncope.

Respiratory, Thoracic, and Mediastinal Disorders

Asthma, bronchospasm, dyspnea, respiratory distress, stridor.

Skin and Subcutaneous Tissue Disorders

Angioedema, erythema, erythema multiforme, facial swelling, pruritus, Stevens-Johnson syndrome, sweating, urticaria.

Vascular Disorders

Henoch-Schönlein purpura, vasculitis.

7 DRUG INTERACTIONS

7.1 Concomitant Vaccine Administration

FLUARIX QUADRIVALENT should not be mixed with any other vaccine in the same syringe or vial.

There are insufficient data to assess the concurrent administration of FLUARIX QUADRIVALENT with other vaccines. When concomitant administration of other vaccines is required, the vaccines should be administered at different injection sites.

7.2 Immunosuppressive Therapies

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater-than-physiologic doses), may reduce the immune response to FLUARIX QUADRIVALENT.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to FLUARIX QUADRIVALENT during pregnancy. Healthcare providers are encouraged to register women by calling 1-888-452-9622.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. 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.

There are insufficient data on FLUARIX QUADRIVALENT in pregnant women to inform vaccine-associated risks.

A developmental toxicity study was performed in female rats administered FLUARIX QUADRIVALENT prior to mating and during gestation and lactation periods. The total dose was 0.2 mL at each occasion (a single human dose is 0.5 mL). This study revealed no adverse effects on fetal or pre-weaning development due to FLUARIX QUADRIVALENT *(see Data).*

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk: Pregnant women infected with seasonal influenza are at increased risk of severe illness associated with influenza infection compared with non-pregnant women. Pregnant women with influenza may be at increased risk for adverse pregnancy outcomes, including preterm labor and delivery.

Data

Animal Data: In a developmental toxicity study, female rats were administered FLUARIX QUADRIVALENT by intramuscular injection 4 and 2 weeks prior to mating, on gestation Days 3, 8, 11, and 15, and on lactation Day 7. The total dose was 0.2 mL at each occasion (a single human dose is 0.5 mL). No adverse effects on pre-weaning development up to post-natal Day 25 were observed. There were no vaccine-related fetal malformations or variations.

8.2 Lactation

Risk Summary

It is not known whether FLUARIX QUADRIVALENT is excreted in human milk. Data are not available to assess the effects of FLUARIX QUADRIVALENT on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for FLUARIX QUADRIVALENT and any potential adverse effects on the breastfed child from FLUARIX QUADRIVALENT 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

Safety and effectiveness of FLUARIX QUADRIVALENT in children younger than 6 months have not been established.

Safety and effectiveness of FLUARIX QUADRIVALENT in individuals aged 6 months through 17 years have been established *[see Adverse Reactions (6.1), Clinical Studies (14.3)]*.

8.5 Geriatric Use

In a randomized, double-blind (2 arms) and open-label (one arm), active-controlled trial, immunogenicity and safety were evaluated in a cohort of subjects aged 65 years and older who received FLUARIX QUADRIVALENT (n = 1,517); 469 of these subjects were aged 75 years and older. In subjects aged 65 years and older, the geometric mean antibody titers (GMTs) post-vaccination and seroconversion rates were lower than in younger subjects (aged 18 through 64 years) and the frequencies of solicited and unsolicited adverse reactions were generally lower than in younger subjects.

11 DESCRIPTION

FLUARIX QUADRIVALENT, Influenza Vaccine, for intramuscular injection, is a sterile, colorless, and slightly opalescent suspension. FLUARIX QUADRIVALENT is prepared from influenza viruses propagated in embryonated chicken eggs. Each of the influenza viruses is produced and purified separately. After harvesting the virus-containing fluids, each influenza virus is concentrated and purified by zonal centrifugation using a linear sucrose density gradient solution containing detergent to disrupt the viruses. Following dilution, the vaccine is further purified by diafiltration. Each influenza virus solution is inactivated by the consecutive effects of sodium deoxycholate and formaldehyde leading to the production of a "split virus." Each split inactivated virus is then suspended in sodium phosphate-buffered isotonic sodium chloride solution. Each vaccine is formulated from the split inactivated virus solutions.

FLUARIX QUADRIVALENT has been standardized according to U.S. Public Health Service (USPHS) requirements for the 2019-2020 influenza season and is formulated to contain 60 micrograms (mcg) hemagglutinin (HA) per 0.5-mL dose, in the recommended ratio of 15 mcg HA of each of the following 4 influenza virus strains (2 A strains and 2 B strains): A/Brisbane/02/2018 (H1N1) pdm09 (IVR-190), A/Kansas/14/2017 (H3N2) NYMC X-327, B/Maryland/15/2016 NYMC BX-69A (a B/Colorado/06/2017-like virus), and B/Phuket/3073/2013.

FLUARIX QUADRIVALENT is formulated without preservatives. FLUARIX QUADRIVALENT does not contain thimerosal. Each 0.5-mL dose also contains octoxynol-10 (TRITON X-100) ≤0.115 mg, α-tocopheryl hydrogen succinate ≤0.135 mg, and polysorbate 80 (Tween 80) ≤0.550 mg. Each dose may also contain residual amounts of hydrocortisone ≤0.0015 mcg, gentamicin sulfate ≤0.15 mcg, ovalbumin ≤0.050 mcg, formaldehyde ≤5 mcg, and sodium deoxycholate ≤65 mcg from the manufacturing process.

The tip caps and plungers of the prefilled syringes of FLUARIX QUADRIVALENT are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Influenza illness and its complications follow infection with influenza viruses. Global surveillance of influenza identifies yearly antigenic variants. Since 1977, antigenic variants of influenza A (H1N1 and H3N2) viruses and influenza B viruses have been in global circulation.

Public health authorities give annual influenza vaccine composition recommendations. Inactivated influenza vaccines are standardized to contain the hemagglutinins of influenza viruses representing the virus types or subtypes likely to circulate in the United States during the influenza season. Two influenza type B virus lineages (Victoria and Yamagata) are of public health importance because they have co-circulated since 2001. FLUARIX (trivalent influenza vaccine) contains 2 influenza A subtype viruses and one influenza type B virus.

Specific levels of hemagglutination-inhibition (HI) antibody titer post-vaccination with inactivated influenza virus vaccines have not been correlated with protection from influenza illness but the HI antibody titers have been used as a measure of vaccine activity. In some human challenge studies, HI antibody titers of ≥1:40 have been associated with protection from influenza illness in up to 50% of subjects.[1,2] Antibody against one influenza virus type or subtype confers little or no protection against another virus. Furthermore, antibody to one antigenic variant of influenza virus might not protect against a new antigenic variant of the same type or subtype. Frequent development of antigenic variants through antigenic drift is the virological basis for seasonal epidemics and the reason for the usual replacement of one or more influenza viruses in each year's influenza vaccine.

Annual revaccination is recommended because immunity declines during the year after vaccination, and because circulating strains of influenza virus change from year to year.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

FLUARIX QUADRIVALENT has not been evaluated for carcinogenic or mutagenic potential or male infertility in animals. Vaccination of female rats with FLUARIX QUADRIVALENT had no effect on fertility *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

14.1 Efficacy against Influenza

The efficacy experience with FLUARIX is relevant to FLUARIX QUADRIVALENT because both vaccines are manufactured using the same process and have overlapping compositions *[see Description (11)]*.

The efficacy of FLUARIX was evaluated in a randomized, double-blind, placebo-controlled trial conducted in 2 European countries during the 2006-2007 influenza season. Efficacy of FLUARIX, containing A/New Caledonia/20/1999 (H1N1), A/Wisconsin/67/2005 (H3N2), and B/Malaysia/2506/2004 influenza virus strains, was defined as the prevention of culture-confirmed influenza A and/or B cases, for vaccine antigenically matched strains, compared with placebo. Healthy subjects aged 18 through 64 years (mean age: 40 years) were randomized (2:1) to receive FLUARIX (n = 5,103) or placebo (n = 2,549) and monitored for influenza-like illnesses (ILI) starting 2 weeks post-vaccination and lasting for approximately 7 months. In the overall population, 60% of subjects were

female and 99.9% were white. Culture-confirmed influenza was assessed by active and passive surveillance of ILI. Influenza-like illness was defined as at least one general symptom (fever ≥100°F and/or myalgia) and at least one respiratory symptom (cough and/or sore throat). After an episode of ILI, nose and throat swab samples were collected for analysis; attack rates and vaccine efficacy were calculated (Table 7).

Table 7. FLUARIX (Trivalent Formulation): Attack Rates and Vaccine Efficacy against Culture-Confirmed Influenza A and/or B in Adults (Total Vaccinated Cohort)

			Attack Rates (n/N)	Vaccine Efficacy		
	N	n	%	%	Lower Limit	Upper Limit
Antigenically Matched Strains[a]						
FLUARIX	5,103	49	1.0	66.9[b]	51.9	77.4
Placebo	2,549	74	2.9	–	–	–
All Culture-Confirmed Influenza (Matched, Unmatched, and Untyped)[c]						
FLUARIX	5,103	63	1.2	61.6[b]	46.0	72.8
Placebo	2,549	82	3.2	–	–	–

[a] There were no vaccine matched culture-confirmed cases of A/New Caledonia/20/1999 (H1N1) or B/Malaysia/2506/2004 influenza virus strains with FLUARIX or placebo.

[b] Vaccine efficacy for FLUARIX exceeded a pre-defined threshold of 35% for the lower limit of the 2-sided 95% Confidence Interval (CI).

[c] Of the 22 additional cases, 18 were unmatched and 4 were untyped; 15 of the 22 cases were A (H3N2) (11 cases with FLUARIX and 4 cases with placebo).

In a post-hoc exploratory analysis by age, vaccine efficacy (against culture-confirmed influenza A and/or B cases, for vaccine antigenically matched strains) in subjects aged 18 through 49 years was 73.4% (95% CI: 59.3, 82.8) (number of influenza cases: FLUARIX [n = 35/3,602] and placebo [n = 66/1,810]). In subjects aged 50 through 64 years, vaccine efficacy was 13.8% (95% CI: -137.0, 66.3) (number of influenza cases: FLUARIX [n = 14/1,501] and placebo [n = 8/739]). As the trial lacked statistical power to evaluate efficacy within age subgroups, the clinical significance of these results is unknown.

The efficacy of FLUARIX QUADRIVALENT was evaluated in Trial 7, a randomized, observer-blind, non-influenza vaccine-controlled trial conducted in 13 countries in Asia, Europe, and Central America during the 2011-2012 and 2012-2013 Northern Hemisphere influenza seasons, and from 2012 to 2014 during influenza seasons in subtropical countries. Healthy subjects aged 6 through 35 months (mean age: 22 months) were randomized (1:1) to receive FLUARIX QUADRIVALENT (n = 6,006) or a non-influenza control vaccine (n = 6,012). In the overall population, 51% were male; 27% were white, 45% were Asian, and 28% were of other racial/ethnic groups. Children aged 12 months and older with no history of influenza vaccination and children younger than 12 months received 2 doses of FLUARIX QUADRIVALENT or the Non-Influenza Active Comparator vaccine approximately 28 days apart. Children aged 12 months and older with a history of influenza vaccination received one dose.

The influenza virus strain composition of FLUARIX QUADRIVALENT administered in each of the 5 study cohorts followed the World Health Organization (WHO) recommendations (which included 2nd B strain from 2012 onwards) for each influenza season associated with a particular cohort.

Efficacy of FLUARIX QUADRIVALENT was assessed for the prevention of reverse transcriptase polymerase chain reaction (RT-PCR)-confirmed influenza°A and/or B°disease, due to any seasonal

influenza strain, compared with non-influenza control vaccines. Influenza disease included episodes of influenza-like illness (ILI, i.e., fever ≥100.4°F with any of the following: cough, runny nose, nasal congestion, or breathing difficulty) or a consequence of influenza virus infection (acute otitis media or lower respiratory illnesses). Among subjects with RT-PCR-positive influenza A and/or B disease, subjects were further prospectively classified based on the presence of adverse outcomes associated with influenza infection: fever >102.2°F, physician-diagnosed acute otitis media, physician-diagnosed lower respiratory tract illness, physician-diagnosed serious extra-pulmonary complications, hospitalization in the intensive care unit, or supplemental oxygen required for more than 8 hours. Subjects were monitored for influenza disease by passive and active surveillance starting 2 weeks post-vaccination and lasting for approximately 6 months. After an episode of ILI, lower respiratory illness, or acute otitis media, nasal swabs were collected and tested for influenza°A and/or°B by RT-PCR. All RT-PCR-positive specimens were further tested in cell culture and by antigenic characterization to determine whether the viral strains matched those in the vaccine. Vaccine efficacy for subjects with RT-PCR confirmed and culture-confirmed vaccine matching strains (According-to-Protocol (ATP) cohort for efficacy – time to event) is presented in Table 8.

Table 8. Attack Rates and Vaccine Efficacy against Influenza A and/or B in Children Aged 6 through 35 Months[a] (ATP Cohort for Efficacy – Time to Event)

	N[b]	n[c]	Attack Rates (n/N)	Vaccine Efficacy		
			%	%	Lower Limit	Upper Limit
All RT-PCR-Confirmed Influenza						
FLUARIX QUADRIVALENT	5,707	344	6.03	49.8	41.8[d]	56.8
Non-Influenza Comparator[e,f]	5,697	662	11.62	-	-	-
All Culture-Confirmed Influenza						
FLUARIX QUADRIVALENT	5,707	303	5.31	51.2	44.1[g]	57.6
Non-Influenza Comparator[e,f]	5,697	602	10.57	-	-	-
All Antigenically Matched Culture-Confirmed Influenza						
FLUARIX QUADRIVALENT	5,707	88	1.54	60.1	49.1[h]	69.0
Non-Influenza Comparator[e,f]	5,697	216	3.79	-	-	-

ATP = According-to-Protocol; RT-PCR = Reverse Transcriptase Polymerase Chain Reaction.

[a] Trial 7: NCT01439360.

[b] Number of subjects in the ATP cohort for efficacy – time to event, which included subjects who met all eligibility criteria, who were followed for efficacy and complied with the study protocol until the influenza-like episode.

[c] Number of subjects who reported at least one case in the reporting period.

[d] Vaccine efficacy for FLUARIX QUADRIVALENT met the pre-defined criterion for the lower limit of the 2-sided 97.5% CI (>15% for all influenza).

[e] Children younger than 12 months: pneumococcal 13-valent conjugate vaccine [Diphtheria CRM197 Protein] (Wyeth Pharmaceuticals, Inc.).

[f] Children 12 months and older: HAVRIX (Hepatitis A Vaccine) for those with a history of influenza vaccination; or HAVRIX (Dose 1) and a varicella vaccine (U.S. Licensed Manufactured by Merck & Co., Inc. or Non-U.S. Licensed Manufactured by GlaxoSmithKline Biologicals) (Dose 2) for those with no history of influenza vaccination.

[g] Vaccine efficacy for FLUARIX QUADRIVALENT met the pre-defined criterion of >10% for the lower limit of the 2-sided 95% CI.

[h] Vaccine efficacy for FLUARIX QUADRIVALENT met the pre-defined criterion of >15% for the lower limit of the 2-sided 95% CI.

The vaccine efficacy against RT-PCR-confirmed influenza associated with adverse outcomes was 64.6% (97.5% CI 53.2%, 73.5%). The vaccine efficacy against RT-PCR-confirmed influenza associated with adverse outcomes due to A/H1N1, A/H3N2, B/Victoria, and B/Yamagata was 71.4% (95% CI 48.5%, 85.2%), 51.3% (95% CI 32.7%, 65.2%), 86.7% (95% CI 52.8%, 97.9%), and 68.9% (95% CI 50.6%, 81.2%), respectively.

For RT-PCR-confirmed influenza cases associated with adverse outcomes, the incidence of the specified adverse outcomes is presented in Table 9.

Table 9. Incidence of Adverse Outcomes Associated with RT-PCR-Positive Influenza in Children Aged 6 through 35 Months[a] (ATP Cohort for Efficacy- Time to Event)[b]

Influenza-Associated Symptom[e]	FLUARIX QUADRIVALENT n = 5,707			Non-Influenza Active Comparator[c,d] n = 5,697		
	Number of Events	Number of Subjects[f]	%	Number of Events	Number of Subjects[f]	%
Fever >102.2^{0}F/39^{0}C	62	61	1.1	184	183	3.2
Acute otitis media (AOM)[g]	5	5	0.1	15	15	0.3
Physician-diagnosed lower respiratory tract illness[h]	28	28	0.5	62	61	1.1
Physician-diagnosed serious extra-pulmonary complications[i]	2	2	0	3	3	0.1
Hospitalization in the intensive care unit	0	0	0	0	0	0
Supplemental oxygen required for more than 8 hours	0	0	0	0	0	0

ATP = According-to-Protocol; RT-PCR = Reverse transcriptase polymerase chain reaction.

[a] Trial 7: NCT01439360.

[b] Number of subjects in the ATP cohort for efficacy – time to event, which included subjects who met all eligibility criteria, who were followed for efficacy and complied with the study protocol until the influenza-like episode.

[c] Children younger than 12 months: pneumococcal 13-valent conjugate vaccine [Diphtheria CRM197 Protein] (Wyeth Pharmaceuticals, Inc.).

[d] Children 12 months and older: HAVRIX (Hepatitis A Vaccine) for those with a history of influenza vaccination; or HAVRIX (Dose 1) and a varicella vaccine (U.S. Licensed Manufactured by Merck & Co., Inc. or Non-U.S. Licensed Manufactured by GlaxoSmithKline Biologicals) (Dose 2) for those with no history of influenza vaccination.

[e] Subjects who experienced more than one adverse outcome, each outcome was counted in the respective category.

[f] Number of subjects with at least one event in a given category.

[g] Analyses considered AOM cases confirmed by otoscopy.

[h] Pneumonia, lower respiratory tract infection, bronchiolitis, bronchitis, or croup infection as per final diagnosis by physician.

[i] Includes myositis, encephalitis or other neurologic condition including seizure, myocarditis/pericarditis or other serious medical condition as per final diagnosis by physician.

14.2 Immunological Evaluation of FLUARIX QUADRIVALENT in Adults

Trial 1 was a randomized, double-blind (2 arms) and open-label (one arm), active-controlled, safety, immunogenicity, and non-inferiority trial. In this trial, subjects received FLUARIX QUADRIVALENT (n = 1,809) or one of 2 formulations of comparator trivalent influenza vaccine (FLUARIX, TIV-1, n = 608 or TIV-2, n = 534), each containing an influenza type B virus that corresponded to one of the 2 type B viruses in FLUARIX QUADRIVALENT (a type B virus of the Victoria lineage or a type B virus of the Yamagata lineage). Subjects aged 18 years and older (mean age: 58 years) were evaluated for

immune responses to each of the vaccine antigens 21 days following vaccination. In the overall population, 57% of subjects were female; 69% were white, 27% were Asian, and 4% were of other racial/ethnic groups.

The immunogenicity endpoints were GMTs of serum HI antibodies adjusted for baseline, and the percentage of subjects who achieved seroconversion, defined as a pre-vaccination HI titer of <1:10 with a post-vaccination titer ≥1:40 or at least a 4-fold increase in serum HI antibody titer over baseline to ≥1:40 following vaccination, performed on the According-to-Protocol (ATP) cohort for whom immunogenicity assay results were available after vaccination. FLUARIX QUADRIVALENT was non-inferior to both TIVs based on adjusted GMTs (upper limit of the 2-sided 95% CI for the GMT ratio [TIV/FLUARIX QUADRIVALENT] ≤1.5) and seroconversion rates (upper limit of the 2-sided 95% CI on difference of the TIV minus FLUARIX QUADRIVALENT ≤10%). The antibody response to influenza B strains contained in FLUARIX QUADRIVALENT was higher than the antibody response after vaccination with a TIV containing an influenza B strain from a different lineage. There was no evidence that the addition of the second B strain resulted in immune interference to other strains included in the vaccine (Table 10).

Table 10. FLUARIX QUADRIVALENT: Immune Responses to Each Antigen 21 Days after Vaccination in Adults (ATP Cohort for Immunogenicity)

		Trivalent Influenza Vaccine (TIV)	
	FLUARIX QUADRIVALENT[a]	**TIV-1 (B Victoria)[b]**	**TIV-2 (B Yamagata)[c]**
Geometric Mean Antibody Titer	**n = 1,809 (95% CI)**	**n = 608 (95% CI)**	**n = 534 (95% CI)**
A/California/7/2009 (H1N1)	201.1 (188.1, 215.1)	218.4 (194.2, 245.6)	213.0 (187.6, 241.9)
A/Victoria/210/2009 (H3N2)	314.7 (296.8, 333.6)	298.2 (268.4, 331.3)	340.4 (304.3, 380.9)
B/Brisbane/60/2008 (Victoria lineage)	404.6 (386.6, 423.4)	393.8 (362.7, 427.6)	258.5 (234.6, 284.8)
B/Brisbane/3/2007 (Yamagata lineage)	601.8 (573.3, 631.6)	386.6 (351.5, 425.3)	582.5 (534.6, 634.7)
Seroconversion[d]	**n = 1,801 % (95% CI)**	**n = 605 % (95% CI)**	**n = 530 % (95% CI)**
A/California/7/2009 (H1N1)	77.5 (75.5, 79.4)	77.2 (73.6, 80.5)	80.2 (76.5, 83.5)
A/Victoria/210/2009 (H3N2)	71.5 (69.3, 73.5)	65.8 (61.9, 69.6)	70.0 (65.9, 73.9)
B/Brisbane/60/2008 (Victoria lineage)	58.1 (55.8, 60.4)	55.4 (51.3, 59.4)	47.5 (43.2, 51.9)
B/Brisbane/3/2007 (Yamagata lineage)	61.7 (59.5, 64.0)	45.6 (41.6, 49.7)	59.1 (54.7, 63.3)

ATP = According-to-protocol; CI = Confidence Interval.

ATP cohort for immunogenicity included subjects for whom assay results were available after vaccination for at least one trial vaccine antigen.

[a] Contained the same composition as FLUARIX (trivalent formulation) manufactured for the 2010-2011 season and an additional influenza type B virus of Yamagata lineage.

[b] Contained the same composition as FLUARIX manufactured for the 2010-2011 season (2 influenza A subtype viruses and an influenza type B virus of Victoria lineage).

[c] Contained the same 2 influenza A subtype viruses as FLUARIX manufactured for the 2010-2011 season and an influenza type B virus of Yamagata lineage.

[d] Seroconversion defined as a pre-vaccination HI titer of <1:10 with a post-vaccination titer ≥1:40 or at least a 4-fold increase in serum titers of HI antibodies to ≥1:40.

14.3 Immunological Evaluation of FLUARIX QUADRIVALENT in Children

Trial 7 was a randomized, observer-blind, non-influenza vaccine-controlled trial evaluating the efficacy of FLUARIX QUADRIVALENT. In this trial, subjects aged 6 through 35 months received FLUARIX QUADRIVALENT (n = 6,006) or a non-influenza control vaccine (n = 6,012). Immune responses to each of the vaccine antigens were evaluated in sera 28 days following 1 or 2 doses in a subgroup of subjects (n = 753 for FLUARIX QUADRIVALENT, n = 579 for control in the ATP cohort for immunogenicity).

Immunogenicity endpoints (GMTs and the percentage of subjects who achieved seroconversion) were analyzed based on the ATP cohort for whom immunogenicity assay results were available after vaccination. Antibody responses for all 4 influenza strains are presented in Table 11.

Table 11. FLUARIX QUADRIVALENT: Immune Responses to Each Antigen 28 Days after Last Vaccination in Children Aged 6 through 35 Months[a] (ATP Cohort for Immunogenicity)

	FLUARIX QUADRIVALENT	**Non-Influenza Active Comparator[b,c]**
Geometric Mean Antibody Titer	**n = 750-753 (95% CI)**	**n = 578-579 (95% CI)**
A (H1N1)	165.3 (148.6, 183.8)	12.6 (11.1, 14.3)
A (H3N2)	132.1 (119.1, 146.5)	14.7 (12.9, 16.7)
B (Victoria lineage)	92.6 (82.3, 104.1)	9.2 (8.4, 10.1)
B (Yamagata lineage)	121.4 (110.1, 133.8)	7.6 (7.0, 8.3)
Seroconversion[d]	**n = 742-746 % (95% CI)**	**n = 566-568 % (95% CI)**
A (H1N1)	80.2 (77.2, 83.0)	3.5 (2.2, 5.4)
A (H3N2)	68.8 (65.3, 72.1)	4.2 (2.7, 6.2)
B (Victoria lineage)	69.3 (65.8, 72.6)	0.9 (0.3, 2.0)
B (Yamagata lineage)	81.2 (78.2, 84.0)	2.3 (1.2, 3.9)

ATP = According-to-protocol; CI = Confidence Interval.
ATP cohort for immunogenicity included subjects for whom assay results were available after vaccination for at least one trial vaccine antigen.
[a] Trial 7: NCT01439360.
[b] Children younger than 12 months: pneumococcal 13-valent conjugate vaccine [Diphtheria CRM197 Protein] (Wyeth Pharmaceuticals, Inc.).
[c] Children 12 months and older: HAVRIX (Hepatitis A Vaccine) for those with a history of influenza vaccination; or HAVRIX (Dose 1) and a varicella vaccine (U.S. Licensed Manufactured by Merck & Co., Inc. or Non-U.S. Licensed Manufactured by GlaxoSmithKline Biologicals) (Dose 2) for those with no history of influenza vaccination.
[d] Seroconversion defined as a pre-vaccination HI titer of <1:10 with a post-vaccination titer ≥1:40 or at least a 4-fold increase in serum titers of HI antibodies to ≥1:40.

Trial 2 was a randomized, double-blind, active-controlled, safety, immunogenicity, and non-inferiority trial. In this trial, subjects received FLUARIX QUADRIVALENT (n = 791) or one of 2 formulations of comparator trivalent influenza vaccine (FLUARIX; TIV-1, n = 819; or TIV-2, n = 801), each containing an influenza type B virus that corresponded to one of the 2 type B viruses in FLUARIX

QUADRIVALENT (a type B virus of the Victoria lineage or a type B virus of the Yamagata lineage). In children aged 3 through 17 years, immune responses to each of the vaccine antigens were evaluated in sera 28 days following 1 or 2 doses. In the overall population, 52% of subjects were male; 56% were white, 29% were Asian, 12% were black, and 3% were of other racial/ethnic groups.

The immunogenicity endpoints were GMTs adjusted for baseline, and the percentage of subjects who achieved seroconversion, defined as a pre-vaccination HI titer of <1:10 with a post-vaccination titer ≥1:40 or at least a 4-fold increase in serum HI titer over baseline to ≥1:40, following vaccination, performed on the ATP cohort for whom immunogenicity assay results were available after vaccination. FLUARIX QUADRIVALENT was non-inferior to both TIVs based on adjusted GMTs (upper limit of the 2-sided 95% CI for the GMT ratio [TIV/FLUARIX QUADRIVALENT] ≤1.5) and seroconversion rates (upper limit of the 2-sided 95% CI on difference of the TIV minus FLUARIX QUADRIVALENT ≤10%). The antibody response to influenza B strains contained in FLUARIX QUADRIVALENT was higher than the antibody response after vaccination with a TIV containing an influenza B strain from a different lineage. There was no evidence that the addition of the second B strain resulted in immune interference to other strains included in the vaccine (Table 12).

Table 12. FLUARIX QUADRIVALENT: Immune Responses to Each Antigen 28 Days after Last Vaccination in Children Aged 3 through 17 Years (ATP Cohort for Immunogenicity)

		Trivalent Influenza Vaccine (TIV)	
	FLUARIX QUADRIVALENT[a]	TIV-1 (B Victoria)[b]	TIV-2 (B Yamagata)[c]
Geometric Mean Antibody Titer	**n = 791 (95% CI)**	**n = 818 (95% CI)**	**n = 801 (95% CI)**
A/California/7/2009 (H1N1)	386.2 (357.3, 417.4)	433.2 (401.0, 468.0)	422.3 (390.5, 456.5)
A/Victoria/210/2009 (H3N2)	228.8 (215.0, 243.4)	227.3 (213.3, 242.3)	234.0 (219.1, 249.9)
B/Brisbane/60/2008 (Victoria lineage)	244.2 (227.5, 262.1)	245.6 (229.2, 263.2)	88.4 (81.5, 95.8)
B/Brisbane/3/2007 (Yamagata lineage)	569.6 (533.6, 608.1)	224.7 (207.9, 242.9)	643.3 (603.2, 686.1)
Seroconversion[d]	**n = 790 % (95% CI)**	**n = 818 % (95% CI)**	**n = 800 % (95% CI)**
A/California/7/2009 (H1N1)	91.4 (89.2, 93.3)	89.9 (87.6, 91.8)	91.6 (89.5, 93.5)
A/Victoria/210/2009 (H3N2)	72.3 (69.0, 75.4)	70.7 (67.4, 73.8)	71.9 (68.6, 75.0)
B/Brisbane/60/2008 (Victoria lineage)	70.0 (66.7, 73.2)	68.5 (65.2, 71.6)	29.6 (26.5, 32.9)
B/Brisbane/3/2007 (Yamagata lineage)	72.5 (69.3, 75.6)	37.0 (33.7, 40.5)	70.8 (67.5, 73.9)

ATP = According-to-protocol; CI = Confidence Interval.

ATP cohort for immunogenicity included subjects for whom assay results were available after vaccination for at least one trial vaccine antigen.

[a] Contained the same composition as FLUARIX (trivalent formulation) manufactured for the 2010-2011 season and an additional influenza type B virus of Yamagata lineage.

[b] Contained the same composition as FLUARIX manufactured for the 2010-2011 season (2 influenza A subtype viruses and an influenza type B virus of Victoria lineage).

[c] Contained the same 2 influenza A subtype viruses as FLUARIX manufactured for the 2010-2011 season and an influenza B virus of Yamagata lineage.

[d] Seroconversion defined as a pre-vaccination HI titer of <1:10 with a post-vaccination titer ≥1:40 or at least a 4-fold increase in serum titers of HI antibodies to ≥1:40.

15 REFERENCES

1. Hannoun C, Megas F, Piercy J. Immunogenicity and protective efficacy of influenza vaccination. *Virus Res.* 2004;103:133-138.
2. Hobson D, Curry RL, Beare AS, et al. The role of serum haemagglutination-inhibiting antibody in protection against challenge infection with influenza A2 and B viruses. *J Hyg Camb.* 1972;70:767-777.

16 HOW SUPPLIED/STORAGE AND HANDLING

NDC 58160-896-41 Syringe in Package of 10: NDC 58160-896-52

Store refrigerated between 2º and 8ºC (36º and 46ºF). Do not freeze. Discard if the vaccine has been frozen. Store in the original package to protect from light.

17 PATIENT COUNSELING INFORMATION

Provide the following information to the vaccine recipient or guardian:

- Inform of the potential benefits and risks of immunization with FLUARIX QUADRIVALENT.
- Educate regarding potential side effects, emphasizing that: (1) FLUARIX QUADRIVALENT contains non-infectious killed viruses and cannot cause influenza and (2) FLUARIX QUADRIVALENT is intended to provide protection against illness due to influenza viruses only and cannot provide protection against all respiratory illness.
- Encourage women exposed to FLUARIX QUADRIVALENT during pregnancy to enroll in the pregnancy registry *[see Use in Specific Populations (8.1)]*.
- Give the Vaccine Information Statements, which are required by the National Childhood Vaccine Injury Act of 1986 prior to each immunization. These materials are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines).
- Instruct that annual revaccination is recommended.

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FLQ:13PI

MONTHLY ESTIMATES OF THE CHILD POPULATION "SUSCEPTIBLE" TO MEASLES, 1900–1931, BALTIMORE, MD.*

By

A. W. HEDRICH.

(Received for publication September 27, 1932.)

Introductory.

Although epidemics have troubled mankind since the dawn of recorded history, our information as to the factors underlying epidemic movements is still very incomplete, and for the most part rather crude and unquantitative. Thus, there has been, and still exists, a lively difference of opinion, as to the rôle played in epidemic phenomena, by the concentration of persons not previously attacked.

Hamer (1) felt that the number of persons without measles history practically determined (in conjunction with the number of cases present) the number of new cases to be expected in a community in the immediate future. On the basis of this theory, he presented estimates, in 1906, of the mean numbers of susceptibles before and after epidemics in London.

Brownlee (2), on the other hand, in 1909, gave reasons for believing that susceptibility played only a minor rôle in shaping the epidemic cycle, and he pointed to variations in virulence of the infective

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organism as a much more important factor. Brownlee's views, however, were not widely accepted.

Soper (3) in 1928, returned to Hamer's theory, gave it mathematical expression and extension, included seasonal variation of infectivity as a factor and tested the ability of the formulated theory to predict cases. Soper's conservative conclusion (pp. 52–55) was that the law of propagation of measles, as disclosed in the twelve years' data from Glasgow, is not quite so simple that we can get good forecasts merely by premising the relationships formulated by him.* This relationship, he modestly continued, "may be said to give half the picture in a selected period;" but even this demonstration, Isserlis (4) and others have added, represented real progress.

In the discussion of Soper's paper, Crookshank referred to his own theory, as put forth in 1908. Crookshank feels that cognizance should be taken of " people who did not get the *disease,* but who were nevertheless transferred from susceptibles to non-susceptibles." Moreover, he says, "susceptibility is such an extraordinarily relative thing. . . . One might be susceptible if one went to see a case in the middle of the night on an empty stomach, but not susceptible if he saw a case after a meal."

A quite different theory has been propounded by Stocks and Karn (5); namely, that during an epidemic of measles a rather large proportion of the non-immune children who escape the disease acquire a latent infection which establishes a temporary immunity. They intimate that the latent immunization established during a major epidemic outnumbers by three or four to one, the clinically recognizable cases of measles, and they conceive that the resultant temporary immunity, fading gradually, is almost completely lost within about two years. Dr. W. H. Frost and the author have carefully reviewed the work of Stocks and Karn and later work by Stocks (6) bearing on this theory, with the result that we consider the evidence not sufficiently convincing to compel acceptance of a theory of such wide implications.

It is not intended to deny the possibility of immunization against measles by latent or subclinical infection, but it does not seem necessary to conclude that this is of such frequent occurrence or of such

* His formula was of the type, $Z_e = ZS\theta/m$, where Z represents cases during the current two week interval, and Z_e, cases expected during the subsequent interval; S, the number of susceptibles at the beginning of the current two week interval; m, a constant, being the critical number of susceptibles, when each current case gives rise, on the average, to one new case; and θ, a factor varying with season.

fundamental importance in the epidemiology of measles, as is implied in the theory developed by Stocks and Karn.

Definitions for this paper.—In this paper an attempt is made to estimate, month by month, from 1900 to 1931, for a specified area, the child population not previously attacked by measles. In the paper as originally presented as part of a doctor's thesis, in 1928, the expressions, "susceptible," and "persons not previously attacked," were considered practically interchangeable, but in the light of what has been said, this assumption would clearly beg a question which is under debate. The use of "non-immune" to designate the unattacked is open to similar objection. It does, in fact, seem fundamentally unscientific in the present state of our knowledge, to name on a basis of presumptive *immunity,* a group that can at present be classified with certainty only on a basis of *attack.* One might with equal logic use the name "poet" for persons who painted, simply because, so far as one knew, nearly all persons who painted, wrote poetry; and nearly all persons who wrote poetry, painted. *In this paper, therefore, the word "intacts" will, for lack of a more suitable synonym, be used to signify "persons not previously subjected to recognizable attack."*

With respect to measles, the group under discussion can be considered approximately, though probably not exactly, equivalent to "persons not permanently immune," or to "potential susceptibles," on the basis of observations such as the following:

(*a*) Paterson (7) has written of a measles epidemic in Reykjavik, Iceland: "Dr. Gudmunson, who is physician for a large district, stated that in his part of the country, out of a population of 6000 or 7000, he only knew of two or three individuals who did not take measles." Apparently only a small fraction of one per cent escaped.

Similarly, Panum (8), in his historic account of the 1846 measles epidemic in the isolated Faroe Islands, states that of approximately 5028 persons exposed,* about 5000, or some 99 per cent, contracted measles.

* Of the 6626 inhabitants in districts visited by him, 98 had been attacked previously; and some 1500, he reports, had been protected by quarantine. It seems likely that this quarantine was really effective, for the disease was dreaded by the Islanders, who made strenuous efforts to protect themselves. Thus, on the seventeen or so islands, there were fifteen villages, aggregating 1132 population, that escaped entirely. Large parts of other villages escaped, due to quarantine, according to Panum. Thirty-three houses in epidemic sections escaped without cases. All in all, it seems reasonable to accept Panum's statement that about 1500 escaped contact with measles cases. Taking account of 96 previously attacked leaves about 5028 non-immunes exposed to risk.

Dependable data for more thickly settled populations are more difficult to obtain, but the proportion of the population ultimately attacked is apparently not much smaller than the foregoing, if smaller at all. Thus data from surveys by Butler, Henderson, Collins and Sydenstricker, which have been discussed in a previous paper, (9) indicate that about 90 to 95 per cent of city children aged fifteen, gave histories of measles.* An additional proportion suffer attack at older ages—about 3.5 per cent in Baltimore.

(*b*) Panum writes further, "It is quite remarkable that of the many old people still living on the Faroes in the 1846 epidemic, who had had measles in 1781, not one, so far as I could find out by careful enquiry, was attacked a second time. I, myself, saw 98 such old people who were exempt because they had had the disease in their youth." Nevertheless, "high age by no means lessened the susceptibility to measles, since, as far as I know, all the old people who had not gone through with the measles in earlier life, were attacked when exposed to infection; while certain young persons, although constantly exposed, were exempt."

Evidence of this type is weighty, because forgotten earlier cases and confused diagnoses are practically ruled out, something that can rarely be said of accounts alleging second attacks. G. N. Wilson (12), who found 2.9 per cent second attacks reported among 12,119 cases of measles in Aberdeen, Scotland, wrote, "The value of the records of such second and third attacks is probably not great, as it is impossible to eliminate the error due to German measles being mistaken for measles."

In summary, then, since (*a*) large proportions of populations (in the neighborhood of 99 per cent) are known to have contracted measles, and since (*b*) with extremely few, if any exceptions, those attacked, seem permanently immune, it appears that the number of intacts, or persons without measles history, may, within a small error, be taken as equivalent to the population of "potential susceptibles," or "persons not permanently immune."

The estimates of this paper are limited to the population under age fifteen in order to minimize the error due to migration. It is believed

* Wilson (10), Collins (11), and others have pointed out that, in surveys, some cases of German measles are likely to be reported as measles. Over against this inflationary effect must be weighed an error in the opposite direction due to memory lapse, of which there is ample evidence. I have assumed for purposes of this paper that the two errors approximately cancelled one another, and have taken 95 per cent for mean measles history rate as of the 15th birthday, for city children.

that by this limitation not more than 10 per cent of the intacts are excluded, and those are clearly from age groups not as liable to attack as children.

The estimates are further confined to a constant area of Baltimore, namely, that comprising the city prior to the annexation of 1919; this area will for convenience be referred to as "Old Baltimore." It is seen from the following Federal census enumerations that this area maintained, during the early years of this century, an exceptionally stable population under age fifteen. Then came a moderate war boom, followed by a decline in this area. (As in many metropolitan areas, growth has taken place largely in the newer, suburban zones.)

Year	Population under fifteen
1900	150,518
1910	150,110
1920 (1919 annexation excluded)	166,577
1930 (1919 annexation excluded)	160,872

Procedure.

The basic operation in this study was to begin with an arbitrarily assumed number of intacts (defined above) as of January 1, 1900, and to calculate subsequent intacts seriatim by adding monthly gains and deducting losses. Adjustment for the error due to the arbitrary start was made at the end in a manner to be described.

The monthly gains in intacts consist mainly of births, and to a small extent of immigrated children not previously attacked (whether of foreign or domestic origin). The losses are attributable mainly to cases, and to a less degree to death and to emigration of intacts. Moreover, since the desired end result is the intact population under age fifteen, we treat as a loss from this universe, each month, estimated intacts who attain the fifteenth birthday.

In summary, then, we may write:

$$N_f = N + B + I' - C - D' - E' - R', \qquad (1)$$

where N_f and N represent persons without measles history (intacts) at beginning of "following month" and of "current month," respectively; and the remaining terms refer to monthly gains or losses of intacts from births (B), immigrants (I'), cases (C), deaths (D'), emigrants (E') and population "retired" at fifteenth birthday (R'). The accent ($'$), where used, indicates limitation to population not previously attacked. The limitation to ages under fifteen has been discussed.

All of the indicated gain and loss elements except the two migration terms have been determined arithmetically, after adjustment of some of the raw data for incompleteness. Because of the difficulty of estimating intra-national migration, and because, as indicated by slow growth of this area, gain of intacts through migration must have been small—if, indeed, it was positive—the migratory elements were omitted from the calculations of this study. Hence neglecting the terms I' and E', the equation becomes

$$\text{Approximately, } N_f = N + B - C - D' - R'. \qquad (2)$$

Treatment of B, R' and D'.—Turning now to discussion of the arithmetic data, it will be expedient to take up first the births, and the intacts among the "retired" and deceased groups. These elements are far less variable from month to month, than the cases; they were, therefore, combined and treated as constant within single years, in order to save labor.

As to births, it was necessary at the outset to correct the raw data for incomplete reporting, and this was done by the method described in an earlier paper (13). Briefly, the corrections rest partly upon tests by the Census Bureau, made by searching the birth records for names from lists of children presumed to be random samples of birth inflow; they rest further upon comparison of reported birth statistics with calculated births derived from census enumerations of the corresponding cohorts of children, after allowance for deaths, and for other factors. It was found that the completeness of reporting was about 60 per cent in 1900, and rose in growth curve fashion to about 99 per cent in 1930. After graduation, these completeness values were used to calculate adjusted annual births.

Intacts to be retired at age 15 (R') were calculated by taking five per cent of the annual numbers of children flowing through fifteenth birthday; this relation following from the datum, referred to above, that approximately 95 per cent of the children at age 15 have previously had measles. The populations used in this connection were arithmetic interpolations between censuses.

Annual numbers of D', were similarly calculated by applying to the annual deaths under age 15, from all causes, a factor representing the mean proportion of intacts among such deceased children. This factor, approximately 88 per cent, is large because of the large proportion of infants among those dying under age 15, almost all without measles history. The calculation of this factor is shown in table

1,* and was briefly as follows: From average age-specific history ratios for the living ($\overline{H}$) shown in fig. 1, and derived as outlined in a footnote to table 1, corresponding intact ratios were obtained by taking $1 - \overline{H}$ at each age. From these, intact ratios for the deceased were obtained by allowance for proportions due to fatal cases.† The re-

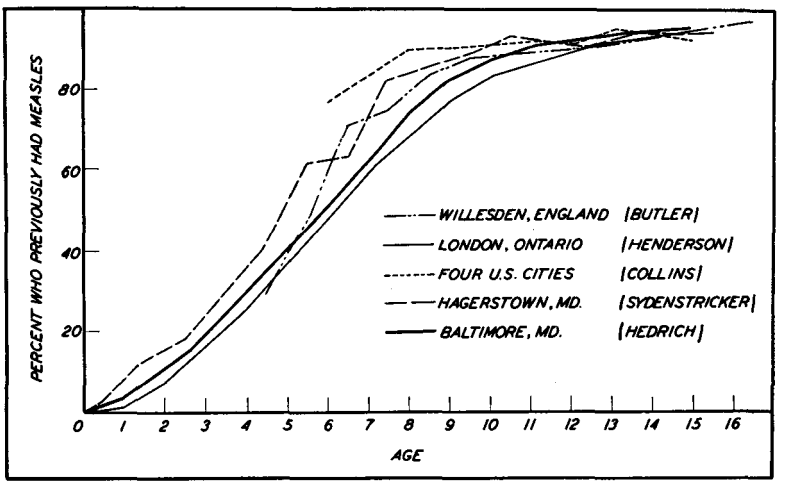

FIG. 1. Four observations of measles history rates by age; also calculated rates for Baltimore.

sulting intact ratios, multiplied into deaths of corresponding age, yielded the desired estimated values of D'.

As the monthly fluctuations of B, D', and R' could have but a minor effect upon the rise and fall of the intact population, they were combined, divided by 12, and treated as a constant net inflow of intacts for the months of any single year. The calculation of these "quasi-constant increments" is shown in table 2.

Correction of cases.—As a first approach, reported cases were cor-

* Table 1 also shows the calculation of the mean proportion of intacts among the living under age 15, namely, 0.423. This constant will be employed in a later calculation of this paper.

† This correction follows because measles deaths do not appear in histories taken in surveys from living children. As an extreme example of the effect of this omission, the death rate from a highly fatal disease, like pneumonic plague in India, might be quite high; yet the history rates taken in surveys might be almost nil, practically none of those attacked having lived to be surveyed. In the case of measles, however, the correction was found to be very small, and might as well have been omitted.

TABLE 1.

Calculation of mean proportions under age 15 without measles history: (A) among living population; (B) among persons dying.

Age interval	A. For living population				B. For persons dying		
	History ratio[a]	Intact ratio[b] =1.0 −(2)	Sum, annual populations 1906-1915	Calculated number intact =(3) ×(4)	Intact ratio[c]	Deaths, 1906–15 (all causes)	Calculated number of intacts =(6) ×(7)
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
(Months)							
0–2	—	—	—	—	0.9986	11,721	11,704
3–5	—	—	—	—	0.9916	3,987	3,955
	0.0141	0.9859	110,109	109,049			
6–8	—	—	—	—	0.9743	2,882	2,807
9–11	—	—	—	—	0.9585	2,408	2,308
(Years)							
1	0.0748	0.9252	100,058	92,574	0.9223	4,241	3,910
2	0.1544	0.8456	107,377	90,787	0.8419	1,623	1,376
3	0.2475	0.7525	106,246	79,950	0.7482	897	671
4	0.3534	0.6466	104,931	67,848	0.6444	723	466
5	0.4604	0.5396	104,258	56,258	0.5376	564	303
6	0.5702	0.4298	104,747	45,020	0.4280	461	197
7	0.6852	0.3148	101,179	31,851	0.3132	380	119
8	0.7853	0.2147	101,200	21,689	0.2134	328	70
9	0.8518	0.1482	98,182	14,551	0.1471	283	42
10	0.8905	0.1094	100,048	10,945	0.1087	278	30
11	0.9140	0.0859	95,430	8,197	0.0852	262	22
12	0.9290	0.0710	101,128	7,180	0.0706	264	20
13	0.9394	0.0606	96,551	5,851	0.0603	269	16
14	0.9464	0.0536	98,335	5,271	0.0532	300	16
Sums	—	—	1,530,279	647,021	—	31,871	28,031

Mean intact ratio for living under age 15

$$= \frac{647{,}021}{1{,}530{,}279} = 0.4228$$

Mean intact ratio for those dying under age 15

$$= \frac{28{,}031}{31{,}871} = 0.8795$$

[a] Refers to mean proportion of population in indicated age band, with history of measles. History ratios as of *birthdays* were first calculated by cumulating from birth to successive anniversaries, the non-fatal case rates of Baltimore, corrected for incompleteness by the method given in reference (9). Means were then taken of adjacent values in pairs, to yield approximate mean history rates over age *intervals*, as given in column (2) above. These history ratios are shown graphically in fig. 1, and are seen to pursue roughly a mid-course between similar ratios from surveys.

[b] Proportion not previously attacked by measles.

[c] Calculated from intact ratio for the living column (3), by subtracting the proportion of all deaths attributable to measles, at given age. Data for the deceased are given by quarter years under age one because of the rapid change of deaths with age in that zone. For the living, the relative change in population (col. 4) is less, and subdivision is therefore unnecessary.

TABLE 2.

Calculation of quasi-constant intact increment, Δ/12.

Year	B Adjusted births	D' Deaths of intacts	R' Intacts retired at 15th birthday	Quasi-constant increment	
				Annual $B - D' - R' = \Delta$	Monthly $\Delta/12$
(1)	(2)	(3)	(4)	(5)	(6)
1900	14,664	3694	550	10,420	868.33
1901	14,902	3283	553	11,066	922.167
1902	15,159	3272	556	11,331	944.250
1903	14,590	3116	560	10,914	909.500
1904	14,538	3086	563	10,889	907.417
1905	15,031	3369	566	11,096	924.667
1906	15,249	3249	569	11,431	952.583
1907	14,803	3254	572	10,977	914.750
1908	14,900[a]	2930	575	11,395	949.583
1909	14,850	3025	578	11,247	937.250
1910	14,800	2868	581	11,351	945.917
1911	14,800	2697	582	11,521	960.083
1912	14,900	2637	582	11,681	973.417
1913	14,990	2716	582	11,692	974.333
1914	15,080	2606	583	11,891	990.917
1915	15,182	2163	583	12,436	1036.333
1916	15,668	2430	583	12,655	1054.583
1917	15,890	2481	583	12,826	1068.833
1918	15,820	3649	583	11,588	965.667
1919	16,131	2158	584	13,389	1115.750
1920	16,994	2233	584	14,177	1181.417
1921	16,948	1872	589	14,487	1207.250
1922	15,856	1854	594	13,408	1117.333
1923	15,848	1836	599	13,413	1117.750
1924	15,503	1712	604	13,187	1098.917
1925	14,612	1674	609	12,329	1027.417
1926	14,023	1739	614	11,670	972.500
1927	14,166	1585	618	11,963	996.917
1928	13,347	1646	623	11,078	923.167
1929	12,499	1364	628	10,507	875.583
1930	12,469	1208	633	10,628	885.667
1931	12,195	1200	638	10,357	863.083

[a] During the years prior to 1914, when the Birth Registration Area was organized, the birth records appear erratic, possibly due to sporadic efforts to improve completeness of birth reporting. For this reason, births for the years 1908–1914 were graphically smoothed before entry in column 2 above.

rected for incomplete notification by a method already described (9*c*), the basis of this method being an inference that the true attack rate under age fifteen averages approximately 6.5 per cent of the population under age fifteen, per year, if taken over a number of complete epidemic cycles. Two difficulties presented themselves in this procedure: (*a*) evidence that child populations were under-enumerated at censuses by 10 per cent or more; and (*b*) that even so small a constant error in the case rate as one per cent per year, for example, would cumulate so as to produce an intolerable error in the calculated intact population toward the end of the long period taken.

As an alternative procedure, therefore, advantage was taken of the approximate equivalence of gains and losses of intacts, if aggregated over a period of years. To illustrate, let us think of the intact population of a community as the contents of a huge reservoir, into which flows a fairly constant stream of intacts composed mainly of births (and to a small extent of migrants, who are here disregarded). Out of the reservoir flows a stream composed of intact losses from death, "retirement" at age fifteen, and principally of a strongly oscillating flow of cases. During epidemics, outflow exceeds inflow and the reservoir level falls; between epidemics, the level rises. Over a period of years, the cumulated outflow must nearly equal cumulated inflow, provided we begin and end at about the same level of the reservoir. (It has already been pointed out that the child population did not increase greatly in Old Baltimore from 1900 to 1930, hence the size of reservoir was fairly constant.) We may, therefore, equate inflow and outflow as follows:

$$\text{Approximately, } \Sigma B = \Sigma C + \Sigma D' + \Sigma R', \tag{3}$$

where Σ indicates summations over a number of epidemic cycles, and the other symbols are defined near equation (1).

All of the terms of the equation represent known quantities, except for the cases, hence we can solve for cases as follows:

$$\text{Approximately, } \Sigma C = \Sigma B - \Sigma D' - \Sigma R'. \tag{4}$$

ΣC here represents a theoretically complete number of cases, provided a time interval is taken long enough to wash out epidemic distortions. It was found by experiment that epidemic fluctuations became sufficiently submerged if reported cases were summed over six year periods, representing roughly three epidemic cycles, on an average; hence, this period was adopted for use with equation (4).

Now, it was early observed that a rise or fall in births was not promptly followed by a corresponding change in the trend of cases; instead, the cases seemed to lag about six years after births. Such a lag might have been expected from the fact that, in Baltimore, the peak in cases comes at about age six (9*d*). Stated in terms of our analogy, intacts tend to remain in the reservoir about six years on an average; hence, in estimating cases by the "residual outflow" method of equation (4), births and intact deaths (which oftenest follow within a few months after birth) were set back six years.

Six year moving sums of theoretical cases were next formed, and by taking ratios to corresponding sums of reported cases, approximate factors were derived for correcting reported cases for incomplete noti-

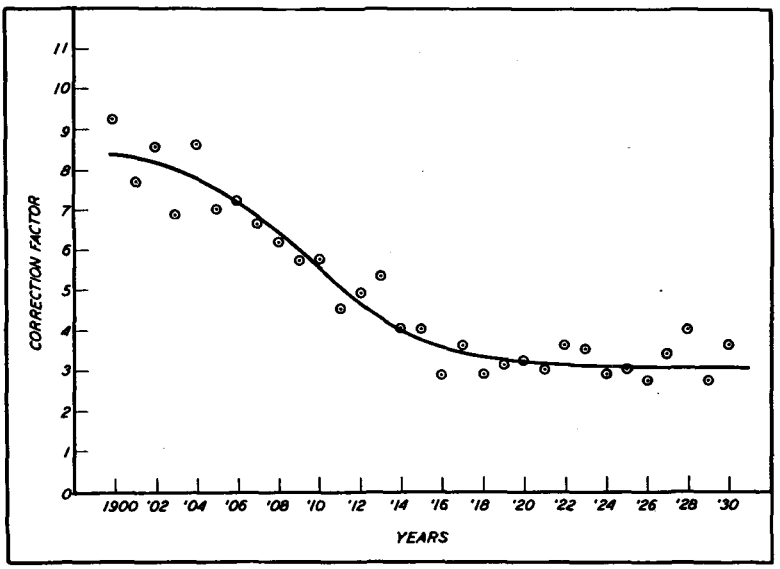

FIG. 2. Factors for correcting reported measles cases for incomplete notification. Baltimore.

fication; these crude correction factors were graduated with a logistic curve. These operations are shown in table 3, and the end results in fig. 2. From the graduation, monthly factors were calculated for correcting the monthly reported cases shown in Appendix Table *A*.

As the correction factor is simply the reciprocal of the completeness of reporting, it follows from the table that the estimated com-

TABLE 3.

Calculation of factors to correct reported measles cases for incomplete notification.

y Year	B =Estimated[a] complete births for year $y-6$	D' Deaths of intacts under age 15 for year $y-6$	R' Intacts retired at age 15	$B-D'-R'$	c =Reported cases	Six year sums[d]		Correction factors[d]	
						$B-D'-R'$ =Theoretical cases	Reported cases	Crude =(7)/(8)	Graduated
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
1897	15,830	3,962	544	11,324	610	—	—	—	—
1898	15,991	4,484	546	10,961	1,316	—	—	—	—
1899	15,484	3,548	548	11,388	550	—	—	—	—
1900	15,904	3,691	550	11,663	2,565	66,849	7,239	9.23	8.41
1901	15,355	3,959	553	10,843	430	66,343	8,673	9.65	8.30
1902	14,906	3,680	556	10,670	1,768	65,769	7,676	8.56	8.18
1903	14,916	3,538	560	10,818	2,044	64,112	9,384	6.83	7.97
1904	14,904	3,954	563	10,387	319	63,164	7,347	8.60	7.76
1905	13,622	3,325	566	9,721	2,258	63,368	9,052	7.00	7.50
1906	14,664	3,694	569	10,715	528	64,010	8,859	7.23	7.20
1907	14,902	3,283	572	11,047	2,135	64,088	9,646	6.64	6.87
1908	15,159	3,272	575	11,312	1,575	64,572	10,422	6.20	6.47
1909	14,590	3,116	578	10,896	2,831	65,921	11,506	5.73	6.01
1910	14,538	3,086	581	10,871	1,095	66,624	11,563	5.76	5.51
1911	15,031	3,369	582	11,080	3,342	66,544	14,701	4.52	5.09
1912	15,249	3,249	582	11,418	585	66,619	13,531	4.92	4.52
1913	14,803	3,254	582	10,967	5,273	66,965	12,456	5.37	4.30
1914	14,900[b]	2,930	583	11,387	405	67,443	16,552	4.07	4.02
1915	14,850	3,025	583	11,242	1,756	67,883	16,885	4.02	3.82
1916	14,800	2,868	583	11,349	5,191	68,145	23,489	2.90	3.61
1917	14,800	2,697	583	11,520	3,675	68,868	18,900	3.64	3.50
1918	14,900	2,637	583	11,680	7,189	69,371	22,445	2.99	3.39
1919	14,990	2,716	584	11,690	684	70,559	22,489	3.14	3.30
1920	15,080	2,606	584	11,890	3,950	71,854	21,479	3.34	3.24
1921	15,182	2,163	589	12,430	1,800	73,144	23,849	3.07	3.20
1922	15,668	2,430	594	12,644	4,181	73,031	20,153	3.62	3.17
1923	15,890	2,481	599	12,810	6,045	74,705	21,098	3.54	3.15
1924	15,820	3,649[c]	604	11,567	3,493	76,962	25,959	2.96	3.14
1925	16,131	2,158	609	13,364	1,629	78,990	24,803	3.18	3.13
1926	16,994	2,233	614	14,147	8,811	79,725	29,409	2.71	3.12
1927	16,948	1,872	618	14,458	644	80,299	23,453	3.42	3.11
1928	15,856	1,854	623	13,379	9,203	81,890	20,253	4.04	3.11
1929	15,848	1,836	628	13,384	100	80,826	29,754	2.72	3.11
1930	15,503	1,712	633	13,158	349	—	—	—	—
1931	14,612	1,674	638	12,300	11,282	—	—	—	—

[a] Births are set back six years because the maximum effect of a given crop of births on the measles case rate is likely, on the average, to take place about six years after birth. Since most of the deaths under age 15 occur under age one, deaths of intacts were likewise set back six years in order to let the deduction affect the cohort of births most directly concerned.

This procedure of setting back births and deaths was followed only in estimating theoretically complete numbers of cases, not in actually calculating intacts in table 2 and appendix table *A*.

[b] See note *a* of table 2.

[c] The excess of deaths is attributable to the influenza epidemic.

[d] The six year sums are centered at January 1 of the years indicated; likewise the correction factors.

pleteness ranged about 1/8.4, or 12 per cent in 1900, to about 1/3.1, or 32 per cent at present.*

Comparison of outflow elements.—Bases have now been indicated for estimating intact outflow from each of the three causes considered. It will be interesting to compare the aggregates. The calculated totals for the years 1901–1926 are:

Type of intact loss	Number	Per cent of total losses
Measles attack	307,649	78.8
Deaths (all causes)	67,911	17.4
Retirement at age 15	15,012	3.8
Total	390,572	100.0

It is noteworthy that about a sixth of the intact losses were by death from various causes. Table 2 shows that this form of outflow was, in Baltimore, about three times as heavy in 1900 as at present.

Intacts by months.—The final step was to calculate, month by month, the child population not previously attacked by measles. The procedure was to begin with an arbitrary number of intacts as of January 1, 1900, and to add gains and deduct losses month by month. For convenience, 75,000 was taken as the beginning number. Each of the remainders so obtained deviated from the true number of intacts by the same amount, namely, the error of the initially assumed number of intacts. This deviation was corrected by employing the datum from table 1, that the average proportion previously unattacked in the population under age 15, is about 42.3 per cent. The mean population for the 32 year period was estimated from census enumerations to be 157,705, hence the calculated mean number of intacts became 66,709. The mean of the monthly intacts on the arbitrary scale from a start of 75,000 was 72,254; subtracting this from the estimated true mean of 66,709 left a negative correction constant of 5545. Applying this to the arbitrary remainders yielded the estimated monthly intacts shown in column (4) of Appendix Table *A*. Intact ratios per hundred population under age fifteen are likewise shown in the table; also in fig. 3, in comparison with monthly case rates.

* The incompleteness of reporting implied by these figures recalls Crookshank's statement (14) that "few people realize the great discrepancy between registered and actual cases; it is colossal." Sydenstricker (15) found that in Hagerstown, Md., 64 per cent of the measles cases were seen by physicians, and of these cases, 40.3 per cent were reported, so that approximately a fourth of all cases were reported. Chapin (16) estimated that approximately half of the cases in Providence were unreported, even at the end of a period of intensive effort. Frost has made an unpublished estimate based upon the data of Brownlee (17) that in Aberdeen, Scotland, only about two-thirds of the cases were reported, even when practitioners were paid 2 shillings, 6 pence for each case reported (10).

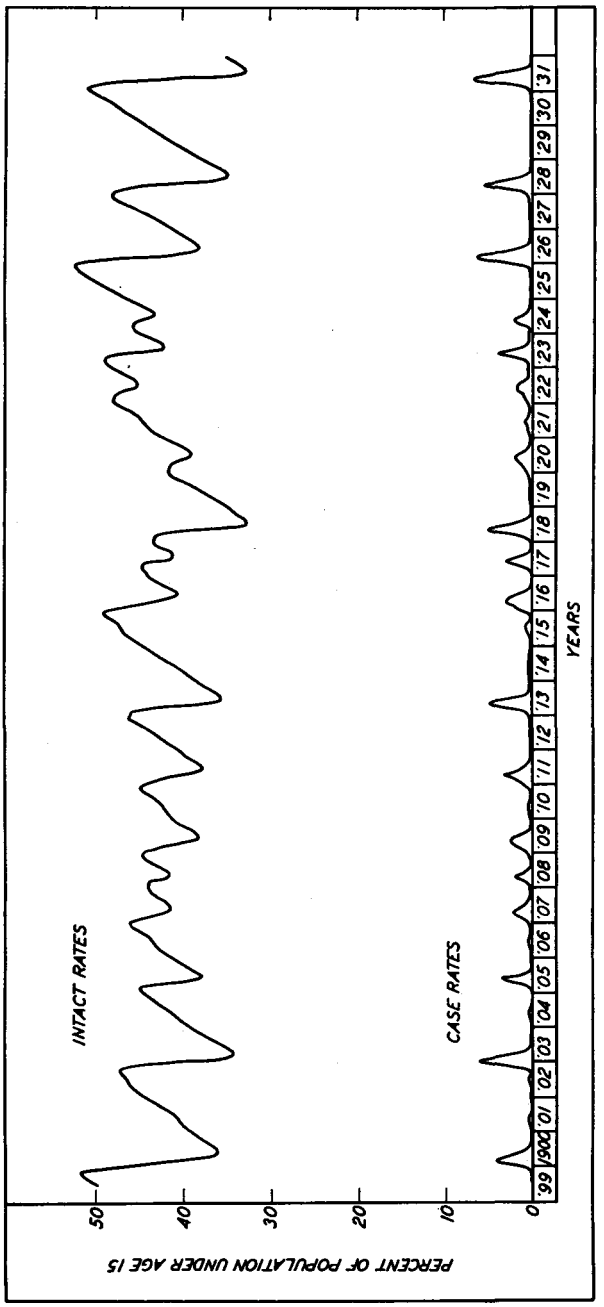

FIG. 3. Estimated complete monthly attack rates from measles; and intact ratios (proportions not previously attacked) for the population under age 15, Old Baltimore, Md.; July, 1899 to December, 1931.

Summary and discussion of results.—At this time, the calculated series of intacts * will be examined mainly from a qualitative angle, and mathematical analysis will not be undertaken.

A few general observations † follow:

(1) During years immediately following heavy epidemics, cases were sufficiently light to permit the intact curve to climb in almost a straight line to the next maximum during a period of about two years, or more (cf. 1929); but during periods of light epidemics, the intact curve showed distinct annual waves (cf. 1907–1908).

(2) The waves of cases and intacts were highly variable, and yet there was a kind of order in this variability, in the form of an alternation of gradual dampening and later re-expansion of the amplitudes of the "epidemic" waves. There is the appearance of a "cycle of epidemic cycles" for the cases, which produced an exaggerated counterpart in the intact curve; the phenomenon is, therefore, seen much more clearly on the intact curve than on the case curve. The damping and later expansion was quite systematic up to about the time of the Great War; for some years thereafter, it was irregular.

The crests of these super-cycles came (*a*) in 1900, or possibly before; (*b*) about 1913–1915, and (*c*) in 1931, or possibly later. The interval between great crests was, therefore, in Baltimore about 15 years. This limited experience gives, of course, no assurance that the same performance will be repeated in the future. An expansion of waves is seen in the case curve for New York City for the years 1909 to about 1923. Damping had apparently not set in by 1931, therefore the super-cycle, if it exists, will have taken much more time between great crests in New York City than in Baltimore. Data from Soper (3*a*) for Glasgow suggest a cycle of this kind with great crests about 18 years apart.

(3) The behavior of the curves in the spring of 1918 was some-

* The reader who may not have read the introduction will find the expression "intacts" defined on page 615.

† The first examination of a graph like fig. 3 stimulates the question: "Why does the intact curve swing in so much greater amplitude than the case curve from which it was derived?" The reason is that the intact curve expresses cumulative effects, whereas the case curve is essentially non-cumulative. Thus, in the case curve, January, February, and March represent summations only within the single months; and the April cases may not be far different in number than January. But intacts at the end of April may be far more or less numerous than on January 1, since the number on the later date is equal to the number on the earlier date plus the *sum* of the gains during the intermediate months, minus the *sum* of the losses. During epidemics the sum of the losses greatly exceeds the gains; between epidemics, *vice versa*.

what abnormal, in that intacts, beginning at about average level, declined during an epidemic to the low point of the three decades. Practically the same minimum was reached in 1931, but in that year the epidemic began with an exceptionally large supply of intact fuel to feed the flame.

Whether the abnormal performances of the intact curve in 1918 represents more than a chance association with the influenza pandemic, of which the first symptoms appeared during the same spring, the author does not feel able to say; but the coincidence seems worthy of mention.

(4) During the 32 year period, the calculated proportion of intacts in the population under age 15 did not rise above 53 per cent, nor fall below 32 per cent. It is evident, as Brownlee and many others have pointed out, that ordinarily measles epidemics do not "wipe out" the susceptible populations. Those escaping attack are mainly infants and young children. Data from Collins (11*a*) and unpublished results of the writer show that the proportion of intacts currently attacked is much greater at early school ages than in infancy.

(5) The greatest relative decline * in intacts during an epidemic occurred in 1931, and amounted to 34 per cent of the previous peak. From this extreme the declines shaded down to zero, small declines occurring oftenest. The frequency distribution of percentage declines of intacts is shown in the following table:

Decline in intacts	Under 10 per cent	10–19 per cent	20–29 per cent	30–39 per cent	Total
Number of instances.....	10†	6	5	2	23

† Five of these were less than one per cent.

The table suggests that on the basis of the Baltimore data, it seems rather meaningless to speak of an average or typical decline in intacts during epidemics; not only was the amount of decline highly variable, but the declines became most frequent as they approached the point of zero magnitude. Stated otherwise, the difficulty is that in Baltimore, at least, the measles incidence in different years presents such variation from light to heavy, that it is difficult to draw a border line between epidemic and non-epidemic, except on an arbitrary basis.

* A decline was taken simply as the amount of drop from a maximum, "maximum" being defined as the point where the intact curve changed from rising slope to falling. Under this definition, no distinction is recognized between "epidemic" and "seasonal" declines.

In conclusion, the writer wishes to urge certain cautions in the use of the calculated results of this paper, because of the heroic corrections of data that were necessary, particularly for reported cases. For this he offers no apology; few if any American data would have been more satisfactory over long time periods; some foreign data are better, but are still far from perfect. The research worker in this branch of epidemiology faces the alternative of struggling with imperfect raw material or of abandoning his search for information.

The mean proportion of intacts was taken at 42.3 per cent on the basis of history surveys in other areas. Most of the latter were smaller places than Baltimore; and it is possible that, for Baltimore, the mean intact rate should be somewhat lower than here indicated, though not a great deal lower.

Because of the approximations and assumptions set forth, the writer is inclined not to stress absolute values of case and intact rates, as much as rates of change of the latter within periods of a few years where errors may cancel out in large degree.

Long-time slope and curvature of the case and intact series are rather sensitive to the curve employed in graduating the correction factors for reported cases; slight differences in slope and curvature are, therefore, not to be taken too seriously. For example, it is not certain that the general slope of the intact curve for the first 13 years is really horizontal, or slightly downward; for as small an increase in the correction factors as one or two per cent per year for the first 13 years, or so, would make the intact curve slope upward. Such a difference would easily fall within the probable error of the graduation.

It is believed, however, that the broad changes in intact cycle enumerated in items (1) to (5) above cannot be attributed to such artifacts; in the opinion of the writer, they represent actual phenomena.

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APPENDIX.

TABLE A. *Calculation of monthly populations under age 15, not previously attacked by measles. 1900–1931. Old Baltimore.*

Month	Reported cases	Corrected cases[a]	Calculated intacts		Month	Reported cases	Corrected cases[a]	Calculated intacts	
			Number[b]	Rate pct.[c]				Number[b]	Rate pct.[c]
(1)	(2)	(3)	(4)	(5)	(1)	(2)	(3)	(4)	(5)
	1900	(Δ/12 = 868)				*1904*	(Δ/12 = 907)		
Jan.	433	3641	69,455	46.2	Jan.	16	125	57,897	38.5
Feb.	737	6193	66,682	44.3	Feb.	14	108	58,679	39.0
Mar.	650	5457	61,357	40.8	Mar.	28	216	59,478	39.6
Apr.	351	2945	56,768	37.7	Apr.	37	285	60,169	40.0
May	236	1978	54,691	36.3	May	100	769	60,791	40.4
June	82	687	53,581	35.6	June	45	345	60,929	40.5
July	29	243	53,762	35.7	July	18	138	61,491	40.9
Aug.	9	75	54,387	36.1	Aug.	11	83	62,260	41.4
Sept.	3	25	55,180	36.7	Sept.	7	53	63,084	42.0
Oct.	15	125	56,023	37.2	Oct.	3	23	63,938	42.5
Nov.	13	108	56,766	37.7	Nov.	8	60	64,822	43.1
Dec.	7	58	57,526	38.2	Dec.	32	241	65,669	43.7
	1901	(Δ/12 = 922)				*1905*	(Δ/12 = 925)		
Jan.	27	224	58,336	38.8	Jan.	39	292	66,335	44.1
Feb.	52	431	59,034	39.2	Feb.	74	553	66,968	44.6
Mar.	67	554	59,525	39.6	Mar.	358	2666	67,340	44.8
Apr.	73	603	59,893	39.8	Apr.	633	4698	65,599	43.7
May	112	923	60,212	40.0	May	689	5096	61,826	41.1
June	52	428	60,211	40.0	June	306	2255	57,655	38.4
July	9	74	60,705	40.4	July	82	60	56,325	37.5
Aug.	1	8	61,553	40.9	Aug.	24	176	57,190	38.1
Sept.	3	25	62,467	41.5	Sept.	19	139	57,939	38.6
Oct.	13	107	63,364	42.1	Oct.	3	22	58,725	39.1
Nov.	9	74	64,179	42.7	Nov.	15	109	59,628	39.7
Dec.	12	98	65,027	43.2	Dec.	16	116	60,444	40.2
	1902	(Δ/12 = 944)				*1906*	(Δ/12 = 953)		
Jan.	18	147	65,851	43.8	Jan.	22	158	61,253	40.8
Feb.	28	228	66,648	44.3	Feb.	13	93	62,048	41.3
Mar.	27	220	67,364	44.8	Mar.	24	172	62,908	41.9
Apr.	47	382	68,088	45.3	Apr.	63	449	63,689	42.4
May	57	462	68,650	45.6	May	114	809	64,193	42.7
June	96	776	69,132	46.0	June	106	750	64,337	42.8
July	80	645	69,300	46.1	July	27	190	64,540	43.0
Aug.	27	217	69,599	46.3	Aug.	25	175	65,303	43.5
Sept.	21	169	70,326	46.8	Sept.	8	56	66,081	44.0
Oct.	92	737	71,101	47.3	Oct.	26	181	66,978	44.6
Nov.	386	3088	71,308	47.4	Nov.	34	236	67,750	45.1
Dec.	889	7099	69,164	46.0	Dec.	66	455	68,467	45.6

APPENDIX—TABLE *A*—*Continued.*

Month	Reported cases	Corrected cases[a]	Calculated intacts		Month	Reported cases	Corrected cases[a]	Calculated intacts	
			Number[b]	Rate pct.[c]				Number[b]	Rate pct.[c]
(1)	(2)	(3)	(4)	(5)	(1)	(2)	(4)	(4)	(5)
	1903	(Δ/12 = 910)				*1907*	(Δ/12 = 915)		
Jan.	1145	9126	63,009	41.9	Jan.	202	1388	68,965	45.9
Feb.	510	4057	54,793	36.4	Feb.	308	2104	68,492	45.6
Mar.	220	1747	51,646	34.3	Mar.	465	3157	67,303	44.8
Apr.	76	602	50,809	33.8	Apr.	473	3193	65,061	43.3
May	41	324	51,117	34.0	May	302	2026	62,783	41.8
June	19	150	51,703	34.4	June	126	840	61,672	41.1
July	8	6	52,463	34.9	July	86	570	61,747	41.1
Aug.	4	3	53,367	35.5	Aug.	23	152	62,092	41.3
Sept.	3	2	54,274	36.1	Sept.	8	53	62,855	41.8
Oct.	6	5	55,182	36.7	Oct.	9	59	63,717	42.4
Nov.	6	5	56,087	37.3	Nov.	66	431	64,573	43.0
Dec.	6	5	56,992	37.9	Dec.	67	435	65,057	43.3
	1908	(Δ/12 = 950)				*1912*	(Δ/12 = 973)		
Jan.	83	537	65,537	43.6	Jan.	35	158	61,931	40.4
Feb.	191	1228	65,950	43.9	Feb.	36	162	62,733	40.9
Mar.	457	2918	65,672	43.7	Mar.	53	239	63,544	41.4
Apr.	360	228	63,704	42.4	Apr.	48	216	64,278	41.9
May	221	1393	62,370	41.5	May	75	337	65,035	42.4
June	62	388	61,927	41.2	June	75	336	65,671	42.8
July	27	168	62,489	41.6	July	49	219	66,308	43.2
Aug.	10	62	63,271	42.1	Aug.	16	71	67,062	43.7
Sept.	4	25	64,159	42.7	Sept.	10	44	67,964	44.3
Oct.	7	43	65,084	43.3	Oct.	16	70	68,893	44.9
Nov.	51	310	65,991	43.9	Nov.	30	131	69,796	45.5
Dec.	102	617	66,631	44.4	Dec.	142	615	70,638	46.1
	1909	(Δ/12 = 937)				*1913*	(Δ/12 = 974)		
Jan.	269	1617	66,964	44.6	Jan.	206	886	70,996	45.8
Feb.	423	2527	66,284	44.2	Feb.	678	2901	71,084	45.9
Mar.	544	3229	64,694	43.1	Mar.	1635	6962	69,157	44.6
Apr.	672	3964	62,402	41.6	Apr.	1670	7076	63,169	40.8
May	515	3019	59,375	39.6	May	770	3246	57,067	36.8
June	233	1357	57,293	38.2	June	180	755	54,795	35.3
July	85	492	56,873	37.9	July	73	304	55,014	35.5
Aug.	8	29	57,318	38.2	Aug.	19	79	55,684	35.9
Sept.	7	40	58,226	38.8	Sept.	5	21	56,579	36.5
Oct.	11	62	59,123	39.4	Oct.	10	41	57,532	37.1
Nov.	27	151	59,998	40.0	Nov.	13	53	58,465	37.7
Dec.	37	206	60,784	40.5	Dec.	14	57	59,386	38.3

APPENDIX—TABLE *A—Continued*

Month	Reported cases	Corrected cases[a]	Calculated intacts		Month	Reported cases	Corrected cases[a]	Calculated intacts	
			Number[b]	Rate pct.[c]				Number[b]	Rate pct.[c]
(1)	(2)	(3)	(4)	(5)	(1)	(2)	(3)	(4)	(5)
	1910	(Δ/12 = 946)				*1914*	(Δ/12 = 991)		
Jan.	83	457	61,515	41.0	Jan.	35	141	60,303	38.5
Feb.	97	532	62,004	41.3	Feb.	47	188	61,153	39.0
Mar.	125	681	62,418	41.6	Mar.	76	304	61,956	39.5
Apr.	129	699	62,683	41.8	Apr.	108	430	62,643	40.0
May	129	695	62,930	41.9	May	61	242	63,204	40.3
June	84	450	63,181	42.1	June	26	103	63,953	40.8
July	53	282	63,677	42.4	July	28	110	64,841	41.4
Aug.	15	79	64,341	42.9	Aug.	5	20	65,722	42.0
Sept.	28	147	65,208	43.4	Sept.	6	23	66,693	42.6
Oct.	36	188	66,007	44.0	Oct.	5	19	67,661	43.2
Nov.	98	507	66,765	44.5	Nov.	5	19	68,633	43.8
Dec.	218	1118	67,204	44.8	Dec.	3	12	69,605	44.4
	1911	(Δ/12 = 960)				*1915*	(Δ/12 = 1036)		
Jan.	402	2046	67,032	44.2	Jan.	10	38	70,584	44.6
Feb.	559	2819	65,946	43.5	Feb.	21	80	71,582	45.2
Mar.	997	4981	64,087	42.2	Mar.	70	265	72,538	45.8
Apr.	573	2836	60,066	39.6	Apr.	153	576	73,309	46.3
May	411	2015	58,190	38.4	May	252	944	73,769	46.6
June	253	1228	57,135	37.7	June	327	1220	73,861	46.7
July	77	370	56,867	37.5	July	114	423	73,677	46.5
Aug.	17	81	57,457	37.9	Aug.	33	122	74,290	46.9
Sept.	4	19	58,336	38.4	Sept.	16	59	75,204	47.5
Oct.	7	33	59,277	39.1	Oct.	16	59	76,181	48.1
Nov.	9	42	60,204	39.7	Nov.	125	455	77,158	48.7
Dec.	33	151	61,122	40.3	Dec.	619	2244	77,739	49.1
	1916	(Δ/12 = 1055)				*1920*	(Δ/12 = 1181)		
Jan.	720	2599	76,531	47.8	Jan.	381	1234	69,326	41.6
Feb.	943	3395	74,987	46.9	Feb.	467	1512	69,273	41.6
Mar.	1235	4434	72,647	45.4	Mar.	602	1947	68,942	41.4
Apr.	1034	3702	69,268	43.3	Apr.	842	2721	68,176	40.9
May	767	2738	66,621	41.7	May	883	2850	66,636	40.0
June	317	1129	64,938	40.6	June	472	1522	64,967	39.0
July	123	437	64,864	40.6	July	127	409	64,626	38.8
Aug.	26	92	65,482	40.9	Aug.	31	100	65,398	39.3
Sept.	17	60	66,445	41.5	Sept.	21	67	66,479	39.9
Oct.	3	11	67,440	42.2	Oct.	20	64	67,593	40.6
Nov.	7	25	68,484	42.8	Nov.	35	112	68,710	41.3
Dec.	9	32	69,514	43.5	Dec.	69	221	69,779	41.9

APPENDIX—TABLE *A*—*Continued.*

Month	Reported cases	Corrected cases[a]	Calculated intacts		Month	Reported cases	Corrected cases[a]	Calculated intacts	
			Number[b]	Rate pct.[c]				Number[b]	Rate pct.[c]
(1)	(2)	(3)	(4)	(5)	(1)	(2)	(3)	(4)	(5)
	1917	(Δ/12 = 1069)				*1921*	(Δ/12 = 1207)		
Jan.	23	81	70,537	43.7	Jan.	106	339	70,739	42.6
Feb.	106	369	71,525	44.3	Feb.	208	665	71,607	43.1
Mar.	340	1180	72,225	44.7	Mar.	178	569	72,149	43.5
Apr.	715	2470	72,114	44.6	Apr.	205	655	72,787	43.9
May	1230	4231	70,713	43.8	May	380	1213	73,339	44.2
June	722	2473	67,551	41.8	June	236	753	73,333	44.2
July	236	805	66,147	40.9	July	60	191	73,787	44.5
Aug.	56	191	66,411	41.1	Aug.	29	92	74,803	45.1
Sept.	42	143	67,289	41.6	Sept.	16	51	75,918	45.7
Oct.	25	85	68,215	42.2	Oct.	22	70	77,074	46.4
Nov.	60	204	69,199	42.8	Nov.	129	409	78,211	47.1
Dec.	120	407	70,064	43.4	Dec.	231	732	79,009	47.6
	1918	(Δ/12 = 966)				*1922*	(Δ/12 = 1117)		
Jan.	370	1254	70,726	43.3	Jan.	365	1155	79,484	48.1
Feb.	547	1848	70,438	43.1	Feb.	436	1380	79,446	48.0
Mar.	1606	5409	69,556	42.6	Mar.	788	2492	79,183	47.9
Apr.	2398	8050	65,113	39.9	Apr.	849	2685	77,808	47.0
May	1670	5588	58,029	35.5	May	818	2587	76,240	46.1
June	429	1431	53,407	32.7	June	513	1622	74,770	45.2
July	98	325	52,942	32.4	July	120	379	74,265	44.9
Aug.	26	86	53,583	32.8	Aug.	30	95	75,003	45.3
Sept.	6	20	54,463	33.4	Sept.	14	44	76,025	46.0
Oct.	3	10	55,409	33.9	Oct.	24	76	77,098	46.6
Nov.	7	23	56,365	34.5	Nov.	130	410	78,139	47.2
Dec.	29	96	57,308	35.1	Dec.	94	296	78,846	47.7
	1919	(Δ/12 = 1116)				*1923*	(Δ/12 = 1118)		
Jan.	45	149	58,178	35.3	Jan.	147	462	79,667	48.3
Feb.	46	152	59,145	35.9	Feb.	265	833	80,323	48.7
Mar.	53	175	60,109	36.5	Mar.	678	2131	80,608	48.9
Apr.	123	405	61,050	37.0	Apr.	1506	4733	79,595	48.3
May	82	270	61,761	37.5	May	2051	6444	75,980	46.1
June	50	165	62,607	38.0	June	920	2890	70,654	42.9
July	13	43	63,558	38.5	July	249	782	68,882	41.8
Aug.	11	36	64,631	39.2	Aug.	87	273	69,218	42.0
Sept.	13	43	65,711	39.9	Sept.	23	72	70,063	42.5
Oct.	27	88	66,784	40.5	Oct.	16	50	71,109	43.1
Nov.	40	130	67,812	41.1	Nov.	41	129	72,177	43.8
Dec.	181	588	68,798	41.7	Dec.	62	194	73,166	44.4

APPENDIX—TABLE *A—Continued.*

Month	Reported cases	Corrected cases[a]	Calculated intacts		Month	Reported cases	Corrected cases[a]	Calculated intacts	
			Number[b]	Rate pct.[c]				Number[b]	Rate pct.[c]
(1)	(2)	(3)	(4)	(5)	(1)	(2)	(3)	(4)	(5)
	1924	(Δ/12 = 1099)				*1928*	(Δ/12 = 923)		
Jan.	121	379	74,090	45.1	Jan.	1158[d]	2648	77,673	47.9
Feb.	301	943	74,810	45.5	Feb.	2371	5357	75,948	46.9
Mar.	680	2130	74,966	45.6	Mar.	3752	8375	71,514	44.1
Apr.	935	2929	73,935	45.0	Apr.	2746	6055	64,062	39.5
May	790	2474	72,105	43.9	May	1792	3902	58,930	36.4
June	447	1400	70,730	43.1	June	320	688	55,951	34.5
July	152	476	70,429	42.9	July	45	96	56,186	34.7
Aug.	36	113	71,052	43.3	Aug.	10	21	57,013	35.2
Sept.	15	47	72,038	43.9	Sept.	5	10	57,915	35.8
Oct.	6	19	73,090	44.5	Oct.	4	8	58,828	36.3
Nov.	3	9	74,170	45.2	Nov.	10	20	59,743	36.9
Dec.	7	22	75,260	45.8	Dec.	16	32	60,646	37.4
	1925	(Δ/12 = 1027)				*1929*	(Δ/12 = 876)		
Jan.	9	28	76,337	46.6	Jan.	12[d]	24	61,537	38.1
Feb.	24	75	77,336	47.2	Feb.	10	19	62,389	38.6
Mar.	22	69	78,288	47.8	Mar.	15	29	63,246	39.2
Apr.	24	75	79,246	48.4	Apr.	17	33	64,089	39.7
May	24	75	80,198	49.0	May	16	31	64,932	40.2
June	77	240	81,150	49.6	June	21	41	65,777	40.7
July	65	203	81,937	50.1	July	9	17	66,612	41.3
Aug.	16	50	82,761	50.6	Aug.	2	4	67,471	41.8
Sept.	23	72	83,738	51.2	Sept.	4	8	68,343	42.3
Oct.	71	222	84,693	51.7	Oct.	6	12	69,211	42.9
Nov.	442	1379	85,498	52.2	Nov.	23	46	70,075	43.4
Dec.	834	2602	85,146	52.0	Dec.	10	20	70,905	43.9
	1926	(Δ/12 = 972)				*1930*	(Δ/12 = 886)		
Jan.	2772	8649	83,571	51.2	Jan.	12[d]	24	71,761	44.6
Feb.	3360	10483	75,894	46.5	Feb.	21	42	72,623	45.1
Mar.	1676	5229	66,383	40.7	Mar.	21	42	73,467	45.7
Apr.	603	1881	62,126	38.1	Apr.	92	188	74,311	46.2
May	227	708	61,217	37.5	May	146	302	75,009	46.6
June	67	209	61,481	37.7	June	52	109	75,593	47.0
July	54	168	62,244	38.2	July	17	36	76,370	47.5
Aug.	26	81	63,048	38.7	Aug.	5	11	77,220	48.0
Sept.	7	22	63,939	39.2	Sept.	6	13	78,095	48.5
Oct.	9	28	64,883	39.8	Oct.	3	7	78,968	49.1
Nov.	10	31	65,827	40.4	Nov.	13	29	79,847	49.6
Dec.	9	28	66,768	40.9	Dec.	63	141	80,704	50.2

APPENDIX—TABLE *A*—*Continued.*

Month	Reported cases	Corrected cases[a]	Calculated intacts		Month	Reported cases	Corrected cases[a]	Calculated intacts	
			Number[b]	Rate pct.[c]				Number[b]	Rate pct.[c]
(1)	(2)	(3)	(4)	(5)	(1)	(2)	(3)	(4)	(5)
	1927	(Δ/12 = 997)				*1931*	(Δ/12 = 863)		
Jan.	16	50	67,712	41.7	Jan.	708[d]	1598	81,449	50.8
Feb.	8	25	68,659	42.2	Feb.	1633	3724	80,714	50.4
Mar.	19	59	69,631	42.8	Mar.	4058	9351	77,853	48.6
Apr.	20	62	70,569	43.4	Apr.	4537	10563	69,365	43.3
May	30	93	71,504	44.0	May	2973	6992	59,665	37.2
June	29	90	72,408	44.5	June	963	2288	53,536	33.4
July	23	72	73,315	45.1	July	102	245	52,111	32.5
Aug.	12	37	74,240	45.7	Aug.	11	27	52,729	32.9
Sept.	8	25	75,200	46.3	Sept.	8	20	53,565	33.4
Oct.	31	96	76,172	46.9	Oct.	5	12	54,408	33.9
Nov.	132	411	77,073	47.4	Nov.	7	17	55,259	34.5
Dec.	316	983	77,659	47.8	Dec.	14	35	56,105	35.0

[a] Cases corrected for incomplete reporting. Correction factors are interpolations between those in column 10, table 3.

[b] Populations under age 15 not previously attacked, estimated as of the first of the month.

[c] Intacts under age 15 per hundred population of like age.

[d] Reported cases given in this table for 1928–1931 relate to total Baltimore. At that time the statistics were changed from a basis of wards to health districts so that reported cases for Old Baltimore (Wards 1–25) could not be obtained by direct addition. However, the "corrected" cases in column (3) relate to Old Baltimore. Correction for area and for completeness was made in one step, without estimating reported cases for Old Baltimore.

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

INFORMED CONSENT ACTION NETWORK,

Plaintiff,

-against-

UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES

Defendant.

STIPULATION

18-cv-03215 (JMF)

WHEREAS, 42 U.S.C. § 300aa-27, entitled "Mandate for safer childhood vaccines," provides as follows:

> (a) General rule
>
> In the administration of this part and other pertinent laws under the jurisdiction of the Secretary [of the Department of Health and Human Services], the Secretary shall—
>
> > (1) promote the development of childhood vaccines that result in fewer and less serious adverse reactions than those vaccines on the market on December 22, 1987, and promote the refinement of such vaccines, and
> >
> > (2) make or assure improvements in, and otherwise use the authorities of the Secretary with respect to, the licensing, manufacturing, processing, testing, labeling, warning, use instructions, distribution, storage, administration, field surveillance, adverse reaction reporting, and recall of reactogenic lots or batches, of vaccines, and research on vaccines, in order to reduce the risks of adverse reactions to vaccines.
>
> . . .
>
> (c) Report
>
> Within 2 years after December 22, 1987, and periodically thereafter, the Secretary shall prepare and transmit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate a report describing the

> actions taken pursuant to subsection (a) of this section during the preceding 2-year period.

WHEREAS, on August 25, 2017, Informed Consent Action Network ("ICAN") submitted a Freedom of Information Act request (the "FOIA Request") to the Department of Health and Human Services ("HHS" or the "Department"), which was assigned control number 2017-01119-FOIA-OS, that sought the following records:

> **Any and all reports transmitted to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate by the Secretary of HHS pursuant to 42 U.S.C. §300aa-27(c).**

WHEREAS, on April 12, 2018, ICAN filed a Complaint for Declaratory and Injunctive Relief in the United States District Court, Southern District of New York against HHS seeking records, if any, responsive to the FOIA Request;

WHEREAS, the HHS Immediate Office of the Secretary ("IOS") maintains the official correspondence file of the Secretary of HHS, including reports to Congress by the Secretary of HHS, and therefore those files were most likely to contain records responsive to the FOIA Request;

WHEREAS, on June 27, 2018, HHS sent ICAN the following response to the FOIA Request:

> The [Department]'s searches for records did not locate any records responsive to your request. The Department of Health and Human Services (HHS) Immediate Office of the Secretary (IOS) conducted a thorough search of its document tracking systems. The Department also conducted a comprehensive review of all relevant indexes of HHS Secretarial Correspondence records maintained at Federal Records Centers that remain in the custody of HHS. These searches did not locate records responsive to your request, or indications that records responsive to your request and in the custody of HHS are located at Federal Records Centers.

WHEREAS, ICAN believes the foregoing response from HHS now resolves all claims asserted in this action;

IT IS HEREBY STIPULATED AND AGREED, by and between the parties by and through their respective counsel:

1. That the above-captioned action is voluntarily dismissed, with prejudice, pursuant to Federal Rule of Civil Procedure 41(a)(1)(A)(ii), each side to bear its own costs, attorney fees, and expenses; and

2. That this stipulation may be signed in counterparts, and that electronic (PDF) signatures may be deemed originals for all purposes.

Dated: July 6, 2018
New York, New York

KENNEDY & MODONNA LLP
Attorney for Plaintiff

By: _____
Robert F. Kennedy, Jr.
48 Dewitt Mills Road
Hurley, NY 12443
(845) 481-2622

Dated: July 6, 2018
New York, New York

GEOFFREY S. BERMAN
United States Attorney
Attorney for Defendant

By: _____
ANTHONY J. SUN
Assistant United States Attorney
86 Chambers Street, Third Floor
New York, New York 10007
(212) 637-2810
anthony.sun@usdoj.gov

SO ORDERED:

_____
HON. JESSE M. FURMAN, U.S.D.J.

Dated: New York, New York
July 6, 2018

Any pending motions are moot. All conferences are vacated. The Clerk of Court is directed to close the case.

Informed Consent Action Network

For Immediate Release: July 13, 2018

US District Court Judge signs order granting Plaintiff, Informed Consent Action Network (ICAN) and counsel, Robert F. Kennedy, Jr., the relief sought in a lawsuit against the US Department of Health and Human Services (HHS)

On Monday, June 9th, the United States District Court for the Southern District of New York signed an order granting Plaintiff, the nonprofit Informed Consent Action Network (ICAN), the relief it sought against the Defendant, the United States Department of Health and Human Services, HHS. ICAN was represented by Robert F. Kennedy, Jr.

In May 2017, ICAN Founder, Del Bigtree, Robert F. Kennedy, Jr.. and a handful of other individuals concerned about vaccine safety were selected by the White House to participate in a seminal meeting with the Counselor to the Secretary of HHS, the heads of the National Institute of Health, NIH, the Center for Disease Control, CDC, and Food and the Drug Administration, FDA. Del Bigtree and Robert F. Kennedy, Jr. suspected that HHS was not fulfilling its critical vaccine safety obligations as required by Congress in The National Childhood Vaccine Injury Act of 1986.

The 1986 Act granted unprecedented, economic immunity to pharmaceutical companies for injuries caused by their products and eviscerated economic incentive for them to manufacture safe vaccine products or improve the safety of existing vaccine products. Congress therefore charged the Secretary of HHS with the explicit responsibility to assure vaccine safety.

Hence, since 1986, HHS has had the primary and virtually sole responsibility to make and assure improvements in the licensing, manufacturing, adverse reaction reporting, research, safety and efficacy testing of vaccines in order to reduce the risk of adverse vaccine reactions. In order to assure HHS meets its vaccine safety obligations, Congress required as part of the 1986 Act that the Secretary of HHS submit a biennial reports to Congress detailing the improvements in vaccine safety made by HHS in the preceding two years.

ICAN therefore filed a Freedom of Information Act, FOIA, request on August 25th, 2017 to HHS seeking copies of the biennial reports that HHS was supposed to submit to Congress, starting in 1988, detailing the improvements it made every two years to vaccine safety. HHS stonewalled ICAN for eight months refusing to provide any substantive response to this request.

ICAN
Informed Consent Action Network

ICAN was therefore forced to file a lawsuit to force HHS to either provide copies of its biennial vaccine safety reports to Congress or admit it never filed these reports. The result of the lawsuit is that HHS had to finally and shockingly admit that it never, not even once, submitted a single biennial report to Congress detailing the improvements in vaccine safety. This speaks volumes to the seriousness by which vaccine safety is treated at HHS and heightens the concern that HHS doesn't have a clue as to the actual safety profile of the now 29 doses, and growing, of vaccines given by one year of age.

In contrast, HHS takes the other portions of the 1986 Act, which require promoting vaccine uptake, very seriously, spending billions annually and generating a steady stream of reports on how to improve vaccine uptake. Regrettably, HHS has chosen to focus on its obligation to increase vaccine uptake and defend against any claim vaccines cause harm in the National Injury Vaccine Compensation Program (aka, the Vaccine Court) to such a degree that it has abandoned its vaccine safety responsibilities. If HHS is not, as confirmed in Court this week, even fulfilling the simple task of filing a biennial report on vaccine safety improvements, there is little hope that HHS is actually tackling the much harder job of actually improving vaccine safety.

For additional information or interviews please contact:
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M-M-R® II
(MEASLES, MUMPS, and RUBELLA VIRUS VACCINE LIVE)

DESCRIPTION

M-M-R® II (Measles, Mumps, and Rubella Virus Vaccine Live) is a live virus vaccine for vaccination against measles (rubeola), mumps, and rubella (German measles).

M-M-R II is a sterile lyophilized preparation of (1) ATTENUVAX® (Measles Virus Vaccine Live), a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture; (2) MUMPSVAX® (Mumps Virus Vaccine Live), the Jeryl Lynn™ (B level) strain of mumps virus propagated in chick embryo cell culture; and (3) MERUVAX® II (Rubella Virus Vaccine Live), the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts.{1,2}

The growth medium for measles and mumps is Medium 199 (a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum) containing SPGA (sucrose, phosphate, glutamate, and recombinant human albumin) as stabilizer and neomycin.

The growth medium for rubella is Minimum Essential Medium (MEM) [a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum] containing recombinant human albumin and neomycin. Sorbitol and hydrolyzed gelatin stabilizer are added to the individual virus harvests.

The cells, virus pools, and fetal bovine serum are all screened for the absence of adventitious agents.

The reconstituted vaccine is for subcutaneous administration. Each 0.5 mL dose contains not less than 1,000 $TCID_{50}$ (tissue culture infectious doses) of measles virus; 12,500 $TCID_{50}$ of mumps virus; and 1,000 $TCID_{50}$ of rubella virus. Each dose of the vaccine is calculated to contain sorbitol (14.5 mg), sodium phosphate, sucrose (1.9 mg), sodium chloride, hydrolyzed gelatin (14.5 mg), recombinant human albumin (≤0.3 mg), fetal bovine serum (<1 ppm), other buffer and media ingredients and approximately 25 mcg of neomycin. The product contains no preservative.

Before reconstitution, the lyophilized vaccine is a light yellow compact crystalline plug. M-M-R II, when reconstituted as directed, is clear yellow.

CLINICAL PHARMACOLOGY

Measles, mumps, and rubella are three common childhood diseases, caused by measles virus, mumps virus (paramyxoviruses), and rubella virus (togavirus), respectively, that may be associated with serious complications and/or death. For example, pneumonia and encephalitis are caused by measles. Mumps is associated with aseptic meningitis, deafness and orchitis; and rubella during pregnancy may cause congenital rubella syndrome in the infants of infected mothers.

The impact of measles, mumps, and rubella vaccination on the natural history of each disease in the United States can be quantified by comparing the maximum number of measles, mumps, and rubella cases reported in a given year prior to vaccine use to the number of cases of each disease reported in 1995. For measles, 894,134 cases reported in 1941 compared to 288 cases reported in 1995 resulted in a 99.97% decrease in reported cases; for mumps, 152,209 cases reported in 1968 compared to 840 cases reported in 1995 resulted in a 99.45% decrease in reported cases; and for rubella, 57,686 cases reported in 1969 compared to 200 cases reported in 1995 resulted in a 99.65% decrease.{3}

Clinical studies of 284 triple seronegative children, 11 months to 7 years of age, demonstrated that M-M-R II is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95%, mumps neutralizing antibodies in 96%, and rubella HI antibodies in 99% of susceptible persons. However, a small percentage (1-5%) of vaccinees may fail to seroconvert after the primary dose (see also INDICATIONS AND USAGE, *Recommended Vaccination Schedule*).

A study{4} of 6-month-old and 15-month-old infants born to vaccine-immunized mothers demonstrated that, following vaccination with ATTENUVAX, 74% of the 6-month-old infants developed detectable neutralizing antibody (NT) titers while 100% of the 15-month-old infants developed NT. This rate of seroconversion is higher than that previously reported for 6-month-old infants born to naturally immune mothers tested by HI assay. When the 6-month-old infants of immunized mothers were revaccinated at 15

months, they developed antibody titers equivalent to the 15-month-old vaccinees. The lower seroconversion rate in 6-month-olds has two possible explanations: 1) Due to the limit of the detection level of the assays (NT and enzyme immunoassay [EIA]), the presence of trace amounts of undetectable maternal antibody might interfere with the seroconversion of infants; or 2) The immune system of 6-month-olds is not always capable of mounting a response to measles vaccine as measured by the two antibody assays.

There is some evidence to suggest that infants who are born to mothers who had wild-type measles and who are vaccinated at less than one year of age may not develop sustained antibody levels when later revaccinated. The advantage of early protection must be weighed against the chance for failure to respond adequately on reimmunization.{5,6}

Efficacy of measles, mumps, and rubella vaccines was established in a series of double-blind controlled field trials which demonstrated a high degree of protective efficacy afforded by the individual vaccine components.{7-12} These studies also established that seroconversion in response to vaccination against measles, mumps, and rubella paralleled protection from these diseases.{13-15}

Following vaccination, antibodies associated with protection can be measured by neutralization assays, HI, or ELISA (enzyme linked immunosorbent assay) tests. Neutralizing and ELISA antibodies to measles, mumps, and rubella viruses are still detectable in most individuals 11 to 13 years after primary vaccination.{16-18} See INDICATIONS AND USAGE, *Non-Pregnant Adolescent and Adult Females*, for Rubella Susceptibility Testing.

The RA 27/3 rubella strain in M-M-R II elicits higher immediate post-vaccination HI, complement-fixing and neutralizing antibody levels than other strains of rubella vaccine{19-25} and has been shown to induce a broader profile of circulating antibodies including anti-theta and anti-iota precipitating antibodies.{26,27} The RA 27/3 rubella strain immunologically simulates natural infection more closely than other rubella vaccine viruses.{27-29} The increased levels and broader profile of antibodies produced by RA 27/3 strain rubella virus vaccine appear to correlate with greater resistance to subclinical reinfection with the wild virus,{27,29-31} and provide greater confidence for lasting immunity.

INDICATIONS AND USAGE

Recommended Vaccination Schedule

M-M-R II is indicated for simultaneous vaccination against measles, mumps, and rubella in individuals 12 months of age or older.

Individuals first vaccinated at 12 months of age or older should be revaccinated prior to elementary school entry. Revaccination is intended to seroconvert those who do not respond to the first dose. The Advisory Committee on Immunization Practices (ACIP) recommends administration of the first dose of M-M-R II at 12 to 15 months of age and administration of the second dose of M-M-R II at 4 to 6 years of age.{32} In addition, some public health jurisdictions mandate the age for revaccination. Consult the complete text of applicable guidelines regarding routine revaccination including that of high-risk adult populations.

Measles Outbreak Schedule

Infants Between 6 to 12 Months of Age

Local health authorities may recommend measles vaccination of infants between 6 to 12 months of age in outbreak situations. This population may fail to respond to the components of the vaccine. Safety and effectiveness of mumps and rubella vaccine in infants less than 12 months of age have not been established. The younger the infant, the lower the likelihood of seroconversion (see CLINICAL PHARMACOLOGY). Such infants should receive a second dose of M-M-R II between 12 to 15 months of age followed by revaccination at elementary school entry.{32}

Unnecessary doses of a vaccine are best avoided by ensuring that written documentation of vaccination is preserved and a copy given to each vaccinee's parent or guardian.

Other Vaccination Considerations

Non-Pregnant Adolescent and Adult Females

Immunization of susceptible non-pregnant adolescent and adult females of childbearing age with live attenuated rubella virus vaccine is indicated if certain precautions are observed (see below and PRECAUTIONS). Vaccinating susceptible postpubertal females confers individual protection against subsequently acquiring rubella infection during pregnancy, which in turn prevents infection of the fetus and consequent congenital rubella injury.{33}

Women of childbearing age should be advised not to become pregnant for 3 months after vaccination and should be informed of the reasons for this precaution.

The ACIP has stated "If it is practical and if reliable laboratory services are available, women of childbearing age who are potential candidates for vaccination can have serologic tests to determine susceptibility to rubella. However, with the exception of premarital and prenatal screening, routinely performing serologic tests for all women of childbearing age to determine susceptibility (so that vaccine is given only to proven susceptible women) can be effective but is expensive. Also, 2 visits to the health-care provider would be necessary — one for screening and one for vaccination. Accordingly, rubella vaccination of a woman who is not known to be pregnant and has no history of vaccination is justifiable without serologic testing — and may be preferable, particularly when costs of serology are high and follow-up of identified susceptible women for vaccination is not assured."{33}

Postpubertal females should be informed of the frequent occurrence of generally self-limited arthralgia and/or arthritis beginning 2 to 4 weeks after vaccination (see ADVERSE REACTIONS).

Postpartum Women

It has been found convenient in many instances to vaccinate rubella-susceptible women in the immediate postpartum period (see PRECAUTIONS, *Nursing Mothers*).

Other Populations

Previously unvaccinated children older than 12 months who are in contact with susceptible pregnant women should receive live attenuated rubella vaccine (such as that contained in monovalent rubella vaccine or in M-M-R II) to reduce the risk of exposure of the pregnant woman.

Individuals planning travel outside the United States, if not immune, can acquire measles, mumps, or rubella and import these diseases into the United States. Therefore, prior to international travel, individuals known to be susceptible to one or more of these diseases can either receive the indicated monovalent vaccine (measles, mumps, or rubella), or a combination vaccine as appropriate. However, M-M-R II is preferred for persons likely to be susceptible to mumps and rubella; and if monovalent measles vaccine is not readily available, travelers should receive M-M-R II regardless of their immune status to mumps or rubella.{34-36}

Vaccination is recommended for susceptible individuals in high-risk groups such as college students, health-care workers, and military personnel.{33,34,37}

According to ACIP recommendations, most persons born in 1956 or earlier are likely to have been infected with measles naturally and generally need not be considered susceptible. All children, adolescents, and adults born after 1956 are considered susceptible and should be vaccinated, if there are no contraindications. This includes persons who may be immune to measles but who lack adequate documentation of immunity such as: (1) physician-diagnosed measles, (2) laboratory evidence of measles immunity, or (3) adequate immunization with live measles vaccine on or after the first birthday.{34}

The ACIP recommends that "Persons vaccinated with inactivated vaccine followed within 3 months by live vaccine should be revaccinated with two doses of live vaccine. Revaccination is particularly important when the risk of exposure to wild-type measles virus is increased, as may occur during international travel."{34}

Post-Exposure Vaccination

Vaccination of individuals exposed to wild-type measles may provide some protection if the vaccine can be administered within 72 hours of exposure. If, however, vaccine is given a few days before exposure, substantial protection may be afforded.{34,38,39} There is no conclusive evidence that vaccination of individuals recently exposed to wild-type mumps or wild-type rubella will provide protection.{33,37}

Use With Other Vaccines

See DOSAGE AND ADMINISTRATION, *Use With Other Vaccines*.

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine, including gelatin.{40}

Do not give M-M-R II to pregnant females; the possible effects of the vaccine on fetal development are unknown at this time. If vaccination of postpubertal females is undertaken, pregnancy should be avoided for three months following vaccination (see INDICATIONS AND USAGE, *Non-Pregnant Adolescent and Adult Females* and PRECAUTIONS, *Pregnancy*).

Anaphylactic or anaphylactoid reactions to neomycin (each dose of reconstituted vaccine contains approximately 25 mcg of neomycin).

Febrile respiratory illness or other active febrile infection. However, the ACIP has recommended that all vaccines can be administered to persons with minor illnesses such as diarrhea, mild upper respiratory infection with or without low-grade fever, or other low-grade febrile illness.{41}

Patients receiving immunosuppressive therapy. This contraindication does not apply to patients who are receiving corticosteroids as replacement therapy, e.g., for Addison's disease.

Individuals with blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems.

Primary and acquired immunodeficiency states, including patients who are immunosuppressed in association with AIDS or other clinical manifestations of infection with human immunodeficiency viruses;{41-43} cellular immune deficiencies; and hypogammaglobulinemic and dysgammaglobulinemic states. Measles inclusion body encephalitis{44} (MIBE), pneumonitis{45} and death as a direct consequence of disseminated measles vaccine virus infection have been reported in immunocompromised individuals inadvertently vaccinated with measles-containing vaccine.

Individuals with a family history of congenital or hereditary immunodeficiency, until the immune competence of the potential vaccine recipient is demonstrated.

WARNINGS

Due caution should be employed in administration of M-M-R II to persons with a history of cerebral injury, individual or family histories of convulsions, or any other condition in which stress due to fever should be avoided. The physician should be alert to the temperature elevation which may occur following vaccination (see ADVERSE REACTIONS).

Hypersensitivity to Eggs

Live measles vaccine and live mumps vaccine are produced in chick embryo cell culture. Persons 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 vaccines containing traces of chick embryo antigen. The potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases. Such individuals may be vaccinated with extreme caution, having adequate treatment on hand should a reaction occur (see PRECAUTIONS).{46}

However, the AAP has stated, "Most children with a history of anaphylactic reactions to eggs have no untoward reactions to measles or MMR vaccine. Persons are not at increased risk if they have egg allergies that are not anaphylactic, and they should be vaccinated in the usual manner. In addition, skin testing of egg-allergic children with vaccine has not been predictive of which children will have an immediate hypersensitivity reaction...Persons with allergies to chickens or chicken feathers are not at increased risk of reaction to the vaccine."{47}

Hypersensitivity to Neomycin

The AAP states, "Persons who have experienced anaphylactic reactions to topically or systemically administered neomycin should not receive measles vaccine. Most often, however, neomycin allergy manifests as a contact dermatitis, which is a delayed-type (cell-mediated) immune response rather than anaphylaxis. In such persons, an adverse reaction to neomycin in the vaccine would be an erythematous, pruritic nodule or papule, 48 to 96 hours after vaccination. A history of contact dermatitis to neomycin is not a contraindication to receiving measles vaccine."{47}

Thrombocytopenia

Individuals with current thrombocytopenia may develop more severe thrombocytopenia following vaccination. In addition, individuals who experienced thrombocytopenia with the first dose of M-M-R II (or its component vaccines) may develop thrombocytopenia with repeat doses. Serologic status may be evaluated to determine whether or not additional doses of vaccine are needed. The potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases (see ADVERSE REACTIONS).

PRECAUTIONS

General

Adequate treatment provisions, including epinephrine injection (1:1000), should be available for immediate use should an anaphylactic or anaphylactoid reaction occur.

Special care should be taken to ensure that the injection does not enter a blood vessel.

Children and young adults who are known to be infected with human immunodeficiency viruses and are not immunosuppressed may be vaccinated. However, vaccinees who are infected with HIV should be monitored closely for vaccine-preventable diseases because immunization may be less effective than for uninfected persons (see CONTRAINDICATIONS).{42,43}

Vaccination should be deferred for 3 months or longer following blood or plasma transfusions, or administration of immune globulin (human).{47}

Excretion of small amounts of the live attenuated rubella virus from the nose or throat has occurred in the majority of susceptible individuals 7 to 28 days after vaccination. There is no confirmed evidence to indicate that such virus is transmitted to susceptible persons who are in contact with the vaccinated individuals. Consequently, transmission through close personal contact, while accepted as a theoretical possibility, is not regarded as a significant risk.{33} However, transmission of the rubella vaccine virus to infants via breast milk has been documented (see *Nursing Mothers*).

There are no reports of transmission of live attenuated measles or mumps viruses from vaccinees to susceptible contacts.

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 test is to be done, it should be administered either before or simultaneously with M-M-R II.

Children under treatment for tuberculosis have not experienced exacerbation of the disease when immunized with live measles virus vaccine;{48} no studies have been reported to date of the effect of measles virus vaccines on untreated tuberculous children. However, individuals with active untreated tuberculosis should not be vaccinated.

As for any vaccine, vaccination with M-M-R II may not result in protection in 100% of vaccinees.

The health-care provider should determine the current health status and previous vaccination history of the vaccinee.

The health-care provider should question the patient, parent, or guardian about reactions to a previous dose of M-M-R II or other measles-, mumps-, or rubella-containing vaccines.

Information for Patients

The health-care provider should provide the vaccine information required to be given with each vaccination to the patient, parent, or guardian.

The health-care provider should inform the patient, parent, or guardian of the benefits and risks associated with vaccination. For risks associated with vaccination see WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

Patients, parents, or guardians should be instructed to report any serious adverse reactions to their health-care provider who in turn should report such events to the U.S. Department of Health and Human Services through the Vaccine Adverse Event Reporting System (VAERS), 1-800-822-7967.{49}

Pregnancy should be avoided for 3 months following vaccination, and patients should be informed of the reasons for this precaution (see INDICATIONS AND USAGE, *Non-Pregnant Adolescent and Adult Females*, CONTRAINDICATIONS, and PRECAUTIONS, *Pregnancy*).

Laboratory Tests

See INDICATIONS AND USAGE, *Non-Pregnant Adolescent and Adult Females*, for Rubella Susceptibility Testing, and CLINICAL PHARMACOLOGY.

Drug Interactions

See DOSAGE AND ADMINISTRATION, *Use With Other Vaccines*.

Immunosuppressive Therapy

The immune status of patients about to undergo immunosuppressive therapy should be evaluated so that the physician can consider whether vaccination prior to the initiation of treatment is indicated (see CONTRAINDICATIONS and PRECAUTIONS).

The ACIP has stated that "patients with leukemia in remission who have not received chemotherapy for at least 3 months may receive live virus vaccines. Short-term (<2 weeks), low- to moderate-dose systemic corticosteroid therapy, topical steroid therapy (e.g. nasal, skin), long-term alternate-day treatment with low to moderate doses of short-acting systemic steroid, and intra-articular, bursal, or tendon injection of corticosteroids are not immunosuppressive in their usual doses and do not contraindicate the administration of [measles, mumps, or rubella vaccine]."{33,34,37}

Immune Globulin

Administration of immune globulins concurrently with M-M-R II may interfere with the expected immune response.{33,34,47}

See also PRECAUTIONS, *General*.

Carcinogenesis, Mutagenesis, Impairment of Fertility

M-M-R II has not been evaluated for carcinogenic or mutagenic potential, or potential to impair fertility.

Pregnancy

Animal reproduction studies have not been conducted with M-M-R II. It is also not known whether M-M-R II can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Therefore, the vaccine should not be administered to pregnant females; furthermore, pregnancy should be avoided for 3 months following vaccination (see INDICATIONS AND USAGE, *Non-Pregnant Adolescent and Adult Females* and CONTRAINDICATIONS).

In counseling women who are inadvertently vaccinated when pregnant or who become pregnant within 3 months of vaccination, the physician should be aware of the following: (1) In a 10-year survey involving over 700 pregnant women who received rubella vaccine within 3 months before or after conception (of whom 189 received the Wistar RA 27/3 strain), none of the newborns had abnormalities compatible with congenital rubella syndrome;{50} (2) Mumps infection during the first trimester of pregnancy may increase the rate of spontaneous abortion. Although mumps vaccine virus has been shown to infect the placenta and fetus, there is no evidence that it causes congenital malformations in humans;{37} and (3) Reports have indicated that contracting wild-type measles during pregnancy enhances fetal risk. Increased rates of spontaneous abortion, stillbirth, congenital defects and prematurity have been observed subsequent to infection with wild-type measles during pregnancy.{51,52} There are no adequate studies of the attenuated (vaccine) strain of measles virus in pregnancy. However, it would be prudent to assume that the vaccine strain of virus is also capable of inducing adverse fetal effects.

Nursing Mothers

It is not known whether measles or mumps vaccine virus is secreted in human milk. Recent studies have shown that lactating postpartum women immunized with live attenuated rubella vaccine may secrete the virus in breast milk and transmit it to breast-fed infants.{53} In the infants with serological evidence of rubella infection, none exhibited severe disease; however, one exhibited mild clinical illness typical of acquired rubella.{54,55} Caution should be exercised when M-M-R II is administered to a nursing woman.

Pediatric Use

Safety and effectiveness of measles vaccine in infants below the age of 6 months have not been established (see also CLINICAL PHARMACOLOGY). Safety and effectiveness of mumps and rubella vaccine in infants less than 12 months of age have not been established.

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. Other reported clinical experience has not identified differences in responses between the elderly and younger subjects.

ADVERSE REACTIONS

The following adverse reactions are listed in decreasing order of severity, without regard to causality, within each body system category and have been reported during clinical trials, with use of the marketed vaccine, or with use of monovalent or bivalent vaccine containing measles, mumps, or rubella:

Body as a Whole

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

Cardiovascular System

Vasculitis.

Digestive System

Pancreatitis; diarrhea; vomiting; parotitis; nausea.

Endocrine System

Diabetes mellitus.

Hemic and Lymphatic System

Thrombocytopenia (see WARNINGS, *Thrombocytopenia*); purpura; regional lymphadenopathy; leukocytosis.

Immune System

Anaphylaxis and anaphylactoid reactions have been reported as well as related phenomena such as angioneurotic edema (including peripheral or facial edema) and bronchial spasm in individuals with or without an allergic history.

Musculoskeletal System

Arthritis; arthralgia; myalgia.

Arthralgia and/or arthritis (usually transient and rarely chronic), and polyneuritis are features of infection with wild-type rubella and vary in frequency and severity with age and sex, being greatest in adult females and least in prepubertal children. This type of involvement as well as myalgia and paresthesia, have also been reported following administration of MERUVAX II.

Chronic arthritis has been associated with wild-type rubella infection and has been related to persistent virus and/or viral antigen isolated from body tissues. Only rarely have vaccine recipients developed chronic joint symptoms.

Following vaccination in children, reactions in joints are uncommon and generally of brief duration. In women, incidence rates for arthritis and arthralgia are generally higher than those seen in children (children: 0-3%; women: 12-26%),{17,56,57} and the reactions tend to be more marked and of longer duration. Symptoms may persist for a matter of months or on rare occasions for years. In adolescent girls, the reactions appear to be intermediate in incidence between those seen in children and in adult women. Even in women older than 35 years, these reactions are generally well tolerated and rarely interfere with normal activities.

Nervous System

Encephalitis; encephalopathy; measles inclusion body encephalitis (MIBE) (see CONTRAINDICATIONS); 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.

Encephalitis and encephalopathy have been reported approximately once for every 3 million doses of M-M-R II or measles-, mumps-, and rubella-containing vaccine administered since licensure of these vaccines.

The risk of serious neurological disorders following live measles virus vaccine administration remains less than the risk of encephalitis and encephalopathy following infection with wild-type measles (1 per 1000 reported cases).{58,59}

In severely immunocompromised individuals who have been inadvertently vaccinated with measles-containing vaccine; measles inclusion body encephalitis, pneumonitis, and fatal outcome as a direct consequence of disseminated measles vaccine virus infection have been reported (see CONTRAINDICATIONS). In this population, disseminated mumps and rubella vaccine virus infection have also been reported.

There have been reports of subacute sclerosing panencephalitis (SSPE) in children who did not have a history of infection with wild-type measles but did receive measles vaccine. Some of these cases may have resulted from unrecognized measles in the first year of life or possibly from the measles vaccination. Based on estimated nationwide measles vaccine distribution, the association of SSPE cases to measles vaccination is about one case per million vaccine doses distributed. This is far less than the association with infection with wild-type measles, 6-22 cases of SSPE per million cases of measles. The results of a retrospective case-controlled study conducted by the Centers for Disease Control and Prevention suggest that the overall effect of measles vaccine has been to protect against SSPE by preventing measles with its inherent higher risk of SSPE.{60}

Cases of aseptic meningitis have been reported to VAERS following measles, mumps, and rubella vaccination. Although a causal relationship between the Urabe strain of mumps vaccine and aseptic meningitis has been shown, there is no evidence to link Jeryl Lynn™ mumps vaccine to aseptic meningitis.

Respiratory System

Pneumonia; pneumonitis (see CONTRAINDICATIONS); sore throat; cough; rhinitis.

Skin

Stevens-Johnson syndrome; erythema multiforme; urticaria; rash; measles-like rash; pruritis.

Local reactions including burning/stinging at injection site; wheal and flare; redness (erythema); swelling; induration; tenderness; vesiculation at injection site; Henoch-Schönlein purpura; acute hemorrhagic edema of infancy.

Special Senses — Ear

Nerve deafness; otitis media.

Special Senses — Eye

Retinitis; optic neuritis; papillitis; retrobulbar neuritis; conjunctivitis.

Urogenital System

Epididymitis; orchitis.

Other

Death from various, and in some cases unknown, causes has been reported rarely following vaccination with measles, mumps, and rubella vaccines; however, a causal relationship has not been established in healthy individuals (see CONTRAINDICATIONS). No deaths or permanent sequelae were reported in a published post-marketing surveillance study in Finland involving 1.5 million children and adults who were vaccinated with M-M-R II during 1982 to 1993.{61}

Under the National Childhood Vaccine Injury Act of 1986, health-care providers and manufacturers are required to record and report certain suspected adverse events occurring within specific time periods after vaccination. However, the U.S. Department of Health and Human Services (DHHS) has established a Vaccine Adverse Event Reporting System (VAERS) which will accept all reports of suspected events.{49} A VAERS report form as well as information regarding reporting requirements can be obtained by calling VAERS 1-800-822-7967.

DOSAGE AND ADMINISTRATION

FOR SUBCUTANEOUS ADMINISTRATION

Do not inject intravascularly.

The dose for any age is 0.5 mL administered subcutaneously, preferably into the outer aspect of the upper arm.

The recommended age for primary vaccination is 12 to 15 months.

Revaccination with M-M-R II is recommended prior to elementary school entry. See also INDICATIONS AND USAGE, *Recommended Vaccination Schedule*.

Children first vaccinated when younger than 12 months of age should receive another dose between 12 to 15 months of age followed by revaccination prior to elementary school entry.{32} See also INDICATIONS AND USAGE, *Measles Outbreak Schedule*.

Immune Globulin (IG) is not to be given concurrently with M-M-R II (see PRECAUTIONS, *General* and PRECAUTIONS, *Drug Interactions*).

CAUTION: A sterile syringe free of preservatives, antiseptics, and detergents should be used for each injection and/or reconstitution of the vaccine because these substances may inactivate the live virus vaccine. A 25 gauge, 5/8" needle is recommended.

To reconstitute, use only the diluent supplied, since it is free of preservatives or other antiviral substances which might inactivate the vaccine.

Single Dose Vial — First withdraw the entire volume of diluent into the syringe to be used for reconstitution. Inject all the diluent in the syringe into the vial of lyophilized vaccine, and agitate to mix thoroughly. If the lyophilized vaccine cannot be dissolved, discard. Withdraw the entire contents into a syringe, inject the total volume of restored vaccine subcutaneously, and discard vial.

It is important to use a separate sterile syringe and needle for each individual patient to prevent transmission of hepatitis B and other infectious agents from one person to another.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. M-M-R II, when reconstituted, is clear yellow.

Use With Other Vaccines

M-M-R II should be given one month before or after administration of other live viral vaccines.

M-M-R II has been administered concurrently with VARIVAX® [Varicella Virus Vaccine Live (Oka/Merck)], and PedvaxHIB® [*Haemophilus b* Conjugate Vaccine (Meningococcal Protein Conjugate)] using separate injection sites and syringes. No impairment of immune response to individually tested vaccine antigens was demonstrated. The type, frequency, and severity of adverse experiences observed with M-M-R II were similar to those seen when each vaccine was given alone.

Routine administration of DTP (diphtheria, tetanus, pertussis) and/or OPV (oral poliovirus vaccine) concurrently with measles, mumps and rubella vaccines is not recommended because there are limited data relating to the simultaneous administration of these antigens.

However, other schedules have been used. The ACIP has stated "Although data are limited concerning the simultaneous administration of the entire recommended vaccine series (i.e., DTaP [or DTwP], IPV [or OPV], Hib with or without Hepatitis B vaccine, and varicella vaccine), data from numerous studies have

indicated no interference between routinely recommended childhood vaccines (either live, attenuated, or killed). These findings support the simultaneous use of all vaccines as recommended."{62}

HOW SUPPLIED

No. 4681 — M-M-R II is supplied as follows: (1) a box of 10 single-dose vials of lyophilized vaccine (package A), **NDC** 0006-4681-00; and (2) a box of 10 vials of diluent (package B). To conserve refrigerator space, the diluent may be stored separately at room temperature.

Storage

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).

Protect the vaccine from light at all times, since such exposure may inactivate the viruses.

Before reconstitution, store the lyophilized vaccine at 36°F to 46°F (2°C to 8°C). The diluent may be stored in the refrigerator with the lyophilized vaccine or separately at room temperature. **Do not freeze the diluent.**

It is recommended that the vaccine be used as soon as possible after reconstitution. Store reconstituted vaccine in the vaccine vial in a dark place at 36°F to 46°F (2°C to 8°C) and discard if not used within 8 hours.

For information regarding stability under conditions other than those recommended, call 1-800-MERCK-90.

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EPIDEMIOLOGIC BASIS FOR ERADICATION OF MEASLES IN 1967

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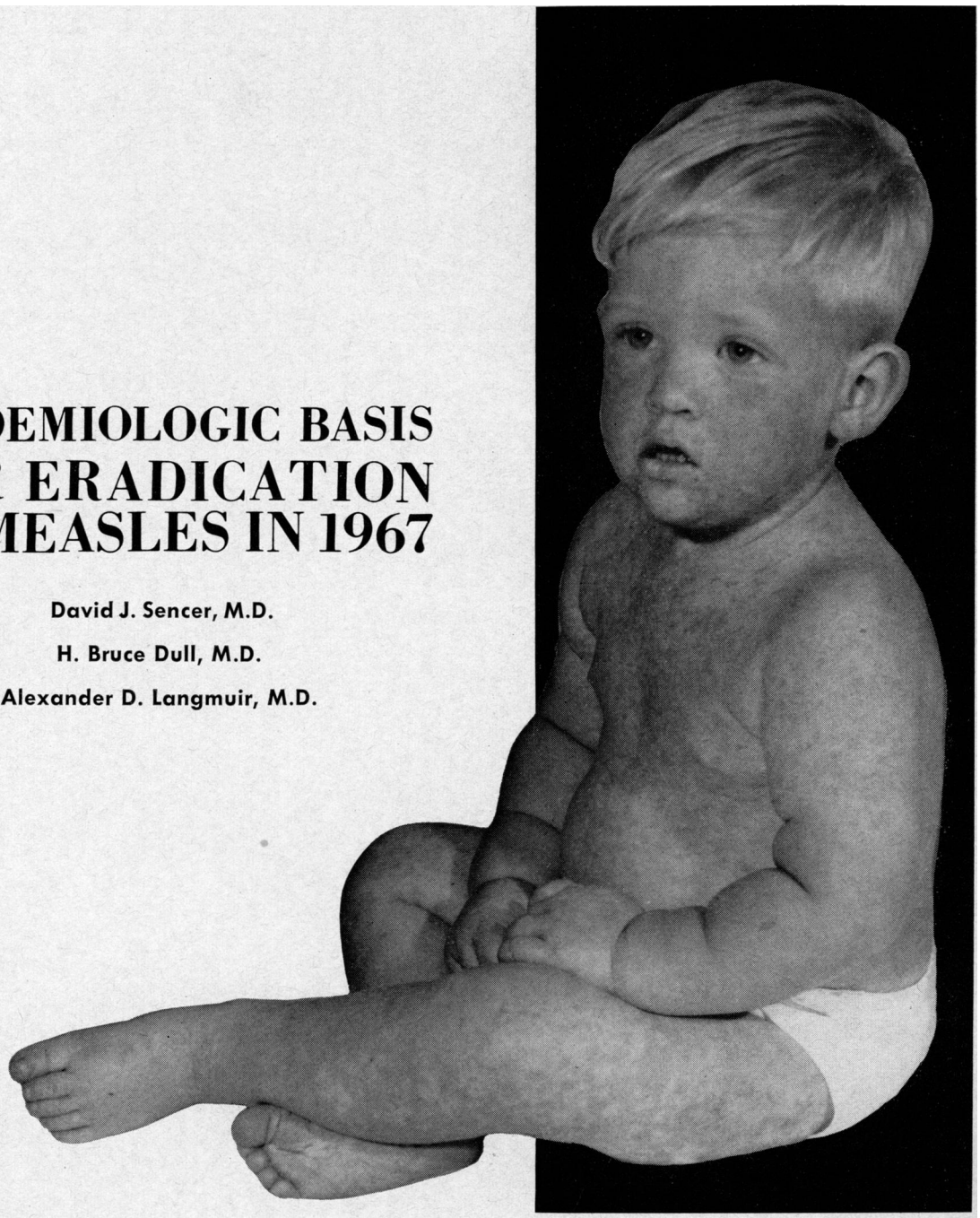

A STATEMENT BY THE PUBLIC HEALTH SERVICE

FOR CENTURIES the measles virus has maintained a remarkably stable ecological relationship with man. The clinical disease is a characteristic syndrome of notable constancy and only moderate severity. Complications are infrequent, and, with adequate medical care, fatality is rare. Susceptibility to the disease after the waning of

maternal immunity is universal; immunity following recovery is solid and lifelong in duration.

The infection spreads by direct contact from person to person and by the airborne route among susceptibles congregated in enclosed spaces. The disease occurs ubiquitously throughout the world in periodic cycles of considerable regularity. With the exception of a few extremely isolated population groups, essentially all children experience the infection sometime before adolescence. The reservoir of infection is man himself. No nonhuman sources of infection are known. Chronic carriers do not exist.

Despite the extent of the epidemiologic knowledge of measles, health officials have been frustrated in their efforts to bring this disease under control. During the past 50 years the doctrine has become widely accepted in health circles that since control measures have failed, man should learn to adapt himself to the measles virus. Thus, by judicious use of immune globulin for modification of the disease among exposed young children at great risk, and by providing adequate medical care to all patients, the damaging effects of the disease could be mitigated. Until very recently, this deep respect for the biological balance of the human race with the measles virus had become accepted doctrine. Eradication was not considered to be scientifically tenable.

All of this has now changed. With the isolation of the measles virus and the development and extensive field testing of several potent and effective vaccines, the tools are at hand to eradicate the infection. With the general application of these tools during the coming months, eradication can be achieved in this country in the year 1967.

This paper states the epidemiologic basis in support of this statement, specifies the essential conditions, and outlines the priorities for attaining this goal.

Theory of Measles Epidemics

Long experience has shown that measles recurs in a characteristic epidemiologic pattern that can be explained fully on the basis of the balance of immunes and susceptibles in the population. In small, closed population groups, such as nurseries or classrooms containing young susceptible children, explosive outbreaks follow promptly on the introduction of a single case. Attack rates are high; the duration of the outbreak is short. The supply of susceptibles becomes exhausted in the course of only a few generations of cases. Despite the subsequent introduction of a new case, another outbreak will not occur until a new crop of susceptibles has been garnered. This may require the passage of 2 or more years.

In more diverse and dispersed population groups, the introduction of a new case of measles is usually followed by an outbreak with a smaller attack rate, spottier distribution, and longer total duration. The proportion of susceptibles is reduced, but the epidemic frequently dies out before the supply of susceptibles is completely exhausted.

In large population centers, as in cities or whole metropolitan areas, measles epidemics recur in 2- to 3-year cycles, with many minor and some major variations in severity and extent. A notable feature of such urban epidemics is their long duration. They usually begin in the fall or early winter, build to a peak in the spring, and continue until the closing of schools. Occasionally, an epidemic will be split over a summer vacation period, with incidence increasing sharply in the early fall following the opening of schools.

The epidemic curve of measles in an urban area represents a composite of many discrete epidemics of shorter duration, beginning at varying times during the epidemic and centering in various local communities, ethnic groups, and school districts that comprise any large population. It is frequently possible to trace the progressive spread of measles from one area to another over the course of a single winter and spring epidemic period.

Most urban epidemics result in large numbers of cases among kindergarten and first- and sec-

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ond-grade school children. In fact, the supply of susceptibles in such groups may be largely exhausted in a relatively short time. Infection is regularly carried back to the home where preschool siblings may become infected. In many homes where infants and preschool children have no school-age siblings, the children have an excellent opportunity to escape infection throughout the epidemic. These are the susceptibles that support the next epidemic a few years later when they congregate in school.

This general experience with measles epidemics has provided the basis for formulating an epidemic theory of measles that can be expressed in simple mathematical terms. The theory accounts reasonably well for the major epidemiologic characteristics of measles epidemics on the basic assumption that incidence is a function of the proportion of the population that is susceptible and the contact rate.

Of particular relevance to the prospects of eradicating measles are the meticulous studies of Hedrich (*1*). He used data from Baltimore, Md., from 1897 to 1927 to quantitate the ebb and flow of susceptibles. He kept a progressive monthly balance sheet, using new births to measure the flow of susceptibles, and corrected estimates of measles cases to measure the flow of immunes. He was thus able to calculate the proportion of the child population of Baltimore that was susceptible at any given time.

While the incidence of measles in Baltimore fluctuated widely from year to year in a roughly 2- to 3-year periodicity, there was a remarkably narrow range of fluctuation in the balance of susceptibles and immunes. Just prior to major epidemics, the proportion of the population under 15 years of age estimated to be susceptible ranged from 45 to 50 percent. At the end of the epidemics, this proportion had fallen only to the level of 30 to 35 percent. Thus a large number of susceptibles escaped infection even during the most severe epidemics.

Examining the evidence from the point of view of immunity, it is evident that when the level of immunity was higher than 55 percent, epidemics did not develop. This is an estimate of the threshold of herd immunity providing protection to the city against a measles epidemic.

Studies in other urban areas comparable to those of Hedrich in Baltimore have not been reported. It must be recognized that the immune threshold of the 55 percent estimated for Baltimore for the period 1897 to 1927 may not have direct applicability to other communities in the United States in 1966. In fact, it is difficult to estimate whether the threshold of herd immunity for an average American city now would be higher or lower than Hedrich's estimate for Baltimore 30 to 70 years ago. Obviously, a considerable variability must be assumed for this threshold from urban area to urban area and within varying ethnic and socioeconomic groups in a single urban area.

There is no reason, however, to question the validity of the basic assumption that the occurrence of measles epidemics depends upon the balance of immunes and susceptibles, and that for all areas and special groups in this country the immune threshold is considerably less than 100 percent.

Therefore, in a country where smallpox, diphtheria, and poliomyelitis have been brought under effective control through immunization of a moderately high proportion, but by no means all infants and children, so also can measles be controlled with the attainment of immunity levels that are reasonable and wholly practical to achieve. Since chronic carriers as in diphtheria, and inapparent infection as in poliomyelitis, do not exist in measles, the course of measles that will follow a nationwide control program will be comparable to that of smallpox; namely, the total disappearance of the infection promptly when the immunity thresholds have been attained.

Essential Conditions for Eradication

With these theoretical considerations, it is now possible to specify the four essential conditions for eradication: (*a*) routine immunization of infants, (*b*) immunization of all susceptible children on entry to school or other place of congregation, (*c*) surveillance, and (*d*) epidemic control.

Routine immunization of infants. All infants should receive measles vaccine at approximately 1 year of age. This practice should be incorporated in the regular schedule of good pediatric practice and well child care. It should become as routine as DTP, polio, and smallpox

immunizations. To the degree that this becomes a universal practice for all infants, the following conditions become of diminishing importance.

Immunization on school entry. All children not immunized in infancy and who escape the natural disease should be immunized against measles at the time of or just before admission to school.

The term "school" must be interpreted broadly to include not only first grade of primary school, but also kindergarten, nursery school, day care homes, and even Sunday schools. While parents should assume primary responsibility for immunization of their children, school authorities may find it distinctly to their advantage also to assume a share of the responsibility to insure that all pupils have been protected. A measles epidemic can be disruptive and frequently costly if funds are made available on the basis of pupil days of attendance.

Surveillance. Effective control depends on knowledge of incidence and epidemiologic characteristics of current cases. Intensive efforts should be initiated by all health authorities—Federal, State, and local—to encourage complete and prompt reporting of all children with measles by name, address, and date of onset. Reports should come not only from practicing physicians, but from school nurses or other designated school officials knowing of absenteeism due to measles. Since measles has been poorly reported up to the present time, some increase in reported incidence above comparable periods in recent years may be expected at the beginning of the eradication program.

The conduct of sample surveys for status of measles immunity is an important aspect of a sound surveillance program. Such surveys are simple to perform, and serve to guide the health authority to areas where intensive immunization efforts are needed.

Epidemic control. Whenever a cluster of cases of measles, or even a single case is reported in a previously uninfected area, the threat of an epidemic is imminent. Immediate steps should be taken to verify the diagnosis, trace the source of infection, detect other unreported cases, and determine exposed susceptible contacts. From this information, a plan for containment of the outbreak can be developed and should be promptly executed. Local resources should be relied on for the main control effort.

The containment plan should include the administration of immune globulin to exposed susceptible contacts and administration of measles vaccine to all available susceptibles in the surrounding community or local area. Particular emphasis should be directed to susceptible children in kindergarten, nursery schools, and the lower primary grades of public schools. Such groups are readily accessible and in face of an imminent epidemic, full cooperation and prompt response can be relied on.

Whether the immunizations are carried out in private physicians' offices, in health department clinics, or in specially arranged clinics in the affected and neighboring schools, should be a matter for local option. The only essential condition is the prompt achievement of a high level of immunization.

When measles has become so widespread that epidemics are already present in several schools and in different communities within a city or county, more extensive communitywide measures must be undertaken. Then the full resources of the health and medical services of the total community, backed by well-coordinated voluntary agencies, will need to be mobilized. Again, priority should be directed first to the immunization of susceptible children in schools or who congregate in other enclosed spaces. If such immunization programs are carried out promptly and effectively, an epidemic of measles can be contained within 2 to 3 weeks. The continuation of an epidemic longer than 3 weeks is a clear indication of the inadequacy of the planned control program.

Conclusion

The availability of potent and effective measles vaccines, which have been tested extensively over the past 4 years, provides the basis for the eradication of measles in any community that will raise its immune thresholds to readily attainable levels. Effective use of these vaccines during the coming winter and spring should insure the eradication of measles from the United States in 1967.

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THE DANGER OF ELIMINATING VACCINE EXEMPTIONS & CURTAILING VACCINE CRITICISM

ICAN
Informed Consent Action Network

Prior to any medical procedure, the U.S. Department of Health & Human Service ("**HHS**") explains that the "voluntary consent of the human subject is absolutely essential."[1] **Coercion invalidates informed consent.**[2] Infringing this right by eliminating vaccine exemptions and curtailing criticism is unethical and un-American given the following facts:

PHARMA HAS NO INCENTIVE TO ASSURE VACCINE SAFETY

1. Immunity from Liability for Vaccine Harms. By the early 1980s, pharmaceutical companies were facing crippling liability for injuries to children caused by their vaccines.[3] Instead of letting these market forces drive them to develop safer vaccines, Congress passed the National Childhood Vaccine Injury Act (the "**1986 Act**") which eliminated pharmaceutical company liability for injuries caused by their vaccine products.[4]

2. Pharmaceutical Company Misconduct. Since 1986, Merck, GSK, Sanofi and Pfizer have paid billions of dollars for misconduct and injuries related to their drug products.[5] These same companies manufacture almost all childhood vaccines, but because of the 1986 Act, cannot similarly be held accountable for misconduct and injuries related to their vaccine products.

HHS CONFLICTED FROM ASSURING VACCINE SAFETY

3. HHS Must Defend Against Any Claim of Vaccine Injury. After eliminating liability for pharmaceutical companies, the 1986 Act established the Vaccine Injury Compensation Program ("**Vaccine Court**"), part of the U.S. Court of Federal Claims, to compensate people injured by vaccines.[6] Under the 1986 Act, HHS is the defendant in Vaccine Court and is legally obligated to defend against any claim that a vaccine causes injury.[7] There is no right to discovery in Vaccine Court and HHS is represented by the formidable resources of the U.S. Department of Justice ("**DOJ**").[8] In nearly every case the injured person bears the burden to prove causation.[9] Despite these hurdles, since 1986, HHS has paid over $4 billion for vaccine injuries.[10]

4. HHS Incriminates Itself if it Publishes or Admits a Vaccine Can Cause a Harm. If HHS publishes any study supporting that a vaccine causes a harm, that study will then be used against HHS in Vaccine Court.[11] This greatly limits HHS's incentive to publish safety studies.

5. CDC's Childhood Vaccine Schedule Was Created by Pharma Insiders. Congress has repeatedly found that the members of the FDA and CDC committees responsible for approving most of the currently licensed and recommended childhood vaccines had serious conflicts of interests with pharmaceutical companies.[12]

VACCINE SAFETY: CONCERNS & LIMITATIONS

6. HHS Fails to Perform Basic Vaccine Safety Requirements. After eliminating the market forces that assured vaccine safety, Congress made HHS directly responsible for vaccine safety pursuant to a section of the 1986 Act entitled the "Mandate for safer childhood vaccines."[13] As HHS recently

[1] https://ori.hhs.gov/chapter-3-The-Protection-of-Human-Subjects-nuremberg-code-directives-human-experimentation
[2] https://www.utcomchatt.org/docs/biomedethics.pdf
[3] https://www.nap.edu/read/2138/chapter/2#2 ("The litigation costs associated with claims of damage from vaccines had forced several companies [by 1986] to end their vaccine … programs as well as to stop producing already licensed vaccines.")
[4] 42 U.S.C. § 300aa-11 ("No person may bring a civil action for damages in the amount greater than $1,000 or in an unspecified amount against a vaccine administrator or manufacturer in a State or Federal court for damages arising from a vaccine-related injury or death."); Bruesewitz v. Wyeth LLC, 562 U.S. 223, 243 (2011) ("the National Childhood Vaccine Injury Act preempts all design-defect claims against vaccine manufacturers brought by plaintiffs who seek compensation for injury or death caused by vaccine side effects")
[5] https://www.citizen.org/sites/default/files/2408.pdf
[6] 42 U.S.C. § 300aa-12 ("In all proceedings brought by the filing of a petition [in Vaccine Court] the Secretary [of HHS] shall be named as the respondent."); https://www.congress.gov/106/crpt/hrpt977/CRPT-106hrpt977.pdf (HHS amended the Vaccine Court rules to make it extremely difficult to obtain compensation and "DOJ attorneys make full use of the apparently limitless resources available to them," "pursued aggressive defenses in compensation cases," "establish[ed] a cadre of attorneys specializing in vaccine injury" and "an expert witness program to challenge claims.")
[7] Ibid.
[8] Ibid.
[9] The 1986 Act created a Vaccine Injury Table (the "**Table**") which was intended to permit the Vaccine Court to quickly compensate certain common vaccine injuries. 42 U.S.C. § 300aa-12. For Table injuries, the burden shifts to HHS to prove the vaccine is not the cause. 42 U.S.C. § 300aa-13. After passage of the 1986 Act, almost 90% of claims were Table claims and quickly settled. Stevens v. Secretary of HHS, No. 99-594V (Office of Special Masters 2001). However, in the 1990s, HHS amended the Table such that now 98% of new claims are off-Table. http://www.gao.gov/assets/670/667136.pdf. As a result, injured children "must prove that the vaccine was the cause" in almost all cases. https://www.ncbi.nlm.nih.gov/nlmcatalog/101633437
[10] https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/data/monthly-stats-february-2019.pdf
[11] *See fn.* 6 and 9.
[12] http://vaccinesafetycommission.org/pdfs/Conflicts-Govt-Reform.pdf
[13] 42 U.S.C. § 300aa-27

conceded in federal court, it has not performed even the basic requirements of this section, such as submitting reports to Congress on how HHS has improved vaccine safety.[14]

7. Pediatric Vaccine Clinical Trials (i) Lack Placebos and (ii) Are Too Short. The pivotal clinical trials relied upon to license childhood vaccines do not include a placebo-control group and safety review periods in these clinical trials are typically only days or months.[15] The safety profile for a pediatric vaccine is therefore not known before it is licensed and routinely used in children.[16]

8. Post-Licensure Safety. After licensure and use by the public, federal law requires that the package insert for each vaccine 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."[17] Inserts for childhood vaccines include over one hundred serious immune, neurological and other chronic conditions that their manufacturers had a basis to believe are caused by their vaccines.[18]

9. Prevalence of Vaccine Harm. The CDC's Vaccine Adverse Events Reporting System ("**VAERS**"), to which doctors and patients may *voluntarily* report adverse vaccine events, received 58,381 reports in 2018, including 412 deaths, 1,237 permanent disabilities, and 4,217 hospitalizations.[19] An HHS-funded three-year review by Harvard Medical School of 715,000 patients stated that "fewer than 1% of vaccine adverse events are reported" to VAERS.[20] This could mean there are a hundredfold more adverse vaccine events than are reported to VAERS. The CDC has nonetheless refused to mandate or automate VAERS reporting.[21]

10. Children Susceptible to Vaccine Injury. While the Institute of Medicine ("**IOM**") has explained that "most individuals who experience an adverse reaction to vaccines have a preexisting susceptibility," HHS and CDC have failed to conduct studies to identify children susceptible to vaccine harms while at the same time recommending vaccines for all children.[22]

11. Carcinogenicity, Mutagenicity & Infertility. Most vaccines have never been evaluated for their potential to cause cancer, mutate genes or cause infertility.[23]

12. Autism. Autism is the most controversial of the claimed vaccine injuries and the one HHS and CDC declare they have thoroughly studied. Most parents with autistic children claim vaccines (including DTaP, Hep B, Hib, PCV13, and IPV, each injected 3 times by 6 months) are a cause of their child's autism.[24] The CDC tells these parents that "Vaccines Do Not Cause Autism."[25] However, there is no science to support this claim for almost all vaccines. For example, reports from the IOM in 1991 and 2012, and HHS in 2014, tried but failed to identify any study to support that DTaP does not cause autism.[26] The same is true for Hep B, Hib, PCV 13, and IPV.[27] The only vaccine actually studied with regard to autism is MMR, and a Senior CDC Scientist claims the CDC did find an increased rate of autism after MMR in the only MMR/autism study ever conducted by the CDC with American children.[28] Moreover, HHS's primary autism expert in Vaccine Court recently provided an affidavit explaining that vaccines can cause autism in some children.[29] Given the lack of studies regarding vaccines and autism, it should come as no surprise that there is a dearth of scientific studies that support the CDC's other claims regarding vaccine safety.

13. HHS Refuses to Conduct Vaccinated Vs. Unvaccinated Studies of Vaccine Schedule. A true epidemic in the U.S. is the fact that 1 in 2 children have an autoimmune, developmental, neurological, or chronic disorder.[30] These conditions have sharply

[14] http://icandecide.org/government/ICAN-HHS-Stipulated-Order-July-2018.pdf
[15] https://icandecide.org/hhs/ICAN-Reply.pdf (see Section I)
[16] Ibid.
[17] https://icandecide.org/hhs/ICAN-Reply.pdf (see Appendix B)
[18] Ibid.
[19] https://wonder.cdc.gov/vaers.html
[20] https://healthit.ahrq.gov/sites/default/files/docs/publication/r18hs017045-lazarus-final-report-2011.pdf
[21] https://icandecide.org/hhs/ICAN-Reply.pdf (see Section III)
[22] https://icandecide.org/hhs/ICAN-Reply.pdf (see Section V)
[23] https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm093833.htm
[24] https://www.ncbi.nlm.nih.gov/pubmed/16685182; https://www.ncbi.nlm.nih.gov/pubmed/25398603; https://www.ncbi.nlm.nih.gov/pubmed/16547798; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1448378/
[25] https://www.cdc.gov/vaccinesafety/concerns/autism.html
[26] https://www.nap.edu/read/1815/chapter/2#7; https://www.nap.edu/read/13164/chapter/12?term=autism#545; https://www.ncbi.nlm.nih.gov/books/NBK230053/pdf/Bookshelf_NBK230053.pdf
[27] https://icandecide.org/hhs/ICAN-Reply.pdf (see Section VI)
[28] http://www.rescuepost.com/files/william-thompson-statement-27-august-2014-3.pdf; https://soundcloud.com/fomotion/cdc-whistle-blower-full-audio; https://www.c-span.org/video/?c4546421/rep-bill-posey-calling-investigation-cdcs-mmr-reasearch-fraud
[29] http://icandecide.org/documents/zimmerman.pdf
[30] https://www.ncbi.nlm.nih.gov/pubmed/21570014

risen in lock-step with the increases in the CDC's recommended vaccine schedule.[31] That schedule has risen from 7 injections of just 2 vaccines in 1986 to the current total of 50 injections of 12 different vaccines.[32] The need to compare health outcomes of vaccinated and unvaccinated children is urgent. In 2017, a seminal study found that babies receiving the DTP vaccine died at 10 times the rate of unvaccinated babies.[33] In another study, children received influenza vaccine or a saline placebo; while both groups had a similar rate of influenza, the vaccinated group had a 440% increased rate of non-influenza infections.[34] A recent pilot study from the School of Public Health at Jackson State University found that 33% of vaccinated preterm babies had a neuro-developmental disorder compared to 0% of the unvaccinated preterm babies; and vaccinated children in this study had an increased risk of 290% for eczema, 390% for allergies, 420% for ADHD, 420% for autism, and 520% for learning disabilities.[35] Nonetheless, HHS and CDC refuse to publish any studies comparing the health outcomes between vaccinated and unvaccinated children.[36]

MMR VACCINE

14. Measles is a Mild Childhood Illness. The mortality rate from measles declined by over 98% between 1900 and 1962 as living conditions improved in this country.[37] In 1962, a year before the first measles vaccine, the CDC reported a total of 408 deaths.[38] That amounts to 1 in 500,000 Americans at a time when measles infected nearly every American.[39]

15. Eliminating Measles Has Increased Cancer Rates. Eliminating measles has increased cancer rates. For example, the International Agency for Research on Cancer found that individuals who never had measles had a 66% increased rate of Non-Hodgkin Lymphoma and a 233% increased rate of Hodgkin Lymphoma.[40] Combined, these cancers killed 20,960 Americans in 2018.[41] As another example, individuals who never had measles, mumps or rubella had a 50% increased rate of ovarian cancer.[42] In 2018, ovarian cancer killed 14,070 Americans.[43] Eliminating measles in this country has caused more deaths from cancer.

16. Eliminating Measles Has Increased Heart Disease. A 22-year prospective study of over 100,000 individuals in Japan revealed that "measles and mumps, especially in case of both infections, were associated with lower risks of mortality from atherosclerotic CVD [heart disease]."[44] Heart disease killed 610,000 Americans in 2018.[45] Eliminating our ecological relationship with measles, mumps and rubella has had serious unintended consequences.

17. Side effects from MMR vaccine. The MMR vaccine has serious risks. For example, the MMR vaccine causes seizures in about 1 in 640 children, five times the rate from measles, as well as "thrombocytopenic purpura," "chronic arthritis," and "brain damage."[46] However, because the MMR was not licensed based on a placebo-controlled clinical trial and post-licensure studies are limited, there are many suspected harms the CDC has yet to confirm or rule out, such as those listed on Merck's package insert for the MMR.[47]

18. Waning Immunity. While the vaccination rate for measles in the United States has been stable over the last 20 years, what has changed is that Americans who have had measles (which confers lifetime immunity) are being replaced by those vaccinated with MMR (which does not typically confer lifetime immunity).[48] MMR produces no immunity in 2% to 10% of vaccinees; and 22 years after two doses of MMR approximately 33% of vaccinees are again

[31] https://www.ncbi.nlm.nih.gov/pubmed/20159870
[32] https://www.cdc.gov/vaccines/schedules/images/schedule1983s.jpg; https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf
[33] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360569/
[34] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404712/
[35] http://www.oatext.com/pdf/JTS-3-186.pdf; http://www.oatext.com/pdf/JTS-3-187.pdf
[36] https://icandecide.org/hhs/ICAN-Reply.pdf (see Section VII)
[37] https://www.cdc.gov/nchs/data/vsus/vsrates1940_60.pdf; https://www.cdc.gov/nchs/data/vsus/VSUS_1962_2A.pdf
[38] https://www.cdc.gov/nchs/data/vsus/VSUS_1962_2A.pdf
[39] Ibid.; https://www.census.gov/library/publications/1962/compendia/statab/83ed.html
[40] https://www.ncbi.nlm.nih.gov/pubmed/16406019
[41] https://seer.cancer.gov/statfacts/html/nhl.html; https://seer.cancer.gov/statfacts/html/hodg.html
[42] https://www.ncbi.nlm.nih.gov/pubmed/16490323
[43] https://seer.cancer.gov/statfacts/html/ovary.html
[44] https://www.ncbi.nlm.nih.gov/pubmed/26122188
[45] https://www.cdc.gov/heartdisease/facts.htm
[46] https://www.hrsa.gov/sites/default/files/vaccinecompensation/vaccineinjurytable.pdf; https://www.cdc.gov/vaccines/hcp/vis/vis-statements/mmr.pdf; https://physiciansforinformedconsent.org/measles/vrs/ (since the measles death from 1959 to 1962 was appx. 400 per 4 million cases https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/e/reported-cases.pdf and death to seizure ratio is appx. 3.25 https://www.cdc.gov/vaccines/pubs/pinkbook/meas.html this amounts to 1 seizure in 3,095 measles cases).
[47] https://www.fda.gov/downloads/BiologicsBloodVaccines/UCM123789.pdf
[48] https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/G/coverage.pdf

potentially susceptible to measles.[49] The proportion after 30 years is even higher.[50] Yet the only focus is on children whose parents have reason to believe the MMR may cause them harm, while ignoring the efficacy issues with this vaccine.

OTHER VACCINES

19. DTaP Vaccine. According to the FDA, those vaccinated with DTaP will have fewer symptoms of pertussis, but will become infected and transmit pertussis, and "will be more susceptible to pertussis throughout their lifetimes."[51] This means the children vaccinated for pertussis are more likely to catch and spread pertussis as asymptomatic carriers, while the unvaccinated are less likely to catch pertussis (and when they do will have symptoms and know to stay home).[52] Since pertussis is very common and more of a concern than measles, as long as children vaccinated for pertussis are permitted to attend school, children not vaccinated for measles should also be permitted to attend school. In any event, the immunity provided by DTaP for pertussis, tetanus, and diphtheria wanes within a few years.[53]

20. Inactivated Polio Vaccine. For the last 20 years, the only polio vaccine used in the U.S. is inactivated polio vaccine ("**IPV**"), which is injected intramuscularly, after it was determined that the oral polio vaccine can cause paralysis.[54] Polio is spread through fecal to oral contamination, and IPV does not prevent colonization and transmission of polio; it only potentially prevents polio from traveling to the spinal column.[55] Hence, those vaccinated or not vaccinated with IPV can equally become infected and transmit polio; but, it is the vaccinated who are considered less likely to have symptoms and thus more likely to spread polio.

21. Chicken Pox Vaccine. Children vaccinated for chicken pox can spread chicken pox virus for six weeks after vaccination.[56] Moreover, the immunity from this vaccine wanes and, absent natural boosting from exposure to chicken pox virus, can lead to shingles.[57] The increased risk of shingles from use of this vaccine is why countries, such as the United Kingdom, have not added it to their routine vaccine schedule.[58]

22. Note. There are additional efficacy and safety issues with the above vaccines and other vaccines not addressed due to space constraints. For example, aluminum adjuvant particles in vaccines, which animal studies reveal deposit in brain and bones, or the millions of snippets of human DNA cultured from the cell lines of aborted fetuses in certain vaccines.[59]

ADDITIONAL INFORMATION

The foregoing highlights a few of the vaccine safety and efficacy issues necessitating the need for informed consent for vaccination and the ability to openly criticize our vaccine policies.

At the least, the following should occur before censoring concerns regarding vaccine safety:

a. Vaccine safety duties should be removed entirely from HHS and placed into an independent board;

b. Pharmaceutical companies should be liable for injuries caused by their vaccine products; and

c. The childhood vaccine schedule and each vaccine should be safety tested in a properly sized long-term placebo-controlled clinical trial.

For additional information or to arrange a presentation, please contact Cat Layton at cat@icandecide.org

[49] https://www.ncbi.nlm.nih.gov/pubmed/17339511
[50] Ibid.
[51] https://www.ncbi.nlm.nih.gov/pubmed/24277828; https://www.ncbi.nlm.nih.gov/pubmed/30793754; https://www.ncbi.nlm.nih.gov/pubmed/29180031 ("neither DTP, nor DTaP or Tdap prevent asymptomatic infection and silent transmission of the pathogen")
[52] Ibid.
[53] Ibid.
[54] http://polioeradication.org/polio-today/polio-prevention/the-vaccines/ipv/
[55] Ibid.
[56] https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142813.pdf
[57] https://www.ncbi.nlm.nih.gov/pubmed/22659447; https://www.ncbi.nlm.nih.gov/pubmed/24275643
[58] https://www.nhs.uk/common-health-questions/childrens-health/why-are-children-in-the-uk-not-vaccinated-against-chickenpox/
[59] http://vaccinepapers.org/wp-content/uploads/vaccine_papers_brochure_8.5x11.pdf; https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf; https://www.ncbi.nlm.nih.gov/pubmed/5949788; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC274969/; https://www.ncbi.nlm.nih.gov/pubmed/29108182

Vaccine Schedule - Birth through 18 years

1983

DTP - 2 months
OPV - 2 months
DTP - 4 months
OPV - 4 months
DTP - 6 months
MMR - 15 months
DTP - 18 months
OPV - 18 months
DTP - 4 years
OPV - 4 years
Td - 15 years

Source: www.CDC.gov

*
Tdap/DTaP - Diphtheria, Tetanus, Pertussis
MMR - Measles, Mumps, Rubella

**
Not included in total doses count.

2019

**Influenza - pregnancy
**Tdap - pregnancy
Hep B - birth
Hep B - 2 months
Rotavirus - 2 months
*DTaP - 2 months
Hib - 2 months
PCV - 2 months
IPV - 2 months
Rotavirus - 4 months
DTaP - 4 months
Hib - 4 months
PCV - 4 months
IPV - 4 months
Hep B - 6 months
Rotavirus - 6 months
DTaP - 6 months
Hib - 6 months
PCV - 6 months
IPV - 6 months
Influenza - 6 months
Influenza - 7 months
Hib - 12 months
PCV - 12 months
*MMR - 12 months
Varicella - 12 months
Hep A - 12 months
DTaP - 18 months
Influenza - 18 months
Hep A - 18 months
Influenza - 30 months
Influenza - 42 months
DTaP - 4 years
IPV - 4 years
MMR - 4 years
Varicella - 4 years
Influenza - 5 years
Influenza - 6 years
Influenza - 7 years
Influenza - 8 years
Influenza - 9 years
Influenza - 10 years
HPV - 11 years
HPV - 11 years
Influenza - 11 years
Tdap - 12 years
Influenza - 12 years
Meningococcal - 12 years
Influenza - 13 years
Influenza - 14 years
Influenza - 15 years
Influenza - 16 years
Meningococcal - 16 years
Influenza - 17 years
Influenza - 18 years

2019
Total doses: 69

1983
Total doses: 24

In 1986, the National Childhood Vaccine Injury Act was signed into law.
This freed vaccine manufacturers of ALL liability resulting from injury or death from their products.

• NCVIA • VAERS • NVICP

To date there is over **4 BILLION DOLLARS** paid out for vaccine injury and death.

Wisconsin United for freedom

www.wisconsinunitedforfreedom.org

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Adacel safely and effectively. See full prescribing information for Adacel.

Adacel® (Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed), Suspension for Intramuscular Injection

Initial U.S. Approval: 2005

RECENT MAJOR CHANGES

Indications and Usage (1)	01/2019
Dosage and Administration (2.2)	01/2019

INDICATIONS AND USAGE

- Adacel is a vaccine indicated for active booster immunization against tetanus, diphtheria and pertussis. Adacel is approved for use in persons 10 through 64 years of age. (1)

DOSAGE AND ADMINISTRATION

For intramuscular injection only.

- Each dose of Adacel is administered as a 0.5 mL injection. (2.1)
- For routine booster vaccination, a first dose of Adacel is administered 5 years or more after the last dose of Diphtheria and Tetanus Toxoids and Acellular Pertussis (DTaP) series or 5 years or more after vaccination with Tetanus and Diphtheria Toxoids Adsorbed (Td). A second dose of Adacel may be administered 8 years or more after the first dose with Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap).
- Adacel may be administered for tetanus prophylaxis for wound management. For management of a tetanus prone wound, a booster dose of Adacel may be administered if at least 5 years have elapsed since previous receipt of a tetanus toxoid containing vaccine.(2.2)

DOSAGE FORMS AND STRENGTHS

- Single-dose vials and prefilled syringes containing a 0.5 mL suspension for injection. (3)

CONTRAINDICATIONS

- Severe allergic reaction (eg, anaphylaxis) to any component of Adacel or any other diphtheria toxoid, tetanus toxoid and pertussis antigen-containing vaccine. (4.1)
- Encephalopathy (eg, coma, decreased level of consciousness, prolonged seizures) within 7 days of administration of a previous pertussis antigen-containing vaccine. (4.2)

WARNINGS AND PRECAUTIONS

- The tip caps of the prefilled syringes may contain natural rubber latex, which may cause allergic reactions in latex sensitive individuals. (5.2, 17)
- If Guillain-Barré syndrome occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the risk for Guillain-Barré syndrome may be increased following a subsequent dose of Adacel vaccine. (5.3)
- Progressive or unstable neurologic conditions are reasons to defer Adacel vaccination. (5.4)
- Persons who experienced an Arthus-type hypersensitivity reaction following a prior dose of a tetanus toxoid-containing vaccine should not receive Adacel unless at least 10 years have elapsed since the last dose of a tetanus toxoid-containing vaccine. (5.5)
- Syncope (fainting) can occur in association with administration of injectable vaccines, including Adacel. Procedures should be in place to prevent falling injury and manage syncopal reactions. (5.7)

ADVERSE REACTIONS

- Following the first vaccination with Adacel, the most common solicited adverse reactions within 0-14 days of vaccination for Adolescents (11-17 years of age)/Adults (18-64 years of age) were: injection site pain (77.8%/65.7%), headache (43.7%/33.9%), body ache or muscle weakness (30.4%/21.9%), tiredness (30.2%/24.3%), injection site swelling (20.9%/21.0%), and injection site erythema (20.8%/24.7%). (6.1)
- Following a second vaccination with Adacel, the most common solicited reactions occurring within 0-7 days of vaccination for Adults (18-64 years of age) were: injection site pain (87.1%), myalgia (58.1%), headache (41.4%), malaise (33.3%), injection site swelling (6.9%), and injection site erythema (6.4%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pharmacovigilance Department, Sanofi Pasteur Inc., Discovery Drive, Swiftwater, PA 18370 at 1-800-822-2463 (1-800-VACCINE) or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

DRUG INTERACTIONS

- When Adacel was administered concomitantly with trivalent inactivated influenza vaccine (TIV) to adults 19-64 years of age, a lower antibody response was observed for pertactin antigen as compared to Adacel administered alone. (7.1, 14.4)
- Immunosuppressive therapies may reduce the immune response to Adacel. (7.2)
- Do not mix Adacel with any other vaccine in the same syringe or vial.

USE IN SPECIFIC POPULATIONS

- Pregnancy Exposure Registry: contact Sanofi Pasteur Inc. at 1-800-822-2463 (1-800-VACCINE). (8.1)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 01/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Adacel® is a vaccine indicated for active booster immunization against tetanus, diphtheria and pertussis. Adacel is approved for use in individuals 10 through 64 years of age.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Preparation for Administration

Just before use, shake the vial or syringe well until a uniform, white, cloudy suspension results. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exist, the vaccine should not be administered.

Withdraw the 0.5 mL dose of vaccine from the single-dose vial using a sterile needle and syringe. Adacel should not be combined through reconstitution or mixed with any other vaccine. Discard unused portion in vial.

2.2 Administration, Dose and Schedule

Adacel is administered as a single 0.5 mL intramuscular injection.

Routine Booster Vaccination

A first dose of Adacel is administered 5 years or more after the last dose of the Diphtheria and Tetanus Toxoids and Acellular Pertussis (DTaP) series or 5 years or more after a dose of Tetanus and Diphtheria Toxoids Adsorbed (Td). A second dose of Adacel may be administered 8 years or more after the first dose of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap).

Wound Management

Adacel may be administered for tetanus prophylaxis for wound management. For management of a tetanus prone wound, a booster dose of Adacel may be administered if at least 5 years have elapsed since previous receipt of a tetanus toxoid containing vaccine.

3 DOSAGE FORMS AND STRENGTHS

Adacel is a suspension for injection available in 0.5 mL single-dose vials and prefilled syringes. [See *HOW SUPPLIED/STORAGE AND HANDLING (16)*.]

4 CONTRAINDICATIONS

4.1 Hypersensitivity

A severe allergic reaction (eg, anaphylaxis) after a previous dose of any tetanus toxoid, diphtheria toxoid or pertussis containing vaccine or any other component of this vaccine is a contraindication to administration of Adacel. [See *DESCRIPTION (11)*.] Because of uncertainty as to which component of the vaccine may be responsible, none of the components should be administered. Alternatively, such individuals may be referred to an allergist for evaluation if further immunizations are to be considered.

4.2 Encephalopathy

Encephalopathy (eg, coma, prolonged seizures, or decreased level of consciousness) within 7 days of a previous dose of a pertussis containing vaccine not attributable to another identifiable cause is a contraindication to administration of any pertussis containing vaccine, including Adacel.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Epinephrine hydrochloride solution (1:1,000) and other appropriate agents and equipment must be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs.

5.2 Latex

For one presentation of Adacel, the tip caps of the prefilled syringes may contain natural rubber latex, which may cause allergic reactions in latex sensitive individuals. The vial stopper is not made with natural rubber latex. [See *HOW SUPPLIED/STORAGE AND HANDLING (16)*.]

5.3 Guillain-Barré Syndrome and Brachial Neuritis

A review by the Institute of Medicine found evidence for acceptance of a causal relation between tetanus toxoid and both brachial neuritis and Guillain-Barré syndrome. (1) If Guillain-Barré syndrome occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the risk for Guillain-Barré syndrome may be increased following a dose of Adacel.

5.4 Progressive or Unstable Neurologic Disorders

Progressive or unstable neurologic conditions are reasons to defer Adacel. It is not known whether administration of Adacel to persons with an unstable or progressive neurologic disorder might hasten manifestations of the disorder or affect the prognosis. Administration of Adacel to persons with an unstable or progressive neurologic disorder may result in diagnostic confusion between manifestations of the underlying illness and possible adverse effects of vaccination.

5.5 Arthus-Type Hypersensitivity

Persons who experienced an Arthus-type hypersensitivity reaction following a prior dose of a tetanus toxoid-containing vaccine should not receive Adacel unless at least 10 years have elapsed since the last dose of a tetanus toxoid containing vaccine.

5.6 Altered Immunocompetence

If Adacel is administered to immunocompromised persons, including persons receiving immunosuppressive therapy, the expected immune response may not be obtained. [See *DRUG INTERACTIONS (7.2).]*

5.7 Syncope

Syncope (fainting) can occur in association with administration of injectable vaccine, including Adacel. Procedures should be in place to prevent falling injury and manage syncopal reactions.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to vaccine use and for approximating rates of those events. As with any vaccine, there is the possibility that broad use of Adacel could reveal adverse reactions not observed in clinical trials.

The safety of a first vaccination with Adacel was evaluated in 5 clinical studies. Three of the studies were conducted in the U.S. and 2 were conducted in Canada. Of the study participants, 86% were Caucasian, 8% Black, 3% Hispanic, 1% Asian and 2% of other ethnic origin. A total of 7,143 individuals 10 through 64 years of age inclusive (4,695 adolescents 10 through 17 years of age and 2,448 adults 18 through 64 years of age) received a single dose of Adacel.

U.S. Adolescent and Adult Study of a First Vaccination with Adacel (Td506)

Clinical study Td506 was a randomized, observer-blind, active-controlled trial that enrolled adolescents 11 through 17 years of age (Adacel N = 1,184; DECAVAC (Tetanus and Diphtheria Toxoids Adsorbed; manufactured by Sanofi Pasteur Inc., Swiftwater, PA) N = 792) and adults 18 through 64 years of age (Adacel N = 1,752; DECAVAC N = 573). Study participants had not received tetanus or diphtheria-containing vaccines within the previous 5 years. Solicited local and systemic reactions and unsolicited adverse events were monitored daily for 14 days post vaccination using a diary card. From days 14 to 28 post vaccination, information on adverse events necessitating a medical contact, such as a telephone call, visit to an emergency room, physician's office or hospitalization, was obtained via telephone interview or at an interim clinic visit. From days 28 to 6 months post vaccination, participants were monitored for unexpected visits to a physician's office or to an emergency room, onset of serious illness, and hospitalizations. Information regarding adverse events that occurred in the 6-month post vaccination time period was obtained from participants via telephone contact. At least 96% of participants completed the 6-month follow-up evaluation.

The frequency of selected solicited adverse reactions (erythema, swelling, pain and fever) occurring during days 0 to 14 following vaccination with Adacel or Td vaccine in adolescents 11 through 17 years of age and adults 18 through 64 years of age are presented in Table 1. Most of these reactions were reported at a similar frequency in recipients of both Adacel and Td vaccine. Pain at the injection site was the most common adverse reaction in 62.9% to 77.8% of all vaccinees. In addition, overall rates of pain were higher in adolescent recipients of Adacel compared to Td vaccine recipients. Rates of moderate and severe pain in adolescents did not significantly differ between the Adacel and Td vaccine groups. Among adults, the rates of pain after receipt of Adacel or Td vaccine did not significantly differ. Fever of 38°C and higher was uncommon, although in the adolescent age group it occurred significantly more frequently in Adacel recipients than Td vaccine recipients.

Table 1: Frequencies of Solicited Injection Site Reactions and Fever for Adolescents and Adults, Days 0-14, Following a First Vaccination with Adacel or Td Vaccine in Study Td506

Adverse Reactions*		Adolescents 11-17 years		Adults 18-64 years	
		Adacel N† = 1,170-1,175 (%)	Td‡ N† = 783-787 (%)	Adacel N† = 1,688-1,698 (%)	Td‡ N† = 551-561 (%)
Injection Site Pain	Any	77.8§	71.0	65.7	62.9
	Moderate¶	18.0	15.6	15.1	10.2
	Severe#	1.5	0.6	1.1	0.9
Injection Site Swelling	Any	20.9	18.3	21.0	17.3
	Moderate¶				
	1.0 to 3.4 cm	6.5	5.7	7.6	5.4
	Severe#				
	≥3.5 cm	6.4	5.5	5.8	5.5
	≥5 cm (2 inches)	2.8	3.6	3.2	2.7
Injection Site Erythema	Any	20.8	19.7	24.7	21.6
	Moderate¶				
	1.0 to 3.4 cm	5.9	4.6	8.0	8.4
	Severe#				
	≥3.5 cm	6.0	5.3	6.2	4.8
	≥5 cm (2 inches)	2.7	2.9	4.0	3.0
Fever	≥38.0°C (≥100.4°F)	5.0§	2.7	1.4	1.1
	≥38.8°C to ≤39.4°C (≥102.0°F to ≤103.0°F)	0.9	0.6	0.4	0.2
	≥39.5°C (≥103.1°F)	0.2	0.1	0.0	0.2

*The study sample size was designed to detect >10% differences between Adacel and Td vaccines for events of 'Any' intensity.

†N = number of participants with available data.

‡Tetanus and Diphtheria Toxoids Adsorbed manufactured by Sanofi Pasteur Inc., Swiftwater, PA.

§Adacel did not meet the non-inferiority criterion for rates of 'Any' Pain in adolescents compared to Td vaccine rates (upper limit of the 95% CI on the difference for Adacel minus Td vaccine was 10.7% whereas the criterion was <10%). For 'Any' Fever the non-inferiority criteria was met, however, 'Any' Fever was statistically higher in adolescents receiving Adacel.

¶Interfered with activities, but did not necessitate medical care or absenteeism.

#Incapacitating, prevented the performance of usual activities, may have/or did necessitate medical care or absenteeism.

The frequency of other solicited adverse reactions (days 0-14) are presented in Table 2. The rates of these reactions following a first vaccination with Adacel were comparable with those observed with Td vaccine. Headache was the most frequent systemic reaction and was usually of mild to moderate intensity.

Table 2: Frequencies of Other Solicited Adverse Reactions for Adolescents and Adults, Days 0-14, Following a First Vaccination with Adacel or Td Vaccine in Study Td506

Adverse Reaction		Adolescents 11-17 years		Adults 18-64 years	
		Adacel N* = 1,174-1,175 (%)	Td† N* = 787 (%)	Adacel N* = 1,697-1,698 (%)	Td† N* = 560-561 (%)
Headache	Any	43.7	40.4	33.9	34.1
	Moderate‡	14.2	11.1	11.4	10.5
	Severe§	2.0	1.5	2.8	2.1
Body Ache or Muscle Weakness	Any	30.4	29.9	21.9	18.8
	Moderate‡	8.5	6.9	6.1	5.7
	Severe§	1.3	0.9	1.2	0.9
Tiredness	Any	30.2	27.3	24.3	20.7
	Moderate‡	9.8	7.5	6.9	6.1
	Severe§	1.2	1.0	1.3	0.5

Table 2: Frequencies of Other Solicited Adverse Reactions for Adolescents and Adults, Days 0-14, Following a First Vaccination with Adacel or Td Vaccine in Study Td506 (continued)

Adverse Reaction		Adolescents 11-17 years		Adults 18-64 years	
		Adacel N* = 1,174-1,175 (%)	Td† N* = 787 (%)	Adacel N* = 1,697-1,698 (%)	Td† N* = 560-561 (%)
Chills	Any	15.1	12.6	8.1	6.6
	Moderate‡	3.2	2.5	1.3	1.6
	Severe§	0.5	0.1	0.7	0.5
Sore and Swollen Joints	Any	11.3	11.7	9.1	7.0
	Moderate‡	2.6	2.5	2.5	2.1
	Severe§	0.3	0.1	0.5	0.5
Nausea	Any	13.3	12.3	9.2	7.9
	Moderate‡	3.2	3.2	2.5	1.8
	Severe§	1.0	0.6	0.8	0.5
Lymph Node Swelling	Any	6.6	5.3	6.5	4.1
	Moderate‡	1.0	0.5	1.2	0.5
	Severe§	0.1	0.0	0.1	0.0
Diarrhea	Any	10.3	10.2	10.3	11.3
	Moderate‡	1.9	2.0	2.2	2.7
	Severe§	0.3	0.0	0.5	0.5
Vomiting	Any	4.6	2.8	3.0	1.8
	Moderate‡	1.2	1.1	1.0	0.9
	Severe§	0.5	0.3	0.5	0.2
Rash	Any	2.7	2.0	2.0	2.3

*N = number of participants with available data.
†Tetanus and Diphtheria Toxoids Adsorbed manufactured by Sanofi Pasteur Inc., Swiftwater, PA.
‡Interfered with activities, but did not necessitate medical care or absenteeism.
§Incapacitating, prevented the performance of usual activities, may have/or did necessitate medical care or absenteeism.

Injection site and systemic solicited reactions occurred at similar rates in Adacel and Td vaccine recipients in the 3 day post-vaccination period. Most injection site reactions occurred within the first 3 days after vaccination (with a mean duration of less than 3 days). The rates of unsolicited adverse events reported from days 14-28 post-vaccination were comparable between the two vaccine groups, as were the rates of unsolicited adverse events from day 28 through 6 months. There were no spontaneous reports of extensive limb swelling of the injected limb in study Td506, nor in the other three studies which also contributed to the safety database for Adacel.

Adult Study of a Second Vaccination with Adacel (Td537)

In a randomized, observer-blind, active-controlled, multi-center study (Td537), adults 18 through 64 years of age who had received a first dose of Adacel 8-12 years previously were enrolled and randomized to receive either Adacel (N = 1002) or a US licensed Td vaccine, TENIVAC (Tetanus and Diphtheria Toxoids Adsorbed; manufactured by Sanofi Pasteur, Limited) (N = 328). Subjects were recruited from the primary licensure study Td506 and the Canadian general public and had not received Td or Tdap vaccine since their initial Adacel dose. The demographic characteristics for study participants were similar for both vaccine groups. The mean ages were 28.9 years for the Adacel group and 29.2 years for the Td group. Overall, there were more female participants in both the Adacel group and Td group; 64.5% and 64.6%, respectively. In both vaccine groups, greater than 94% of subjects identified as white and 99% as non-Hispanic or Latino.

Safety data were collected from all participants who received the study vaccine (N = 999 for the Adacel group; N = 328 for the Td group). Solicited local and systemic reactions and unsolicited adverse events were monitored for 7 days post-vaccination using a diary card. Unsolicited adverse events were collected for approximately 28 days post-vaccination. Serious adverse events were collected throughout the study period (up to 6 months post-vaccination).

Solicited adverse reactions reported to occur during days 0-7 following vaccination are presented in Table 3.

Table 3: Frequencies of Solicited Adverse Reactions 0-7 Days Following a Second Vaccination with Adacel Compared to Td Vaccine in Study Td537 - Safety Analysis Set

Adverse Reaction		Adacel (N=999) (%)	Td Adsorbed* (N=328) (%)
Injection site pain	Any	87.1	87.4
	Grade 2†	28.5	31.4
	Grade 3‡	3.6	2.8
Injection site erythema	Any	6.4	5.5
	Grade 2 (≥51 to ≤100 mm)	2.1	2.8
	Grade 3 (>100 mm)	0.2	0.0
Injection site swelling	Any	6.9	8.0
	Grade 2 (≥51 to ≤100 mm)	2.4	2.2
	Grade 3 (>100 mm)	0.3	0.0
Fever	Any	0.9	1.8
	Grade 2 (≥38.5°C to ≤38.9°C or ≥101.2°F to ≤102.0°F	0.3	0.6
	Grade 3 (≥102.1°F)	0.2	0.3
Headache	Any	41.4	39.1
	Grade 2†	12.4	10.5
	Grade 3‡	2.6	4.0
Malaise	Any	33.3	30.8
	Grade 2†	9.3	9.8
	Grade 3‡	3.0	3.7
Myalgia	Any	58.1	58.2
	Grade 2†	18.7	16.9
	Grade 3‡	3.0	3.1

N = number of participants with available data
*Tetanus and Diphtheria Toxoids Adsorbed manufactured by Sanofi Pasteur Limited, Toronto, Ontario, Canada.
†Some interference with activity
‡Significant; prevents daily activity

Adult Study of a Second Vaccination with Adacel (Td518)

Study Td518 was a descriptive, open-label, post-marketing, multi-center study evaluating the safety of Adacel readministration in adults 5 years following a previous dose of Adacel. The mean age of subjects was 31.7 years, there were more females (52.2%) than males (47.8%) and 89.9% of subjects were Caucasian. Solicited adverse reactions were collected for 14 days following vaccination. SAEs were monitored for 6 months following vaccination. A total of 545 subjects 16-69 years of age were enrolled. All participants in this study received a first dose of Adacel vaccine as part of Sanofi Pasteur studies Td501, Td502, or Td505. Approximately 90% of the participants had at least one solicited injection site reaction. The most frequently reported injection site reactions were pain in 87.6% of subjects, followed by erythema/redness in 28.6%, and swelling in 25.6%. Approximately 77% of the participants had at least one solicited systemic reaction. The most frequently reported solicited systemic adverse reactions in subjects who received a second dose of Adacel were myalgia (61%), followed by headache (53.2%), malaise (38.2%), and fever (6.5%).

Injection Site and Systemic Reactions Following Adacel Given Concomitantly with Hepatitis B Vaccine

In the concomitant vaccination study with Adacel (first vaccination) and Hepatitis B vaccine [Recombivax HB] (Td501) [See *CLINICAL STUDIES (14)*], injection site and systemic adverse events were monitored daily for 14 days post-vaccination using a diary card. Injection site adverse events were only monitored at site/arm of Adacel administration. Unsolicited reactions (including immediate reactions, serious adverse events and events that elicited seeking medical attention) were collected at a clinic visit or via telephone interview for the duration of the trial, ie, up to 6 months post-vaccination.

The rates reported for fever and injection site pain (at the Adacel administration site) were similar when Adacel and Hepatitis B vaccine were given concurrently or separately. However, the rates of injection site erythema (23.4% for concomitant vaccination and 21.4% for separate administration) and swelling (23.9% for concomitant vaccination and 17.9% for separate administration) at the Adacel administration site were increased when coadministered. Swollen and/or sore joints were reported by 22.5% for concomitant vaccination and 17.9% for separate administration. The rates of generalized body aches in the individuals who reported swollen and/or sore joints were 86.7% for concomitant vaccination and 72.2% for separate administration. Most joint complaints were mild in intensity with a mean duration of 1.8 days. The incidence of other solicited and unsolicited adverse events were not different between the 2 study groups.

Injection Site and Systemic Reactions Following Adacel Given Concomitantly with Trivalent Inactivated Influenza Vaccine (TIV)

In the concomitant vaccination study with Adacel (first vaccination) and trivalent inactivated influenza vaccine [Fluzone] (Td502) [See *CLINICAL STUDIES (14)*], injection site and systemic adverse events were monitored for 14 days post-vaccination using a diary card. All unsolicited reactions occurring through day 14 were collected. From day 14 to the end of the trial, ie, up to 84 days, only events that elicited seeking medical attention were collected.

The rates of fever and injection site erythema and swelling were similar for recipients of concurrent and separate administration of Adacel and TIV. However, pain at the Adacel injection site occurred at statistically higher rates following concurrent administration (66.6%) versus separate administration (60.8%). The rates of sore and/or swollen joints were 13% for concurrent administration and 9% for separate administration. Most joint complaints were mild in intensity with a mean duration of 2.0 days. The incidence of other solicited and unsolicited adverse events was similar between the 2 study groups.

Additional Studies

In an additional study (Td505), 1,806 adolescents 11 through 17 years of age received Adacel (first vaccination) as part of the lot consistency study used to support Adacel licensure. This study was a randomized, double-blind, multi-center trial designed to assess lot consistency as measured by the safety and immunogenicity of 3 lots of Adacel when given as a booster dose to adolescents 11 through 17 years of age inclusive. Local and systemic adverse events were monitored for 14 days

post-vaccination using a diary card. Unsolicited adverse events and serious adverse events were collected for 28 days post-vaccination. Pain was the most frequently reported local adverse event occurring in approximately 80% of all participants. Headache was the most frequently reported systemic event occurring in approximately 44% of all participants. Sore and/or swollen joints were reported by approximately 14% of participants. Most joint complaints were mild in intensity with a mean duration of 2.0 days.

An additional 962 adolescents and adults received Adacel in three supportive Canadian studies (TC9704, Td9707 and TD9805) used as the basis for licensure in other countries. Within these clinical trials, the rates of local and systemic reactions following the first vaccination with Adacel were similar to those reported in the four principal trials in the U.S. with the exception of a higher rate (86%) of adults experiencing "any" local injection site pain. The rate of severe pain (0.8%), however, was comparable to the rates reported in four principal trials conducted in the US. There was one spontaneous report of whole-arm swelling of the injected limb among the 277 Td vaccine recipients, and two spontaneous reports among the 962 Adacel recipients in the supportive Canadian studies.

An additional study (Td519) enrolled 1,302 individuals in an open label, two-arm, multicenter trial (651 participants in each group) to evaluate the safety and immunogenicity of a first vaccination with Adacel administered to persons 10 to <11 years of age compared to persons 11 to <12 years of age. Immediate reactions were monitored for 20 minutes post-vaccination. Solicited local and systemic adverse events were monitored for 7 days post-vaccination using a diary card. Unsolicited and serious adverse events were collected for approximately 30 days post-vaccination. Similar rates of immediate, solicited and unsolicited adverse reactions were reported in each of the two age cohorts. One serious adverse event, not related to vaccination, was reported in the younger age group.

Serious Adverse Events

Throughout the 6-month follow-up period following a first vaccination with Adacel in study Td506, SAEs were reported in 1.5% of Adacel recipients and in 1.4% of Td vaccine recipients. Two SAEs in adults were neuropathic events that occurred within 28 days of Adacel administration; one severe migraine with unilateral facial paralysis and one diagnosis of nerve compression in neck and left arm. Similar or lower rates of serious adverse events were reported in the other trials following a first vaccination with Adacel in participants up to 64 years of age and no additional neuropathic events were reported. In study Td537 when a second vaccination of Adacel was administered 8-12 years following the initial vaccination of Adacel, a total of 8 participants (0.8%) in the Adacel group and 1 participant (0.3%) in the Td group reported SAEs during the 6-month follow-up period. All SAEs were considered by the investigator to be unrelated to the study vaccine.

In study Td518, seven participants experienced an SAE, all of which were considered by the investigator to be unrelated to the study vaccine.

6.2 Postmarketing Experience

The following adverse events of Adacel have been spontaneously reported in the US and other countries. Because these events are reported voluntarily from a population of uncertain size, it may not be possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

The following adverse events were included based on one or more of the following factors: severity, frequency of reporting, or strength of evidence for a causal relationship to Adacel.

- ***Immune system disorders***
  Anaphylactic reaction, hypersensitivity reaction (angioedema, edema, rash, hypotension)
- ***Nervous system disorders***
  Paresthesia, hypoesthesia, Guillain-Barré syndrome, brachial neuritis, facial palsy, convulsion, syncope, myelitis
- ***Cardiac disorders***
  Myocarditis
- ***Skin and subcutaneous tissue disorders***
  Pruritus, urticaria
- ***Musculoskeletal and connective tissue disorders***
  Myositis, muscle spasm
- ***General disorders and administration site conditions***
  Large injection site reactions (>50 mm), extensive limb swelling from the injection site beyond one or both joints
  Injection site bruising, sterile abscess, Arthus hypersensitivity

7 DRUG INTERACTIONS

7.1 Concomitant Vaccine Administration

When Adacel is administered concomitantly with other injectable vaccines or Tetanus Immune Globulin, they should be given with separate syringes and at different injection sites. Adacel should not be mixed with any other vaccine in the same syringe or vial.

Trivalent Inactivated Influenza Vaccine (TIV)

In a clinical study Adacel (first vaccination) was administered concomitantly with a US-licensed trivalent inactivated influenza vaccine (TIV). [See *ADVERSE REACTIONS (6.1)* and *CLINICAL STUDIES (14)*.] No interference in tetanus and diphtheria seroprotection rates and responses to influenza vaccine, detoxified pertussis toxin (PT), fimbriae types 2 and 3 (FIM) or filamentous hemagglutinin (FHA) were observed when Adacel vaccine was administered concomitantly with TIV compared to separate administration. A lower pertactin (PRN) GMC was observed when Adacel was administered concomitantly with TIV compared to separate administration.

7.2 Immunosuppressive Treatments

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses), may reduce the immune response to vaccines. [See *WARNINGS AND PRECAUTIONS (5.6)*.]

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Adacel during pregnancy. Women who receive Adacel during pregnancy are encouraged to contact directly, or have their healthcare professional contact, Sanofi Pasteur Inc. at 1-800-822-2463 (1-800-VACCINE).

Risk Summary

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. There are no adequate and well-controlled studies of Adacel administration in pregnant women in the U.S.

Available data suggest the rates of major birth defects and miscarriage in women who receive Adacel within 30 days prior to pregnancy or during pregnancy are consistent with estimated background rates. *(*See *Data)*

Two developmental toxicity studies were performed in female rabbits given 0.5 mL (a single human dose) of Adacel twice prior and during gestation. The studies revealed no evidence of harm to the fetus due to Adacel. *(*See *Data)*

Data

Human Data

An assessment of data from the ongoing pregnancy registry over 12 years (2005-2017) included 1518 reports of exposure to Adacel vaccine from 30 days before or at any time during pregnancy. Of these reports, 543 had known pregnancy outcomes available and were enrolled in the registry prior to the outcomes being known. Among the 543 pregnancies with known outcomes, the timing of Adacel vaccination was not known for 126 of the pregnancies.

Of the prospectively followed pregnancies for whom the timing of Adacel vaccination was known, 374 women received Adacel during the 30 days prior to conception through the second trimester. Outcomes among these prospectively followed pregnancies included 5 infants with major birth defects and 25 cases of miscarriage.

Animal Data

The effect of Adacel on embryo-fetal and pre-weaning development was evaluated in two developmental toxicity studies in female rabbits. Animals were administered 0.5 mL (a single human dose) of Adacel twice prior to gestation, during the period of organogenesis (gestation day 6) and later during pregnancy on gestation day 29. No adverse effects on pregnancy, parturition, lactation, embryo-fetal or pre-weaning development were observed. There were no vaccine related fetal malformations or other evidence of teratogenesis noted in this study.

8.2 Lactation

Risk Summary

It is not known whether Adacel vaccine components are excreted in human milk. Data are not available to assess the effect of administration of Adacel on breast-fed infants or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Adacel and any potential adverse effects on the breastfed child from Adacel 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

Adacel is not approved for individuals less than 10 years of age. Safety and effectiveness of Adacel in persons less than 10 years of age in the U.S. have not been established.

8.5 Geriatric Use

Adacel is not approved for use in individuals 65 years of age and older.

In a clinical study, individuals 65 years of age and older received a single dose of Adacel. Based on prespecified criteria, persons 65 years of age and older who received a dose of Adacel had lower geometric mean concentrations of antibodies to PT, PRN and FIM when compared to infants who had received a primary series of DAPTACEL®, Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP). [See *CLINICAL STUDIES (14)* for description of DAPTACEL.]

11 DESCRIPTION

Adacel is a sterile isotonic suspension of tetanus and diphtheria toxoids and pertussis antigens adsorbed on aluminum phosphate, for intramuscular injection.

Each 0.5 mL dose contains 5 Lf tetanus toxoid (T), 2 Lf diphtheria toxoid (d), and acellular pertussis antigens [2.5 mcg detoxified pertussis toxin (PT), 5 mcg filamentous hemagglutinin (FHA), 3 mcg pertactin (PRN), 5 mcg fimbriae types 2 and 3 (FIM)]. Other ingredients per 0.5 mL dose include 1.5 mg aluminum phosphate (0.33 mg aluminum) as the adjuvant, ≤5 mcg residual formaldehyde, <50 ng residual glutaraldehyde and 3.3 mg (0.6% v/v) 2-phenoxyethanol (not as a preservative). The antigens are the same as those in DAPTACEL; however, Adacel is formulated with reduced quantities of diphtheria and detoxified PT.

The acellular pertussis vaccine components are produced from *Bordetella pertussis* cultures grown in Stainer-Scholte medium (2) modified by the addition of casamino acids and dimethyl-beta-cyclodextrin. PT, FHA and PRN are isolated separately from the supernatant culture medium. FIM are extracted and copurified from the bacterial cells. The pertussis antigens are purified by sequential filtration, salt-precipitation, ultrafiltration and chromatography. PT is detoxified with glutaraldehyde, FHA is treated with formaldehyde, and the residual aldehydes are removed by ultrafiltration. The individual antigens are adsorbed onto aluminum phosphate.

The tetanus toxin is produced from *Clostridium tetani* grown in modified Mueller-Miller casamino acid medium without beef heart infusion. (3) Tetanus toxin is detoxified with formaldehyde and purified by ammonium sulfate fractionation and diafiltration. *Corynebacterium diphtheriae* is grown in modified Mueller's growth medium. (4) After purification by ammonium sulfate fractionation, diphtheria toxin is detoxified with formaldehyde and diafiltered.

The adsorbed diphtheria, tetanus and acellular pertussis components are combined with aluminum phosphate (as adjuvant), 2-phenoxyethanol (not as a preservative) and water for injection. Adacel does not contain a preservative.

In the guinea pig potency test, the tetanus component induces at least 2 neutralizing units/mL of serum and the diphtheria component induces at least 0.5 neutralizing units/mL of serum. The potency of the acellular pertussis vaccine components is evaluated by the antibody response of immunized mice to detoxified PT, FHA, PRN and FIM as measured by enzyme-linked immunosorbent assay (ELISA).

Diphtheria and tetanus toxoids are individually adsorbed onto aluminum phosphate.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Tetanus

Tetanus is a disease manifested primarily by neuromuscular dysfunction caused by a potent exotoxin released by *C tetani*.

Protection against disease is due to the development of neutralizing antibodies to tetanus toxin. A serum tetanus antitoxin level of at least 0.01 IU/mL, measured by neutralization assay is considered the minimum protective level. (5) (6)

Diphtheria

Diphtheria is an acute toxin-mediated disease caused by toxigenic strains of *C diphtheriae*. Protection against disease is due to the development of neutralizing antibodies to diphtheria toxin. A serum diphtheria antitoxin level of 0.01 IU/mL is the lowest level giving some degree of protection. Antitoxin levels of at least 0.1 IU/mL are generally regarded as protective. (5) Levels of 1.0 IU/mL have been associated with long-term protection. (7)

Pertussis

Pertussis (whooping cough) is a respiratory disease caused by *B pertussis*. This Gram-negative coccobacillus produces a variety of biologically active components, though their role in either the pathogenesis of, or immunity to, pertussis has not been clearly defined.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Adacel has not been evaluated for carcinogenic or mutagenic potential, or impairment of male fertility.

14 CLINICAL STUDIES

The effectiveness of the tetanus toxoid and diphtheria toxoid used in Adacel was based on the immune response to these antigens compared to a US licensed Tetanus and Diphtheria Toxoids Adsorbed For Adult Use (Td) vaccine manufactured by Sanofi Pasteur Inc., Swiftwater, PA. The primary measures for immune response to the diphtheria and tetanus toxoids were the percentage of participants attaining an antibody level of at least 0.1 IU/mL.

The effectiveness of the pertussis antigens used in Adacel was evaluated based on a comparison of pertussis antibody levels achieved in recipients of Adacel with those obtained in infants after three or four doses of DAPTACEL. For the first dose of Adacel, the comparisons were to infants who received three doses of DAPTACEL in the Sweden I Efficacy trial. For the second dose of Adacel, for the evaluation of FHA, PRN, and FIM antibody levels, the comparisons were to infants who received three doses of DAPTACEL in the Sweden I Efficacy trial; for evaluation of PT antibody levels, the comparison was to infants who received four doses of DAPTACEL in a US safety and immunogenicity study (Study M5A10). In the Sweden I Efficacy Trial, three doses of DAPTACEL vaccine were shown to confer a protective efficacy of 84.9% (95% CI: 80.1%, 88.6%) against WHO defined pertussis (21 days of paroxysmal cough with laboratory-confirmed *B pertussis* infection or epidemiological link to a confirmed case). The protective efficacy against mild pertussis (defined as at least one day of cough with laboratory-confirmed *B pertussis* infection) was 77.9% (95% CI: 72.6%, 82.2%). (8)

In addition, the ability of Adacel to elicit a booster response (defined as rise in antibody concentration after vaccination) to the tetanus, diphtheria and pertussis antigens following vaccination was evaluated.

14.1 Immunological Evaluation in Adolescents and Adults, 11 through 64 Years of Age Following a First Vaccination with Adacel

Study Td506 was a comparative, multi-center, randomized, observer-blind, controlled trial which enrolled 4,480 participants; 2,053 adolescents (11-17 years of age) and 2,427 adults (18-64 years of age). Enrollment was stratified by age to ensure adequate representation across the entire age range. Participants had not received a tetanus or diphtheria toxoid containing vaccine within the previous 5 years. After enrollment participants were randomized to receive one dose of either Adacel or Td vaccine. A total of 4,461 randomized participants were vaccinated. The per-protocol immunogenicity subset included 1,270 Adacel recipients and 1,026 Td vaccine recipients. Sera were obtained before and approximately 35 days after vaccination. [Blinding procedures for safety assessments are described in *ADVERSE REACTIONS (6).*]

Demographic characteristics were similar within age groups and between the vaccine groups. A total of 76% of the adolescents and 1.1% of the adults reported a history of receiving 5 previous doses of diphtheria-tetanus-pertussis containing vaccines. Anti-tetanus and anti-diphtheria seroprotection rates (≥0.1 IU/mL) and booster response rates were comparable between Adacel and Td vaccines. (See Table 4 and Table 5.) Adacel induced pertussis antibody levels that were non-inferior to those of Swedish infants who received three doses of DAPTACEL vaccine (Sweden I Efficacy Study). (See Table 6.) Acceptable booster responses to each of the pertussis antigens were also demonstrated, ie, the percentage of participants with a booster response exceeded the predefined lower limit. (See Table 7.)

Table 4: Pre-vaccination and Post-vaccination Antibody Responses and Booster Response Rates to Tetanus Toxoid Following A First Vaccination with Adacel Vaccine as Compared to Td Vaccine in Adolescents and Adults 11 through 64 Years of Age (Td506)

			Anti-Tetanus toxoid (IU/mL)				
			Pre-vaccination			1 Month Post-vaccination	
Age Group (years)	Vaccine	N*	% ≥0.10 (95% CI)	% ≥1.0 (95% CI)	% ≥0.10 (95% CI)	% ≥1.0 (95% CI)	% Booster† (95% CI)
11-17	Adacel	527	99.6 (98.6, 100.0)	44.6 (40.3, 49.0)	100.0‡ (99.3, 100.0)	99.6§ (98.6, 100.0)	91.7‡ (89.0, 93.9)
	Td¶	516	99.2 (98.0, 99.8)	43.8 (39.5, 48.2)	100.0 (99.3, 100.0)	99.4 (98.3, 99.9)	91.3 (88.5, 93.6)
18-64	Adacel	742-743	97.3 (95.9, 98.3)	72.9 (69.6, 76.1)	100.0‡ (99.5, 100.0)	97.8§ (96.5, 98.8)	63.1‡ (59.5, 66.6)
	Td¶	509	95.9 (93.8, 97.4)	70.3 (66.2, 74.3)	99.8 (98.9, 100.0)	98.2 (96.7, 99.2)	66.8 (62.5, 70.9)

*N = number of participants in the per-protocol population with available data.

†Booster response is defined as: A 4-fold rise in antibody concentration, if the pre-vaccination concentration was equal to or below the cut-off value and a 2-fold rise in antibody concentration if the pre-vaccination concentration was above the cut-off value. The cut-off value for tetanus was 2.7 IU/mL.

‡Seroprotection rates at ≥0.10 IU/mL and booster response rates to Adacel were non-inferior to Td vaccine (upper limit of the 95% CI on the difference for Td vaccine minus Adacel <10%).

§Seroprotection rates at ≥1.0 IU/mL were not prospectively defined as a primary endpoint.

¶Tetanus and Diphtheria Toxoids Adsorbed manufactured by Sanofi Pasteur Inc., Swiftwater, PA.

Table 5: Pre-vaccination and Post-vaccination Antibody Responses and Booster Response Rates to Diphtheria Toxoid Following A First Vaccination with Adacel as Compared to Td Vaccine in Adolescents and Adults 11 through 64 Years of Age (Td506)

			Anti-Diphtheria toxin (IU/mL)				
			Pre-vaccination			1 Month Post-vaccination	
Age Group (years)	Vaccine	N*	% ≥0.10 (95% CI)	% ≥1.0 (95% CI)	% ≥0.10 (95% CI)	% ≥1.0 (95% CI)	% Booster† (95% CI)
11-17	Adacel	527	72.5 (68.5, 76.3)	15.7 (12.7, 19.1)	99.8‡ (98.9, 100.0)	98.7§ (97.3, 99.5)	95.1‡ (92.9, 96.8)
	Td¶	515-516	70.7 (66.5, 74.6)	17.3 (14.1, 20.8)	99.8 (98.9, 100.0)	98.4 (97.0, 99.3)	95.0 (92.7, 96.7)
18-64	Adacel	739-741	62.6 (59.0, 66.1)	14.3 (11.9, 17.0)	94.1‡ (92.1, 95.7)	78.0§ (74.8, 80.9)	87.4‡ (84.8, 89.7)
	Td¶	506-507	63.3 (59.0, 67.5)	16.0 (12.9, 19.5)	95.1 (92.8, 96.8)	79.9 (76.1, 83.3)	83.4 (79.9, 86.5)

*N = number of participants in the per-protocol population with available data.

†Booster response is defined as: A 4-fold rise in antibody concentration, if the pre-vaccination concentration was equal to or below the cut-off value and a 2-fold rise in antibody concentration if the pre-vaccination concentration was above the cut-off value. The cut-off value for diphtheria was 2.56 IU/mL.

‡Seroprotection rates at ≥0.10 IU/mL and booster response rates to Adacel were non-inferior to Td vaccine (upper limit of the 95% CI on the difference for Td vaccine minus Adacel <10%).

§Seroprotection rates at ≥1.0 IU/mL were not prospectively defined as a primary endpoint.

¶Tetanus and Diphtheria Toxoids Adsorbed manufactured by Sanofi Pasteur Inc., Swiftwater, PA.

Table 6: Ratio of Pertussis Antibody Geometric Mean Concentrations (GMCs)* Observed One Month Following A First Vaccination with Adacel in Adolescents and Adults 11 through 64 Years of Age Compared with Those Observed in Infants One Month following Vaccination at 2,4 and 6 Months of Age in the Efficacy Trial with DAPTACEL (Sweden I Efficacy Study)

	Adolescents 11-17 Years of Age	Adults 18-64 Years of Age
	Adacel†/DAPTACEL‡ GMC Ratio (95% CIs)	Adacel§/DAPTACEL‡ GMC Ratio (95% CIs)
Anti-PT	3.6 (2.8, 4.5)¶	2.1 (1.6, 2.7)¶
Anti-FHA	5.4 (4.5, 6.5)¶	4.8 (3.9, 5.9)¶
Anti-PRN	3.2 (2.5, 4.1)¶	3.2 (2.3, 4.4)¶
Anti-FIM	5.3 (3.9, 7.1)¶	2.5 (1.8, 3.5)¶

*Antibody GMCs, measured in arbitrary ELISA units were calculated separately for infants, adolescents and adults.

†N = 524 to 526, number of adolescents in the per-protocol population with available data for Adacel.

‡N = 80, number of infants who received DAPTACEL with available data post dose 3 (Sweden Efficacy I).

§N = 741, number of adults in the per-protocol population with available data for Adacel.

¶GMC following Adacel was non-inferior to GMC following DAPTACEL (lower limit of 95% CI on the ratio of GMC for Adacel divided by DAPTACEL >0.67).

Table 7: Booster Response Rates to the Pertussis Antigens Observed One Month Following a First Vaccination with Adacel in Adolescents and Adults 11 through 64 Years of Age

	Adolescents 11-17 Years of Age		Adults 18-64 Years of Age		Predefined Acceptable Rates* %†
	N‡	% (95% CI)	N‡	% (95% CI)	
Anti-PT	524	92.0 (89.3, 94.2)	739	84.4 (81.6, 87.0)	81.2
Anti-FHA	526	85.6 (82.3, 88.4)	739	82.7 (79.8, 85.3)	77.6
Anti-PRN	525	94.5 (92.2, 96.3)	739	93.8 (91.8, 95.4)	86.4

Table 7: Booster Response Rates to the Pertussis Antigens Observed One Month Following a First Vaccination with Adacel in Adolescents and Adults 11 through 64 Years of Age (continued)

	Adolescents 11-17 Years of Age		Adults 18-64 Years of Age		Predefined Acceptable Rates* %†
	N‡	% (95% CI)	N‡	% (95% CI)	
Anti-FIM	526	94.9 (92.6, 96.6)	739	85.9 (83.2, 88.4)	82.4

*The acceptable response rate for each antigen was defined as the lower limit of the 95% CI for the rate being no more than 10% lower than the response rate observed in previous clinical trials.
†A booster response for each antigen was defined as a 4-fold rise in antibody concentration if the pre-vaccination concentration was equal to or below the cut-off value and a 2-fold rise in antibody concentration if the pre-vaccination concentration was above the cut-off value. The cut-off values for pertussis antigens were established based on antibody data from both adolescents and adults in previous clinical trials. The cut-off values were 85 EU/mL for PT, 170 EU/mL for FHA, 115 EU/mL for PRN and 285 EU/mL for FIM.
‡N = number of participants in the per-protocol population with available data.

Study Td519 assessed the comparative immunogenicity of a first vaccination with Adacel administered to adolescents (10 to <11 years of age and 11 to <12 years of age) [See *ADVERSE REACTIONS (6.1)*.] In this study non-inferiority was demonstrated for booster responses to tetanus and diphtheria toxoids, GMCs to the pertussis antigens (PT, FHA, PRN and FIM) and booster responses to the pertussis antigens PT, FHA and PRN. For FIM, non-inferiority was not demonstrated as the lower bound of the 95% CI of the difference in booster response rates (-5.96%) did not meet the predefined criterion (>-5% when the booster response in the older age group was >95%).

14.2 Immunological Evaluation in Adults, 18 through 64 Years of Age Following a Second Vaccination with Adacel

In study Td537 [See *ADVERSE REACTIONS (6.1)*.], subjects 18 to 64 years of age who had received a dose of Adacel 8-12 years previously, were randomized to receive a second dose of Adacel or Td vaccine (Tetanus and Diphtheria Toxoids Adsorbed manufactured by Sanofi Pasteur, Limited). Blood samples for immunogenicity analyses were obtained from participants pre-vaccination and approximately 28 days post-vaccination. The per-protocol analysis set was used for all immunogenicity analyses, and included 948 participants in the Adacel group and 317 participants in the Td control vaccine group. Of the study participants, 35% were male. Of subjects who reported a racial/ethnic demographic, 95% were Caucasian, 2% Black, 0.5% American Indian or Alaska native, 1% Asian and 1.5% were of mixed or other origin.

A tetanus antitoxoid level of ≥ 0.1 IU/mL, measured by the ELISA used in this study was considered protective. An anti-diphtheria anti-toxin level of ≥ 0.1 IU/mL was considered protective. Pre-vaccination and post-vaccination seroprotection rates and booster response rates are presented in Table 8.

Table 8: Pre-vaccination and Post-vaccination Seroprotection Rates and Booster Response Rates to Tetanus Toxoid and Diphtheria Toxoid Following a Second Vaccination with Adacel Compared to Td Vaccine in Persons 18 through 64 Years of Age, Per Protocol Analysis Set

	Vaccine	N*	Pre-vaccination		1 month post-vaccination		
			≥1.0 IU/mL (95% CI)	≥0.1 IU/mL (95% CI)	≥1.0 IU/mL (95% CI))†	≥1.0 IU/mL (95% CI)‡	%Booster§ (95% CI)
Anti-Tetanus Toxoid (ELISA - IU/mL)	Adacel	944-948	97.2 (96.0; 98.2)	62.3 (59.1; 65.4)	100.0 (99.6; 100.0)	99.9 (99.4; 100.0)	74.5¶ # (71.6; 77.2)
	Td Adsorbed	315-317	96.5 (93.8; 98.2)	63.8 (58.2; 69.1)	100.0 (98.8; 100.0)	100.0 (98.8; 100.0)	81.6¶ # (76.9; 85.7)
Anti-Diphtheria Toxin (ELISA - IU/mL)	Adacel	945-948	84.7 (82.2; 86.9)	29.1 (26.2; 32.1)	99.8 (99.2; 100.0)	94.9 (93.3; 96.2)	83.2¶ (80.6; 85.5)
	Td Adsorbed	315-317	83.8 (79.3; 87.7)	29.8 (24.8; 35.2)	99.4 (97.7; 99.9)	94.0 (90.8; 96.4)	84.1¶ (79.6; 88.0)

*N = number of participants in the per-protocol population with available data.
†Seroprotection rates at ≥0.10 IU/mL for Adacel were non-inferior to Td for diphtheria toxin and tetanus toxoid (upper limit of the 95% CI on the difference for Td vaccine minus Adacel <10%).
‡Seroprotection rates at ≥1.0 IU/mL were not prospectively defined as a primary or secondary endpoint.
§Booster response is defined as a minimum rise in antibody concentration from pre to post-vaccination. The minimum rise is at least 2 times if the pre-vaccination concentration is above the cutoff value, or at least 4 times if it is at or below the cutoff value. The cutoff values for to tetanus and diphtheria are 2.7 IU/mL and 2.56 IU/mL, respectively.
¶n/M: defines the number n of participants with booster response / the number M of subjects with available data to evaluate booster response. There were (n/M) 703/944, 257/315, 786/945 and 265/315 for Adacel/Tetanus, Td Adsorbed/Tetanus, Adacel/Diphtheria, and Td Adsorbed/Diphtheria, respectively.
#Booster response rates for tetanus toxoid in Adacel did not meet the pre-specified non-inferiority criteria.
ÞTetanus and Diphtheria Toxoids Adsorbed manufactured by Sanofi Pasteur Limited, Toronto, Ontario, Canada.

For all pertussis antigens (PT, FHA, PRN and FIM), post-vaccination anti-pertussis GMCs in the Adacel group were non-inferior to GMCs induced by 3 or 4 doses of DAPTACEL in historical studies as are presented in Table 9.

Table 9: Ratio of Pertussis Antibody Geometric Mean Concentrations (GMCs) Observed One Month Following a Second Vaccination with Adacel in Adults Compared with Those Observed in Infants One Month following Vaccination with 3 or 4 Doses of DAPTACEL (Per-Protocol Analysis Set)

Antigen	Adacel			DAPTACEL*			Adacel/DAPTACEL*	
	N	GMC (EU/mL)	(95% CI)	N	GMC (EU/mL)	(95% CI)	GMC Ratio	(95% CI)†
PT	935	102	(94.9; 110)	366	98.1	(90.9; 106)	1.04	(0.92; 1.18)
FHA	948	209	(200; 217)	80	39.9	(34.6; 46.1)	5.22	(4.51; 6.05)
PRN	948	318	(302; 334)	80	108	(91.4; 128)	2.94	(2.46; 3.51)
FIM	948	745	(711; 781)	80	341	(270; 431)	2.18	(1.84; 2.60)

*DAPTACEL: Historical controls who received DAPTACEL in Sanofi Pasteur studies. PT antibody GMC were compared to GMC following 4 doses of DAPTACEL in M5A10. FHA, PRN and FIM antibody GMCs were compared to GMCs following 3 doses of Daptacel in the Sweden I Efficacy trial.
†For each pertussis antigen, non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the GMC ratio (Adacel divided by the historical control) was > 0.66.

Booster response rates for PT and FHA were non-inferior in Adacel participants compared to pre-specified criteria for booster response rates, but non-inferiority was not achieved for PRN and FIM booster response rates (See Table 10).

Table 10: Comparison of Booster Response* Rates for Pertussis Antigens Following a Second Vaccination with Adacel (Per-Protocol Analysis Set)

	Adacel (N=948)		Pre-specified criteria for Booster Response Rates†	Adacel minus Pre-specified Booster Response Rates†	
Antigen	**n/M**	**% (95% CI)**	**%**	**Difference (%)**	**(95% CI)‡**
PT	693/894	77.5 (74.6; 80.2)	61.4	16.12	(13.27; 18.73)
FHA	651/945	68.9 (65.8; 71.8)	73.1	-4.21	(-7.23; -1.34)
PRN	617/945	65.3 (62.2; 68.3)	83.9	-18.61	(-21.7; -15.6)
FIM	537/945	56.8 (53.6; 60.0)	75.9	-19.07	(-22.3; -16.0)

N= number of subjects analyzed according to Per-Protocol Analysis Set
M=number of subjects with available data for the considered endpoint
n= number of subjects fulfilling the item listed in the first column
*Booster response is defined as a minimum rise in antibody concentration from pre to post-vaccination. The minimum rise is at least 2-fold if the pre-vaccination concentration is above the cutoff value, or at least 4-fold if it is at or below the cutoff value. The cutoff values for Study Td537 for the pertussis antigens are: 93 EU/mL for PT, 170 EU/mL for FHA, 115 EU/mL for PRN, and 285 EU/mL for FIM.
†Pre-specified criteria for booster response rates were derived from participants 21 to <65 years of age who received Adacel in Study Td506.
‡Non-inferiority in booster response rate for each pertussis antigen was demonstrated if the lower limit of the 2-sided 95% CI of the difference of booster response rates between participants receiving Adacel in Study Td537 and expected booster response rates based on Study Td506 was >-10%.

14.3 Concomitant Hepatitis B Vaccine Administration

The concomitant use of Adacel (first vaccination) and hepatitis B (Hep B) vaccine (Recombivax HB®, 10 mcg per dose using a two-dose regimen, manufactured by Merck and Co., Inc.) was evaluated in a multi-center, open-labeled, randomized, controlled study that enrolled 410 adolescents, 11 through 14 years of age inclusive. One group received Adacel and Hep B vaccines concurrently (N = 206). The other group (N = 204) received Adacel at the first visit, then 4-6 weeks later received Hep B vaccine. The second dose of Hep B vaccine was given 4-6 weeks after the first dose. Serum samples were obtained prior to and 4-6 weeks after Adacel administration, as well as 4-6 weeks after the 2nd dose of Hep B for all participants. No interference was observed in the immune responses to any of the vaccine antigens when Adacel and Hep B vaccines were given concurrently or separately. [See *ADVERSE REACTIONS (6.1)*.]

14.4 Concomitant Influenza Vaccine Administration

The concomitant use of Adacel (first vaccination) and trivalent inactivated influenza vaccine (TIV, Fluzone®, manufactured by Sanofi Pasteur Inc., Swiftwater, PA) was evaluated in a multi-center, open-labeled, randomized, controlled study conducted in 720 adults, 19-64 years of age inclusive. In one group, participants received Adacel and TIV vaccines concurrently (N = 359). The other group received TIV at the first visit, then 4-6 weeks later received Adacel (N = 361). Sera were obtained prior to and 4-6 weeks after Adacel, as well as 4-6 weeks after the TIV. The immune responses were comparable for concurrent and separate administration of Adacel and TIV vaccines for diphtheria (percent of participants with seroprotective concentration ≥0.10 IU/mL and booster responses), tetanus (percent of participants with seroprotective concentration ≥0.10 IU/mL), pertussis antigens (booster responses and GMCs except lower PRN GMC in the concomitant group, lower bound of the 90% CI was 0.61 and the prespecified criterion was ≥0.67) and influenza antigens (percent of participants with hemagglutination-inhibition [HI] antibody titer ≥1:40 IU/mL and ≥4-fold rise in HI titer). Although tetanus booster response rates were significantly lower in the group receiving the vaccines concurrently versus separately, greater than 98% of participants in both groups achieved seroprotective levels of ≥0.1 IU/mL. [See *ADVERSE REACTIONS (6.1)*.]

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16 HOW SUPPLIED/STORAGE AND HANDLING

Syringe, without needle, single-dose – NDC 49281-400-89 (not made with natural rubber latex); in package of 5 syringes, NDC 49281-400-20.

Syringe, without needle, single-dose – NDC 49281-400-88; in package of 5 syringes, NDC 49281-400-15. The tip caps of the prefilled syringes may contain natural rubber latex. No other components are made with natural rubber latex.

Vial, single-dose – NDC 49281-400-58; in package of 5 vials; NDC 49281-400-05. The vial stopper is not made with natural rubber latex. Discard unused portion in vial.

Vial, single-dose – NDC 49281-400-58; in package of 10 vials; NDC 49281-400-10. The vial stopper is not made with natural rubber latex. Discard unused portion in vial.

Not all pack sizes may be marketed.

Adacel should be stored at 2°C to 8°C (35°F to 46°F). DO NOT FREEZE. Product which has been exposed to freezing should not be used. Do not use after expiration date shown on the label.

17 PATIENT COUNSELING INFORMATION

Before administration of Adacel, healthcare providers should inform the patient, parent or guardian of the benefits and risks of the vaccine and the importance of receiving recommended booster dose unless a contraindication to further immunization exists.

The healthcare provider should inform the patient, parent or guardian about the potential for adverse reactions that have been temporally associated with Adacel or other vaccines containing similar components. The healthcare provider should provide the Vaccine Information Statements (VISs) that are required by the National Childhood Vaccine Injury Act of 1986 to be given with each immunization. The patient, parent or guardian should be instructed to report any serious adverse reactions to their healthcare provider.

Pregnancy Exposure Registry

[See *USE IN SPECIFIC POPULATIONS (8.1)*.]

Manufactured by:
Sanofi Pasteur Limited
Toronto Ontario Canada

Distributed by:
Sanofi Pasteur Inc.
Swiftwater PA 18370 USA

Adacel® is a registered trademark of Sanofi, its affiliates, and its subsidiaries.

R11-0119 USA

TRDAP-FPLR-SL-JAN19 Rx Only

UNDENIABLE VACCINATION FACTS:

1. US supreme court ruled vaccines “unavoidably UNsafe” in 2011 . 1 Bruesewitz v. Wyeth LLC, http://www.supremecourt.gov/opinions/10pdf/09-152.pdf

2. According to David Kessler, former commissioner of the FDA, "only about one percent of serious events [adverse drug reactions] are reported." Human and Experimental Toxicology, 31(10) 1012–1021, DOI: 10.1177/0960327112440111, Relative trends in hospitalizations and mortality among infants by the number of vaccine doses and age, based on the Vaccine Adverse Event Reporting System (VAERS), 1990–2010

3. In 1986 Congress passed the “National Childhood Vaccine Injury Act” which removed financial liability from vaccine manufacturers and placed it on taxpayers with a $ 0.75 tax on every vaccine given. (42 U.S.C. § 300aa-1 et seq., and Bruesewitz, supra.) The National Vaccine injury compensation program has paid out over $4.1 BILLION for vaccine injuries and deaths since 1989. http://www.hrsa.gov/vaccinecompensation/

4. Approximately 5% of the vaccine injuries and deaths reported to VAERS.gov ever reach Vaccine Court. The majority of families are forced to carry the physical and financial burden of caring for an injured child themselves as are taxpayers via schools and Medicare. Only a FRACTION of the above cases ever receive payout from the NVICP because families are responsible to ‘PROVE’ the vaccine caused the death or injury. “while individuals may file VICP claims for these vaccines, each petitioner must demonstrate that the vaccine that was administered caused the alleged injury.” 51% of Claims take 5+ years to Adjudicate. http://www.gao.gov/assets/670/667135.pdf

5. Vaccines Have “NOT been evaluated for carcinogenic or mutagenic potential, or potential to impair fertility” – as stated in package inserts. (Take notice of section 13.1 ie: MMRII insert top page 6, and in the other vaccine inserts as well.) http://www.merck.com/product/usa/pi_circulars/m/mmr_ii/mmr_ii_pi.pdf

6. The pharmaceutical industry is the biggest defrauder of the federal government under the False Claims Act. (http://www.fraudwhistleblowersblog.com/2014/02/) 1 In a recent 5-year period, $19.2 billion were returned from attempts to defraud federal health programs, more than twice that of the previous 5 years. (False Claims Act, Feb 2014 archive.)

7. Religious beliefs are protected under the US constitution:

> 14th Amendment (section 1) US Supreme court rulings state parents have the “right to parent their children” including Medical Decisions…without state intervention-unless the state has deemed them “unfit”. (Troxel v. Granville, 530 U.S. 57 [2000])
>
> 1st Amendment of the US Constitution ONLY requires a “Religious Belief” to be “religious in nature” and “sincerely held.” (Sherr and Levy vs. Northport East-Northport

Union Free School District, 672 F. Supp. 81, [E.D.N.Y., 1987]; Mason v. General Brown Cent. School Dist., 851 F.2d 47 [2nd Cir. 1988], Lewis v. Sobel, 710 F. Supp. 506, 512 [S.D.N.Y. 1989]; and Farina v. The Board of Education, 116 F. Supp.2d 503 [S.D.N.Y. 2000] are cases that cite United States v. Seeger, 380 U.S. 163, 85 S.Ct. 850 and other U.S. Supreme Court cases)

8. Universal Declaration on Bioethics and Human Rights:

U.N. Article 3 – Human dignity and human rights 1. Human dignity, human rights and fundamental freedoms are to be fully respected. 2. The interests and welfare of the individual should have priority over the sole interest of science or society.

U.N. Article 28 – Denial of acts contrary to human rights, fundamental freedoms and human dignity: Nothing in this Declaration may be interpreted as implying for any State, group or person any claim to engage in any activity or to perform any act contrary to human rights, fundamental freedoms and human dignity.

U.N. Article 6 – Consent: Any preventive, diagnostic and therapeutic medical intervention is only to be carried out with the prior, free and informed consent of the person concerned, based on adequate information. The consent should, where appropriate, be express and may be withdrawn by the person concerned at any time and for any reason without disadvantage or prejudice.
http://portal.unesco.org/en/ev.php-URL_ID=31058&URL_DO=DO_TOPIC&URL_SECTION=201.html

Syllabus

NOTE: Where it is feasible, a syllabus (headnote) will be released, as is being done in connection with this case, at the time the opinion is issued. The syllabus constitutes no part of the opinion of the Court but has been prepared by the Reporter of Decisions for the convenience of the reader. See *United States* v. *Detroit Timber & Lumber Co.,* 200 U. S. 321, 337.

SUPREME COURT OF THE UNITED STATES

Syllabus

BRUESEWITZ ET AL. *v.* WYETH LLC, FKA WYETH, INC., ET AL.

CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

No. 09–152. Argued October 12, 2010—Decided February 22, 2011

The National Childhood Vaccine Injury Act of 1986 (NCVIA or Act) created a no-fault compensation program to stabilize a vaccine market adversely affected by an increase in vaccine-related tort litigation and to facilitate compensation to claimants who found pursuing legitimate vaccine-inflicted injuries too costly and difficult. The Act provides that a party alleging a vaccine-related injury may file a petition for compensation in the Court of Federal Claims, naming the Health and Human Services Secretary as the respondent; that the court must resolve the case by a specified deadline; and that the claimant can then decide whether to accept the court's judgment or reject it and seek tort relief from the vaccine manufacturer. Awards are paid out of a fund created by an excise tax on each vaccine dose. As a *quid pro quo,* manufacturers enjoy significant tort-liability protections. Most importantly, the Act eliminates manufacturer liability for a vaccine's unavoidable, adverse side effects.

Hannah Bruesewitz's parents filed a vaccine-injury petition in the Court of Federal Claims, claiming that Hannah became disabled after receiving a diphtheria, tetanus, and pertussis (DTP) vaccine manufactured by Lederle Laboratories (now owned by respondent Wyeth). After that court denied their claim, they elected to reject the unfavorable judgment and filed suit in Pennsylvania state court, alleging, *inter alia,* that the defective design of Lederle's DTP vaccine caused Hannah's disabilities, and that Lederle was subject to strict liability and liability for negligent design under Pennsylvania common law. Wyeth removed the suit to the Federal District Court. It granted Wyeth summary judgment, holding that the relevant Pennsylvania law was preempted by 42 U. S. C. §300aa–22(b)(1), which

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provides that "[n]o vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the injury or death resulted from side-effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings." The Third Circuit affirmed.

Held: The NCVIA preempts all design-defect claims against vaccine manufacturers brought by plaintiffs seeking compensation for injury or death caused by a vaccine's side effects. Pp. 7–19.

(a) Section 300aa–22(b)(1)'s text suggests that a vaccine's design is not open to question in a tort action. If a manufacturer could be held liable for failure to use a different design, the "even though" clause would do no work. A vaccine side effect could alway*s* have been avoidable by use of a different vaccine not containing the harmful element. The language of the provision thus suggests the design is not subject to question in a tort action. What the statute establishes as a complete defense must be unavoidability (given safe manufacture and warning) with respect to the particular design. This conclusion is supported by the fact that, although products-liability law establishes three grounds for liability—defective manufacture, inadequate directions or warnings, and defective design—the Act mentions only manufacture and warnings. It thus seems that the Act's failure to mention design-defect liability is "by deliberate choice, not inadvertence." *Barnhart* v. *Peabody Coal Co.*, 537 U. S. 149, 168. Pp. 7–8.

(b) Contrary to petitioners' argument, there is no reason to believe that §300aa–22(b)(1)'s term "unavoidable" is a term of art incorporating Restatement (Second) of Torts §402A, Comment *k,* which exempts from strict liability rules "unavoidably unsafe products." "Unavoidable" is hardly a rarely used word, and cases interpreting comment *k* attach special significance only to the term "unavoidably unsafe products," not the word "unavoidable" standing alone. Moreover, reading the phrase "side effects that were unavoidable" to exempt injuries caused by flawed design would require treating "even though" as a coordinating conjunction linking independent ideas when it is a concessive, subordinating conjunction conveying that one clause weakens or qualifies the other. The canon against superfluity does not undermine this Court's interpretation because petitioners' competing interpretation has superfluity problems of its own. Pp. 8–12.

(c) The structure of the NCVIA and of vaccine regulation in general reinforces what §300aa–22(b)(1)'s text suggests. Design defects do not merit a single mention in the Act or in Food and Drug Administration regulations that pervasively regulate the drug manufacturing process. This lack of guidance for design defects, combined with

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the extensive guidance for the two liability grounds specifically mentioned in the Act, strongly suggests that design defects were not mentioned because they are not a basis for liability. The Act's mandates lead to the same conclusion. It provides for federal agency improvement of vaccine design and for federally prescribed compensation, which are other means for achieving the two beneficial effects of design-defect torts—prompting the development of improved designs, and providing compensation for inflicted injuries. The Act's structural *quid pro quo* also leads to the same conclusion. The vaccine manufacturers fund an informal, efficient compensation program for vaccine injuries in exchange for avoiding costly tort litigation and the occasional disproportionate jury verdict. Taxing their product to fund the compensation program, while leaving their liability for design defect virtually unaltered, would hardly coax them back into the market. Pp. 13–16.

561 F. 3d 233, affirmed.

SCALIA, J., delivered the opinion of the Court, in which ROBERTS, C. J., and KENNEDY, THOMAS, BREYER, and ALITO, JJ., joined. BREYER, J., filed a concurring opinion. SOTOMAYOR, J., filed a dissenting opinion, in which GINSBURG, J., joined. KAGAN, J., took no part in the consideration or decision of the case.

SUPREME COURT OF THE UNITED STATES

No. 09–152

RUSSELL BRUESEWITZ, ET AL., PETITIONERS *v.* WYETH LLC, FKA WYETH, INC., FKA WYETH LABORATORIES, ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

[February 22, 2011]

JUSTICE SCALIA delivered the opinion of the Court.

We consider whether a preemption provision enacted in the National Childhood Vaccine Injury Act of 1986 (NCVIA)[1] bars state-law design-defect claims against vaccine manufacturers.

I

A

For the last 66 years, vaccines have been subject to the same federal premarket approval process as prescription drugs, and compensation for vaccine-related injuries has been left largely to the States.[2] Under that regime, the elimination of communicable diseases through vaccination became "one of the greatest achievements" of public health in the 20th century.[3] But in the 1970's and 1980's vac-

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[1] 42 U. S. C. §300aa–22(b)(1).

[2] See P. Hutt, R. Merrill, & L. Grossman, Food and Drug Law 912–913, 1458 (3d ed. 2007).

[3] Centers for Disease Control, Achievements in Public Health, 1900–1999: Impact of Vaccines Universally Recommended for Children, 48 Morbidity and Mortality Weekly Report 243, 247 (Apr. 2, 1999).

cines became, one might say, victims of their own success. They had been so effective in preventing infectious diseases that the public became much less alarmed at the threat of those diseases,[4] and much more concerned with the risk of injury from the vaccines themselves.[5]

Much of the concern centered around vaccines against diphtheria, tetanus, and pertussis (DTP), which were blamed for children's disabilities and developmental delays. This led to a massive increase in vaccine-related tort litigation. Whereas between 1978 and 1981 only nine product-liability suits were filed against DTP manufacturers, by the mid-1980's the suits numbered more than 200 each year.[6] This destabilized the DTP vaccine market, causing two of the three domestic manufacturers to withdraw; and the remaining manufacturer, Lederle Laboratories, estimated that its potential tort liability exceeded its annual sales by a factor of 200.[7] Vaccine shortages arose when Lederle had production problems in 1984.[8]

Despite the large number of suits, there were many complaints that obtaining compensation for legitimate vaccine-inflicted injuries was too costly and difficult.[9] A

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[4] See Mortimer, Immunization Against Infectious Disease, 200 Science 902, 906 (1978).

[5] See National Vaccine Advisory Committee, A Comprehensive Review of Federal Vaccine Safety Programs and Public Health Activities 2–3 (Dec. 2008) (hereinafter NVAC), http://www.hhs.gov/nvpo/nvac/documents/vaccine-safety-review.pdf (as visited Feb. 18, 2011, and available in Clerk of Court's case file).

[6] See Sing & Willian, Supplying Vaccines: An Overview of the Market and Regulatory Context, in Supplying Vaccines: An Economic Analysis of Critical Issues 45, 51–52 (M. Pauly, C. Robinson, S. Sepe, M. Sing, & M. William eds. 1996).

[7] See *id.,* at 52.

[8] See Centers for Disease Control, Diptheria-Tetanus-Pertussis Vaccine Shortage, 33 Morbidity and Mortality Weekly Report 695–696 (Dec. 14, 1984).

[9] See Apolinsky & Van Detta, Rethinking Liability for Vaccine Injury, 19 Cornell J. L. & Pub. Pol'y 537, 550–551 (2010); T. Burke, Lawyers,

significant number of parents were already declining vaccination for their children,[10] and concerns about compensation threatened to depress vaccination rates even further.[11] This was a source of concern to public health officials, since vaccines are effective in preventing outbreaks of disease only if a large percentage of the population is vaccinated.[12]

To stabilize the vaccine market and facilitate compensation, Congress enacted the NCVIA in 1986. The Act establishes a no-fault compensation program "designed to work faster and with greater ease than the civil tort system." *Shalala* v. *Whitecotton*, 514 U. S. 268, 269 (1995). A person injured by a vaccine, or his legal guardian, may file a petition for compensation in the United States Court of Federal Claims, naming the Secretary of Health and Human Services as the respondent.[13] A special master then makes an informal adjudication of the petition within (except for two limited exceptions) 240 days.[14] The Court of Federal Claims must review objections to the special master's decision and enter final judgment under a similarly tight statutory deadline.[15] At that point, a claimant has two options: to accept the court's judgment and forgo a traditional tort suit for damages, or to reject the judgment and seek tort relief from the vaccine manufacturer.[16]

Fast, informal adjudication is made possible by the Act's Vaccine Injury Table, which lists the vaccines covered under the Act; describes each vaccine's compensable,

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Lawsuits, and Legal Rights: The Battle over Litigation in American Society 146 (2002).

[10] Mortimer, *supra*, at 906.

[11] See Hagan, 45 Food Drug Cosm. L. J. 477, 479 (1990).

[12] See R. Merrill, Introduction to Epidemiology 65–68 (2010).

[13] See 42 U. S. C. §300aa–11(a)(1).

[14] See §300aa–12(d)(3).

[15] See §300aa–12(e), (g).

[16] See §300aa–21(a).

adverse side effects; and indicates how soon after vaccination those side effects should first manifest themselves.[17] Claimants who show that a listed injury first manifested itself at the appropriate time are prima facie entitled to compensation.[18] No showing of causation is necessary; the Secretary bears the burden of disproving causation.[19] A claimant may also recover for unlisted side effects, and for listed side effects that occur at times other than those specified in the Table, but for those the claimant must prove causation.[20] Unlike in tort suits, claimants under the Act are not required to show that the administered vaccine was defectively manufactured, labeled, or designed.

Successful claimants receive compensation for medical, rehabilitation, counseling, special education, and vocational training expenses; diminished earning capacity; pain and suffering; and $250,000 for vaccine-related deaths.[21] Attorney's fees are provided, not only for successful cases, but even for unsuccessful claims that are not frivolous.[22] These awards are paid out of a fund created by an excise tax on each vaccine dose.[23]

The *quid pro quo* for this, designed to stabilize the vaccine market, was the provision of significant tort-liability protections for vaccine manufacturers. The Act requires claimants to seek relief through the compensation program before filing suit for more than $1,000.[24] Manufacturers are generally immunized from liability for fail-

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[17] See §300aa–14(a); 42 CFR §100.3 (2009) (current Vaccine Injury Table).

[18] See 42 U. S. C. §§300aa–11(c)(1), 300aa–13(a)(1)(A).

[19] See §300aa–13(a)(1)(B).

[20] See §300aa–11(c)(1)(C)(ii).

[21] See §300aa–15(a).

[22] See §300aa–15(e).

[23] See §300aa–15(i)(2); 26 U. S. C. §§4131, 9510.

[24] See 42 U. S. C. §300aa–11(a)(2).

ure to warn if they have complied with all regulatory requirements (including but not limited to warning requirements) and have given the warning either to the claimant or the claimant's physician.[25] They are immunized from liability for punitive damages absent failure to comply with regulatory requirements, "fraud," "intentional and wrongful withholding of information," or other "criminal or illegal activity."[26] And most relevant to the present case, the Act expressly eliminates liability for a vaccine's unavoidable, adverse side effects:

> "No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings."[27]

B

The vaccine at issue here is a DTP vaccine manufactured by Lederle Laboratories. It first received federal approval in 1948 and received supplemental approvals in 1953 and 1970. Respondent Wyeth purchased Lederle in 1994 and stopped manufacturing the vaccine in 1998.

Hannah Bruesewitz was born on October 20, 1991. Her pediatrician administered doses of the DTP vaccine according to the Center for Disease Control's recommended childhood immunization schedule. Within 24 hours of her April 1992 vaccination, Hannah started to experience

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[25] See §300aa–22(b)(2), (c). The immunity does not apply if the plaintiff establishes by clear and convincing evidence that the manufacturer was negligent, or was guilty of fraud, intentional and wrongful withholding of information, or other unlawful activity. See §§300aa–22(b)(2), 300aa–23(d)(2).

[26] §300aa–23(d)(2).

[27] §300aa–22(b)(1).

seizures.[28] She suffered over 100 seizures during the next month, and her doctors eventually diagnosed her with "residual seizure disorder" and "developmental delay."[29] Hannah, now a teenager, is still diagnosed with both conditions.

In April 1995, Hannah's parents, Russell and Robalee Bruesewitz, filed a vaccine injury petition in the United States Court of Federal Claims, alleging that Hannah suffered from on-Table residual seizure disorder and encephalopathy injuries.[30] A Special Master denied their claims on various grounds, though they were awarded $126,800 in attorney's fees and costs. The Bruesewitzes elected to reject the unfavorable judgment, and in October 2005 filed this lawsuit in Pennsylvania state court. Their complaint alleged (as relevant here) that defective design of Lederle's DTP vaccine caused Hannah's disabilities, and that Lederle was subject to strict liability, and liability for negligent design, under Pennsylvania common law.[31]

Wyeth removed the suit to the United States District Court for the Eastern District of Pennsylvania, which granted Wyeth summary judgment on the strict-liability and negligence design-defect claims, holding that the Pennsylvania law providing those causes of action was preempted by 42 U. S. C. §300aa–22(b)(1).[32] The United States Court of Appeals for the Third Circuit affirmed.[33] We granted certiorari. 559 U. S. ___ (2010).

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[28] See *Bruesewitz* v. *Secretary of Health and Human Servs.*, No. 95–0266V, 2002 WL 31965744, *3 (Ct. Cl., Dec. 20, 2002).

[29] 561 F. 3d 233, 236 (CA3 2009).

[30] See *id.,* at *1.

[31] See 561 F. 3d at 237. The complaint also made claims based upon failure to warn and defective manufacture. These are no longer at issue.

[32] See *id.,* at 237–238.

[33] *Id.,* at 235.

II

A

We set forth again the statutory text at issue:

> "No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings."[34]

The "even though" clause clarifies the word that precedes it. It delineates the preventative measures that a vaccine manufacturer *must* have taken for a side-effect to be considered "unavoidable" under the statute. Provided that there was proper manufacture and warning, any remaining side effects, including those resulting from design defects, are deemed to have been unavoidable. State-law design-defect claims are therefore preempted.

If a manufacturer could be held liable for failure to use a different design, the word "unavoidable" would do no work. A side effect of a vaccine could *always* have been avoidable by use of a differently designed vaccine not containing the harmful element. The language of the provision thus suggests that the *design* of the vaccine is a given, not subject to question in the tort action. What the statute establishes as a complete defense must be unavoidability (given safe manufacture and warning) *with respect to the particular design*. Which plainly implies that the design itself is not open to question.[35]

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[34] 42 U. S. C. §300aa–22(b)(1).

[35] The dissent advocates for another possibility: "[A] side effect is 'unavoidable' . . . where there is no feasible alternative design that would eliminate the side effect of the vaccine without compromising its cost and utility." *Post*, at 15 (opinion of SOTOMAYOR, J.). The dissent makes no effort to ground that position in the text of §300aa–22(b)(1).

A further textual indication leads to the same conclusion. Products-liability law establishes a classic and well known triumvirate of grounds for liability: defective manufacture, inadequate directions or warnings, and defective design.[36] If all three were intended to be preserved, it would be strange to mention specifically only two, and leave the third to implication. It would have been much easier (and much more natural) to provide that manufacturers would be liable for "defective manufacture, defective directions or warning, and defective design." It seems that the statute fails to mention design-defect liability "by deliberate choice, not inadvertence." *Barnhart* v. *Peabody Coal Co.*, 537 U. S. 149, 168 (2003). *Expressio unius, exclusio alterius.*

B

The dissent's principal textual argument is mistaken. We agree with its premise that "'side effects that were unavoidable' must refer to side effects caused by a vaccine's *design*."[37] We do not comprehend, however, the second step of its reasoning, which is that the use of the conditional term "if" in the introductory phrase "if the injury or death resulted from side effects that were unavoidable" "plainly implies that some side effects stemming from a vaccine's design are 'unavoidable,' while

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We doubt that Congress would introduce such an amorphous test by implication when it otherwise micromanages vaccine manufacturers. See *infra*, at 13–14. We have no idea how much more expensive an alternative design can be before it "compromis[es]" a vaccine's cost or how much efficacy an alternative design can sacrifice to improve safety. Neither does the dissent. And neither will the judges who must rule on motions to dismiss, motions for summary judgment, and motions for judgment as a matter of law. Which means that the test would probably have no real-world effect.

[36] W. Keeton, D. Dobbs, R. Keeton, & D. Owen, Prosser and Keeton on Law of Torts 695 (5th ed. 1984); Restatement (Third) of Torts §2 (1999).

[37] *Post*, at 3.

others are avoidable."[38] That is not so. The "if" clause makes total sense whether the design to which "unavoidable" refers is (as the dissent believes) any feasible design (making the side effects of the design used for the vaccine at issue avoidable), or (as we believe) the particular design used for the vaccine at issue (making its side effects unavoidable). Under the latter view, the condition established by the "if" clause is that the vaccine have been properly labeled and manufactured; and under the former, that it have been properly *designed*, labeled, and manufactured. Neither view renders the "if" clause a nullity. Which of the two variants must be preferred is addressed by our textual analysis, and is in no way determined by the "if" clause.

Petitioners' and the dissent's textual argument also rests upon the proposition that the word "unavoidable" in §300aa–22(b)(1) is a term of art that incorporates comment *k* to Restatement (Second) of Torts §402A (1963–1964).[39] The Restatement generally holds a manufacturer strictly liable for harm to person or property caused by "any product in a defective condition unreasonably dangerous to the user."[40] Comment *k* exempts from this strict-liability rule "unavoidably unsafe products." An unavoidably unsafe product is defined by a hodge-podge of criteria and a few examples, such as the Pasteur rabies vaccine and experimental pharmaceuticals. Despite this lack of clarity, petitioners seize upon one phrase in the comment *k* analysis, and assert that by 1986 a majority of courts had made this a *sine qua non* requirement for an "unavoidably unsafe product": a case-specific showing that the product was "quite incapable of being made safer for

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[38] *Ibid.*

[39] See Brief for Petitioners 29.

[40] Restatement §402A, p. 347.

[its] intended . . . use."[41]

We have no need to consider the finer points of comment *k*. Whatever consistent judicial gloss that comment may have been given in 1986, there is no reason to believe that §300aa–22(b)(1) was invoking it. The comment creates a special category of "unavoidably unsafe products," while the statute refers to "side effects that were unavoidable." That the latter uses the adjective "unavoidable" and the former the adverb "unavoidably" does not establish that Congress had comment *k* in mind. "Unavoidable" is hardly a rarely used word. Even the cases petitioners cite as putting a definitive gloss on comment *k* use the precise phrase "unavoidably unsafe product";[42] none attaches special significance to the term "unavoidable" standing alone.

The textual problems with petitioners' interpretation do

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[41] *Id.,* Comment *k*, p. 353; Petitioners cite, *inter alia*, *Kearl* v. *Lederle Labs.*, 172 Cal. App. 3d 812, 828–830, 218 Cal. Rptr. 453, 463–464 (1985); *Belle Bonfils Memorial Blood Bank* v. *Hansen*, 665 P. 2d 118, 122 (Colo. 1983).

Though it is not pertinent to our analysis, we point out that a large number of courts disagreed with that reading of comment *k*, and took it to say that manufacturers did not face strict liability for side effects of properly manufactured prescription drugs that were accompanied by adequate warnings. See, *e.g., Brown* v. *Superior Court*, 227 Cal. Rptr. 768, 772–775 (Cal. App. 1986), (officially depublished), aff'd 44 Cal. 3d 1049, 751 P. 2d 470 (1988); *McKee* v. *Moore*, 648 P. 2d 21, 23 (Okla. 1982); *Stone* v. *Smith, Kline & French Labs.*, 447 So. 2d 1301, 1303–1304 (Ala. 1984); *Lindsay* v. *Ortho Pharm. Corp.*, 637 F. 2d 87, 90–91 (CA2 1980) (applying N. Y. law); *Wolfgruber* v. *Upjohn Co.*, 72 App. Div. 2d 59, 61, 423 N. Y. S. 2d 95, 96 (1979); *Chambers* v. *G. D. Searle & Co.*, 441 F. Supp. 377, 380–381 (D Md. 1975); *Basko* v. *Sterling Drug, Inc.*, 416 F. 2d 417, 425 (CA2 1969) (applying Conn. law).

[42] See, *e.g., Johnson* v. *American Cyanamid Co.*, 239 Kan. 279, 285, 718 P. 2d 1318, 1323 (1986); *Feldman* v. *Lederle Labs.*, 97 N. J. 429, 440, 446–447, 479 A. 2d 374, 380, 383–384 (1984); *Belle Bonfils Memorial Blood Bank supra*, at 121–123; *Cassisi* v. *Maytag Co.*, 396 So. 2d 1140, 1144, n. 4, 1146 (Fla. App. 1981); *Racer* v. *Utterman*, 629 S. W. 2d 387, 393 (Mo. App. 1981).

not end there. The phrase "even though" in the clause "even though the vaccine was properly prepared and [labeled]" is meant to signal the unexpected: unavoidable side effects persist *despite* best manufacturing and labeling practices.[43] But petitioners' reading eliminates any opposition between the "even though" clause—called a concessive subordinate clause by grammarians—and the word "unavoidable."[44] Their reading makes preemption turn equally on unavoidability, proper preparation, and proper labeling. Thus, the dissent twice refers to the requirements of proper preparation and proper labeling as "two additional prerequisites" for preemption independent of unavoidability.[45] The primary textual justification for the dissent's position depends on that independence.[46] But linking independent ideas is the job of a coordinating junction like "and," not a subordinating junction like "even though."[47]

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[43] The dissent's assertion that we treat "even though" as a synonym for "because" misses the subtle distinction between "because" and "despite." See *post,* at 17, n. 14. "Even though" is a close cousin of the latter. See Webster's New International Dictionary 709, 2631 (2d ed. 1957). The statement "the car accident was unavoidable despite his quick reflexes" indicates that quick reflexes could not avoid the accident, and leaves open two unstated possibilities: (1) that other, unstated means of avoiding the accident besides quick reflexes existed, but came up short as well; or (2) that quick reflexes were the only possible way to avoid the accident. Our interpretation of §300aa–22(b)(1) explains why we think Congress meant the latter in this context. (Incidentally, the statement "the car accident was unavoidable because of his quick reflexes" makes no sense.)

[44] See W. Follett, Modern American Usage: A Guide 61 (1966).

[45] *Post*, at 9, 17.

[46] *Post*, at 3–5.

[47] The dissent responds that these "additional prerequisites" act "in a concessive, subordinating fashion," *post,* at 17, n. 14 (internal quotation marks and brackets omitted). But that is no more true of the dissent's conjunctive interpretation of the present text than it is of *all* provisions that set forth additional requirements—meaning that we could eliminate "even though" from our English lexicon, its function being entirely

Petitioners and the dissent contend that the interpretation we propose would render part of §300aa–22(b)(1) superfluous: Congress could have more tersely and more clearly preempted design-defect claims by barring liability "if . . . the vaccine was properly prepared and was accompanied by proper directions and warnings." The intervening passage ("the injury or death resulted from side effects that were unavoidable even though") is unnecessary. True enough. But the rule against giving a portion of text an interpretation which renders it superfluous does not prescribe that a passage which could have been more terse does not mean what it says. The rule applies only if verbosity and prolixity can be eliminated by giving the offending passage, or the remainder of the text, a competing interpretation. That is not the case here.[48] To be sure, petitioners' and the dissent's interpretation gives independent meaning to the intervening passage (the supposed meaning of comment *k*); but it does so only at the expense of rendering the remainder of the provision superfluous. Since a vaccine is not "quite incapable of being made safer for [its] intended use" if manufacturing defects could have been eliminated or better warnings provided, the entire "even though" clause is a useless appendage.[49] It would suffice to say "if the injury or death resulted from side effects that were unavoidable"—full stop.

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performed by "and." No, we think "even though" has a distinctive concessive, subordinating role to play.

[48] Because the dissent has a superfluity problem of its own, its reliance on *Bates* v. *Dow Agrosciences LLC*, 544 U. S. 431 (2005), is misplaced. See *id.,* at 449 (adopting an interpretation that was "the only one that makes sense of each phrase" in the relevant statute).

[49] That is true regardless of whether §300aa–22(b)(1) incorporates comment *k*. See Restatement §402A, Comment *k*, pp. 353, 354 (noting that "unavoidably unsafe products" are exempt from strict liability "with the qualification that they are properly prepared and marketed, and proper warning is given").

III

The structure of the NCVIA and of vaccine regulation in general reinforces what the text of §300aa–22(b)(1) suggests. A vaccine's license spells out the manufacturing method that must be followed and the directions and warnings that must accompany the product.[50] Manufacturers ordinarily must obtain the Food and Drug Administration's (FDA) approval before modifying either.[51] Deviations from the license thus provide objective evidence of manufacturing defects or inadequate warnings. Further objective evidence comes from the FDA's regulations—more than 90 of them[52]—that pervasively regulate the manufacturing process, down to the requirements for plumbing and ventilation systems at each manufacturing facility.[53] Material noncompliance with any one of them, or with any other FDA regulation, could cost the manufacturer its regulatory-compliance defense.[54]

Design defects, in contrast, do not merit a single mention in the NCVIA or the FDA's regulations. Indeed, the FDA has never even spelled out in regulations the criteria it uses to decide whether a vaccine is safe and effective for its intended use.[55] And the decision is surely not an easy one. Drug manufacturers often could trade a little less efficacy for a little more safety, but the safest design is not always the best one. Striking the right balance between safety and efficacy is especially difficult with respect to vaccines, which affect public as well as individual health. Yet the Act, which in every other respect micromanages manufacturers, is silent on how to evaluate competing designs. Are manufacturers liable only for failing to em-

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[50] See 42 U. S. C. §262(a), (j); 21 CFR §§601.2(a), 314.105(b) (2010).
[51] See §601.12.
[52] See §§211.1 *et seq.*, 600.10–600.15, 600.21–600.22, 820.1 *et seq.*
[53] See §§211.46, 211.48.
[54] See 42 U. S. C. §300aa–22(b)(2).
[55] Hutt, Merrill, & Grossman, Food and Drug Law, at 685, 891.

ploy an alternative design that the FDA has approved for distribution (an approval it takes years to obtain[56])? Or does it suffice that a vaccine design has been approved in other countries? Or could there be liability for failure to use a design that exists only in a lab? Neither the Act nor the FDA regulations provide an answer, leaving the universe of alternative designs to be limited only by an expert's imagination.

Jurors, of course, often decide similar questions with little guidance, and we do not suggest that the absence of guidance alone suggests preemption. But the lack of guidance for design defects combined with the extensive guidance for the two grounds of liability specifically mentioned in the Act strongly suggests that design defects were not mentioned because they are not a basis for liability.

The mandates contained in the Act lead to the same conclusion. Design-defect torts, broadly speaking, have two beneficial effects: (1) prompting the development of improved designs, and (2) providing compensation for inflicted injuries. The NCVIA provides other means for achieving both effects. We have already discussed the Act's generous compensation scheme. And the Act provides many means of improving vaccine design. It directs the Secretary of Health and Human Services to promote "the development of childhood vaccines that result in fewer and less serious adverse reactions."[57] It establishes a National Vaccine Program, whose Director is "to achieve optimal prevention of human infectious diseases . . . and to achieve optimal prevention against adverse reactions."[58] The Program is to set priorities for federal vaccine research, and to coordinate federal vaccine safety and effi-

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[56] See Sing & William, Supplying Vaccines, at 66–67.

[57] 42 U. S. C. §300aa–27(a)(1).

[58] §300aa–1.

cacy testing.[59] The Act requires vaccine manufacturers and health-care providers to report adverse side effects,[60] and provides for monitoring of vaccine safety through a collaboration with eight managed-care organizations.[61] And of course whenever the FDA concludes that a vaccine is unsafe, it may revoke the license.[62]

These provisions for federal agency improvement of vaccine design, and for federally prescribed compensation, once again suggest that §300aa–22(b)(1)'s silence regarding design-defect liability was not inadvertent. It instead reflects a sensible choice to leave complex epidemiological judgments about vaccine design to the FDA and the National Vaccine Program rather than juries.[63]

And finally, the Act's structural *quid pro quo* leads to the same conclusion: The vaccine manufacturers fund from their sales an informal, efficient compensation program for vaccine injuries;[64] in exchange they avoid costly tort litigation and the occasional disproportionate jury verdict.[65] But design-defect allegations are the most speculative and difficult type of products liability claim to

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[59] See §§300aa–2(a)(1)–(3), 300aa–3.

[60] See §300aa–25(b).

[61] See NVAC 18–19.

[62] See 21 CFR §601.5(b)(1)(vi) (2010).

[63] The dissent quotes just part of this sentence, to make it appear that we believe complex epidemiological judgments ought to be assigned in that fashion. See *post*, at 26. We do not state our preference, but merely note that it is Congress's expressed preference—and in order to preclude the argument that it is absurd to think Congress enacted such a thing, we assert that the choice is reasonable and express some of the reasons why. Leaving it to the jury may (or may not) be reasonable as well; we express no view.

[64] See 42 U. S. C. §300aa–15(i)(2); Pub. L. 99–660, §323(a), 100 Stat. 3784. The dissent's unsupported speculation that demand in the vaccine market is inelastic, see *post*, at 24, n. 22, sheds no light on whether Congress regarded the tax as a *quid pro quo*, most Members of Congress being neither professional economists nor law-and-economics scholars.

[65] See 42 U. S. C. §§300aa–11(a)(2), 300aa–22.

litigate. Taxing vaccine manufacturers' product to fund the compensation program, while leaving their liability for design defect virtually unaltered, would hardly coax manufacturers back into the market.

The dissent believes the Act's mandates are irrelevant because they do not spur innovation in precisely the same way as state-law tort systems.[66] That is a novel suggestion. Although we previously have expressed doubt that Congress would quietly preempt product-liability claims without providing a federal substitute, see *Medtronic, Inc.* v. *Lohr*, 518 U. S. 470, 486–488 (1996) (plurality opinion), we have never suggested we would be skeptical of preemption unless the congressional substitute operated like the tort system. We decline to adopt that stance today. The dissent's belief that the FDA and the National Vaccine Program cannot alone spur adequate vaccine innovation is probably questionable, but surely beside the point.

IV

Since our interpretation of §300aa–22(b)(1) is the only interpretation supported by the text and structure of the NCVIA, even those of us who believe legislative history is a legitimate tool of statutory interpretation have no need to resort to it. In any case, the dissent's contention that it would contradict our conclusion is mistaken.

The dissent's legislative history relies on the following syllogism: A 1986 House Committee Report states that §300aa–22(b)(1) "sets forth the principle contained in Comment k of Section 402A of the Restatement of Torts (Second);"[67] in 1986 comment *k* was "commonly understood" to require a case-specific showing that "no feasible alternative design" existed; Congress therefore must have intended §300aa–22(b)(1) to require that showing.[68] The

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[66] See *post*, at 21–24.

[67] H. R. Rep. No. 99–908, pt. 1, p. 25 (1986) (hereinafter 1986 Report).

[68] *Post*, at 7–8.

syllogism ignores unhelpful statements in the Report and relies upon a term of art that did not exist in 1986.

Immediately after the language quoted by the dissent, the 1986 Report notes the difficulty a jury would have in faithfully assessing whether a feasible alternative design exists when an innocent "young child, often badly injured or killed" is the plaintiff.[69] Eliminating that concern is why the Report's authors "strongly believ[e] that Comment k is appropriate and necessary as the policy for civil actions seeking damages in tort."[70] The dissent's interpretation of §300aa–22(b)(1) and its version of "the principle in Comment K" adopted by the 1986 Report leave that concern unaddressed.

The dissent buries another unfavorable piece of legislative history. Because the Report believes that §300aa–22(b)(1) should incorporate "the principle in Comment K" and because the Act provides a generous no-fault compensation scheme, the Report counsels injured parties who cannot prove a manufacturing or labeling defect to "pursue recompense in the compensation system, not the tort system."[71] That counsel echoes our interpretation of §300aa–22(b)(1).

Not to worry, the dissent retorts, a Committee Report by a later Congress "authoritative[ly]" vindicates its interpretation.[72] Post-enactment legislative history (a contradiction in terms) is not a legitimate tool of statutory interpretation. See *Jones* v. *United States*, 526 U. S. 227, 238

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[69] 1986 Report, at 26; see *ibid.* ("[E]ven if the defendant manufacturer may have made as safe a vaccine as anyone reasonably could expect, a court or jury undoubtedly will find it difficult to rule in favor of the 'innocent' manufacturer if the equally 'innocent' child has to bear the risk of loss with no other possibility of recompense").

[70] *Ibid.*

[71] *Ibid.*

[72] *Post*, at 12. This is a courageous adverb since we have previously held that the only authoritative source of statutory meaning is the text that has passed through the Article I process. See *Exxon Mobil Corp.* v. *Allapattah Services, Inc.*, 545 U. S. 546, 568 (2005).

(1999); *United States* v. *Mine Workers*, 330 U. S. 258, 281–282 (1947). Real (pre-enactment) legislative history is persuasive to some because it is thought to shed light on what legislators understood an ambiguous statutory text to mean when they voted to enact it into law. See *Exxon Mobil Corp.* v. *Allapattah Services, Inc.*, 545 U. S. 546, 568 (2005). But post-enactment legislative history by definition "could have had no effect on the congressional vote," *District of Columbia* v. *Heller*, 554 U. S. 570, 605 (2008).

It does not matter that §300aa–22(b)(1) did not take effect until the later Congress passed the excise tax that funds the compensation scheme,[73] and that the supposedly dispositive Committee Report is attached to that funding legislation.[74] Those who voted on the relevant statutory language were not necessarily the same persons who crafted the statements in the later Committee Report; or if they were did not necessarily have the same views at that earlier time; and no one voting at that earlier time could possibly have been informed by those later statements. Permitting the legislative history of subsequent funding legislation to alter the meaning of a statute would set a dangerous precedent. Many provisions of federal law depend on appropriations or include sunset provisions;[75] they cannot be made the device for unenacted statutory revision.

That brings us to the second flaw in the dissent's syllogism: Comment *k* did not have a "commonly understood meaning"[76] in the mid-1980's. Some courts thought it required a case-specific showing that a product was "unavoidably unsafe"; many others thought it categorically exempted certain types of products from strict liability.[77]

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[73] Pub. L. 99–960, §323(a), 100 Stat. 3784.

[74] H. R. Rep. No. 100–391, pt. 1, p. 701 (1987).

[75] See, *e.g.,* Pub. L. 104–208, §§401, 403(a), 110 Stat. 3009–655 to 3009–656, 3009–659 to 3009–662, as amended, note following 8 U. S. C. §1324a (2006 ed., Supp. III) (E-Verify program expires Sept. 30, 2012).

[76] *Post*, at 8.

[77] See n. 39, *supra; post*, at 7–8, n. 5.

When "all (or nearly all) of the" relevant judicial decisions have given a term or concept a consistent judicial gloss, we presume Congress intended the term or concept to have that meaning when it incorporated it into a later-enacted statute. *Merck & Co.* v. *Reynolds*, 559 U. S. ___, ___ (2010) (SCALIA, J., concurring in part and concurring in judgment) (slip op., at 5). The consistent gloss represents the public understanding of the term. We cannot make the same assumption when widespread disagreement exists among the lower courts. We must make do with giving the term its most plausible meaning using the traditional tools of statutory interpretation. That is what we have done today.

* * *

For the foregoing reasons, we hold that the National Childhood Vaccine Injury Act preempts all design-defect claims against vaccine manufacturers brought by plaintiffs who seek compensation for injury or death caused by vaccine side effects. The judgment of the Court of Appeals is affirmed.

It is so ordered.

JUSTICE KAGAN took no part in the consideration or decision of this case.

SUPREME COURT OF THE UNITED STATES

No. 09–152

RUSSELL BRUESEWITZ, ET AL., PETITIONERS *v.* WYETH LLC, FKA WYETH, INC., FKA WYETH LABORATORIES, ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

[February 22, 2011]

JUSTICE BREYER, concurring.

I join the Court's judgment and opinion. In my view, the Court has the better of the purely textual argument. But the textual question considered alone is a close one. Hence, like the dissent, I would look to other sources, including legislative history, statutory purpose, and the views of the federal administrative agency, here supported by expert medical opinion. Unlike the dissent, however, I believe these other sources reinforce the Court's conclusion.

I

House Committee Report 99–908 contains an "authoritative" account of Congress' intent in drafting the pre-emption clause of the National Childhood Vaccine Injury Act of 1986 (NCVIA or Act). See *Garcia* v. *United States*, 469 U. S. 70, 76 (1984) ("[T]he authoritative source for finding the Legislature's intent lies in the Committee Reports on the bill"). That Report says that, "if" vaccine-injured persons

> "cannot demonstrate under applicable law either that a vaccine was improperly prepared or that it was accompanied by improper directions or inadequate warnings [they] should pursue recompense in the

> compensation system, not the tort system." H. R. Rep. No. 99–908, pt. 1, p. 24 (1986) (hereinafter H. R. Rep.).

The Report lists two specific kinds of tort suits that the clause does not pre-empt (suits based on improper manufacturing and improper labeling), while going on to state that compensation for other tort claims, *e.g.*, design-defect claims, lies in "the [NCVIA's no-fault] compensation system, not the tort system." *Ibid.*

The strongest contrary argument rests upon the Report's earlier description of the statute as "set[ting] forth the principle contained in Comment k" (of the Restatement Second of Torts' *strict liability* section, 402A) that "a vaccine manufacturer should not be liable for injuries or deaths resulting from *unavoidable* side effects." *Id.*, at 23 (emphasis added). But the appearance of the word "unavoidable" in this last-mentioned sentence cannot provide petitioners with much help. That is because nothing in the Report suggests that the statute means the word "unavoidable" to summon up an otherwise unmentioned third exception encompassing suits based on design defects. Nor can the Report's reference to comment *k* fill the gap. The Report itself refers, not to comment *k*'s details, but only to its "*principle,*" namely, that vaccine manufacturers should *not* be held liable for unavoidable injuries. It says nothing at all about who—judge, jury, or federal safety agency—should decide whether a safer vaccine could have been designed. Indeed, at the time Congress wrote this Report, different state courts had come to very different conclusions about that matter. See Cupp, Rethinking Conscious Design Liability for Prescription Drugs: The *Restatement (Third)* Standard Versus a Negligence Approach, 63 Geo. Wash. L. Rev. 76, 79 (1994–1995) ("[C]ourts [had] adopted a broad range of conflicting interpretations" of comment *k*). Neither the word "unavoid-

able" nor the phrase "the principle of Comment k" tells us which courts' view Congress intended to adopt. Silence cannot tell us to follow those States where juries decided the design-defect question.

II

The legislative history describes the statute more generally as trying to protect the lives of children, in part by ending "the instability and unpredictability of the childhood vaccine market." H. R. Rep., at 7; see *ante,* at 2–3. As the Committee Report makes clear, routine vaccination is "one of the most spectacularly effective public health initiatives this country has ever undertaken." H. R. Rep., at 4. Before the development of routine whooping cough vaccination, for example, "nearly all children" in the United States caught the disease and more than 4,000 people died annually, most of them infants. U. S. Dept. of Health and Human Services, Centers for Disease Control and Prevention, What Would Happen if We Stopped Vaccinations? http://www.cdc.gov/vaccines/vac-gen/whatifstop.htm (all Internet materials as visited Feb. 17, 2011, and available in Clerk of Court's case file); Preventing Tetanus, Diphtheria, and Pertussis Among Adolescents: Use of Tetanus Toxoid, Reduced Diptheria Toxoid and Acellular Pertussis Vaccines, 55 Morbidity and Mortality Weekly Report, No. RR–3, p. 2 (Mar. 24, 2006) (hereinafter Preventing Tetanus) (statistics for 1934–1943), http://www.cdc.gov/mmwr/PDF/rr/rr5503.pdf; U. S. Dept. of Health and Human Services, Centers for Disease Control and Prevention, Epidemiology and Prevention of Vaccine-Preventable Diseases 200 (11th ed. rev. May 2009). After vaccination became common, the number of annual cases of whooping cough declined from over 200,000 to about 2,300, and the number of deaths from about 4,000 to about 12. Preventing Tetanus 2; Childhood Immunizations, House Committee on Energy and Com-

merce, 99th Cong., 2d Sess., 10 (Comm. Print 1986) (hereinafter Childhood Immunizations).

But these gains are fragile; "[t]he causative agents for these preventable childhood illnesses are ever present in the environment, waiting for the opportunity to attack the unprotected individual." Hearing on S. 827 before the Senate Committee on Labor and Human Resources, 99th Cong., 2d Sess., pt. 2, pp. 20–21 (1985) (hereinafter Hearings) (testimony of the American Academy of Pediatrics); see California Dept. of Public Health, Pertussis Report (Jan. 7, 2011), www.cdph.ca.gov/programs/immunize/Documents/PertussisReport2011–01–07.pdf (In 2010, 8,383 people in California caught whooping cough, and 10 infants died). Even a brief period when vaccination programs are disrupted can lead to children's deaths. Hearings 20–21; see Gangarosa et al., Impact of Anti-Vaccine Movements on Pertussis Control: The Untold Story, 351 Lancet 356–361 (Jan. 31, 1998) (when vaccination programs are disrupted, the number of cases of whooping cough skyrockets, increasing by orders of magnitude).

In considering the NCVIA, Congress found that a sharp increase in tort suits brought against whooping cough and other vaccine manufacturers between 1980 and 1985 had "prompted manufacturers to question their continued participation in the vaccine market." H. R. Rep., at 4; Childhood Immunizations 85–86. Indeed, two whooping cough vaccine manufacturers withdrew from the market, and other vaccine manufacturers, "fac[ing] great difficulty in obtaining [product liability] insurance," told Congress that they were considering "a similar course of action." H. R. Rep., at 4; Childhood Immunizations 68–70. The Committee Report explains that, since there were only one or two manufacturers of many childhood vaccines, "[t]he loss of any of the existing manufacturers of childhood vaccines . . . could create a genuine public health hazard"; it "would present the very real possibility of vaccine short-

ages, and, in turn, increasing numbers of unimmunized children, and, perhaps, a resurgence of preventable diseases." H. R. Rep., at 5. At the same time, Congress sought to provide generous compensation to those whom vaccines injured—as determined by an expert compensation program. *Id.,* at 5, 24.

Given these broad general purposes, to read the preemption clause as preserving design-defect suits seems anomalous. The Department of Health and Human Services (HHS) decides when a vaccine is safe enough to be licensed and which licensed vaccines, with which associated injuries, should be placed on the Vaccine Injury Table. 42 U. S. C. §300aa–14; *ante,* at 3–4; A Comprehensive Review of Federal Vaccine Safety Programs and Public Health Activities 13–15, 32–34 (Dec. 2008), http://www.hhs.gov/nvpo/nvac/documents/vaccine-safety-review.pdf. A special master in the Act's compensation program determines whether someone has suffered an injury listed on the Injury Table and, if not, whether the vaccine nonetheless caused the injury. *Ante,* at 3–4; §300aa–13. To allow a jury in effect to second-guess those determinations is to substitute less expert for more expert judgment, thereby threatening manufacturers with liability (indeed, strict liability) in instances where any conflict between experts and nonexperts is likely to be particularly severe—instances where Congress intended the contrary. That is because potential tort plaintiffs are unlikely to bring suit unless the specialized compensation program has determined that they are not entitled to compensation (say, because it concludes that the vaccine did not cause the injury). Brief for United States as *Amicus Curiae* 28 ("99.8% of successful Compensation Program claimants have accepted their awards, foregoing any tort remedies against vaccine manufacturers"). It is difficult to reconcile these potential conflicts and the resulting tort liabilities with a statute that seeks to diminish

manufacturers' product liability while simultaneously augmenting the role of experts in making compensation decisions.

III

The United States, reflecting the views of HHS, urges the Court to read the Act as I and the majority would do. It notes that the compensation program's listed vaccines have survived rigorous administrative safety review. It says that to read the Act as permitting design-defect lawsuits could lead to a recurrence of "exactly the crisis that precipitated the Act," namely withdrawals of vaccines or vaccine manufacturers from the market, "disserv[ing] the Act's central purposes," and hampering the ability of the agency's "expert regulators, in conjunction with the medical community, [to] control the availability and withdrawal of a given vaccine." Brief for United States as *Amicus Curiae* 30, 31.

The United States is supported in this claim by leading public health organizations, including the American Academy of Pediatrics, the American Academy of Family Physicians, the American College of Preventive Medicine, the American Public Health Association, the American Medical Association, the March of Dimes Foundation, the Pediatric Infectious Diseases Society, and 15 other similar organizations. Brief for American Academy of Pediatrics et al. as *Amici Curiae* (hereinafter AAP Brief). The American Academy of Pediatrics has also supported the retention of vaccine manufacturer tort liability (provided that federal law structured state-law liability conditions in ways that would take proper account of federal agency views about safety). Hearings 14–15. But it nonetheless tells us here, in respect to the specific question before us, that the petitioners' interpretation of the Act would undermine its basic purposes by threatening to "halt the future production and development of childhood vaccines

in this country," *i.e.,* by "threaten[ing] a resurgence of the very problems which . . . caused Congress to intervene" by enacting this statute. AAP Brief 24 (internal quotation marks omitted).

I would give significant weight to the views of HHS. The law charges HHS with responsibility for overseeing vaccine production and safety. It is "likely to have a thorough understanding" of the complicated and technical subject matter of immunization policy, and it is comparatively more "qualified to comprehend the likely impact of state requirements." *Geier* v. *American Honda Motor Co., Inc.*, 529 U. S. 861, 883 (2000) (internal quotation marks omitted); see *Medtronic, Inc.* v. *Lohr*, 518 U. S. 470, 506 (1996) (BREYER, J., concurring in part and concurring in judgment) (the agency is in the best position to determine "whether (or the extent to which) state requirements may interfere with federal objectives"). HHS's position is particularly persuasive here because expert public health organizations support its views and the matter concerns a medical and scientific question of great importance: how best to save the lives of children. See *Skidmore* v. *Swift & Co.*, 323 U. S. 134 (1944).

In sum, congressional reports and history, the statute's basic purpose as revealed by that history, and the views of the expert agency along with those of relevant medical and scientific associations, all support the Court's conclusions. I consequently agree with the Court.

SUPREME COURT OF THE UNITED STATES

No. 09–152

RUSSELL BRUESEWITZ, ET AL., PETITIONERS *v.* WYETH LLC, FKA WYETH, INC., FKA WYETH LABORATORIES, ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

[February 22, 2011]

JUSTICE SOTOMAYOR, with whom JUSTICE GINSBURG joins, dissenting.

Vaccine manufacturers have long been subject to a legal duty, rooted in basic principles of products liability law, to improve the designs of their vaccines in light of advances in science and technology. Until today, that duty was enforceable through a traditional state-law tort action for defective design. In holding that §22(b)(1) of the National Childhood Vaccine Injury Act of 1986 (Vaccine Act or Act), 42 U. S. C. §300aa–22(b)(1), pre-empts all design defect claims for injuries stemming from vaccines covered under the Act, the Court imposes its own bare policy preference over the considered judgment of Congress. In doing so, the Court excises 13 words from the statutory text, misconstrues the Act's legislative history, and disturbs the careful balance Congress struck between compensating vaccine-injured children and stabilizing the childhood vaccine market. Its decision leaves a regulatory vacuum in which no one ensures that vaccine manufacturers adequately take account of scientific and technological advancements when designing or distributing their products. Because nothing in the text, structure, or legislative history of the Vaccine Act remotely suggests that Congress intended such a result, I respectfully dissent.

I

A

Section 22 of the Vaccine Act provides "[s]tandards of responsibility" to govern civil actions against vaccine manufacturers. 42 U. S. C. §300aa–22. Section 22(a) sets forth the "[g]eneral rule" that "State law shall apply to a civil action brought for damages for a vaccine-related injury or death." §300aa–22(a). This baseline rule that state law applies is subject to three narrow exceptions, one of which, §22(b)(1), is at issue in this case. Section 22(b)(1) provides:

> "No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings." §300aa–22(b)(1).

The provision contains two key clauses: "if the injury or death resulted from side effects that were unavoidable" (the "if" clause), and "even though the vaccine was properly prepared and was accompanied by proper directions and warnings" (the "even though" clause).

Blackletter products liability law generally recognizes three different types of product defects: design defects, manufacturing defects, and labeling defects (*e.g.*, failure to warn).[1] The reference in the "even though" clause to a "properly prepared" vaccine "accompanied by proper directions and warnings" is an obvious reference to two such defects—manufacturing and labeling defects. The plain terms of the "even though" clause thus indicate that

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[1] W. Keeton, D. Dobbs, R. Keeton, & D. Owen, Prosser and Keeton on Law of Torts 695 (5th ed. 1984).

§22(b)(1) applies only where neither kind of defect is present. Because §22(b)(1) is invoked by vaccine manufacturers as a defense to tort liability, it follows that the "even though" clause requires a vaccine manufacturer in each civil action to demonstrate that its vaccine is free from manufacturing and labeling defects to fall within the liability exemption of §22(b)(1).[2]

Given that the "even though" clause requires the absence of manufacturing and labeling defects, the "if" clause's reference to "side effects that were unavoidable" must refer to side effects caused by something other than manufacturing and labeling defects. The only remaining kind of product defect recognized under traditional products liability law is a design defect. Thus, "side effects that were unavoidable" must refer to side effects caused by a vaccine's *design* that were "unavoidable." Because §22(b)(1) uses the conditional term "if," moreover, the text plainly implies that some side effects stemming from a vaccine's design are "unavoidable," while others are avoidable. See Webster's Third New International Dictionary 1124 (2002) ("if" means "in the event that," "so long as," or "on condition that"). Accordingly, because the "if" clause (like the "even though" clause) sets forth a condition to invoke §22(b)(1)'s defense to tort liability, Congress must also have intended a vaccine manufacturer to demonstrate in each civil action that the particular side effects of a vaccine's design were "unavoidable."

Congress' use of conditional "if" clauses in two other provisions of the Vaccine Act supports the conclusion that §22(b)(1) requires an inquiry in each case in which a manufacturer seeks to invoke the provision's exception to

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[2] See *Silkwood* v. *Kerr-McGee Corp.*, 464 U. S. 238, 255 (1984); *Brown* v. *Earthboard Sports USA, Inc.*, 481 F. 3d 901, 912 (CA6 2007) ("'[F]ederal preemption is an affirmative defense upon which the defendants bear the burden of proof'" (quoting *Fifth Third Bank* v. *CSX Corp.*, 415 F. 3d 741, 745 (CA7 2005))).

state tort liability. In §22(b)(2), Congress created a presumption that, for purposes of §22(b)(1), "a vaccine shall be presumed to be accompanied by proper directions and warnings if the vaccine manufacturer shows that it complied in all material respects with" federal labeling requirements. 42 U. S. C. §300aa–22(b)(2). Similarly, in §23(d)(2), Congress created an exemption from punitive damages "[i]f . . . the manufacturer shows that it complied, in all material respects," with applicable federal laws, unless it engages in "fraud," "intentional and wrongful withholding of information" from federal regulators, or "other criminal or illegal activity." §300aa–23(d)(2). It would be highly anomalous for Congress to use a conditional "if" clause in §§22(b)(2) and 23(d)(2) to require a specific inquiry in each case while using the same conditional "if" clause in §22(b)(1) to denote a categorical exemption from liability. Cf. *Erlenbaugh* v. *United States*, 409 U. S. 239, 243 (1972) ("[A] legislative body generally uses a particular word with a consistent meaning in a given context").

Indeed, when Congress intends to pre-empt design defect claims categorically, it does so using categorical (*e.g.*, "all") and/or declarative language (*e.g.*, "shall"), rather than a conditional term ("if"). For example, in a related context, Congress has authorized the Secretary of Health and Human Services to designate a vaccine designed to prevent a pandemic or epidemic as a "covered countermeasure." 42 U. S. C. §§247d–6d(b), (i)(1), (i)(7)(A)(i). With respect to such "covered countermeasure[s]," Congress provided that subject to certain exceptions, "a covered person *shall* be immune from suit and liability under Federal and State law with respect to *all* claims for loss caused by, arising out of, relating to, or resulting from the administration to or the use by an individual of a covered countermeasure," §247d–6d(a)(1) (emphasis added), including specifically claims relating to

"the design" of the countermeasure, §247d–6d(a)(2)(B).

The plain text and structure of the Vaccine Act thus compel the conclusion that §22(b)(1) pre-empts some—but not all—design defect claims. Contrary to the majority's and respondent's categorical reading, petitioners correctly contend that, where a plaintiff has proved that she has suffered an injury resulting from a side effect caused by a vaccine's design, a vaccine manufacturer may invoke §22(b)(1)'s liability exemption only if it demonstrates that the side effect stemming from the particular vaccine's design is "unavoidable," and that the vaccine is otherwise free from manufacturing and labeling defects.[3]

B

The legislative history confirms petitioners' interpretation of §22(b)(1) and sheds further light on its pre-emptive scope. The House Energy and Commerce Committee Report accompanying the Vaccine Act, H. R. Rep. No. 99–908, pt. 1 (1986) (hereinafter 1986 Report), explains in relevant part:

> "*Subsection (b)—Unavoidable Adverse Side Effects; Direct Warnings*.—This provision sets forth the principle contained in Comment K of Section 402A of the Restatement of Torts (Second) that a vaccine manufacturer should not be liable for injuries or deaths resulting from unavoidable side effects even though the vaccine was properly prepared and accompanied by proper directions and warnings.
>
> "The Committee has set forth Comment K in this bill because it intends that the principle in Comment K regarding 'unavoidably unsafe' products, i.e., those products which in the present state of human skill and knowledge cannot be made safe, apply to the vac-

[3] This leaves the question of what precisely §22(b)(1) means by "unavoidable" side effects, which I address in the next section.

> cines covered in the bill and that such products not be the subject of liability in the tort system." *Id.*, at 25–26.

The Report expressly adopts comment *k* of §402A of the Restatement of Torts (Second) (1963–1964) (hereinafter Restatement), which provides that "unavoidably unsafe" products—*i.e.*, those that "in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use"—are not defective.[4] As "[a]n outstanding example" of an "[u]navoidably unsafe" product, comment *k* cites "the vaccine for the Pasteur treatment of rabies, which not uncommonly leads to very serious and damaging consequences when it is injected";

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[4] Comment *k* provides as follows:

"*Unavoidably unsafe products*. There are some products which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use. These are especially common in the field of drugs. An outstanding example is the vaccine for the Pasteur treatment of rabies, which not uncommonly leads to very serious and damaging consequences when it is injected. Since the disease itself invariably leads to a dreadful death, both the marketing and the use of the vaccine are fully justified, notwithstanding the unavoidable high degree of risk which they involve. Such a product, properly prepared, and accompanied by proper directions and warning, is not defective, nor is it *unreasonably* dangerous. The same is true of many other drugs, vaccines, and the like, many of which for this very reason cannot legally be sold except to physicians, or under the prescription of a physician. It is also true in particular of many new or experimental drugs as to which, because of lack of time and opportunity for sufficient medical experience, there can be no assurance of safety, or perhaps even of purity of ingredients, but such experience as there is justifies the marketing and use of the drug notwithstanding a medically recognizable risk. The seller of such products, again with the qualification that they are properly prepared and marketed, and proper warning is given, where the situation calls for it, is not to be held to strict liability for unfortunate consequences attending their use, merely because he has undertaken to supply the public with an apparently useful and desirable product, attended with a known but apparently reasonable risk." Restatement 353–354.

"[s]ince the disease itself invariably leads to a dreadful death, both the marketing and the use of the vaccine are fully justified, notwithstanding the unavoidable high degree of risk which they involve." *Id.*, at 353. Comment *k* thus provides that "seller[s]" of "[u]navoidably unsafe" products are "not to be held to strict liability" provided that such products "are properly prepared and marketed, and proper warning is given." *Ibid.*

As the 1986 Report explains, Congress intended that the "principle in Comment K regarding 'unavoidably unsafe' products" apply to the vaccines covered in the bill. 1986 Report 26. That intent, in turn, is manifested in the plain text of §22(b)(1)—in particular, Congress' use of the word "unavoidable," as well as the phrases "properly prepared" and "accompanied by proper directions and warnings," which were taken nearly verbatim from comment *k*. 42 U. S. C. §300aa–22(b)(1); see Restatement 353–354 ("Such a[n unavoidably unsafe] product, properly prepared, and accompanied by proper directions and warning, is not defective"). By the time of the Vaccine Act's enactment in 1986, numerous state and federal courts had interpreted comment *k* to mean that a product is "unavoidably unsafe" when, given proper manufacture and labeling, no feasible alternative design would reduce the safety risks without compromising the product's cost and utility.[5] Given Con-

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[5] See, *e.g.*, *Smith ex rel. Smith* v. *Wyeth Labs., Inc.*, No. Civ. A 84–2002, 1986 WL 720792, *5 (SD W. Va., Aug. 21, 1986) ("[A] prescription drug is not 'unavoidably unsafe' when its dangers can be eliminated through design changes that do not unduly affect its cost or utility"); *Kearl* v. *Lederle Labs.*, 172 Cal. App. 3d 812, 830, 218 Cal. Rptr. 453, 464 (1985) ("unavoidability" turns on "(i) whether the product was designed to minimize—to the extent scientifically knowable at the time it was distributed—the risk inherent in the product, and (ii) the availability . . . of any alternative product that would have *as effectively* accomplished the *full intended purpose* of the subject product"), disapproved in part by *Brown* v. *Superior Ct.*, 44 Cal. 3d 1049, 751 P. 2d 470 (1988); *Belle Bonfils Memorial Blood Bank* v. *Hansen*, 665 P. 2d 118,

gress' expressed intent to codify the "principle in Comment K," 1986 Report 26, the term "unavoidable" in §22(b)(1) is best understood as a term of art, which incorporates the commonly understood meaning of "unavoidably unsafe" products under comment *k* at the time of the Act's enactment in 1986. See *McDermott Int'l, Inc.* v. *Wilander*, 498 U. S. 337, 342 (1991) ("[W]e assume that when a statute uses . . . a term [of art], Congress intended it to have its established meaning"); *Morissette* v. *United States*, 342 U. S. 246, 263 (1952) (same).[6] Similarly, courts applying

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122 (Colo. 1983) ("[A]pplicability of comment k . . . depends upon the coexistence of several factors," including that "the product's benefits must not be achievable in another manner; and the risk must be unavoidable under the present state of knowledge"); see also 1 L. Frumer & M. Friedman, Products Liability §§8.07[1]–[2], pp. 8–277 to 8–278 (2010) (comment *k* applies "only to defects in design," and there "must be no feasible alternative design which on balance accomplishes the subject product's purpose with a lesser risk" (internal quotation marks omitted)). To be sure, a number of courts at the time of the Vaccine Act's enactment had interpreted comment *k* to preclude design defect claims categorically for certain kinds of products, see *Hill* v. *Searle Labs.*, 884 F. 2d 1064, 1068 (CA8 1989) (collecting cases), but as indicated by the sources cited above, the courts that had construed comment *k* to apply on a case-specific basis generally agreed on the basic elements of what constituted an "unavoidably unsafe" product. See also n. 8, *infra*. The majority's suggestion that "judges who must rule on motions to dismiss, motions for summary judgment, and motions for judgment as a matter of law" are incapable of adjudicating claims alleging "unavoidable" side effects, *ante*, at 7–8, n. 35, is thus belied by the experience of the many courts that had adjudicated such claims for years by the time of the Vaccine Act's enactment.

[6]The majority refuses to recognize that "unavoidable" is a term of art derived from comment *k*, suggesting that "'[u]navoidable' is hardly a rarely used word." *Ante*, at 10. In fact, however, "unavoidable" is an extremely rare word in the relevant context. It appears exactly *once* (*i.e.*, in §300aa–22(b)(1)) in the entirety of Title 42 of the U. S. Code ("Public Health and Welfare"), which governs, *inter alia*, Social Security, see 42 U. S. C. §301 *et seq.*, Medicare, see §1395 *et seq.*, and several other of the Federal Government's largest entitlement programs. The singular rarity in which Congress used the term supports the conclu-

comment *k* had long required manufacturers invoking the defense to demonstrate that their products were not only "unavoidably unsafe" but also properly manufactured and labeled.[7] By requiring "prope[r] prepar[ation]" and "proper directions and warnings" in §22(b)(1), Congress plainly intended to incorporate these additional comment *k* requirements.

The 1986 Report thus confirms petitioners' interpretation of §22(b)(1). The Report makes clear that "side effects that were unavoidable" in §22(b)(1) refers to side effects stemming from a vaccine's design that were "unavoidable." By explaining what Congress meant by the term "unavoidable," moreover, the Report also confirms that whether a side effect is "unavoidable" for purposes of §22(b)(1) involves a specific inquiry in each case as to whether the vaccine "in the present state of human skill and knowledge cannot be made safe," 1986 Report 26—*i.e.*, whether a feasible alternative design existed that would have eliminated the adverse side effects of the vaccine without compromising its cost and utility. See Brief for Kenneth W. Starr et al. as *Amici Curiae* 14–15 ("If a particular plaintiff could show that her injury at issue was avoidable . . . through the use of a feasible alternative design for a specific vaccine, then she would satisfy the plain language of the statute, because she would have demonstrated that the side effects were *not* unavoidable"). Finally, the Report confirms that the "even though" clause is properly read to establish two additional prerequisites—proper manufacturing and proper labeling—to qualify for

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sion that "unavoidable" is a term of art.

[7] See, *e.g.*, *Brochu* v. *Ortho Pharmaceutical Corp.*, 642 F. 2d 652, 657 (CA1 1981); *Needham* v. *White Labs., Inc.*, 639 F. 2d 394, 402 (CA7 1981); *Reyes* v. *Wyeth Labs.*, 498 F. 2d 1264, 1274–1275 (CA5 1974); *Davis* v. *Wyeth Labs.*, 399 F. 2d 121, 127–129 (CA9 1968); *Feldman* v. *Lederle Labs.*, 97 N. J. 429, 448, 479 A. 2d 374, 384 (1984); see also *Toner* v. *Lederle Labs.*, 112 Idaho 328, 336, 732 P. 2d 297, 305 (1987).

§22(b)(1)'s liability exemption.[8]

In addition to the 1986 Report, one other piece of the Act's legislative history provides further confirmation of the petitioners' textual reading of §22(b)(1). When Congress enacted the Vaccine Act in 1986, it did not initially include a source of payment for the no-fault compensation program the Act established. The Act thus "made the compensation program and accompanying tort reforms contingent on the enactment of a tax to provide funding

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[8]Respondent suggests an alternative reading of the 1986 Report. According to respondent, "the principle in Comment K" is simply that of nonliability for "unavoidably unsafe" products, and thus Congress' stated intent in the 1986 Report to apply the "principle in Comment K" to "the vaccines covered in the bill" means that Congress viewed the covered vaccines as a class to be "'unavoidably unsafe.'" 1986 Report 25–26; Brief for Respondent 42. The concurrence makes a similar argument. *Ante*, at 1–2 (opinion of BREYER, J.). This interpretation finds some support in the 1986 Report, which states that "if [injured individuals] cannot demonstrate under applicable law either that a vaccine was improperly prepared or that it was accompanied by improper directions or inadequate warnings [they] should pursue recompense in the compensation system, not the tort system." 1986 Report 26. It also finds some support in the pre-Vaccine Act case law, which reflected considerable disagreement in the courts over "whether comment k applies to pharmaceutical products across the board or only on a case-by-case basis." Ausness, Unavoidably Unsafe Products and Strict Products Liability: What Liability Rule Should be Applied to the Sellers of Pharmaceutical Products? 78 Ky. L. J. 705, 708, and n. 11 (1989–1990) (collecting cases). This interpretation, however, is undermined by the fact that Congress has never directed the Food and Drug Administration (FDA) or any other federal agency to review vaccines for optimal vaccine design, see *infra*, at 20–22, and n. 19, and thus it seems highly unlikely that Congress intended to eliminate the traditional mechanism for such review (*i.e.*, design defect liability), particularly given its express retention of state tort law in the Vaccine Act, see 42 U. S. C. §300aa–22(a). In any event, to the extent there is ambiguity as to how precisely Congress intended the "principle in Comment K" to apply to the covered vaccines, that ambiguity is explicitly resolved in petitioners' favor by the 1987 House Energy and Commerce Committee Report, H. R. Rep. No. 100–391, pt. 1, pp. 690–691 (hereinafter 1987 Report). See *infra* this page and 11–12.

for the compensation." 1987 Report 690. In 1987, Congress passed legislation to fund the compensation program. The House Energy and Commerce Committee Report[9] accompanying that legislation specifically stated that "the codification of Comment (k) of The Restatement (Second) of Torts was not intended to decide as a matter of law the circumstances in which a vaccine should be deemed unavoidably unsafe." *Id.*, at 691. The Committee noted that "[a]n amendment to establish . . . that a manufacturer's failure to develop [a] safer vaccine was not grounds for liability was rejected by the Committee during its original consideration of the Act." *Ibid.* In light of that rejection, the Committee emphasized that "there should be no misunderstanding that the Act undertook to decide as a matter of law whether vaccines were unavoidably unsafe or not," and that "[t]his question is left to the courts to determine in accordance with applicable law." *Ibid.*

To be sure, postenactment legislative history created by a subsequent Congress is ordinarily a hazardous basis from which to infer the intent of the enacting Congress. See *Sullivan* v. *Finkelstein*, 496 U. S. 617, 631–632 (1990) (SCALIA, J., concurring in part). But unlike ordinary postenactment legislative history, which is justifiably given little or no weight, the 1987 Report reflects the intent of the Congress that enacted the funding legislation necessary to give operative effect to the principal provisions of the Vaccine Act, including §22(b)(1).[10] Congress in

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[9] The Third Circuit's opinion below expressed uncertainty as to whether the 1987 Report was authored by the House Budget Committee or the House Energy and Commerce Committee. See 561 F. 3d 233, 250 (2009). As petitioners explain, although the Budget Committee compiled and issued the Report, the Energy and Commerce Committee wrote and approved the relevant language. Title IV of the Report, entitled "Committee on Energy and Commerce," comprises "two Committee Prints approved by the Committee on Energy and Commerce for inclusion in the forthcoming reconciliation bill." 1987 Report 377, 380.

[10] The majority suggests that the 1987 legislation creating the fund-

1987 had a number of options before it, including adopting an entirely different compensation scheme, as the Reagan administration was proposing;[11] establishing different limitations on tort liability, including eliminating design defect liability, as pharmaceutical industry leaders were advocating;[12] or not funding the compensation program at all, which would have effectively nullified the relevant portions of the Act. Because the tort reforms in the 1986 Act, including §22(b)(1), had no operative legal effect unless and until Congress provided funding for the compensation program, the views of the Congress that enacted that funding legislation are a proper and, indeed, authoritative guide to the meaning of §22(b)(1). Those views, as reflected in the 1987 Report, provide unequivocal confir-

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ing mechanism is akin to appropriations legislation and that giving weight to the legislative history of such legislation "would set a dangerous precedent." *Ante*, at 18. The difference, of course, is that appropriations legislation ordinarily funds congressional enactments that already have operative legal effect; in contrast, operation of the tort reforms in the 1986 Act, including §22(b)(1), was expressly conditioned on the enactment of a separate tax to fund the compensation program. See §323(a), 100 Stat. 3784. Accordingly, this Court's general reluctance to view appropriations legislation as modifying substantive legislation, see, *e.g.*, *TVA* v. *Hill*, 437 U. S. 153, 190 (1978), has no bearing here.

[11] See 1987 Report 700 (describing the administration's alternative proposal).

[12] See, *e.g.*, Hearings on Funding of the Childhood Vaccine Program before the Subcommittee on Select Revenue Measures of the House Committee on Ways and Means, 100th Cong., 1st Sess., 85 (1987) ("[T]he liability provisions of the 1986 Act should be amended to assure that manufacturers will not be found liable in the tort system if they have fully complied with applicable government regulations. In particular, manufacturers should not face liability under a 'design defect' theory in cases where plaintiffs challenge the decisions of public health authorities and federal regulators that the licensed vaccines are the best available way to protect children from deadly diseases" (statement of Robert B. Johnson, President, Lederle Laboratories Division, American Cyanamid Co.)).

mation of petitioners' reading of §22(b)(1).

In sum, the text, structure, and legislative history of the Vaccine Act are fully consistent with petitioners' reading of §22(b)(1). Accordingly, I believe §22(b)(1) exempts vaccine manufacturers from tort liability only upon a showing by the manufacturer in each case that the vaccine was properly manufactured and labeled, and that the side effects stemming from the vaccine's design could not have been prevented by a feasible alternative design that would have eliminated the adverse side effects without compromising the vaccine's cost and utility.

II

In contrast to the interpretation of §22(b)(1) set forth above, the majority's interpretation does considerable violence to the statutory text, misconstrues the legislative history, and draws the wrong conclusions from the structure of the Vaccine Act and the broader federal scheme regulating vaccines.

A

As a textual matter, the majority's interpretation of §22(b)(1) is fundamentally flawed in three central respects. First, the majority's categorical reading rests on a faulty and untenable premise. Second, its reading functionally excises 13 words from the statutory text, including the key term "unavoidable." And third, the majority entirely ignores the Vaccine Act's default rule preserving state tort law.

To begin, the majority states that "[a] side effect of a vaccine could *always* have been avoidable by use of a differently designed vaccine not containing the harmful element." *Ante*, at 7. From that premise, the majority concludes that the statute must mean that "the *design* of the vaccine is a given, not subject to question in the tort action," because construing the statute otherwise would

render §22(b)(1) a nullity. *Ibid.* A tort claimant, according to the majority, will always be able to point to a differently designed vaccine not containing the "harmful element," and if that were sufficient to show that a vaccine's side effects were not "unavoidable," the statute would preempt nothing.

The starting premise of the majority's interpretation, however, is fatally flawed. Although in the most literal sense, as the majority notes, a side effect can always be avoided "by use of a differently designed vaccine not containing the harmful element," *ibid.*, this interpretation of "unavoidable" would effectively read the term out of the statute, and Congress could not have intended that result. Indeed, §22(b)(1) specifically uses the conditional phrase "if the injury or death resulted from side effects that were unavoidable," which plainly indicates that Congress contemplated that there would be some instances in which a vaccine's side effects are "unavoidable" and other instances in which they are not. See *supra*, at 3. The majority's premise that a vaccine's side effects can always be "avoid[ed] by use of a differently designed vaccine not containing the harmful element," *ante*, at 7, entirely ignores the fact that removing the "harmful element" will often result in a less effective (or entirely ineffective) vaccine. A vaccine, by its nature, ordinarily employs a killed or weakened form of a bacteria or virus to stimulate antibody production;[13] removing that bacteria or virus might remove the "harmful element," but it would also necessarily render the vaccine inert. As explained above, the legislative history of the Vaccine Act and the cases interpreting comment *k* make clear that a side effect is

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[13] See American Academy of Pediatrics, Questions and Answers about Vaccine Ingredients (Oct. 2008), http://www.aap.org/immunization/families/faq/Vaccineingredients.pdf (all Internet materials as visited Feb. 18, 2011, and available in Clerk of Court's case file).

"unavoidable" for purposes of §22(b)(1) only where there is no feasible alternative design that would eliminate the side effect of the vaccine without compromising its cost and utility. See *supra*, at 7. The majority's premise—that side effects stemming from a vaccine's design are always avoidable—is thus belied by the statutory text and legislative history of §22(b)(1). And because its starting premise is invalid, its conclusion—that the design of a vaccine is not subject to challenge in a tort action—is also necessarily invalid.

The majority's reading suffers from an even more fundamental defect. If Congress intended to exempt vaccine manufacturers categorically from all design defect liability, it more logically would have provided: "No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the vaccine was properly prepared and was accompanied by proper directions and warnings." There would have been no need for Congress to include the additional 13 words "the injury or death resulted from side effects that were unavoidable even though." See *TRW Inc.* v. *Andrews*, 534 U. S. 19, 31 (2001) (noting "cardinal principle of statutory construction that a statute ought, upon the whole, to be so construed that, if it can be prevented, no clause, sentence, or word shall be superfluous, void, or insignificant" (internal quotation marks omitted)).

In *Bates* v. *Dow Agrosciences LLC*, 544 U. S. 431 (2005), this Court considered an analogous situation where an express pre-emption provision stated that certain States "'shall not impose or continue in effect any requirements for labeling or packaging in addition to or different from those required under this subchapter.'" *Id.*, at 436 (quoting 7 U. S. C. §136v(b) (2000 ed.)). The *Bates* Court stated:

> "Conspicuously absent from the submissions by [respondent] and the United States is any plausible alternative interpretation of 'in addition to or different from' that would give that phrase meaning. Instead, they appear to favor reading those words out of the statute, which would leave the following: 'Such State shall not impose or continue in effect any requirements for labeling or packaging.' This amputated version of [the statute] would no doubt have clearly and succinctly commanded the pre-emption of *all* state requirements concerning labeling. That Congress added the remainder of the provision is evidence of its intent to draw a distinction between state labeling requirements that are pre-empted and those that are not." 544 U. S., at 448–449.

As with the statutory interpretation rejected by this Court in *Bates*, the majority's interpretation of §22(b)(1) functionally excises 13 words out of the statute, including the key term "unavoidable." See *Duncan* v. *Walker*, 533 U. S. 167, 174 (2001) ("We are especially unwilling" to treat a statutory term as surplusage "when the term occupies so pivotal a place in the statutory scheme"). Although the resulting "amputated version" of the statutory provision "would no doubt have clearly and succinctly commanded the pre-emption of *all* state" design defect claims, the fact "[t]hat Congress added the remainder of the provision" is strong evidence of its intent not to pre-empt design defect claims categorically. *Bates*, 544 U. S., at 449; see also *American Home Prods. Corp.* v. *Ferrari*, 284 Ga. 384, 393, 668 S. E. 2d 236, 242 (2008) ("'If Congress had intended to deprive injured parties of a long available form of compensation, it surely would have expressed that intent more clearly'" (quoting *Bates*, 544 U. S., at 449)), cert. pending, No. 08–1120.

Strikingly, the majority concedes that its interpretation

renders 13 words of the statute entirely superfluous. See *ante*, at 12 ("The intervening passage ('the injury or death resulted from side effects that were unavoidable even though') is unnecessary. True enough"). Nevertheless, the majority contends that "the rule against giving a portion of text an interpretation which renders it superfluous . . . applies only if verbosity and prolixity can be eliminated by giving the offending passage, or the remainder of the text, a competing interpretation." *Ibid.* According to the majority, petitioners' reading of §22(b)(1) renders the "even though" clause superfluous because, to reach petitioners' desired outcome, "[i]t would suffice to say 'if the injury or death resulted from side effects that were unavoidable'—full stop." *Ibid.* As explained above, however, the "even though" clause establishes two additional prerequisites—proper manufacturing and proper labeling—to qualify for §22(b)(1)'s exemption from liability. Contrary to the majority's contention, then, the "even though" clause serves an important function by limiting the scope of the preemption afforded by the preceding "if" clause.[14]

The majority's only other textual argument is based on

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[14] In this manner, the "even though" clause functions in a "concessive subordinat[ing]" fashion, *ante*, at 11, in accord with normal grammatical usage. According to the majority, however, the "even though" clause "clarifies the word that precedes it" by "delineat[ing]" the conditions that make a side effect "unavoidable" under the statute. *Ante*, at 7. The majority's interpretation hardly treats the clause as "concessive," and indeed strains the meaning of "even though." In the majority's view, proper manufacturing and labeling are the sole prerequisites that render a vaccine's side effects unavoidable. Thus, an injurious side effect is unavoidable *because* the vaccine was properly prepared and labeled, not "even though" it was. The two conjunctions are not equivalent: The sentence "I am happy *even though* it is raining" can hardly be read to mean that "I am happy *because* it is raining." In any event, the more fundamental point is that petitioners' interpretation actually gives meaning to the words "even though," whereas the majority concedes that its interpretation effectively reads those words entirely out of the statute. See *supra* this page.

the *expressio unius*, *exclusio alterius* canon. According to the majority, because blackletter products liability law generally recognizes three different types of product defects, "[i]f all three were intended to be preserved, it would be strange [for Congress] to mention specifically only two"—namely, manufacturing and labeling defects in the "even though" clause—"and leave the third to implication." *Ante*, at 8. The majority's argument, however, ignores that the default rule under the Vaccine Act is that state law is preserved. As explained above, §22(a) expressly provides that the "[g]eneral rule" is that "State law shall apply to a civil action brought for damages for a vaccine-related injury or death." 42 U. S. C. §300aa–22(a). Because §22(a) already preserves state-law design defect claims (to the extent the exemption in §22(b)(1) does not apply), there was no need for Congress separately and expressly to preserve design defect claims in §22(b)(1). Indeed, Congress' principal aim in enacting §22(b)(1) was not to preserve manufacturing and labeling claims (those, too, were already preserved by §22(a)), but rather, to federalize comment *k*-type protection for "unavoidably unsafe" vaccines. The "even though" clause simply functions to limit the applicability of that defense. The lack of express language in §22(b)(1) specifically preserving design defect claims thus cannot fairly be understood as impliedly (and categorically) pre-empting such traditional state tort claims, which had already been preserved by §22(a).[15]

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[15]This Court, moreover, has long operated on "the assumption that the historic police powers of the States are not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress." *Altria Group, Inc.* v. *Good*, 555 U. S. ___, ___ (2008) (slip op., at 5) (internal quotation marks and alteration omitted). Given the long history of state regulation of vaccines, see Brief for Petitioners 3–6, the presumption provides an additional reason not to read §22(b)(1) as pre-empting all design defect claims, especially given Congress' inclusion of

The majority also suggests that if Congress wished to preserve design defect claims, it could have simply provided that manufacturers would be liable for "defective manufacture, defective directions or warning, and defective design." *Ante*, at 8 (internal quotation marks omitted). Putting aside the fact that §22(a) already preserves design defect claims (to the extent §22(b)(1) does not apply), the majority's proposed solution would not have fully effectuated Congress' intent. As the legislative history makes clear, Congress used the term "unavoidable" to effectuate its intent that the "principle in Comment K regarding 'unavoidably unsafe' products . . . apply to the vaccines covered in the bill." 1986 Report 26; see also 1987 Report 691. At the time of the Vaccine Act's enactment in 1986, at least one State had expressly rejected comment *k*,[16] while many others had not addressed the applicability of comment *k* specifically to vaccines or applied comment *k* to civil actions proceeding on a theory other than strict liability (*e.g.*, negligence[17]). A statute

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an express saving clause in the same statutory section, see 42 U. S. C. §300aa–22(a), and its use of the conditional "if" clause in defining the pre-emptive scope of the provision. See *Bates* v. *Dow Agrosciences LLC*, 544 U. S. 431, 449 (2005) ("In areas of traditional state regulation, we assume that a federal statute has not supplanted state law unless Congress has made such an intention clear and manifest" (internal quotation marks omitted)).

[16] See *Collins* v. *Eli Lilly Co.*, 116 Wis. 2d 166, 197, 342 N. W. 2d 37, 52 (1984) ("We conclude that the rule embodied in comment k is too restrictive and, therefore, not commensurate with strict products liability law in Wisconsin"). *Collins* did, however, "recognize that in some exigent circumstances it may be necessary to place a drug on the market before adequate testing can be done." *Ibid.* It thus adopted a narrower defense (based on "exigent circumstances") than that recognized in other jurisdictions that had expressly adopted comment *k*.

[17] See, *e.g.*, *Kearl*, 172 Cal. App. 3d, at 831, n. 15, 218 Cal. Rptr., at 465, n. 15 ("[T]he unavoidably dangerous product doctrine merely exempts the product from a strict liability design defect analysis; a plaintiff remains free to pursue his design defect theory on the basis of

that simply stated that vaccine manufacturers would be liable for "defective design" would be silent as to the availability of a comment *k*-type defense for "unavoidably unsafe" vaccines, and thus would not have fully achieved Congress' aim of extending greater liability protection to vaccine manufacturers by providing comment *k*-type protection in all civil actions as a matter of federal law.

B

The majority's structural arguments fare no better than its textual ones. The principal thrust of the majority's position is that, since nothing in the Vaccine Act or the FDA's regulations governing vaccines expressly mentions design defects, Congress must have intended to remove issues concerning the design of FDA-licensed vaccines from the tort system. *Ante*, at 13. The flaw in that reasoning, of course, is that the FDA's silence on design defects existed long before the Vaccine Act was enacted. Indeed, the majority itself concedes that the "FDA has never even spelled out in regulations the criteria it uses to decide whether a vaccine is safe and effective for its intended use."[18] *Ibid.* And yet it is undisputed that prior to the Act, vaccine manufacturers had long been subject to liability under state tort law for defective vaccine design. That the Vaccine Act did not itself set forth a comprehensive regulatory scheme with respect to design defects is thus best understood to mean not that Congress suddenly decided to change course *sub silentio* and pre-empt a

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negligence"); *Toner*, 112 Idaho, at 340, 732 P. 2d, at 309–310 ("The authorities universally agree that where a product is deemed unavoidably unsafe, the plaintiff is deprived of the advantage of a strict liability cause of action, but may proceed under a negligence cause of action").

[18] See 42 U. S. C. §262(a)(2)(C)(i)(I) ("The Secretary shall approve a biologics license application . . . on the basis of a demonstration that . . . the biological product that is the subject of the application is safe, pure, and potent").

longstanding, traditional category of state tort law, but rather, that Congress intended to leave the status quo alone (except, of course, with respect to those aspects of state tort law that the Act expressly altered). See 1987 Report 691 ("It is not the Committee's intention to preclude court actions under applicable law. The Committee's intent at the time of considering the Act . . . was . . . to leave otherwise applicable law unaffected, except as expressly altered by the Act").

The majority also suggests that Congress necessarily intended to pre-empt design defect claims since the aim of such tort suits is to promote the development of improved designs and provide compensation for injured individuals, and the Vaccine Act "provides other means for achieving both effects"—most notably through the no-fault compensation program and the National Vaccine Program. *Ante*, at 14, and nn. 57–60 (citing 42 U. S. C. §§300aa–1, 300aa–2(a)(1)–(3), 300aa–3, 300aa–25(b), 300aa–27(a)(1)). But the majority's position elides a significant difference between state tort law and the federal regulatory scheme. Although the Vaccine Act charges the Secretary of Health and Human Services with the obligation to "promote the development of childhood vaccines" and "make or assure improvements in . . . vaccines, and research on vaccines," §300aa–27(a), neither the Act nor any other provision of federal law places a legal *duty* on vaccine manufacturers to improve the design of their vaccines to account for scientific and technological advances. Indeed, the FDA does not condition approval of a vaccine on it being the most optimally designed among reasonably available alternatives, nor does it (or any other federal entity) ensure that licensed vaccines keep pace with technological and scientific advances.[19] Rather, the function of ensuring

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[19] See, *e.g.*, *Hurley* v. *Lederle Labs.*, 863 F. 2d 1173, 1177 (CA5 1988) ("[T]he FDA is a passive agency: it considers whether to approve

that vaccines are optimally designed in light of existing science and technology has traditionally been left to the States through the imposition of damages for design defects. Cf. *Bates*, 544 U. S., at 451 ("'[T]he specter of damage actions may provide manufacturers with added dynamic incentives to continue to keep abreast of all possible injuries stemming from use of their product[s] so as to forestall such actions through product improvement'"); *Wyeth* v. *Levine*, 555 U. S. ___, ___ (2009) (slip op., at 22–

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vaccine designs only if and when manufacturers come forward with a proposal"); *Jones* v. *Lederle Labs.*, 695 F. Supp. 700, 711 (EDNY 1988) ("[T]he agency takes the drugs and manufacturers as it finds them. While its goal is to oversee inoculation with the best possible vaccine, it is limited to reviewing only those drugs submitted by various manufacturers, regardless of their flaws"). Although the FDA has authority under existing regulations to revoke a manufacturer's biologics licenses, that authority can be exercised only where (as relevant here) "[t]he licensed product is not safe and effective for all of its intended uses." 21 CFR §601.5(b)(1)(vi) (2010); see §600.3(p) (defining "safety" as "relative freedom from harmful effect to persons affected, directly or indirectly, by a product when prudently administered, taking into consideration the character of the product in relation to the condition of the recipient at the time"). The regulation does not authorize the FDA to revoke a biologics license for a manufacturer's failure to adopt an optimal vaccine design in light of existing science and technology. See Conk, Is There a Design Defect in the Restatement (Third) of Torts: Products Liability? 109 Yale L. J. 1087, 1128–1129 (1999–2000) ("The FDA does not claim to review products for optimal design . . . . FDA review thus asks less of drug . . . manufacturers than the common law of products liability asks of other kinds of manufacturers"). At oral argument, counsel for *amicus* United States stated that the Centers for Disease Control and Prevention (CDC) routinely performs comparative analyses of vaccines that are already on the market. See Tr. of Oral Arg. 44–45; *id.*, at 52–53 (describing CDC's comparison of Sabin and Salk polio vaccines). Neither the United States nor any of the parties, however, has represented that CDC examines whether a safer alternative vaccine *could have been designed* given practical and scientific limits, the central inquiry in a state tort law action for design defect. CDC does not issue biologics licenses, moreover, and thus has no authority to require a manufacturer to adopt a different vaccine design.

23) (noting that the FDA has "traditionally regarded state law as a complementary form of drug regulation" as "[s]tate tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly").[20] The importance of the States' traditional regulatory role is only underscored by the unique features of the vaccine market, in which there are "only one or two manufacturers for a majority of the vaccines listed on the routine childhood immunization schedule." Brief for Respondent 55. The normal competitive forces that spur innovation and improvements to existing product lines in other markets thus operate with less force in the vaccine market, particularly for vaccines that have already been released and marketed to the public. Absent a clear statutory mandate to the contrary, there is no reason to think that Congress intended in the vaccine context to eliminate the traditional incentive and deterrence functions served by state tort liability in favor of a federal regulatory scheme providing only carrots and no sticks.[21] See *Levine*, 555 U. S., at ___ (slip op., at 18) ("The

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[20] Indeed, we observed in *Levine* that the FDA is perpetually understaffed and underfunded, see 555 U. S., at ___, n. 11 (slip op., at 22, n. 11), and the agency has been criticized in the past for its slow response in failing to withdraw or warn about potentially dangerous products, see, *e.g.*, L. Leveton, H. Sox, & M. Soto, Institute of Medicine, HIV and the Blood Supply: An Analysis of Crisis Decisionmaking (1995) (criticizing FDA response to transmission of AIDS through blood supply). These practical shortcomings reinforce the conclusion that "state law offers an additional, and important, layer of consumer protection that complements FDA regulation." *Levine*, 555 U. S., at ___ (slip op., at 23).

[21] The majority mischaracterizes my position as expressing a general "skeptic[ism] of preemption unless the congressional substitute operate[s] like the tort system." *Ante*, at 16. Congress could, of course, adopt a regulatory regime that operates differently from state tort systems, and such a difference is not necessarily a reason to question Congress' pre-emptive intent. In the specific context of the Vaccine Act, however, the relevant point is that this Court should not lightly assume

case for federal pre-emption is particularly weak where Congress has indicated its awareness of the operation of state law in a field of federal interest, and has nonetheless decided to stand by both concepts and to tolerate whatever tension there is between them." (internal quotation marks and alteration omitted)).

III

In enacting the Vaccine Act, Congress established a carefully wrought federal scheme that balances the competing interests of vaccine-injured persons and vaccine manufacturers. As the legislative history indicates, the Act addressed "two overriding concerns": "(a) the inadequacy—from both the perspective of vaccine-injured persons as well as vaccine manufacturers—of the current approach to compensating those who have been damaged by a vaccine; and (b) the instability and unpredictability of the childhood vaccine market." 1986 Report 7. When viewed in the context of the Vaccine Act as a whole, §22(b)(1) is just one part of a broader statutory scheme that balances the need for compensating vaccine-injured children with added liability protections for vaccine manufacturers to ensure a stable childhood vaccine market.

The principal innovation of the Act was the creation of the no-fault compensation program—a scheme funded entirely through an excise tax on vaccines.[22] Through that

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that Congress intended *sub silentio* to displace a longstanding species of state tort liability where, as here, Congress specifically included an express saving clause preserving state law, there is a long history of state-law regulation of vaccine design, and pre-emption of state law would leave an important regulatory function—*i.e.*, ensuring optimal vaccine design—entirely unaddressed by the congressional substitute.

[22]The majority's suggestion that "vaccine manufacturers fund from their sales" the compensation program is misleading. *Ante*, at 15. Although the manufacturers nominally pay the tax, the amount of the tax is specifically included in the vaccine price charged to purchasers. See CDC Vaccine Price List (Feb. 15, 2011), http://www.cdc.gov/

program, Congress relieved vaccine manufacturers of the burden of compensating victims of vaccine-related injuries in the vast majority of cases[23]—an extremely significant economic benefit that "functionally creat[es] a valuable insurance policy for vaccine-related injuries." Reply Brief for Petitioners 10. The structure and legislative history, moreover, point clearly to Congress' intention to divert would-be tort claimants into the compensation program, rather than eliminate a longstanding category of traditional tort claims. See 1986 Report 13 ("The Committee anticipates that the speed of the compensation program, the low transaction costs of the system, the no-fault nature of the required findings, and the relative certainty and generosity of the system's awards will divert a significant number of potential plaintiffs from litigation"). Indeed, although complete pre-emption of tort claims would have eliminated the principal source of the "unpredictability" in the vaccine market, Congress specifically chose *not* to pre-empt state tort claims categorically. See 42 U. S. C. §300aa–22(a) (providing as a "[g]eneral rule" that "State law shall apply to a civil action brought for damages for a vaccine-related injury or death"). That decision reflects Congress' recognition that court actions are essential

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vaccines/programs/vfc/cdc-vac-price-list.htm. Accordingly, the only way the vaccine manufacturers can be said to actually "fund" the compensation program is if the cost of the excise tax has an impact on the number of vaccines sold by the vaccine manufacturer. The majority points to no evidence that the excise tax—which ordinarily amounts to 75 cents per dose, 26 U. S. C. §4131(b)—has any impact whatsoever on the demand for vaccines.

[23] See Brief for United States as *Amicus Curiae* 28 ("Department of Justice records indicate that 99.8% of successful Compensation Program claimants have accepted their awards, foregoing any tort remedies against vaccine manufacturers"); S. Plotkin, W. Orenstein, & P. Offit, Vaccines 1673 (5th ed. 2008) (noting that "[v]irtually all . . . petitioners, even those who were not awarded compensation" under the compensation program, choose to accept the program's determination).

because they provide injured persons with significant procedural tools—including, most importantly, civil discovery—that are not available in administrative proceedings under the compensation program. See §§300aa–12(d)(2)(E), (d)(3). Congress thus clearly believed there was still an important function to be played by state tort law.

Instead of eliminating design defect liability entirely, Congress enacted numerous measures to reduce manufacturers' liability exposure, including a limited regulatory compliance presumption of adequate warnings, see §300aa–22(b)(2), elimination of claims based on failure to provide direct warnings to patients, §300aa–22(c), a heightened standard for punitive damages, §300aa–23(d)(2), and, of course, immunity from damages for "unavoidable" side effects, §300aa–22(b)(1). Considered in light of the Vaccine Act as a whole, §22(b)(1)'s exemption from liability for unavoidably unsafe vaccines is just one part of a broader statutory scheme that reflects Congress' careful balance between providing adequate compensation for vaccine-injured children and conferring substantial benefits on vaccine manufacturers to ensure a stable and predictable childhood vaccine supply.

The majority's decision today disturbs that careful balance based on a bare policy preference that it is better "to leave complex epidemiological judgments about vaccine design to the FDA and the National Vaccine Program rather than juries." *Ante*, at 15.[24] To be sure, reasonable minds can disagree about the wisdom of having juries weigh the relative costs and benefits of a particular vaccine design. But whatever the merits of the majority's

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[24] JUSTICE BREYER's separate concurrence is even more explicitly policy driven, reflecting his own preference for the "more expert judgment" of federal agencies over the "less expert" judgment of juries. *Ante*, at 5.

policy preference, the decision to bar all design defect claims against vaccine manufacturers is one that Congress must make, not this Court.[25] By construing §22(b)(1) to

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[25] Respondent notes that there are some 5,000 petitions alleging a causal link between certain vaccines and autism spectrum disorders that are currently pending in an omnibus proceeding in the Court of Federal Claims (Vaccine Court). Brief for Respondent 56–57. According to respondent, a ruling that §22(b)(1) does not pre-empt design defect claims could unleash a "crushing wave" of tort litigation that would bankrupt vaccine manufacturers and deplete vaccine supply. *Id.*, at 28. This concern underlies many of the policy arguments in respondent's brief and appears to underlie the majority and concurring opinions in this case. In the absence of any empirical data, however, the prospect of an onslaught of autism-related tort litigation by claimants denied relief by the Vaccine Court seems wholly speculative. As an initial matter, the special masters in the autism cases have thus far uniformly rejected the alleged causal link between vaccines and autism. See Brief for American Academy of Pediatrics et al. as *Amici Curiae* 20–21, n. 4 (collecting cases). To be sure, those rulings do not necessarily mean that no such causal link exists, cf. Brief for United States as *Amicus Curiae* 29 (noting that injuries have been added to the Vaccine Injury Table for existing vaccines), or that claimants will not ultimately be able to prove such a link in a state tort action, particularly with the added tool of civil discovery. But these rulings do highlight the substantial hurdles to recovery a claimant faces. See *Schafer* v. *American Cyanamid Co.*, 20 F. 3d 1, 5 (CA1 1994) ("[A] petitioner to whom the Vaccine Court gives nothing may see no point in trying to overcome tort law's yet more serious obstacles to recovery"). Trial courts, moreover, have considerable experience in efficiently handling and disposing of meritless products liability claims, and decades of tort litigation (including for design defect) in the prescription-drug context have not led to shortages in prescription drugs. Despite the doomsday predictions of respondent and the various *amici* cited by the concurrence, *ante*, at 6–7, the possibility of a torrent of meritless lawsuits bankrupting manufacturers and causing vaccine shortages seems remote at best. More fundamentally, whatever the merits of these policy arguments, the issue in this case is what Congress has decided, and as to that question, the text, structure, and legislative history compel the conclusion that Congress intended to leave the courthouse doors open for children who have suffered severe injuries from defectively designed vaccines. The majority's policy-driven decision to the contrary usurps Congress' role and deprives such vaccine-injured children of a key remedy that Congress intended them to have.

pre-empt all design defect claims against vaccine manufacturers for covered vaccines, the majority's decision leaves a regulatory vacuum in which no one—neither the FDA nor any other federal agency, nor state and federal juries—ensures that vaccine manufacturers adequately take account of scientific and technological advancements. This concern is especially acute with respect to vaccines that have already been released and marketed to the public. Manufacturers, given the lack of robust competition in the vaccine market, will often have little or no incentive to improve the designs of vaccines that are already generating significant profit margins. Nothing in the text, structure, or legislative history remotely suggests that Congress intended that result.

I respectfully dissent.

Vaccine Schedule - Birth through 18 years

1983

DTP - 2 months
OPV - 2 months
DTP - 4 months
OPV - 4 months
DTP - 6 months
MMR - 15 months
DTP - 18 months
OPV - 18 months
DTP - 4 years
OPV - 4 years
Td - 15 years

Source: www.CDC.gov

Influenza - pregnancy
Tdap - pregnancy
Hep B - birth
Hep B - 2 months
Rotavirus - 2 months
DTaP - 2 months
Hib - 2 months
PCV - 2 months
IPV - 2 months
Rotavirus - 4 months
DTaP - 4 months
Hib - 4 months
PCV - 4 months
IPV - 4 months
Hep B - 6 months
Rotavirus - 6 months
DTaP - 6 months
Hib - 6 months
PCV - 6 months
IPV - 6 months
Influenza - 6 months
Influenza - 7 months

2019

Hib - 12 months
PCV - 12 months
MMR - 12 months
Varicella - 12 months
Hep A - 12 months
DTaP - 18 months
Influenza - 18 months
Hep A - 18 months
Influenza - 30 months
Influenza - 42 months
DTaP - 4 years
IPV - 4 years
MMR - 4 years
Varicella - 4 years
Influenza - 5 years
Influenza - 6 years
Influenza - 7 years
Influenza - 8 years
Influenza - 9 years
Influenza - 10 years
HPV - 11 years
HPV - 11 years
Influenza - 11 years
Tdap - 12 years
Influenza - 12 years
Meningococcal - 12 years
Influenza - 13 years
Influenza - 14 years
Influenza - 15 years
Influenza - 16 years
Meningococcal - 16 years
Influenza - 17 years
Influenza - 18 years

2019
Total doses: 69

1983
Total doses: 24

In 1986, the National Childhood Vaccine Injury Act was signed into law.
This freed vaccine manufacturers of ALL liability resulting from injury or death from their products.

- NCVIA
- VAERS
- NVICP

To date there is over **4 BILLION DOLLARS** paid out for vaccine injury and death.

Wisconsin United for freedom

www.wisconsinunitedforfreedom.org

VACCINE DOSES for U.S. CHILDREN

1962	1983	2018	
5	**24**	**72**	
Doses	**Doses**	**Doses**	
Polio	DTP (2 months)	Influenza (pregnancy)	Influenza (18 months)
Smallpox	OPV (2 months)	DTaP (pregnancy)	Hep A (18 months)
DTP	DTP)4 months)	Hep B (birth)	Influenza (30 months)
	OPV (4 months)	Hep B (2 months)	Influenza (42 months)
	DTP (6 months)	Rotavirus (2 months)	DTaP (4 years)
	MMR (15 months)	DTaP (2 months)	IPV (4 years)
	DTP (18 months)	HIB (2 months)	MMR (4 years)
	OPV (18 months)	PCV (2 months)	Varicella (4 years)
	DTP (4 years)	IPV (2 months)	Influenza (5 years)
	OPV (4 years)	Rotavirus (4 months)	Influenza (6 years)
	Td (15 years)	DTaP (4 months)	Influenza (7 years)
		HIB (4 months)	Influenza (8 years)
		PCV (4 months)	Influenza (9 years)
		IPV (4 months)	HPV (9 years)
		Hep B (6 months)	Influenza (10 years)
		Rotavirus (6 months)	HPV (10 years)
		DTaP (6 months)	Influenza (11 years)
		HIB (6 months)	HPV (11 years)
		PCV (6 months)	DtaP (12 years)
		IPV (6 months)	Influenza (12 years)
		Influenza (6 months)	Meningococcal (12 years)
		Influenza (7 months)	Influenza (13 years)
		HIB (12 months)	Influenza (14 years)
		PCV (12 months)	Influenza (15 years)
		MMR (12 months)	Influenza (16 years)
		Varicella (12 months)	Meningococcal (16 years)
		Hep A (12 months)	Influenza (17 years)
		DTaP (18 months)	Influenza (18 years)

**In 1986, pharmaceutical companies producing vaccines were given full federal protection from lawsuits resulting from vaccine injury or death via the Childhood Vaccine Act passed by Congress. If vaccines are so safe, why did they need a law to protect from liability?*
*After this law, vaccines became **HIGHLY** profitable. There are almost 300 vaccines in development, and mandatory vaccine laws for children – and **ADULTS** – being pushed in most states.*

*The US gives 2-3x more vaccines to children than most developed countries, yet we have skyrocketing rates of childhood issues that are **NOT** seen in other countries. Things like asthma, childhood diabetes, food allergies, childhood leukemia, developmental delays, tics, ADHD, autism, lupus, arthritis, eczema, epilepsy, Alzheimers, brain damage, etc… **It's NOT a coincidence***

*Vaccines contain toxic chemicals that do **NOT** belong in our bodies, such as aluminum, (known to cause brain and developmental damage even in small doses), polysorbate 80, MSG and formaldehyde (known to cause cancer in humans).*

RESEARCH, don't REGRET

www.LearnTheRisk.org

VACCINE DOSES for U.S. CHILDREN

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	OPV (18 months)	PCV (2 months)	Varicella (4 years)
	DTP (4 years)	IPV (2 months)	Influenza (5 years)
	OPV (4 years)	Rotavirus (4 months)	Influenza (6 years)
	Td (15 years)	DTaP (4 months)	Influenza (7 years)
		HIB (4 months)	Influenza (8 years)
		PCV (4 months)	Influenza (9 years)
		IPV (4 months)	HPV (9 years)
		Hep B (6 months)	Influenza (10 years)
		Rotavirus (6 months)	HPV (10 years)
		DTaP (6 months)	Influenza (11 years)
		HIB (6 months)	HPV (11 years)
		PCV (6 months)	DtaP (12 years)
		IPV (6 months)	Influenza (12 years)
		Influenza (6 months)	Meningococcal (12 years)
		Influenza (7 months)	Influenza (13 years)
		HIB (12 months)	Influenza (14 years)
		PCV (12 months)	Influenza (15 years)
		MMR (12 months)	Influenza (16 years)
		Varicella (12 months)	Meningococcal (16 years)
		Hep A (12 months)	Influenza (17 years)
		DTaP (18 months)	Influenza (18 years)

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RESEARCH, don't REGRET

www.LearnTheRisk.org

Vaccine Excipient Summary

Excipients Included in U.S. Vaccines, by Vaccine

In addition to weakened or killed disease antigens (viruses or bacteria), vaccines contain very small amounts of other ingredients – excipients.

Some excipients are added to a vaccine for a specific purpose. These include:
Preservatives, to prevent contamination. For example, thimerosal.
Adjuvants, to help stimulate a stronger immune response. For example, aluminum salts.
Stabilizers, to keep the vaccine potent during transportation and storage. For example, sugars or gelatin.

Others are residual trace amounts of materials that were used during the manufacturing process and removed. These can include:
Cell culture materials, used to grow the vaccine antigens. For example, egg protein, various culture media.
Inactivating ingredients, used to kill viruses or inactivate toxins. For example, formaldehyde.
Antibiotics, used to prevent contamination by bacteria. For example, neomycin.

The following table lists substances, other than active ingredients (i.e., antigens), shown in the manufacturers' package insert (PI) as being contained in the final formulation of each vaccine. **Note: Substances used in the manufacture of a vaccine but not listed as contained in the final product (e.g., culture media) can be found in each PI, but are not shown on this table.** Each PI, which can be found on the FDA's website (see below) contains a description of that vaccine's manufacturing process, including the amount and purpose of each substance. In most PIs, this information is found in Section 11: "Description."

All information was extracted from manufacturers' package inserts.
If in doubt about whether a PI has been updated since this table was prepared, check the FDA's website at:
http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm

Vaccine	Contains
Adenovirus	monosodium glutamate, sucrose, D-mannose, D-fructose, dextrose, human serum albumin, potassium phosphate, plasdone C, anhydrous lactose, microcrystalline cellulose, polacrilin potassium, magnesium stearate, cellulose acetate phthalate, alcohol, acetone, castor oil, FD&C Yellow #6 aluminum lake dye
Anthrax (Biothrax)	aluminum hydroxide, sodium chloride, benzethonium chloride, formaldehyde
BCG (Tice)	glycerin, asparagine, citric acid, potassium phosphate, magnesium sulfate, iron ammonium citrate, lactose
Cholera (Vaxchora)	ascorbic acid, hydrolyzed casein, sodium chloride, sucrose, dried lactose, sodium bicarbonate, sodium carbonate
DT (Sanofi)	aluminum phosphate, isotonic sodium chloride, formaldehyde
DTaP (Daptacel)	aluminum phosphate, formaldehyde, glutaraldehyde, 2-phenoxyethanol
DTaP (Infanrix)	formaldehyde, aluminum hydroxide, sodium chloride, polysorbate 80 (Tween 80)
DTaP-IPV (Kinrix)	Formaldehyde, aluminum hydroxide, sodium chloride, polysorbate 80 (Tween 80), neomycin sulfate, polymyxin B
DTaP-IPV (Quadracel)	formaldehyde, aluminum phosphate, 2-phenoxyethanol, polysorbate 80, glutaraldehyde, neomycin, polymyxin B sulfate, bovine serum albumin
DTaP-HepB-IPV (Pediarix)	formaldehyde, aluminum hydroxide, aluminum phosphate, sodium chloride, polysorbate 80 (Tween 80), neomycin sulfate, polymyxin B, yeast protein
DTaP-IPV/Hib (Pentacel)	aluminum phosphate, polysorbate 80, sucrose, formaldehyde, glutaraldehyde, bovine serum albumin, 2-phenoxyethanol, neomycin, polymyxin B sulfate
Hib (ActHIB)	sodium chloride, formaldehyde, sucrose
Hib (Hiberix)	formaldehyde, sodium chloride, lactose
Hib (PedvaxHIB)	amorphous aluminum hydroxyphosphate sulfate, sodium chloride
Hep A (Havrix)	MRC-5 cellular proteins, formalin, aluminum hydroxide, amino acid supplement, phosphate-buffered saline solution, polysorbate 20, neomycin sulfate, aminoglycoside antibiotic
Hep A (Vaqta)	amorphous aluminum hydroxyphosphate sulfate, non-viral protein, DNA, bovine albumin, formaldehyde, neomycin, sodium borate, sodium chloride, other process chemical residuals
Hep B (Engerix-B)	aluminum hydroxide, yeast protein, sodium chloride, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate
Hep B (Recombivax)	formaldehyde, potassium aluminum sulfate, amorphous aluminum hydroxyphosphate sulfate, yeast protein

Vaccine	Contains
Hep B (Heplisav-B)	yeast protein, yeast DNA, deoxycholate, phosphorothioate linked oligodeoxynucleotide, sodium phosphate, dibasic dodecahydrate, sodium chloride, monobasic dehydrate, polysorbate 80
Hep A/Hep B (Twinrix)	MRC-5 human diploid cells, formalin, aluminum phosphate, aluminum hydroxide, amino acids, sodium chloride, phosphate buffer, polysorbate 20, neomycin sulfate, yeast protein, water
Human Papillomavirus (HPV) (Gardasil 9)	amorphous aluminum hydroxyphosphate sulfate, sodium chloride, L-histidine, polysorbate 80, sodium borate, yeast protein
Influenza (Afluria) Trivalent & Quadrivalent	sodium chloride, monobasic sodium phosphate, dibasic sodium phosphate, monobasic potassium phosphate, potassium chloride, calcium chloride, sodium taurodeoxycholate, ovalbumin, sucrose, neomycin sulfate, polymyxin B, beta-propiolactone, thimerosal (multi-dose vials)
Influenza (Fluad)	squalene, polysorbate 80, sorbitan trioleate, sodium citrate dehydrate, citric acid monohydrate, neomycin, kanamycin, barium, hydrocortisone, egg proteins, cetyltrimethylammonium bromide (CTAB), formaldehyde
Influenza (Fluarix) Quadrivalent	octoxynol-10 (TRITON X-100), α-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80), hydrocortisone, gentamicin sulfate, ovalbumin, formaldehyde, sodium deoxycholate, sodium phosphate-buffered isotonic sodium chloride
Influenza (Flublok) Quadrivalent	sodium chloride, monobasic sodium phosphate, dibasic sodium phosphate, polysorbate 20 (Tween 20), baculovirus and *Spodoptera frugiperda* cell proteins, baculovirus and cellular DNA, Triton X-100
Influenza (Flucelvax) Quadrivalent	Madin Darby Canine Kidney (MDCK) cell protein, phosphate buffered saline, protein other than HA, MDCK cell DNA, polysorbate 80, cetyltrimethlyammonium bromide, and β-propiolactone, Thimerosal (multi-dose vials)
Influenza (Flulaval) Quadrivalent	ovalbumin, formaldehyde, sodium deoxycholate, α-tocopheryl hydrogen succinate, polysorbate 80, thimerosal (multi-dose vials), phosphate-buffered saline solution
Influenza (Fluzone) Quadrivalent	formaldehyde, egg protein, octylphenol ethoxylate (Triton X-100), sodium phosphate-buffered isotonic sodium chloride solution, thimerosal (multi-dose vials)
Influenza (Fluzone) High Dose	egg protein, octylphenol ethoxylate (Triton X-100), sodium phosphate-buffered isotonic sodium chloride solution, formaldehyde
Influenza (FluMist) Quadrivalent	monosodium glutamate, hydrolyzed porcine gelatin, arginine, sucrose, dibasic potassium phosphate, monobasic potassium phosphate, ovalbumin, gentamicin sulfate, ethylenediaminetetraacetic acid (EDTA)
Japanese Encephalitis (Ixiaro)	aluminum hydroxide, protamine sulfate, formaldehyde, bovine serum albumin, Vero cell DNA, sodium metabisulphite, Vero cell protein
Meningococcal (MenACWY-Menactra)	sodium phosphate-buffered isotonic sodium chloride solution, formaldehyde, diphtheria toxoid
Meningococcal (MenACWY-Menveo)	formaldehyde, CRM_{197} protein
Meningococcal (MenB – Bexsero)	aluminum hydroxide, sodium chloride, histidine, sucrose, kanamycin
Meningococcal (MenB – Trumenba)	polysorbate 80, aluminum phosphate, histidine buffered saline
MMR (MMR-II)	vitamins, amino acids, fetal bovine serum, sucrose, glutamate, recombinant human albumin, neomycin, sorbitol, hydrolyzed gelatin, sodium phosphate, sodium chloride
MMRV (ProQuad) (Frozen: Recombinant Albumin)	MRC-5 cells including DNA and protein, sucrose, hydrolyzed gelatin, sodium chloride, sorbitol, monosodium L-glutamate, sodium phosphate dibasic, recombinant human albumin, sodium bicarbonate, potassium phosphate monobasic, potassium chloride; potassium phosphate dibasic, neomycin, bovine calf serum
MMRV (ProQuad) (Frozen: Human Serum Albumin)	MRC-5 cells including DNA and protein, sucrose, hydrolyzed gelatin, sodium chloride, sorbitol, monosodium L-glutamate, sodium phosphate dibasic, human albumin, sodium bicarbonate, potassium phosphate monobasic, potassium chloride; potassium phosphate dibasic, neomycin, bovine calf serum
MMRV (ProQuad) (Refrigerator Stable)	MRC-5 cells including DNA and protein, sucrose, hydrolyzed gelatin, urea, sodium chloride, sorbitol, monosodium L-glutamate, sodium phosphate, recombinant human albumin, sodium bicarbonate, potassium phosphate, potassium chloride, neomycin, bovine serum albumin

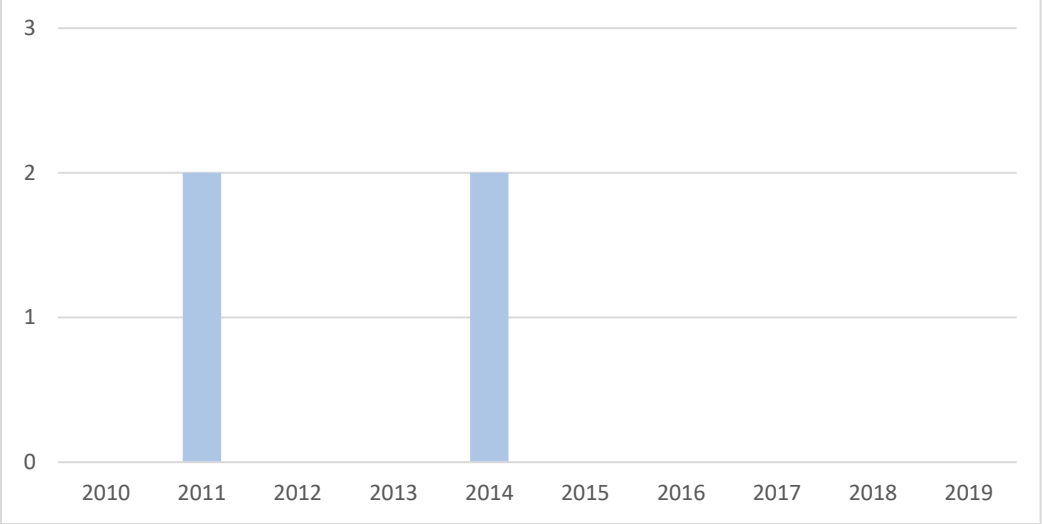
Vaccine	Contains
Pneumococcal (PCV13 – Prevnar 13)	CRM_{197} carrier protein, polysorbate 80, succinate buffer, aluminum phosphate
Pneumococcal (PPSV-23 – Pneumovax)	phenol
Polio (IPV – Ipol)	calf bovine serum albumin, 2-phenoxyethanol, formaldehyde, neomycin, streptomycin, polymyxin B, M-199 medium
Rabies (Imovax)	human albumin, neomycin sulfate, phenol red, beta-propriolactone
Rabies (RabAvert)	chicken protein, polygeline (processed bovine gelatin), human serum albumin, potassium glutamate, sodium EDTA, ovalbumin, neomycin, chlortetracycline, amphotericin B
Rotavirus (RotaTeq)	sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, cell culture media, fetal bovine serum *[DNA from porcine circoviruses (PCV) 1 and 2 has been detected in RotaTeq. PCV-1 and PCV-2 are not known to cause disease in humans.]*
Rotavirus (Rotarix)	Dextran, Dulbecco's Modified Eagle Medium (sodium chloride, potassium chloride, magnesium sulfate, ferric (III) nitrate, sodium phosphate, sodium pyruvate, D-glucose, concentrated vitamin solution, L-cystine, L-tyrosine, amino acids, L-glutamine, calcium chloride, sodium hydrogenocarbonate, and phenol red), sorbitol, sucrose, calcium carbonate, sterile water, xanthan *[Porcine circovirus type 1 (PCV-1) is present in Rotarix. PCV-1 is not known to cause disease in humans.]*
Smallpox (Vaccinia) (ACAM2000)	HEPES, 2% human serum albumin, 0.5 - 0.7% sodium chloride USP, 5% Mannitol USP, neomycin, polymyxin B, 50% Glycerin USP, 0.25% phenol USP
Td (Tenivac)	aluminum phosphate, formaldehyde, ammonium sulfate, sodium chloride, water
Td (Mass Biologics)	aluminum phosphate, formaldehyde, thimerosal
Tdap (Adacel)	aluminum phosphate, formaldehyde, 2-phenoxyethanol, glutaraldehyde
Tdap (Boostrix)	formaldehyde, aluminum hydroxide, sodium chloride, polysorbate 80
Typhoid (Typhim Vi)	formaldehyde, phenol, polydimethylsiloxane, disodium phosphate, monosodium phosphate, sodium chloride, sterile water
Typhoid (Vivotif Ty21a)	sucrose, ascorbic acid, amino acids, lactose, magnesium stearate. gelatin
Varicella (Varivax) *Frozen*	MRC-5 human diploid cells, including DNA & protein, sucrose, hydrolyzed gelatin, sodium chloride, monosodium L-glutamate, sodium phosphate dibasic, sodium phosphate monobasic, potassium phosphate monobasic, potassium chloride, EDTA, neomycin, fetal bovine serum
Varicella (Varivax) *Refrigerator Stable*	MRC-5 human diploid cells, including DNA & protein, sucrose, hydrolyzed gelatin, sodium chloride, monosodium L-glutamate, urea, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride, neomycin, bovine calf serum
Yellow Fever (YF-Vax)	sorbitol, gelatin, sodium chloride, egg protein
Zoster (Shingles) (Zostavax) *Frozen*	MRC-5 human diploid cells, including DNA & protein, sucrose, hydrolyzed porcine gelatin, sodium chloride, monosodium L-glutamate, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride; neomycin, bovine calf serum
Zoster (Shingles) (Zostavax) *Refrigerator Stable*	MRC-5 human diploid cells, including DNA & protein, sucrose, hydrolyzed porcine gelatin, urea, sodium chloride, monosodium L-glutamate, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride, neomycin, bovine calf serum
Zoster (Shingles) (Shingrix)	sucrose, sodium chloride, dioleoyl phosphatidylcholine (DOPC), 3-*O*-desacl-4'monophosphoryl lipid A (MPL), QS-21 (a saponin purified from plant extract *Quillaja saponaria* Molina), potassium dihydrogen phosphate, cholesterol, sodium dihydrogen phosphate dihydrate, disodium phosphate anhydrous, dipotassium phosphate, polysorbate 80, host cell protein and DNA

A table listing vaccine excipients and media *by excipient* is published by the Institute for Vaccine Safety at Johns Hopkins University, and can be found at http://www.vaccinesafety.edu/components-Excipients.htm.

January 2019

NUMBER OF MEASLES CASES REPORTED BY YEAR IN WISCONSIN

2010-2019 (as of September 12, 2019)



In 2014, two Wisconsin residents were infected with measles. One was believed to be infected at a U.S. airport while waiting for a domestic flight and the other had travelled internationally.

Source: Wisconsin Department of Health. Vaccine-Preventable Diseases Surveillance Summary Wisconsin, 2018 P-02321 (April 2019)

Measles outbreaks ARE NOT occurring in our Wisconsin Schools

In 2019, there have been 1,241 reported cases of measles in the U.S. out of a population of over 329,000,000. The percentage of people infected with measles in the U.S. in 2019 is 0.0003772%. The death rate from measles in the U.S. in 2019 is 0.

Sources: U.S. Census Bureau U.S Population (Accessed Sept 17, 2019); CDC Measles Cases and Outbreaks Sept. 12, 2019

Wisconsin's vaccination rates have remained stable. In 2018-2019, only 1.1% of Wisconsin students had waived all immunizations.

In 2018-2019, 4.6% of parents opted to use the Personal Conviction Exemption. Most parents who opt for an exemption have children who are **partially vaccinated**. A vaccine exemption is filed regardless of whether the exemption is filed for one dose or all doses. The Wisconsin Department of Health **does not collect data** to determine the exact number of vaccines or type of vaccine that are being waived by Pre-K through 12th grade students.

Source: Wisconsin Department of Health – WISCONSIN SCHOOL IMMUNIZATION RATES 2018-2019 SCHOOL YEAR. P-01894 (Rev. 04/2019)

According to the Wisconsin Department of Health:

Schools are required to submit vaccination data by the 40th day of the school year. While only 91.9% of students met the minimum requirement at the time the data was submitted, we do not know whether or not the minimum requirement data increased. The Wisconsin Department of Health ***DOES NOT FOLLOW UP*** with schools to find out whether children who are "behind schedule", "in process" or who have "no records" are in compliance **at any point** during the school year.

According the CDC:

"Vaccination coverage among kindergartners remained high; however, schools can improve coverage by following up with students who are provisionally enrolled, in a grace period, or lacking complete documentation of required vaccinations."

Source: CDC Vaccination Coverage for Selected Vaccines and Exemption Rates Among Children in Kindergarten — United States, 2017–18 School Year *MMWR* Oct. 12, 2018; 67(40);1115–1122

VACCINE FACTS

Vaccine manufacturers, the doctors, and providers who administer vaccines are completely shielded from liability for vaccine injuries and deaths. The law passed by Congress in 1986 establishing the National Vaccine Injury Compensation Program [i] and the 2011 Supreme Court Decision BRUESEWITZ ET AL. *v*. WYETH LLC, FKA WYETH, INC., ET AL [ii] took away the right for those injured or killed by vaccines to sue the vaccine manufacturer in a civil court of law. There are **NO incentives** for pharmaceutical companies to assure that their products are safe.

Since 1989, the U.S. Government has paid out over $4.1 billion dollars to vaccine victims through the National Vaccine Compensation Program.[iii] This money does not come from the pharmaceutical companies who make the vaccines that cause these injuries and death. The program is funded by U.S. taxpayers, through a 75 cent tax levied on all administered vaccines.[iv]

The CDC currently recommends that all children receive 50 doses of 14 different vaccines between the day of birth and age six and at least 69 doses of 16 vaccines between the day of birth and age eighteen.[v] This more than doubles the government childhood schedule of 34 doses of 11 different vaccines in the year 2000.[vi] In the past 15 years, 35 doses and 5 more unique vaccines have been added to the schedule. While adding vaccine after vaccine and dose after dose, **the CDC has yet to do a *single study* on whether or not this ever growing vaccine schedule is actually safe for our children.** There is no end in sight to the number of vaccines that could be added to the schedule, with over 260 vaccines currently in development.[vii]

The U.S. Vaccine Market alone was $36.45 Billion in 2018 and expected to reach $50.42 billion by 2023.[viii] This is a powerful industry with lots of resources to lobby and influence policy to remove parental rights to be able to delay or decline a vaccine. The industry benefits from forced vaccination. In the first 3 months of 2019, the 10 largest pharmaceutical companies have spent over $31 million dollars on Congressional Lobbying efforts. Merck, the maker of the MMR vaccine, has spent over $4.36 million dollars to lobby Congress.[ix]

Vaccine risks are facts, not opinions. As of May 31, 2019, **in Wisconsin alone,** there have been more than **11,794 reports** of vaccine reactions, hospitalizations, injuries and deaths following vaccinations made to the federal Vaccine Adverse Events Reporting System (VAERS), including **65 related deaths, 648 hospitalizations, and 208 related disabilities**.[x] VAERS is a VOLUNTARY reporting system and a 3 year review completed by the Harvard Medical School and funded by the U.S. Health and Human Services (HHS) found that **"fewer than 1% of vaccine adverse events are reported"** to VAERS.[xi]

The 2013 IOM Committee, which examined the safety of the current federally recommended early childhood vaccine schedule found that it had not been fully scientifically evaluated: ***"Most vaccine-related research focuses on the outcomes of single immunizations or combinations of vaccines administered at a single visit. Although each new vaccine is evaluated in the context of the overall immunization schedule that existed at the time of review of that vaccine, elements of the schedule are not evaluated once it is adjusted to accommodate a new vaccine.***

Thus, key elements of the entire schedule – the number, frequency, timing, order and age at administration of vaccines – have not been systematically examined in research studies." [xii]

References

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[i] U.S. Code 42 USC CHAPTER 6A, SUBCHAPTER XIX, Part 2: National Vaccine Injury Compensation Program From Title 42—THE PUBLIC HEALTH AND WELFARE - CHAPTER 6A—PUBLIC HEALTH SERVICE SUBCHAPTER XIX—VACCINES

[ii] U.S. Code 42 USC CHAPTER 6A, SUBCHAPTER XIX, Part 2: National Vaccine Injury Compensation Program From Title 42—THE PUBLIC HEALTH AND WELFARE - CHAPTER 6A—PUBLIC HEALTH SERVICE SUBCHAPTER XIX—VACCINES

[iii] U.S. Department of Health and Human Services. National Vaccine Injury Compensation Program Data—Sept 1, 2019. *National Vaccine Injury Compensation Program*. Sept.1, 2019

[iv] U.S. Department of Health and Human Services. About the National Vaccine Injury Compensation Program. *National Vaccine Injury Compensation Program*. June 2019

[v] CDC Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2019 Feb. 5, 2019

[vi] CDC Notice to Readers: Recommended Childhood Immunization Schedule -- United States, 2000 *MMWR* Jan. 21, 2000; 49(02);35-38,47

[vii] Pharmaceutical Research and Manufacturers of America (PHRMA) VACCINES: HARNESSING SCIENCE TO DRIVE INNOVATION FOR PATIENTS Oct. 2017

[viii] Markets and Markets Vaccines Market worth $50.42 billion by 2023 *Press Release*. No Date

[ix] Blankenship K, Pharma lobbyists flood the zone in D.C., with Pfizer and Amgen leading the way *Fierce Pharma* Apr. 23, 2019

[x] Vaccine Adverse Events Reporting System. Wisconsin VAERS Data as of May. 31, 2019. (Accessed Sept. 17, 2019)

[xi] AHRQ Electronic Support for Public Health–Vaccine Adverse Event Reporting System (ESP:VAERS) Dec 1, 2007-Sep. 30, 2010

[xii] Institute of Medicine Committee on the Assessment of Studies of Health Outcomes Related to the Recommended Childhood Immunization Schedule. The Childhood Immunization Schedule and Safety: Stakeholder Concerns, Scientific Evidence and Future Studies. Conclusions About Scientific Findings. Summary: Pages 10-11 Washington, DC: *The National Academies Press* 2013.

Wisconsin Vaccination and Exemption Rates

Wisconsin Student Immunization Law Compliance Results Public and Private Schools Kindergarten (and Pre-K) through 12th Grade, By School Year [1]

Wisconsin's vaccination rates have remained stable. In 2018-2019, only 1.1% of Wisconsin students had waived all immunizations. [2]

2018-2019 Wisconsin Medical Waiver: 0.3%

2018-2019 Wisconsin Religious Waiver: 0.4%

2018-2019 Wisconsin Personal Conviction Waiver: 4.6%

A vaccine exemption is filed regardless of whether the exemption is filed for one dose or all doses. The Wisconsin Department of Health does not collect data to determine the exact number of vaccines or type of vaccine that are being waived by Pre-K through 12th grade students.

Percentage of Wisconsin day care center attendees ages 2 through 4 years who met each Immunization compliance category, by assessment year[3]

"Vaccination rates have remained stable since 2011-12."[4]

Compliance Category	2011-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18
No Record	3.0%	2.7%	2.5%	2.2%	2.4%	3.9%	3.2%
Polio (3 or more doses)	92.7%	93.2%	93.0%	92.4%	93.7%	92.5%	93.3%
DTaP (4 or more doses)	91.6%	91.5%	91.3%	91.2%	91.9%	91.2%	91.5%
MMR (1 dose)	93.5%	93.7%	92.4%	92.9%	94.4%	93.5%	93.7%
Hib (3 or more doses)	92.3%	93.1%	92.6%	92.1%	93.2%	92.2%	92.7%
PCV (3 or more doses)	92.3%	93.2%	91.9%	92.2%	93.9%	93.0%	93.1%
Hep B (3 or more doses)	92.5%	92.7%	91.2%	91.8%	92.7%	92.2%	93.0%
Varicella (1 dose)	91.9%	92.3%	91.1%	91.6%	93.1%	92.3%	92.8%
Waived All Vaccines						1.2%	1.3%
Waived One or More Vaccines	3.1%	2.8%	3.1%	3.0%	3.1%	2.5%	2.6%
Health Waiver						0.1%	0.2%
Religious Waiver						0.3%	0.3%
Personal Conviction Waiver						2.0%	2.1%

Preserve our freedoms. Please vote NO to AB248/SB262.

References

[1] Wisconsin Student Immunization Law Compliance Results - Public and Private Schools Kindergarten (and Pre-K) through 12th Grade, By School Year - Wisconsin Dept. of Health P-02204 (Rev. 04/2019) (https://tinyurl.com/yy52otok)

[2] Wisconsin School Immunization Rates 2018-2019 School Year P-01894 (Rev. 04/2019) (https://tinyurl.com/yxg5uojb)

[3] CHILD CARE CENTER IMMUNIZATION ASSESSMENT RESULTS WISCONSIN | 2017-2018 - Wisconsin Dept. of Health - P-01445 (Rev. 08/2018)(https://tinyurl.com/yy52otok)

[4] Ibid

Vaccine Excipient & Media Summary

Excipients Included in U.S. Vaccines, by Vaccine

In addition to weakened or killed disease antigens (viruses or bacteria), vaccines contain very small amounts of other ingredients – excipients or media.

Some excipients are added to a vaccine for a specific purpose. These include:
Preservatives, to prevent contamination. For example, thimerosal.
Adjuvants, to help stimulate a stronger immune response. For example, aluminum salts.
Stabilizers, to keep the vaccine potent during transportation and storage. For example, sugars or gelatin.

Others are residual trace amounts of materials that were used during the manufacturing process and removed. These include:
Cell culture materials, used to grow the vaccine antigens. For example, egg protein, various culture media.
Inactivating ingredients, used to kill viruses or inactivate toxins. For example, formaldehyde.
Antibiotics, used to prevent contamination by bacteria. For example, neomycin.

The following table lists all components, other than antigens, shown in the manufacturers' package insert (PI) for each vaccine. Each of these PIs, which can be found on the FDA's website (see below) contains a description of that vaccine's manufacturing process, including the amount and purpose of each substance. In most PIs, this information is found in Section 11: "Description."

All information was extracted from manufacturers' package inserts, current as of January 6, 2017.
If in doubt about whether a PI has been updated since then, check the FDA's website at:
http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm

Vaccine	Contains
Adenovirus	human-diploid fibroblast cell cultures (strain WI-38), Dulbecco's Modified Eagle's Medium, fetal bovine serum, sodium bicarbonate, monosodium glutamate, sucrose, D-mannose, D-fructose, dextrose, human serum albumin, potassium phosphate, plasdone C, anhydrous lactose, microcrystalline cellulose, polacrilin potassium, magnesium stearate, microcrystalline cellulose, magnesium stearate, cellulose acetate phthalate, alcohol, acetone, castor oil, FD&C Yellow #6 aluminum lake dye
Anthrax (Biothrax)	amino acids, vitamins, inorganic salts, sugars, aluminum hydroxide, sodium chloride, benzethonium chloride, formaldehyde
BCG (Tice)	glycerin, asparagine, citric acid, potassium phosphate, magnesium sulfate, iron ammonium citrate, lactose
Cholera (Vaxchora)	casamino acids, yeast extract, mineral salts, anti-foaming agent, ascorbic acid, hydrolyzed casein, sodium chloride, sucrose, dried lactose, sodium bicarbonate, sodium carbonate
DT (Sanofi)	aluminum phosphate, isotonic sodium chloride, formaldehyde, casein, cystine, maltose, uracil, inorganic salts, vitamins, dextrose
DTaP (Daptacel)	aluminum phosphate, formaldehyde, glutaraldehyde, 2-phenoxyethanol, Stainer-Scholte medium, casamino acids, dimethyl-beta-cyclodextrin, Mueller's growth medium, ammonium sulfate, modified Mueller-Miller casamino acid medium without beef heart infusion, 2-phenoxyethanol
DTaP (Infanrix)	Fenton medium containing a bovine extract, modified Latham medium derived from bovine casein, formaldehyde, modified Stainer-Scholte liquid medium, glutaraldehyde, aluminum hydroxide, sodium chloride, polysorbate 80 (Tween 80)
DTaP-IPV (Kinrix)	Fenton medium containing a bovine extract, modified Latham medium derived from bovine casein, formaldehyde, modified Stainer-Scholte liquid medium, glutaraldehyde, aluminum hydroxide, VERO cells, a continuous line of monkey kidney cells, Calf serum lactalbumin hydrolysate, sodium chloride, polysorbate 80 (Tween 80), neomycin sulfate, polymyxin B
DTaP-IPV (Quadracel)	modified Mueller's growth medium, ammonium sulfate, modified Mueller-Miller casamino acid medium without beef heart infusion, formaldehyde, ammonium sulfate aluminum phosphate, Stainer-Scholte medium, casamino acids, dimethyl-beta-cyclodextrin, MRC-5 cells, normal human diploid cells, CMRL 1969 medium supplemented with calf serum, Medium 199 without calf serum, 2-phenoxyethanol, polysorbate 80, glutaraldehyde, neomycin, polymyxin B sulfate

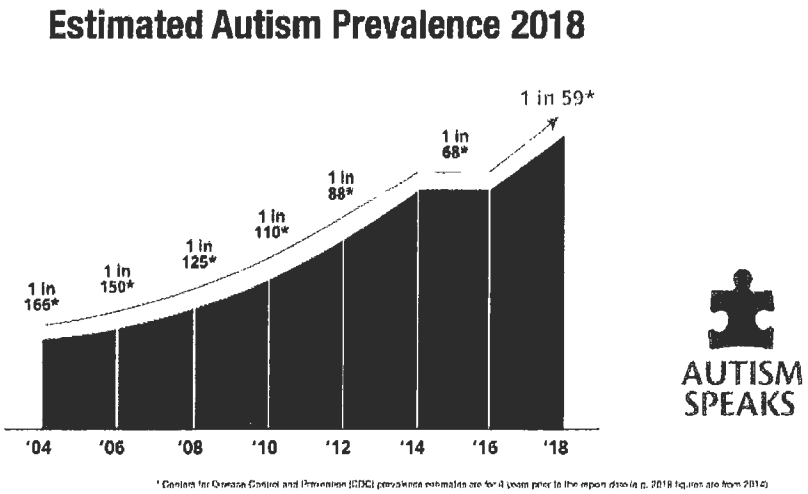
Vaccine	Contains
DTaP-HepB-IPV (Pediarix)	Fenton medium containing a bovine extract, modified Latham medium derived from bovine casein, formaldehyde, modified Stainer-Scholte liquid medium, VERO cells, a continuous line of monkey kidney cells, calf serum and lactalbumin hydrolysate, aluminum hydroxide, aluminum phosphate, aluminum salts, sodium chloride, polysorbate 80 (Tween 80), neomycin sulfate, polymyxin B, yeast protein.
DTaP-IPV/Hib (Pentacel)	aluminum phosphate, polysorbate 80, sucrose, formaldehyde, glutaraldehyde, bovine serum albumin, 2-phenoxyethanol, neomycin, polymyxin B sulfate, modified Mueller's growth medium, ammonium sulfate, modified Mueller-Miller casamino acid medium without beef heart infusion, Stainer-Scholte medium, casamino acids, dimethyl-beta-cyclodextrin. glutaraldehyde, MRC-5 cells (a line of normal human diploid cells), CMRL 1969 medium supplemented with calf serum, Medium 199 without calf serum, modified Mueller and Miller medium
Hib (ActHIB)	sodium chloride, modified Mueller and Miller medium (the culture medium contains milk-derived raw materials [casein derivatives]), formaldehyde, sucrose
Hib (Hiberix)	saline, synthetic medium, formaldehyde, sodium chloride, lactose
Hib (PedvaxHIB)	complex fermentation media, amorphous aluminum hydroxyphosphate sulfate, sodium chloride
Hib/Mening. CY (MenHibrix)	saline, semi-synthetic media, formaldehyde, sucrose, tris (trometamol)-HCl
Hep A (Havrix)	MRC-5 human diploid cells, formalin, aluminum hydroxide, amino acid supplement, phosphate-buffered saline solution, polysorbate 20, neomycin sulfate, aminoglycoside antibiotic
Hep A (Vaqta)	MRC-5 diploid fibroblasts, amorphous aluminum hydroxyphosphate sulfate, non-viral protein, DNA, bovine albumin, formaldehyde, neomycin, sodium borate, sodium chloride
Hep B (Engerix-B)	aluminum hydroxide, yeast protein, sodium chloride, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate
Hep B (Recombivax)	soy peptone, dextrose, amino acids, mineral salts, phosphate buffer, formaldehyde, potassium aluminum sulfate, amorphous aluminum hydroxyphosphate sulfate, yeast protein
Hep A/Hep B (Twinrix)	MRC-5 human diploid cells, formalin, aluminum phosphate, aluminum hydroxide, amino acids, sodium chloride, phosphate buffer, polysorbate 20, neomycin sulfate, yeast protein
Human Papillomavirus (HPV) (Gardasil)	vitamins, amino acids, mineral salts, carbohydrates, amorphous aluminum hydroxyphosphate sulfate, sodium chloride, L-histidine, polysorbate 80, sodium borate, yeast protein
Human Papillomavirus (HPV) (Gardasil 9)	vitamins, amino acids, mineral salts, carbohydrates, amorphous aluminum hydroxyphosphate sulfate, sodium chloride, L-histidine, polysorbate 80, sodium borate, yeast protein
Influenza (Afluria) Trivalent & Quadrivalent	sodium chloride, monobasic sodium phosphate, dibasic sodium phosphate, monobasic potassium phosphate, potassium chloride, calcium chloride, sodium taurodeoxycholate, ovalbumin, sucrose, neomycin sulfate, polymyxin B, beta-propiolactone, thimerosal (multi-dose vials)
Influenza (Fluad)	squalene, polysorbate 80, sorbitan trioleate, sodium citrate dehydrate, citric acid monohydrate, neomycin, kanamycin, barium, egg proteins, CTAB (cetyltrimethylammonium bromide), formaldehyde
Influenza (Fluarix) Trivalent & Quadrivalent	octoxynol-10 (TRITON X-100), α-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80), hydrocortisone, gentamicin sulfate, ovalbumin, formaldehyde, sodium deoxycholate, sodium phosphate-buffered isotonic sodium chloride
Influenza (Flublok) Trivalent & Quadrivalent	sodium chloride, monobasic sodium phosphate, dibasic sodium phosphate, polysorbate 20 (Tween 20), baculovirus and *Spodoptera frugiperda* cell proteins, baculovirus and cellular DNA, Triton X-100, lipids, vitamins, amino acids, mineral salts
Influenza (Flucelvax) Trivalent & Quadrivalent	Madin Darby Canine Kidney (MDCK) cell protein, protein other than HA, MDCK cell DNA, polysorbate 80, cetyltrimethlyammonium bromide, and β-propiolactone
Influenza (Flulaval) Trivalent & Quadrivalent	ovalbumin, formaldehyde, sodium deoxycholate, α-tocopheryl hydrogen succinate, polysorbate 80, thimerosal (multi-dose vials)
Influenza (Fluvirin)	ovalbumin, polymyxin, neomycin, betapropiolactone, nonylphenol ethoxylate, thimerosal
Influenza (Fluzone) Quadrivalent	egg protein, octylphenol ethoxylate (Triton X-100), sodium phosphate-buffered isotonic sodium chloride solution, thimerosal (multi-dose vials), sucrose

Vaccine	Contains
Influenza (Fluzone) High Dose	egg protein, octylphenol ethoxylate (Triton X-100), sodium phosphate-buffered isotonic sodium chloride solution, formaldehyde, sucrose
Influenza (Fluzone) Intradermal	egg protein, octylphenol ethoxylate (Triton X-100), sodium phosphate-buffered isotonic sodium chloride solution, sucrose
Influenza (FluMist) Quadrivalent	monosodium glutamate, hydrolyzed porcine gelatin, arginine, sucrose, dibasic potassium phosphate, monobasic potassium phosphate, ovalbumin, gentamicin sulfate, ethylenediaminetetraacetic acid (EDTA)
Japanese Encephalitis (Ixiaro)	aluminum hydroxide, protamine sulfate, formaldehyde, bovine serum albumin, host cell DNA, sodium metabisulphite, host cell protein
Meningococcal (MenACWY-Menactra)	Watson Scherp media containing casamino acid, modified culture medium containing hydrolyzed casein, ammonium sulfate, sodium phosphate, formaldehyde, sodium chloride
Meningococcal (MenACWY-Menveo)	formaldehyde, amino acids, yeast extract, Franz complete medium, CY medium
Meningococcal (MPSV4-Menomune)	Mueller Hinton casein agar, Watson Scherp casamino acid media, thimerosal (multi-dose vials), lactose
Meningococcal (MenB – Bexsero)	aluminum hydroxide, *E. coli*, histidine, sucrose, deoxycholate, kanamycin
Meningococcal (MenB – Trumenba)	defined fermentation growth media, polysorbate 80, histidine buffered saline.
MMR (MMR-II)	chick embryo cell culture, WI-38 human diploid lung fibroblasts, vitamins, amino acids, fetal bovine serum, sucrose, glutamate, recombinant human albumin, neomycin, sorbitol, hydrolyzed gelatin, sodium phosphate, sodium chloride
MMRV (ProQuad) (Frozen)	chick embryo cell culture, WI-38 human diploid lung fibroblasts MRC-5 cells, sucrose, hydrolyzed gelatin, sodium chloride, sorbitol, monosodium L-glutamate, sodium phosphate dibasic, human albumin, sodium bicarbonate, potassium phosphate monobasic, potassium chloride; potassium phosphate dibasic, neomycin, bovine calf serum
MMRV (ProQuad) (Refrigerator Stable)	chick embryo cell culture, WI-38 human diploid lung fibroblasts, MRC-5 cells, sucrose, hydrolyzed gelatin, urea, sodium chloride, sorbitol, monosodium L-glutamate, sodium phosphate, recombinant human albumin, sodium bicarbonate, potassium phosphate potassium chloride, neomycin, bovine serum albumin
Pneumococcal (PCV13 – Prevnar 13)	soy peptone broth, casamino acids and yeast extract-based medium, CRM197 carrier protein, polysorbate 80, succinate buffer, aluminum phosphate
Pneumococcal (PPSV-23 – Pneumovax)	phenol
Polio (IPV – Ipol)	Eagle MEM modified medium, calf bovine serum, M-199 without calf bovine serum, vero cells (a continuous line of monkey kidney cells), phenoxyethanol, formaldehyde, neomycin, streptomycin, polymyxin B
Rabies (Imovax)	human albumin, neomycin sulfate, phenol red indicator, MRC-5 human diploid cells, beta-propriolactone
Rabies (RabAvert)	chicken fibroblasts, β-propiolactone, polygeline (processed bovine gelatin), human serum albumin, bovine serum, potassium glutamate, sodium EDTA, ovalbumin neomycin, chlortetracycline, amphotericin B
Rotavirus (RotaTeq)	sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, cell culture media, fetal bovine serum, vero cells *[DNA from porcine circoviruses (PCV) 1 and 2 has been detected in RotaTeq. PCV-1 and PCV-2 are not known to cause disease in humans.]*
Rotavirus (Rotarix)	amino acids, dextran, Dulbecco's Modified Eagle Medium (sodium chloride, potassium chloride, magnesium sulfate, ferric (III) nitrate, sodium phosphate, sodium pyruvate, D-glucose, concentrated vitamin solution, L-cystine, L-tyrosine, amino acids solution, L-250 glutamine, calcium chloride, sodium hydrogenocarbonate, and phenol red), sorbitol, sucrose, calcium carbonate, sterile water, xanthan *[Porcine circovirus type 1 (PCV-1) is present in Rotarix. PCV-1 is not known to cause disease in humans.]*
Smallpox (Vaccinia – ACAM2000)	African Green Monkey kidney (Vero) cells, HEPES, human serum albumin, sodium chloride, neomycin, polymyxin B, Glycerin, phenol

CDC increases estimate of autism's prevalence by 15 percent, to 1 in 59 children

Autism Speaks calls on nation's leaders to adequately fund critically needed research and support services

April 26, 2018



* Centers for Disease Control and Prevention (CDC) prevalence estimates are for 4 years prior to the report date (e.g. 2018 figures are from 2014)

The Centers for Disease Control and Prevention (CDC) today released its biennial update of autism's estimated prevalence among the nation's children, based on an analysis of 2014 medical records and, where available, educational records of 8-year-old children from 11 monitoring sites across the United States.

The new estimate represents a 15 percent increase in prevalence nationally: to 1 in 59 children, from 1 in 68 two years previous.

However, prevalence estimates varied widely between monitoring sites, with significantly higher numbers at sites where researchers had full access to school records. This suggests that the new national numbers reflect a persistent undercount of autism's true prevalence among the nation's children.

"These findings demonstrate that while progress has been made on some fronts, there is still much work to do," says Autism Speaks President and Chief Executive Officer Angela Geiger. "They urgently warrant a significant increase in life-enhancing research and access to high quality services for people with autism across the spectrum and throughout their lifespan."

Autism Speaks calls on legislators, public health agencies and the National Institutes of Health to advance research that helps us better understand the increased prevalence and the complex medical needs that often accompany autism. In doing so, policy makers should follow the U.S. Interagency Autism Coordinating Committee's recommendation to double the autism research budget.

Autism Speaks also urges government leaders to advance policies that better provide individualized support and services in areas including education, transition to adulthood, residential options and employment.

Key findings of the new report include:

- Nationally, 1 in 59 children had a diagnosis of autism spectrum disorder (ASD) by age 8 in 2014, a 15 percent increase over 2012.
- But estimated rates varied, with a high of 1 in 34 in New Jersey (a 20 percent increase), where researchers had better access to education records. On the low side, autism's estimated prevalence in Arkansas was just 1 in 77. "This suggests that the new national prevalence estimate of 1 in 59 still reflects a significant undercount of autism's true prevalence among our children," says Autism Speaks Chief Science Officer Thomas Frazier. "And without more and better research, we can't know how much higher it really is."
- The gender gap in autism has decreased. While boys were 4 times more likely to be diagnosed than girls (1 in 37 versus 1 in 151) in 2014, the difference was narrower than in 2012, when boys were 4.5 times more frequently diagnosed than girls. This appears

Vaccination Rebuttal

Introduction...I'm speaking to you as a scientist and a healthcare provider educated in human physiology. Vaccination debate is always very emotional, rather than scientific, which is unfortunate and doesn't really lend itself to adequately understanding the issues. I'd like to keep this discussion scientific.

Autism...Autism, as may already know, is a developmental neurologic disorder with characteristics of damage to parts of the brain causing abnormal brain function. Autism prevalence has skyrocketed over the past decade to an unbelievable prevalence in the US of 168/10,000 or 1 in 59 children in 2014. This is not a small problem; it is an incredibly serious situation. One of the primary ways that brain damage occurs is the influx of harmful chemicals into the brain from the bloodstream. In a fully developed brain, there should be very little noxious chemical exchange from the blood to the brain. That protection from harmful chemicals is accomplished by a physiological system called the "Blood Brain Barrier".

Blood Brain Barrier (BBB)...The barrier between our blood and our brains that protects the very delicate cells of our brain. When mature and properly formed, it doesn't allow potentially damaging chemicals, that enter our bloodstream, to pass from a person's blood to their brains. Much of the stuff in your blood should never reach your brain so it's held out by a door, that door is the BBB. The BBB consists of small capillaries in the brain that are much less permeable than in any other area of the body.

When is the BBB formed...Complete formation doesn't occur until at least 6 months of age and can take until the age of 7 depending

on the individual. Up to the point of complete formation, there are large holes in the BBB. As a result of those holes and porosity, in instances such as injecting toxic chemicals into their bodies, babies and young children's brains are exposed to harmful substances in the blood that are never supposed to reach the brain.

Arthur Guyton...He's the #1 physiologist in all of history who wrote 80 textbooks on physiology or, in other words, how our body functions. His textbooks are used in every medical school in every country of the world. His comments on the physiologic importance of the BBB are essentially as follows...Neurons of the brain require an exactly controlled environment, or their function becomes abnormal and therefore, the function of the brain becomes abnormal. Autism is a condition with abnormal brain function.

Hormesis...Term used by toxicologists to describe things that are good for you in smaller doses and bad for you in too high a quantity. For example, even fruits and vegetables can be harmful if in too high a quantity. Not everything is hermetic though...nonhormetic substances are toxins and harm you in any quantity. As soon as you come into contact with a non-hormetic substance, it harms us or damages the tissue it comes in contact with.

Contents of Vaccinations...Are there any non-hormetic substances in vaccinations? Here is a list of the ingredients in each vaccine obtained from the US Centers of Disease Control or CDC website. There are several non-hormetic substances in many of the vaccines. Among the most harmful is Aluminum. Some of those chemicals are Aluminum Hydroxide, Aluminum Hydroxyphosphate Sulfate, Potassium Aluminum Sulfate, Formaldehyde, Formalin, Phenol, Ethanol, Detergent, Alcohol,

Monosodium Glutamate, Thimerosal (Mercury). In addition, there are several more substance that are very likely harmful to the infants and children receiving them in a vaccination such as WI-38 Human Diploid Lung Fibroblaste, Polysorbate 80, Phenol, FD&C Yellow #6 Aluminum Lake Dye, Benzethonium Chloride, Bovine Extract, 2-phenoxethanol, Polysorbate 20, Insect Cell, Ethylene Diamine Tetraacetic Acid (EDTA) Cetyltrimethylamonium and Madin Darby Canine Kidney (MDCK) etc.

Vaccine Adverse Effects...On 9-30-19, I performed a search of the Pub Med website which generated 34,387 articles related to the adverse effects of vaccinations. Pub Med is the electronic search engine for the National Medical Library of America in Bethesda, MD. It consists of over 24 million scientific articles that are considered truthful.

Vaccinations are touted to be safe and harmless. However, how could they possibly be safe and harmless when there are 34,387 articles surrounding adverse (harmful, damaging, dangerous, destructive poisonous unhealthy etc.) effects of vaccinations?

Regulation/Enforcement of Vaccinations...With all due respect, in my opinion, no regulatory body, or individual within that regulatory body, should be able to make important health choices for anyone's children unless they can converse intelligently on the physiology of the human body and completely define, and understand, the Blood Brain Barrier within the human brain.

Centers for Disease Control and Prevention

Morbidity and Mortality Weekly Report (*MMWR*)

Surveillance Summaries / April 12, 2019 / 68(2);1–19

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Abstract

Problem/Condition: Autism spectrum disorder (ASD) is estimated to affect up to 3% of children in the United States. Public health surveillance for ASD among children aged 4 years provides information about trends in prevalence, characteristics of children with ASD, and progress made toward decreasing the age of identification of ASD so that evidence-based interventions can begin as early as possible.

Period Covered: 2010, 2012, and 2014.

Description of System: The Early Autism and Developmental Disabilities Monitoring (Early ADDM) Network is an active surveillance system that provides biennial estimates of the prevalence and characteristics of ASD among children aged 4 years whose parents or guardians lived within designated sites. During surveillance years 2010, 2012, or 2014, data were collected in seven sites: Arizona, Colorado, Missouri, New Jersey, North Carolina, Utah, and Wisconsin. The Early ADDM Network is a subset of the broader ADDM Network (which included 13 total sites over the same period) that has been conducting ASD surveillance among children aged 8 years since 2000. Each Early ADDM site covers a smaller geographic area than the broader ADDM Network. Early ADDM ASD surveillance is conducted in two phases using the same methods and project staff members as the ADDM Network. The first phase consists of reviewing and abstracting data from children's records, including comprehensive evaluations performed by community professionals. Sources for these evaluations include general pediatric health clinics and specialized programs for children with developmental disabilities. In addition, special education records (for children aged ≥3 years) were reviewed for Arizona, Colorado, New Jersey, North Carolina, and Utah, and early intervention records (for children aged 0 to <3 years) were reviewed for New Jersey, North Carolina, Utah, and Wisconsin; in Wisconsin, early intervention records were reviewed for 2014 only. The second phase involves a review of the abstracted evaluations by trained clinicians using a standardized case definition and method. A child is considered to meet the surveillance case definition for ASD if one or more comprehensive evaluations of that child completed by a qualified professional describes behaviors consistent with the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision* (DSM-IV-TR) diagnostic criteria for any of the following conditions: autistic disorder, pervasive developmental disorder–not otherwise specified (PDD-NOS, including atypical autism), or Asperger disorder (2010, 2012, and 2014). For 2014 only, prevalence estimates based on surveillance case definitions according to DSM-IV-TR and the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) were compared. This report provides estimates of overall ASD prevalence and prevalence by sex and race/ethnicity; characteristics of children aged 4 years with ASD, including age at first developmental evaluation, age at ASD diagnosis, and cognitive function; and trends in ASD prevalence and characteristics among Early ADDM sites with data for all 3 surveillance years (2010, 2012, and 2014), including comparisons with children aged 8

years living in the same geographic area. Analyses of time trends in ASD prevalence are restricted to the three sites that contributed data for all 3 surveillance years with consistent data sources (Arizona, Missouri, and New Jersey).

Results: The overall ASD prevalence was 13.4 per 1,000 children aged 4 years in 2010, 15.3 in 2012, and 17.0 in 2014 for Early ADDM sites with data for the specific years. ASD prevalence was determined using a surveillance case definition based on DSM-IV-TR. Within each surveillance year, ASD prevalence among children aged 4 years varied across surveillance sites and was lowest each year for Missouri (8.5, 8.1, and 9.6 per 1,000, for 2010, 2012, and 2014, respectively) and highest each year for New Jersey (19.7, 22.1, and 28.4 per 1,000, for the same years, respectively). Aggregated prevalence estimates were higher for sites that reviewed education and health care records than for sites that reviewed only health care records. Among all participating sites and years, ASD prevalence among children aged 4 years was consistently higher among boys than girls; prevalence ratios ranged from 2.6 (Arizona and Wisconsin in 2010) to 5.2 boys per one girl (Colorado in 2014). In 2010, ASD prevalence was higher among non-Hispanic white children than among Hispanic children in Arizona and non-Hispanic black children in Missouri; no other differences were observed by race/ethnicity. Among four sites with ≥60% data on cognitive test scores (Arizona, New Jersey, North Carolina, and Utah), the frequency of co-occurring intellectual disabilities was significantly higher among children aged 4 years than among those aged 8 years for each site in each surveillance year except Arizona in 2010. The percentage of children with ASD who had a first evaluation by age 36 months ranged from 48.8% in Missouri in 2012 to 88.9% in Wisconsin in 2014. The percentage of children with a previous ASD diagnosis from a community provider varied by site, ranging from 43.0% for Arizona in 2012 to 86.5% for Missouri in 2012. The median age at earliest known ASD diagnosis varied from 28 months in North Carolina in 2014 to 39.0 months in Missouri and Wisconsin in 2012. In 2014, the ASD prevalence based on the DSM-IV-TR case definition was 20% higher than the prevalence based on the DSM-5 (17.0 versus 14.1 per 1,000, respectively).

Trends in ASD prevalence and characteristics among children aged 4 years during the study period were assessed for the three sites with data for all 3 years and consistent data sources (Arizona, Missouri, and New Jersey) using the DSM-IV-TR case definition; prevalence was higher in 2014 than in 2010 among children aged 4 years in New Jersey and was stable in Arizona and Missouri. In Missouri, ASD prevalence was higher among children aged 8 years than among children aged 4 years. The percentage of children with ASD who had a comprehensive evaluation by age 36 months was stable in Arizona and Missouri and decreased in New Jersey. In the three sites, no change occurred in the age at earliest known ASD diagnosis during 2010–2014.

Interpretation: The findings suggest that ASD prevalence among children aged 4 years was higher in 2014 than in 2010 in one site and remained stable in others. Among children with ASD, the frequency of cognitive impairment was higher among children aged 4 years than among those aged 8 years and suggests that surveillance at age 4 years might more often include children with more severe symptoms or those with co-occurring conditions such as intellectual disability. In the sites with data for all years and consistent data sources, no change in the age at earliest known ASD diagnosis was found, and children received their first developmental evaluation at the same or a later age in 2014 compared with 2010. Delays in the initiation of a first developmental evaluation might adversely affect children by delaying access to treatment and special services that can improve outcomes for children with ASD.

Public Health Action: Efforts to increase awareness of ASD and improve the identification of ASD by community providers can facilitate early diagnosis of children with ASD. Heterogeneity of results across sites suggests that community-level differences in evaluation and diagnostic services as well as access to data sources might affect estimates of ASD prevalence and age of identification. Continuing improvements in providing

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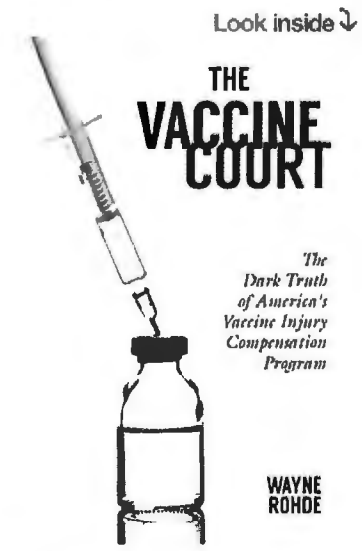

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Vaccine Excipient & Media Summary

Excipients Included in U.S. Vaccines, by Vaccine

This table includes not only vaccine ingredients (e.g., adjuvants and preservatives), but also substances used during the manufacturing process, including vaccine-production media, that are removed from the final product and present only in trace quantities. In addition to the substances listed, most vaccines contain Sodium Chloride (table salt).

Last Updated February 2015

All reasonable efforts have been made to ensure the accuracy of this information, but manufacturers may change product contents before that information is reflected here. If in doubt, check the manufacturer's package insert.

Vaccine	Contains	Source: Manufacturer's P.I. Dated
Adenovirus	sucrose, D-mannose, D-fructose, dextrose, potassium phosphate, plasdone C, anhydrous lactose, micro crystalline cellulose, polacrilin potassium, magnesium stearate, cellulose acetate phthalate, alcohol, acetone, castor oil, FD&C Yellow #6 aluminum lake dye, human serum albumin, fetal bovine serum, sodium bicarbonate, human-diploid fibroblast cell cultures (WI-38), Dulbecco's Modified Eagle's Medium, monosodium glutamate	March 2011
Anthrax (Biothrax)	aluminum hydroxide, benzethonium chloride, formaldehyde, amino acids, vitamins, inorganic salts and sugars	May 2012
BCG (Tice)	glycerin, asparagine, citric acid, potassium phosphate, magnesium sulfate, Iron ammonium citrate, lactose	February 2009
DT (Sanofi)	aluminum potassium sulfate, peptone, bovine extract, formaldehyde, thimerosal (trace), modified Mueller and Miller medium, ammonium sulfate	December 2005
DTaP (Daptacel)	aluminum phosphate, formaldehyde, glutaraldehyde, 2-Phenoxyethanol, Stainer-Scholte medium, modified Mueller's growth medium, modified Mueller-Miller casamino acid medium (without beef heart infusion), dimethyl 1-beta-cyclodextrin, ammonium sulfate	October 2013
DTaP (Infanrix)	formaldehyde, glutaraldehyde, aluminum hydroxide, polysorbate 80, Fenton medium (containing bovine extract), modified Latham medium (derived from bovine casein), modified Stainer-Scholte liquid medium	November 2013
DTaP-IPV (Kinrix)	formaldehyde, glutaraldehyde, aluminum hydroxide, Vero (monkey kidney) cells, calf serum, lactalbumin hydrolysate, polysorbate 80, neomycin sulfate, polymyxin B, Fenton medium (containing bovine extract), modified Latham medium (derived from bovine casein), modified Stainer-Scholte liquid medium	November 2013
DTaP-HepB-IPV (Pediarix)	formaldehyde, gluteraldehyde, aluminum hydroxide, aluminum phosphate, lactalbumin hydrolysate, polysorbate 80, neomycin sulfate, polymyxin B, yeast protein, calf serum, Fenton medium (containing bovine extract), modified Latham medium (derived from bovine casein), modified Stainer-Scholte liquid medium, Vero (monkey kidney) cells	November 2013
DTaP-IPV/Hib (Pentacel)	aluminum phosphate, polysorbate 80, formaldehyde, sucrose, gutaraldehyde, bovine serum albumin, 2-phenoxethanol, neomycin, polymyxin B sulfate, Mueller's Growth Medium, Mueller-Miller casamino acid medium (without beef heart infusion), Stainer-Scholte medium (modified by the addition of casamino acids and dimethyl-beta-cyclodextrin), MRC-5 (human diploid) cells, CMRL 1969 medium (supplemented with calf serum), ammonium sulfate, and medium 199	October 2013
Hib (ActHIB)	ammonium sulfate, formalin, sucrose, Modified Mueller and Miller medium	January 2014
Hib (Hiberix)	formaldehyde, lactose, semi-synthetic medium	March 2012
Hib (PedvaxHIB)	aluminum hydroxphosphate sulfate, ethanol, enzymes, phenol, detergent, complex fermentation medium	December 2010

Appendix B

Vaccine	Contains	Source: Manufacturer's P.I. Dated
Hib/Hep B (Comvax)	yeast (vaccine contains no detectable yeast DNA), nicotinamide adenine dinucleotide, hemin chloride, soy peptone, dextrose, mineral salts, amino acids, formaldehyde, potassium aluminum sulfate, amorphous aluminum hydroxyphosphate sulfate, sodium borate, phenol, ethanol, enzymes, detergent	December 2010
Hib/Mening. CY (MenHibrix)	tris (trometamol)-HCl, sucrose, formaldehyde, synthetic medium, semi-synthetic medium	2012
Hep A (Havrix)	aluminum hydroxide, amino acid supplement, polysorbate 20, formalin, neomycin sulfate, MRC-5 cellular proteins	December 2013
Hep A (Vaqta)	amorphous aluminum hydroxyphosphate sulfate, bovine albumin, formaldehyde, neomycin, sodium borate, MRC-5 (human diploid) cells	February 2014
Hep B (Engerix-B)	aluminum hydroxide, yeast protein, phosphate buffers, sodium dihydrogen phosphate dihydrate	December 2013
Hep B (Recombivax)	yeast protein, soy peptone, dextrose, amino acids, mineral salts, potassium aluminum sulfate, amorphous aluminum hydroxyphosphate sulfate, formaldehyde, phosphate buffer	May 2014
Hep A/Hep B (Twinrix)	formalin, yeast protein, aluminum phosphate, aluminum hydroxide, amino acids, phosphate buffer, polysorbate 20, neomycin sulfate, MRC-5 human diploid cells	August 2012
Human Papillomavirus (HPV) (Cerverix)	vitamins, amino acids, lipids, mineral salts, aluminum hydroxide, sodium dihydrogen phosphate dehydrate, 3-O-desacyl-4' Monophosphoryl lipid A, insect cell, bacterial, and viral protein	November 2013
Human Papillomavirus (HPV) (Gardasil)	yeast protein, vitamins, amino acids, mineral salts, carbohydrates, amorphous aluminum hydroxyphosphate sulfate, L-histidine, polysorbate 80, sodium borate	June 2014
Human Papillomavirus (HPV) (Gardasil 9)	yeast protein, vitamins, amino acids, mineral salts, carbohydrates, amorphous aluminum hydroxyphosphate sulfate, L-histidine, polysorbate 80, sodium borate	December 2014
Influenza (Afluria)	beta-propiolactone, thimerosol (multi-dose vials only), monobasic sodium phosphate, dibasic sodium phosphate, monobasic potassium phosphate, potassium chloride, calcium chloride, sodium taurodeoxycholate, neomycin sulfate, polymyxin B, egg protein, sucrose	December 2013
Influenza (Agriflu)	egg proteins, formaldehyde, polysorbate 80, cetyltrimethylammonium bromide, neomycin sulfate, kanamycin, barium	2013
Influenza (Fluarix) Trivalent and Quadrivalent	octoxynol-10 (Triton X-100), α-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80), hydrocortisone, gentamicin sulfate, ovalbumin, formaldehyde, sodium deoxycholate, sucrose, phosphate buffer	June 2014
Influenza (Flublok)	monobasic sodium phosphate, dibasic sodium phosphate, polysorbate 20, baculovirus and host cell proteins, baculovirus and cellular DNA, Triton X-100, lipids, vitamins, amino acids, mineral salts	March 2014
Influenza (Flucelvax)	Madin Darby Canine Kidney (MDCK) cell protein, MDCK cell DNA, polysorbate 80, cetyltrimethlyammonium bromide, β-propiolactone, phosphate buffer	March 2014
Influenza (Fluvirin)	nonylphenol ethoxylate, thimerosal (multidose vial–trace only in prefilled syringe), polymyxin, neomycin, beta-propiolactone, egg proteins, phosphate buffer	February 2014
Influenza (Flulaval) Trivalent and Quadrivalent	thimerosal, formaldehyde, sodium deoxycholate, egg proteins, phosphate buffer	February 2013
Influenza (Fluzone: Standard (Trivalent and Quadrivalent), High-Dose, & Intradermal)	formaldehyde, octylphenol ethoxylate (Triton X-100), gelatin (standard trivalent formulation only), thimerosal (multi-dose vial only) , egg protein, phosphate buffers, sucrose	2014

Vaccine	Contains	Source: Manufacturer's P.I. Dated
Influenza (FluMist) Quadrivalent	ethylene diamine tetraacetic acid (EDTA), monosodium glutamate, hydrolyzed porcine gelatin, arginine, sucrose, dibasic potassium phosphate, monobasic potassium phosphate, gentamicin sulfate, egg protein	July 2013
Japanese Encephalitis (Ixiaro)	aluminum hydroxide, Vero cells, protamine sulfate, formaldehyde, bovine serum albumin, sodium metabisulphite, sucrose	May 2013
Meningococcal (MCV4-Menactra)	formaldehyde, phosphate buffers, Mueller Hinton agar, Watson Scherp media, Modified Mueller and Miller medium, detergent, alcohol, ammonium sulfate	April 2013
Meningococcal (MCV4-Menveo)	formaldehyde, amino acids, yeast extract, Franz complete medium, CY medium	August 2013
Meningococcal (MPSV4-Menomune)	thimerosal (multi-dose vial only), lactose, Mueller Hinton casein agar, Watson Scherp media, detergent, alcohol	April 2013
Meningococcal (MenB – Bexsero)	aluminum hydroxide, *E. coli*, histidine, sucrose, deoxycholate, kanomycin	2015
Meningococcal (MenB – Trumenba)	polysorbate 80, histodine, *E. coli*, fermentation growth media	October 2015
MMR (MMR-II)	Medium 199 (vitamins, amino acids, fetal bovine serum, sucrose, glutamate) , Minimum Essential Medium, phosphate, recombinant human albumin, neomycin, sorbitol, hydrolyzed gelatin, chick embryo cell culture, WI-38 human diploid lung fibroblasts	June 2014
MMRV (ProQuad)	sucrose, hydrolyzed gelatin, sorbitol, monosodium L-glutamate, sodium phosphate dibasic, human albumin, sodium bicarbonate, potassium phosphate monobasic, potassium chloride, potassium phosphate dibasic, neomycin, bovine calf serum, chick embryo cell culture, WI-38 human diploid lung fibroblasts, MRC-5 cells	March 2014
Pneumococcal (PCV13 – Prevnar 13)	casamino acids, yeast, ammonium sulfate, Polysorbate 80, succinate buffer, aluminum phosphate, soy peptone broth	January 2014
Pneumococcal (PPSV-23 – Pneumovax)	phenol	May 2014
Polio (IPV – Ipol)	2-phenoxyethanol, formaldehyde, neomycin, streptomycin, polymyxin B, monkey kidney cells, Eagle MEM modified medium, calf serum protein, Medium 199	May 2013
Rabies (Imovax)	Human albumin, neomycin sulfate, phenol red indicator, MRC-5 human diploid cells, beta-propriolactone	April 2013
Rabies (RabAvert)	β-propiolactone, potassium glutamate, chicken protein, egg protein, neomycin, chlortetracycline, amphotericin B, human serum albumin, polygeline (processed bovine gelatin), sodium EDTA, bovine serum	March 2012
Rotavirus (RotaTeq)	sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, cell culture media, fetal bovine serum, vero cells *[DNA from porcine circoviruses (PCV) 1 and 2 has been detected in RotaTeq. PCV-1 and PCV-2 are not known to cause disease in humans.]*	June 2013
Rotavirus (Rotarix)	amino acids, dextran, sorbitol, sucrose, calcium carbonate, xanthan, Dulbecco's Modified Eagle Medium (potassium chloride, magnesium sulfate, ferric (III) nitrate, sodium phosphate, sodium pyruvate, D-glucose, concentrated vitamin solution, L-cystine, L-tyrosine, amino acids solution, L-glutamine, calcium chloride, sodium hydrogenocarbonate, and phenol red) *[Porcine circovirus type 1 (PCV-1) is present in Rotarix. PCV-1 is not known to cause disease in humans.]*	May 2014
Smallpox (Vaccinia – ACAM2000)	human serum albumin, mannitol, neomycin, glycerin, polymyxin B, phenol, Vero cells, HEPES	September 2009

Appendix B

Vaccine	Contains	Source: Manufacturer's P.I. Dated
Td (Decavac)	aluminum potassium sulfate, peptone, formaldehyde, thimerosal, bovine muscle tissue (US sourced), Mueller and Miller medium, ammonium sulfate	March 2011
Td (Tenivac)	aluminum phosphate, formaldehyde, modified Mueller-Miller casamino acid medium without beef heart infusion, ammonium sulfate	April 2013
Td (Mass Biologics)	aluminum phosphate, formaldehyde, thimerosal (trace), ammonium phosphate, modified Mueller's media (containing bovine extracts)	February 2011
Tdap (Adacel)	aluminum phosphate, formaldehyde, glutaraldehyde, 2-phenoxyethanol, ammonium sulfate, Stainer-Scholte medium, dimethyl-beta-cyclodextrin, modified Mueller's growth medium, Mueller-Miller casamino acid medium (without beef heart infusion)	March 2014
Tdap (Boostrix)	formaldehyde, glutaraldehyde, aluminum hydroxide, polysorbate 80 (Tween 80), Latham medium derived from bovine casein, Fenton medium containing a bovine extract, Stainer-Scholte liquid medium	February 2013
Typhoid (inactivated – Typhim Vi)	hexadecyltrimethylammonium bromide, formaldehyde, phenol, polydimethylsiloxane, disodium phosphate, monosodium phosphate, semi-synthetic medium	March 2014
Typhoid (oral – Ty21a)	yeast extract, casein, dextrose, galactose, sucrose, ascorbic acid, amino acids, lactose, magnesium stearate. gelatin	September 2013
Varicella (Varivax)	sucrose, phosphate, glutamate, gelatin, monosodium L-glutamate, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride, sodium phosphate monobasic, potassium chloride, EDTA, residual components of MRC-5 cells including DNA and protein, neomycin, fetal bovine serum, human diploid cell cultures (WI-38), embryonic guinea pig cell cultures, human embryonic lung cultures	March 2014
Yellow Fever (YF-Vax)	sorbitol, gelatin, egg protein	May 2013
Zoster (Shingles – Zostavax)	sucrose, hydrolyzed porcine gelatin, monosodium L-glutamate, sodium phosphate dibasic, potassium phosphate monobasic, neomycin, potassium chloride, residual components of MRC-5 cells including DNA and protein, bovine calf serum	February 2014

A table listing vaccine excipients and media *by excipient* can be found in:

Grabenstein JD. *ImmunoFacts: Vaccines and Immunologic Drugs* – 2013 (38th revision). St Louis, MO: Wolters Kluwer Health, 2012.

B

Vaccine Injured Families

Please Hear Our Stories

* Testimony from WI families
* National Deaths and Injuries

4-Month-Old Wisconsin Baby Donates Organs After Receiving 7 Vaccine Doses

Parents in Wisconsin are grieving over the loss of their infant son following routine vaccinations. Less than one day after receiving seven vaccine doses at his four-month baby checkup, Zaire Corvell Thomas went into cardiac arrest and stopped breathing in his sleep. His mother and emergency responders helped save him.

Once at the hospital, Zaire was put on life support. Within twelve hours, his parents were being pressured to donate his organs. Zaire was hardly given a chance to recover when his beating heart and liver were taken from his living body four days later.

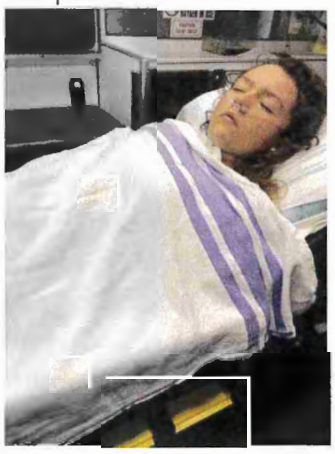
Prior to this happening, Zaire's mother thought vaccines were safe and was an organ donor. She no longer feels this way and asks parents to please research vaccines before allowing your child to get injected with what is in them. It took her losing her son to realize he was never protected from any vaccine; instead he was used for profit. After learning of the deceptive practices used to get increased consent for organ donations, Zaire's parents question if their son could've survived.

Zaire's parents live with such grief and guilt, wishing they had been more aware of the truth, feeling they helped harm their son by trusting the doctors so much. Their lives have been shattered over this. In the process of coping with the loss of their baby, Zaire's parents want to share their story, in hopes to bring attention to issues involving vaccines and organ donations.

Vaccine Injury Stories

Fond du Lac County, WI: Ashlyn is an "A" student in Middle School. She plays in band and is in several sports including football, softball, track and dance. She has many friends and loves her social time. She's involved in anything she can be and loves to helps the community and volunteer. She has always been a positive, happy girl.

At Ashlyn's 13-year-old checkup, she was given the HPV Vaccination. Before leaving the Doctor's office, she had a lump on her arm. The next 3 days following the vaccination, Ashlyn had a temperature over 101 degrees. A few days later she started experiencing constant muscle and joint pain in her legs and arms. 59 day after the vaccination on Tuesday, May 8, 2018 my fun loving 13-year-old's life changed. She was at track practice and wasn't feeling well. She went into the locker room and got dizzy. She remembers nothing but waking up on the floor. I took her to the ER and was told she was dehydrated but fine. The next day I took her to her family doctor just to get her checked out. She agreed that this was probably the problem. That Thursday at school she "passed out" but we noticed she had some movement in her hand. I took her back to her doctor and they did blood work. All was normal. Friday May 11th was the school dance. On the way home Ashlyn "passed out" in the back seat. We could not wake her. Her right hand was shaking and we had no response from her. I called 911 and drove her as far as Sherwood to meet the ambulance. They took her to Theda Clark. There we were told she needed to see a cardiologist to rule out a heart problem. At this time, they did not think the hand shaking was a big deal. Saturday, Sunday same things, "passing out" with shaking in her right hand but now I noticed her right leg was shaking too. We took her back to the doctors and we were told they sounded more like seizures then just "passing out". She had more on Monday and Tuesday at school. Wednesday May 16, 2018, she was taken by ambulance to Children's in Milwaukee after having a violent seizure. They hooked her up to EEG's and she had CT scans and a lot of blood work. She had a seizure when the EEG was on. The results showed non epileptic seizures. On Friday, July 6, 2018 Ashlyn was taken to the ER after falling when having a seizure and hitting her head on concrete floor. There I was introduced to an ER Doctor that practices in Milwaukee. She was very informative and has seen girls like Ashlyn before. She confirmed that yes, this is a side effect from the vaccination and yes, that is what is causing Ashlyn's seizures. We are now struggling to find doctors that know how to help her. We are struggling to find her the help she needs to control this. We are being told this may not be reversible, it altered her hormones. Ashlyn has seen numerus doctors including at Children's Hospital in Milwaukee and Madison. Currently we travel to Minnesota to Children's Hospital of St. Paul for her Neurologist. Ashlyn also sees a Phycologist and Naturalists weekly. She continues to struggle with seizures and passing out. We never know when or where they will happen. He social life has changed. Her sports have been affected. She continues to try and stay strong but that is hard to do at this point. On May 8, 2019, the 1-year mark from Ashlyn's first episode, she has had 165 non-epileptic events, over 45 passing out events, 26 ER visits, 22 Ambulance rides, 4 extended hospital stays, approximately 175 Doctor appointments and over 25 missing days of school. Her future at this point is unknown.



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I am a mother of 8. I started as any other mother. Brought my kids to the doctor routinely got any recommended shots for them. Even after my second started to develop asthma and allergies at a young age, I did not think anything of it. It was not until my third stopped breathing after her two month vaccines that I started to give them any thought. However, I continued to vaccinate on schedule while researching them more. As I did, I discovered, mostly reading the manufactures inserts, that not only were they most likely the cause of my daughter's breathing episodes but they were also most likely the result of my son's declining health. With our five children that followed my husband and me, with our doctor's support, decided not to vaccinate them. Not only are they in great health but not one suffers from the so-called hereditary issues of asthma and allergies that our vaccinated children have struggled. Basic math would tell you that if it is simply a matter of genes that more of our unvaccinated children should suffer the same fate as their vaccinated siblings. Preserving parents' rights to choose is of utmost importance, in all areas. There is never going to be a one size fits all and the manufacturer's warnings and side effects for vaccines should NOT be ignored.

Thank you,

Mom of Eight
De Pere, WI

Hello. I am a mother of four, an honors graduate who was pre-med (emphasis in microbiology), and am currently working on a bachelor's in math. My husband is a PhD statistician and a professor at a local university. 15 years ago, when I had my first child I was very pro-vaccination. I liked to delay with her though because I did know that so many as an infant could be detrimental. No physician ever cared that we delayed. Then, 2 1/2 years later, I had my second daughter. At this point, I started to question vaccines a bit more. In just a few short years, more vaccines were added to the schedule. One of those was for rotavirus; my oldest had never had that vaccine, but had the disease as a 10 month old and recovered just fine.

With my second child, I continued with delayed vaccinations and was never questioned. Four years after she was born, I had my third child and at that point I was really starting to question vaccines more. While I was pregnant with him they told me I needed a flu shot. With my older two flu shots were a no-no during pregnancy. Suddenly they wanted me to get one? I told our pediatrician that we would be holding off on hepatitis vaccines for my third because I just did not see the need, as he would have no exposure. She agreed with me. I needed to get my two older daughters "caught up" for school. I had them vaccinated with DTaP, flu, and MMR. What a mistake that was. Within days, I thought my second daughter had the flu. She was very sick for a week. I found it curious that no one else in the house had gotten sick. Within weeks, she had this mysterious stomach bug again. No one else got sick again and I was starting get suspicious.

My son was one year old and I decided to find out what was really in a vaccine. My doctor had always told me they were safe and effective after all. As a pre-med student, I had never once looked up vaccine ingredients. I was disgusted. As a microbiologist, I re-visited all the "vaccine-preventable diseases" and saw how benign they truly are. Then I did some research on the Blood Brain Barrier. At that point, I decided we would no longer vaccinate. I was suspicious that the vaccines I had caught her up on caused my daughter's GI issues. It would take me years, but eventually my worst fears would be proven true. As I started to dive into the research, I learned that my childhood was one long bad adverse event to vaccines. I was constantly sick and the schedule was much smaller back in the 80's. I was the kid constantly sick with strep, bronchitis, ear infections, chronic migraines, sinus infections, etc. I had tubes put in my ears and all was fine until I received the MMR vaccinate in 1994. All of a sudden, I was having ear and sinus infections again. I was again fine until vaccinations for college. I spent my first semester sick with sinus and ear infections, kidney infections. I was prescribed allergy meds that did not help. I was told after my third child that I needed a TDAP booster so he would not get pertussis. I agreed and had a horrible allergic reaction.

Vaccine Injury Stories

Sick again with my allergies as bad as they had ever been. It was a miserable year as a new mom. In 2012, my son turned 1 and my 2nd daughter had her boosters and was ill within days. Those were the last vaccines they ever received. In 2013, I learned I was pregnant with my fourth child. I started my care with hospital midwives who liked to push every procedure they can. This time they wanted me to get a DTaP while pregnant. I questioned them as to why they would give that during pregnancy especially when I just had one 3 years prior with a reaction. They did not care. It was to protect baby. They had no science to share with me and I refused. I also transferred my care out of hospital with home birth midwives. My daughter was born in April 2014 without me having had flu or DTaP vaccines. She did not receive vitamin K or hepatitis B at birth. I am not HEP+ nor would she be exposed. I also decided she would not go to a pediatrician or receive any more vaccines and at age 5 she has never seen one. She has been sick 4 times in her life (3 viral bugs and chicken pox), but somehow she is a threat to vaccinated children? In November 2017, my 12yr old finally had a name for her persistent GI issues. She has Idiopathic Gastroparesis, but we all knew that the vaccines caused this. In this time, we found out we have allergies to thimerosal (still found in all vaccines in trace amounts) and polysorbate along with sensitivities to MSG. I have partial hearing loss from all the ruptured eardrums I suffered as a child. I am on year round allergy meds. I suffer from POTS, a known condition related to vaccines. My 12 year old has suffered for 7 years from vaccines and her conditions are worse than any of mine. Hers are only controlled with diet and at times, that is not enough. She is in pain and has had to miss school, sports, and family functions. There is no cure for her. She is 12 and will have to live with this for the rest of her life. Her former doctors do not care. I did not receive informed consent that this could possibly happen to my daughter. I was simply told that vaccines are safe and effective. You may now understand why I have no trust or faith in allopathic doctors. We prefer naturopaths who treat the whole body and use natural supplements to help the immune system. That is working a lot better for us.

Please take look at the 14th amendment of the United States Constitution and the equal protection laws. Any kind of mandatory vaccination law is a violation of the equal protection laws, as my children would no longer be able to attend public schools. They are all exemplary students and would suffer if not allowed in school. As educators, my husband and I could very much homeschool our kids, but that is not the point. There should always be a choice. As a scientist, I have yet to find a double blind placebo safety study for ANY vaccine (had I known this when my oldest was born, we would have never started any vaccines). That is sickening, terrifying, and bad science. If I presented research like that, I would be laughed at and my drug would not be approved. Take the liability or do not pass this law. That is what any parent asks. I would be happy to provide you with further research or the chance to talk to my daughter and myself. She would be happy to let anyone know her struggles with vaccine induced gastroparesis.

Sincerely, Rebecca Edwards

 Before I had kids, I really was just like everyone else. I trusted everything my doctors had to say and never questioned any of it. I even got the flu shot while pregnant with my first child. It was not until he had, what in my eyes, a severe reaction to his 2-month vaccines that I woke up. He was lethargic to the point of being a ragdoll. His elevated fever lasted for days. He subsequently had ear infections and gastrointestinal issues that include being prescribed an antacid at around 4 months old. He just was not a normal, happy baby. He would arch his back and cry out in pain because his gut was wrecked. Colic, they called it. More like an excuse for any inconsolable baby. I knew what was wrong with my son. His little body was reacting to the toxic ingredients that were in those 2 month vaccines and it was having a very hard time. His first year of life was not that of a typical newborn. While what we experienced was horrible, it truly was mild compared to the devastation vaccines have caused to so many other families.

I know in my heart that these vaccines did and would continue to harm my child. My right, as a parent, is to choose what goes into my child's body. I choose to abstain from vaccination due to the vast amount of research I have done. That research being brought forth by dozens and dozens of doctors and scientists alike, proving the harm that CAN occur with

vaccination. From the genetic susceptibility such as methylation issues to the toxic, overload of aluminum adjuvants, formaldehyde, polysorbate 80, fetal and animal DNA, antibiotics and more. I should have the right to choose for myself and for my children to refuse these ingredients to be directly injected into our bloodstream and bypassing any God given defense mechanisms my body may possess. My children should be free to peruse a public education whilst remaining vaccine-free based solely off their parent's philosophical views. My children do not harbor disease. If my children are sick, they stay home. While the recently vaccinated, being asymptomatic, remain active in the public unaware they themselves are spreading the disease they were vaccinated for. I implore you, as representatives of the people, to educate yourselves further on vaccination, their ingredients, the Vaccine Adverse Events Reporting System and please, always remember - WE are the parents.

Thank you,

Amber Psket
Cedarburg resident Wife and Mother of 2 boys
414-324-4672

Hello and thank you for your time. I started out as most people do when they first have children. I just "trusted" that doctors had all the knowledge. Therefore, I took my son in for all his appointments and got his vaccinations on time. I had no idea I could even choose not to do it. The risks you are told about during the visit are not all inclusive so parents are left with a feeling like "what do I have to lose?" If I had only known what I do today.

My son Oliver had been developing socially on time through his entire first year. I have videos of him laughing at me making funny sounds and faces, chasing his brother in his walker, playing pat-a-cake with his dad, and peek-a-boo with his brother. He consistently turned to look at me when I called his name and would reciprocate my affection toward him.

It all started to change after he was about 15 months old. He started gravitating towards objects more than people and did a lot of repetitive things like pushing buttons and running back and forth. He stopped looking to me when I would call his name and no longer enjoyed the playful connection he had with his brother. He seemed irritable and had constant ear infections. He would bang his head back against objects and rock back and forth. Then came the tiptoe walking, weeklong constipation, screeching and screaming, obsessions over electronics and the constant eloping out of the house. He was miserable and could not fall asleep at night. I did not know what autism was until he was referred for services around the age of two. He was diagnosed autistic at age 3 after failed attempts at speech and behavioral therapy. It was frustrating not knowing why my son who was developing so beautifully just vanished before my eyes.

An employee at the CDC by the name of Dr. William Thompson came forward in 2014 stating that important data was omitted in a study published in 2004 regarding MMR vaccine and autism. Finally really questioning whether vaccines could have caused this I dug into my home videos to find that indeed my son's regression into autism began around 15 months, which was when he received the vaccine set that included the MMR. I have been studying vaccines to this day and am appalled to learn of the aborted fetal DNA, aluminum, mercury, and much more that are injected into our children. The lack of inert placebos in the clinical trials of vaccines is an absolute disgrace! Vaccine safety is a train wreck and it is nothing as I had originally thought when I first decided to trust my doctor.

If we no longer have personal exemptions to vaccines we give up our rights to say "no" to any or all vaccines if we so wish, no matter how unsafe, unnecessary, or immoral we think they may be. With a list of 270 new ones coming our way, the vaccine schedule will just keep growing. Rates for autism have been on a steady incline ever since the vaccine schedule became bloated. A society bogged down by the weight of enough people unable to care for themselves or

communicate effectively will surely crumble. You can watch my son's regression at the link below.
https://youtu.be/SccZrtOF5QM?fbclid=IwAR19kSv0KkUPTtiHiqaCI5_Vu497ao3lfnxg6ZqFja9De1VLyiGTlso0fH8

Thank you again for your time!

Sincerely, Rhea Kitowski
Junction City, WI

The Wenk Family

I was one of those PRO vaccine jerks. I used to stand on my soapbox telling the anti-vaxxers how my kids would protect theirs and were providing herd immunity etc. Then with baby #3 I felt something was off and wanted to delay at least the MMR vaccine until 2. I did it at 18 months and she changed so much she lost most of her words. I was told it was from the trauma of her having an intussusception although I had no clue the rotavirus vaccine caused that at the time. Then my baby #4 had his "normal" 2 month vaccines after the doctor bullied me into it and told me if I refused the vaccines he would call CPS. Within 24 hours of those shots my healthy, happy baby had a fever of 105 then he broke out in a rash all over his body. The urgent care told me it was roseola and refused to even entertain the idea of a vaccine reaction. Overnight his body went stiff while he was lying next to me; stiff like rigor mortis was setting in while he was still alive. So we rushed to the children's hospital and it was concluded he was having an adverse reaction to the DTaP vaccine. He stayed in the hospital for a week but made a "full" recovery. I say that with the quotation marks because he then had skin issues after that. That is the day I started my research on vaccines and held off on all my kids' vaccines moving forward. I found a new doctor for my kids, one who is so damn smart and knows the dangers of vaccines.

Then 7 months later, all my fully vaccinated kids got whooping cough and were hospitalized. My baby boy who did not receive any more vaccines after the scare stayed healthy. He never got whooping cough. 🤔 That is when my wheels went crazy with researching. My first three kids all have asthma and have had multiple ear infections. My first child has ADHD and had 12 ear infections before he turned 2. My third child has SPD and my second child has had kidney issues and RSV multiple times. All three of them get pneumonia at least 1 time a year. My third child has had 28 ears infections in 5 years, including 24 of them before she was 3. She also has had her tonsils and adenoids removed. She has had 3 sets of ear tubes. My fourth child (no more vaccines) has been sick approximately 3 times in his 6 years of life. (only had his 2 month shots) My fifth child hasn't had any vaccines and she has had nothing in 3 years of life; no ear infections, no breathing issues, no behavioral issues. Just a healthy perfect little girl.

Truly, Lyric Wenk

Vaccines have affected me personally and I would like to share my vaccine injury story. I was a Medical Laboratory Technologist and about two and a half years ago, the company I was working for decided to force everyone to get the flu shot. They did this because if they did not reach a certain percentage of employees who got their flu shot, they would not get their Medicare reimbursement money. You could decline it but would then have to wear a mask for the entire flu season. The flu season around here is usually about six months, give or take! I am from Merrill, WI and work in Wausau, WI. That is about half of your working career being forced to wear a mask. I was not ok with this so I broke down and got my flu shot. Shortly afterwards did I became very sick. The entire winter I was sick and my body could not get better. I started seeing a holistic nutritionist and I slowly got better. We also discovered that my body's inability to get better was caused from the flu shot. Now, let's fast forward to the next year of flu season, about a year and a half ago. I still was not ok with having to wear a mask, so I unwilling got my flu shot, again. I was terrified because of what had happened the previous year.

A few weeks after receiving my flu shot, I developed a rash on my neck. It itched and was super red all the time! I thought that maybe it was due to the cold weather. I was still seeing my holistic nutritionist and after some time she finally said this rash has to be due to food because it was not getting better. After further work with the holistic nutritionist, we discovered that it was eggs causing the reaction. Every single time I ate something with eggs in it my neck was reacting. We thought what would have caused this. The flu shot! The flu shot has eggs in it! I never had this problem before and I was completely devastated. Over the past year since we discovered this, we also found out that soy was causing my neck to react as well. By changing my diet and supporting my body and immune system, my neck is slowly getting better. We still have a ways to go though! I have had to completely change my diet and I am in constant fear when I do not eat at home if there is even the slightest amount of eggs or soy in something. I regret getting my flu shot last year and was forced to come to terms with wearing a mask. I spent many hours having anxiety and crying over having to wear a mask at work.

I starting preparing for this year's flu season I got a medical exemption, in case they didn't give an option this year I didn't want to be fired. The time came around and I gladly declined my flu shot and wear my mask now. About a month ago, I started a new job as well where I do not have to deal with this. It is not my fault that my body cannot get the flu shot. I should not have to be punished and humiliated every day at work. It scares me to think what would happen if I ever HAD to get it again!

Mandating vaccines is not ok. Everyone's body reacts differently to foreign things being put into their bodies! I am not very surprised by how my body ended up reacting after repeated flu shots because my grandmother had many allergies and immunity problems as well. This is why personal exemptions are so important! Family history of problems is a very real reason to decline vaccines. Even if someone does not have a family history of vaccine injuries, immunity problems, etc. it is still important to keep personal exemptions an option! I own my body and should be allowed to control what I put it, NOT the government. We are not government property!

Sincerely, Jessica

 Tyler's Story

I fully believed in vaccines and never questioned them, but something told me not to get Tyler's kindergarten shots. I put them off as long as I could, but the intimidating letters from the health department scared me into it. They fooled me into thinking he could not go to school unless he got them. As absurd as that seemed to me (how can they force medical procedures?!) I was a single parent at the time, and homeschooling was not an option. Therefore, I took him to the clinic.

I held him down as the nurses injected him several times. They assured me "You're doing the right thing" "He'll thank you later". I recall asking "...and you're sure this is safe?" They chuckled and said "Oh yes, of course." After his tears dried, he was given a sucker and we went home. We had supper and went to bed early because he was exceptionally tired, which I attributed to the excess tears and energy spent from being worked up at the clinic.

Around 10pm, Tyler shook me awake. He was struggling to breathe, gasping desperately for air. I thought he was choking but he shook his head "no" when asked if he had tried eating or swallowing anything. I threw him in the car and raced to the ER, only a few blocks away. When we arrived he was nearly unconscious and not getting any air. Things after that point were a blur. Doctors and/or nurses immediately swarmed us. They asked me a bunch of questions. The one I recall most vividly was "Did he have shots today?" With that information, they went to work stopping his anaphylactic reaction and they kept him for observation. During this time, they told me repeatedly, "Do not get him anymore shots".

Fast forward to his next "well child visit". The doctor insisted Tyler finish his next round of shots. I was shocked and told him to review his chart, that he almost died from the last set. The doctor reviewed the chart and said, "All I see is an ER visit due to an acute asthma attack". That is how I learned that, instead of documenting his vaccine reaction, they diagnosed him with asthma. I questioned a colleague, a doctor, about this and he said that documenting a vaccine reaction would be committing career suicide.

Tyler is now 13. He has a diagnosis of asthma that he does not actually have, and he did not receive a medical exemption from vaccines, even though they nearly took his life. He relies on his personal exemption to attend school. We rarely need a doctor except for sports physicals, at which we are always harassed about getting him caught up, even after I explain that he almost died. They laugh at us. Tell us it did not happen. They tell us the doctors in the ER were wrong and ask us what they can do to convince us to inject him again. Can you imagine? Imagine if I had told them he almost died after eating a strawberry and then they recommended that I feed him strawberries. It is insanity! I watched my son nearly die. The very people who did it to him now mock us for it. Vaccines are medical procedures that come with a warning stating it could kill the recipient. Some people who even qualify for them do not receive them because doctors do not document vaccine injuries. Tyler, and many others like him, rely on personal exemptions because their vaccine injury was not properly documented and physicians are truly taught to deny that they exist. Thank you for your time, and for reading Tyler's story. There are many more children like him.

Kind regards,

The Rogers (David, Amy, Tyler, Bo & Evan)
Stevens Point, WI

 I questioned vaccines with my oldest son's pediatricians right away. I asked why so many more are required for kids versus when I was a kid and I got the sales pitch in response. Back then, our county HHS office administered vaccines. I chose to select which vaccines my son received and I choose to delay live ones. Every nurse at the office badgered me for saying no to certain ones. I eventually just did not bring him in. One nurse screamed (literally yelled) at me for waiting too long so now he could not drink a solution for one of the vaccines. I said, "That's fine, I don't want him to have that anyways." She said my baby would die without it. Of course, as a new mom, this gave me anxiety but I read about it and realized she was wrong. At my son's 6-year-old check up the pediatrician said he needed chicken pox and MMR, which he didn't get any doses of at all. I asked about safety of both and safety of having both at once. The pediatrician said, "Oh they are perfectly safe, no risks." In hindsight, she never even gave me the inserts. I had him get those and that is my biggest regret. A few months later, my son had several digestive issues and burped up food several times an hour. We saw his pediatrician at the time and I questioned vaccines and was told that wasn't the source of these issues. We were referred to the children's hospital and had many tests and again I questioned that doctor about vaccine reaction and even asked if there was a way to report and she said no. We saw another specialist and I questioned again and was told no yet again.

My son still has digestive problems and burps up food and no medical provider can explain why. One friend, who is a nurse practitioner, said he has food allergies so we are looking at an elimination diet. Fast forward to me researching vaccines. I then put the puzzle pieces together and realized that indeed food allergies and digestive issues are both linked to vaccines. These side effects are listed in the inserts that I was never given.

My story: For years I felt exhausted to the point I wanted to sleep all day. I saw more than 30 doctors and nurse practitioners and all of them said it's "normal ", you're a working mom. I was told by several doctors to quit my job and go on welfare and then I can sleep when I need to. I kept reading and searching (and working full time because my work ethic doesn't allow me to give up). Years went by and finally a doctor listened to me and did more in depth lab tests that

revealed a whole host of autoimmune diseases with Hashimoto's thyroiditis being most likely primary issue. Rheumatoid arthritis, Sjogren's disease and the list goes on as it seems like each checkup reveals something else. According to research, autoimmune diseases are linked to vaccines. The number of people with autoimmune disorders is astounding and it is ever increasing. I have now read that because I have autoimmune diseases, my kids are at risk and vaccines can induce that in them, whereas every doctor told me vaccines for my kids are completely safe. There must be a choice.

Thank you.

 I had been trying to conceive a baby after a miscarriage and was hoping to have a healthy baby to call my own, to kiss, to hold, breastfeed, and to nurture. Watch my baby take his or her first steps, eat first spoon full of purees, say their first word, teach how to use the big kids potty, dress my baby up for first day of preschool, sing ABC's and 123's but what was dealt to me instead was way beyond I could fathom . When I tested positive on a pregnancy test I was so excited to be growing this tiny human inside my womb. To make sure this was a viable pregnancy I made an appointment at well-known local Woman's Center. I wanted to establish a healthy rapport with my OBGYN and follow us closely to prevent any adverse events. First visit we retested my urine and tested my HCG levels everything was fine. She then recommended the flu vaccine and Rhogam because of my blood type without informed consent. I was only told its was to protect me and the baby so I will not get sick and risk losing the baby and that was the last thing I wanted to do so we proceeded with vaccination for the flu and the Rhogam . I felt on top of the world and I was finally complete until my 16 week ultrasound them my whole world came to a whole end .During the ultrasound they noticed some abnormalities with his anatomy of the fetus brain and revealed the gender I WAS HAVING A BOY!!! The initial diagnosis was Downs Syndrome and I was in complete denial because my Downs syndrome screening before the vaccination came back negative for the potential of any anomalies. I followed up with my OBGYN and rescheduled another ultrasound to get a better look at what was going on with my son. When I followed up with my OBGYN she dropped me as her patient and referred me to the High risk fetal concerns clinic. From there that dream of recording my babies firsts went out the window and my new nightmare began. I talk as though I do not love my son. I love my baby; he will always be my oversized baby! However, the inner grief I suffer when I see NORMAL FAMILIES take their NORMAL CHILDREN to school, playdates, Chuck E Cheese, out in public my heart is filled with resentment and guilt. My life instead consists of heart monitors, wheelchairs, ventilators, suction machines, medicine cabinets and making sure my baby stays stable enough to get to appointments. God forbid we are in the middle of a storm where we could likely lose power, which is my son's lifeline. I should have done my research or my treating physician should have informed me prior to a medical procedure I knew zero about. I know without a shadow of doubt I would not be in pain everyday knowing somebody out there is responsible for this. In my heart, I just knew I was doing the right thing as a first time mom! I never knew that syringe would seal the fate of what is now my new normal. My son is now 4 years old. He cannot walk, talk, eat by mouth nor absorb food; he is exclusively TPN, which is I.V nutrition. He cannot breath on his own without the help of mechanical ventilation. Not thinking about the fact that he had an adverse reaction to the flu vaccine, I kept vaccinating and our troubles were not over. For a month straight after his DTAP, varicella, rotavirus, MMR vaccine my son would scream high pitched all day everyday for hours. I just thought that is what babies do, particularly babies with special needs and a host of health problems. After my son received the rotavirus vaccine and contracted rotavirus, he nearly died of 104 temperature, projectile vomiting and explosive diarrhea at children's hospital. When my baby tested positive for rotavirus they looked in his immunization chart and he received against it. So why did my sweet little guy have rotavirus? He never fully recovered from the virus and getting him to tolerate Gtube feeds is difficult. I just wish for my OBGYN to have given me the option to have a healthy baby and a normal life. It takes 4 hours to pack up my baby to go to a doctor so they can tell you what they THINK is wrong with your kid but they really do not know. I have to deal with the isolation of being a special needs parent, learn how to use lifesaving machinery and teaching those who went to school for years to work in the medical field on how to use it. I would not wish the feeling of isolation, living in a hospital

room for months on end, watching your precious baby pricked and prodded on anyone. All the while just wishing you can turn back the hands of time and decline the one thing that turned your life on its head and that is VACCINES. They say correlation does not equal causation; tell that to my son's two perfectly healthy baby brothers who did not have mercury pouring into their developing bodies while still in the womb.

My name is Judith Jolly, RN, BSN. I reside in Columbia County, Wisconsin. As a registered nurse, I have administered vaccines as well as cared for several severely injured vaccine children. I am reaching out to you to respectful request that be no action taken to change our current school and childcare vaccination laws and exemptions.

Vaccine injuries are real. The government admitted this fact in 1986, with the creation of The National Childhood Vaccine Injury Act of 1986. This law acknowledged that vaccine injuries and deaths occur and that there should be financial compensation to persons who are vaccine injured. As of January 2, 2019, there have been payouts over 4 billion to individuals and families who have had their lives irreversibly altered by vaccines. Yet, nearly 2 out of 3 vaccine injury claims are ultimately denied, leaving many families to face lifelong financial burdens because of their injuries.ii The claims court, designed to be a simple "administrative" process, has now become a battleground for vaccine-injured victims seeking the promised compensation from the Vaccine Injury Act of 1986. Most vaccine injury claims take many years to adjudicate because the Departments of Health and Justice use a nearly endless amount of taxpayer dollars to fight against awarding compensation for the majority of children and adults who apply.

There are significant gaps in scientific knowledge about the biological mechanisms of vaccine injury and death. In the past 25 years, the Institute of Medicine (IOM) has acknowledged that there are genetic predispositions and individual susceptibility that may increase the risk of vaccine injury. In most cases, doctors find it difficult to predict who will be harmed by vaccination. In 2012, the Institute of Medicine stated that for eight routinely used vaccines (MMR, DTaP, hepatitis B, hepatitis A, varicella zoster, pneumococcal, influenza and meningococcal), there were too few scientifically sound studies published to determine whether more than 100 serious brain and immune system problems, such as multiple sclerosis, arthritis, lupus, stroke, SIDS, autism and asthma, were or were not caused by the vaccines. iv In 2013, The Institute of Medicine stated the following – "key elements of the entire schedule – the number, frequency, timing, order and age at administration of vaccines – have not been systematically examined in research studies."

As a nurse, I learned to respect the rights of my patients and families. Informed consent was required for all care provided. Patients have the right to know the all risks associated with any medical procedures. Coercion and bullying have no place in healthcare and is a serious ethics violation. Sadly, this is longer the case. Parents of vaccine injured children as well as individuals who question vaccine safety have become targets of verbal abuse and bullying by legislators, healthcare providers and the media. There are numerous campaigns aimed to end bullying and verbal abuse in our schools and workplaces, yet vaccine injured and vaccine hesitant parents and individuals continue to be attacked and in the media and by legislators.

The First Principle of the Nuremberg Code is "The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision." vi Vaccine mandates that do not allow for exemptions are a violation of this code and should not be acceptable in a democratic country. Vaccines come with risks, both known and unknown. When there is a risk involved, there MUST be a choice.

Vaccine Injury Stories

Tamara L: "Against the SCREAMING in my gut, we went ahead with my sons 2mo vaccines. He was only 5 weeks adjusted. What ensued was 6 days of agony. Screaming. Not eating. Not sleeping. Pitch black projectile diarrhea. High fevers. Dr said it must be coincidental. Likely a "virus". Ah NO. I was sick wondering if he would come out of it. The photo I took of him showed exactly how he was. When he wasn't screaming for hours he was completely out of it. Wouldn't interact, respond, no emotion. Nothing. Thankfully he did eventually bounce back but shortly after started showing symptoms of my disorder. Dysautonomia. Raynauds. We haven't had one shot since. He will be 2 1/2 next month. this was him the day after the vax."

Tara H: "My son 6 month shots, 105 temp and encephalitis. My daughter chronic ear infections and respiratory infections, most gut damage, random high fever spikes of 104-105, ODD. My oldest: asthma, chronic ear infections , chronic vomiting. My friend's baby died after her 6 month shots, her intestine wrapped around itself and was the 4th most common reaction listed on the insert"

Andrea D: "Myself fainting spells and diagnosed with dysautonomia after HPV vaccine. Second child went limp and had motor deficits after Dtap."

Christi M: "Both my brother and I received the MMR on schedule back in the 90's. My mom said we changed overnight, we became monsters. In addition to that, I got put on Ritalin by the age of 3 and stayed on different drugs for ADHD until I graduated. My brother also was diagnosed with ADHD but not till HS. I suffered from chronic ear infections also. My family (sister,dad,myself) are all immune compromised as well (hashimotos, reynauds, lupus)."

Sarah P: "Developed lazy eye after HepB in infancy. Have struggled with depression, bouts of anxiety and rage, PCOS, insulin resistance, and chronic fatigue with brain fog. I suffer vertigo and migraines frequently."

Sara H: "My business partner's son went unconscious and needed to be resuscitated after his 6 month vaccines. His brain swelled and caused Cerebral palsy. He died at age 17. All was verified to be a vaccine reaction by his pediatrician and a neurologist and my partner got nothing. The vaccine courts called it viral encephalitis even though the child's doctors disagreed 😢"

Becca L: "My mom was told when I was a child in the 80s that I was allergic to thimerosal but it was better to take a risk of allergic reaction than get measles. My whole childhood was spent sick and in pain. My little body was constantly reacting. I had awful migraines, eczema, monthly ear infections, strep throat every 6 months, etc. finally went away in my teens when I was no longer being vaccinated. at age 29 found out I was also allergic to polysorbate after a reaction. I have

partial hearing loss from all of the allergic reactions that causes my eardrums to rupture and POTS. Also, year round allergies that I didn't have before age 29.

My 12 year old was injured at age 5 when I went to "catch" her up for kindergarten. About a week later she was very ill. I thought she had the flu. But no one else in the house got sick. Then it came back a few weeks later and she would repeat the cycle every few weeks. That's when I knew something was wrong. I was given heartburn meds to give her. What a joke as they did nothing. I was told she will grow out of it. About 2 years ago I finally had a name for her disease. She has gastroparesis from a reaction to a vaccine when I went to get her caught up. There is no cure. We can manage the symptoms but she will always have issues. Any more vaccines would likely do more damage to her vagus nerve.

My cousin took her second daughter in for her two-month vaccines. Later that night her husband heard over the monitor some weird sounds. Their daughter had stopped breathing. They got her to come back but she was taken to the hospital by ambulance. That was 10 years ago. Neither of her daughters have been vaccinated since.

My dad was given a flu shot and is immunocompromised. Not only did he end up with the flu and pneumonia that year, he also almost died from encephalitis. Years of rehab."

Kayla R: " In high school I received a tetanus shot. My entire arm had excruciating pain, turned dark purplish from shoulder to black fingers, and lost circulation for 2 days. We didn't know better to take pics or report. I also suspect my food sensitivities and Reynauds disease stem from shots but have no way to verify as i was also raised on the standard American diet"

Elizabeth L: "My oldest daughter was damaged by the Dtap. She has low muscle tone. Her legs took lots of PT to get her moving at 16/17 months. She received a flu shot when she was 6 and could barely move the arm for a few weeks. 7 years later she still has a lump at the injection site. Middle child was hospitalized after round of shots at 18 months.... 2 ear infection, restrictive airway and bacterial pneumonia. Recovered. Didn't know better. Same child at 4 year old shots for kindergarten he began getting horrible belly pain. Began projectile vomiting. For no reasons. Except vaccines. Seen at Mayo Clinic and determined it was cyclic vomiting syndrome. My Youngest has eczema. Partially vaccinated up to 12 months. No more."

Savannah B: "My brother in 1985. Reacted to DTap (or whatever was used at that time... Mom cannot remember) at 2 and 4 months. Had a fever of 105, non stop screaming for hours, etc. Doctors said his symptoms were not from the vaccine and that it was weird timing. My mom said NO more to the shot at 6 months and the doctor told her she had to. She said she didn't care she wasn't doing it and he'd probably die if she did it again. He got other shots but she continued to refuse DTap. For myself I had terrible each infections as a child as well as awful eczema. My

mom said it was terrible and would crack and bleed. As an adult, I had terrible perioral dermatitis, also could be called eczema around my mouth for months and couldn't figure out what was going on. It wasn't until a few months ago I realized for 2 years this flared up (and lasted a good month or more each time) after I got a flu shot which became mandatory for my job. I also had breathing issues around this time which impacted my running. I was diagnosed with borderline asthma and given an inhaler to use as needed. I quit that job, partly because of the flu shot (still not knowing it was connected to the skin issues) and haven't gotten any vaccines since that last flu shot in 2015. I've had no eczema or skin issues since that time. No way to prove it was the flu shot but so coincidence that the flare up was a week after the flu shot and I've had no more issues."

Melissa S: "My daughter had her 1 year vaccines (MMR, Hep A, Chicken Pox) and ended up in the ER 16 hours later with swelling grossly throughout the R side of her body, lymph nodes the size of golf balls, and her joints on the R side of her body were red and hot and painful. They quarantined her, performed X rays, MRI's blood work, etc and were unable to determine a cause. Her lymphatic system went haywire. The Immunologist that was on her case said given the time frame of her vaccines and her symptoms it was most likely the cause BUT she could not document that because it was controversial! Her system remained stressed and her eosinophils were extremely elevated for almost 2 years. We underwent further testing and the specialists determined she had a reactive RA type of reaction most likely stemming from the Rubella part of the MMR shot. Our daughter is now 8 and still struggles with side effects, weakened overall immune system, elevated eosinophils, and taxed lymphatic system."

Maggie L: " My stepdaughter got a booster MMR two years ago when "the measles were coming to town"...without my husband's consent. She was a smart little 4 year old with very clear speech and a large vocabulary. Within a week of that vaccination, she developed a terrible stutter. It is still difficult for her to get out the simplest of words.

My stepson (who is fully vaccinated and will continue to be, per his mother) is 7 years old. He has had ear tubes in and out since he was 2 years old due to chronic ear infections. He has permanent hearing loss. He has dealt with severe speech delays his entire life, still in speech therapy twice a week at school. He has eczema all over his back and in his ears. He also deals with extreme constipation. I feel all of this is vaccine related."

Amanda N: "Both of my boys reacted to MMR. My oldest lost all of his speech, etc at about 15 months and my middle had a high fever that couldn't be broken for about 2 weeks. He ended up in Children's ER with what we now suspect (after talking to 2 different doctors) was brain swelling after numerous episodes of writhing in pain and uncontrollable, primal screaming for hours on end. Children's told us it was constipation and sent us home. They cannot get a medical exemption."

Vaccine Injury Stories

Bernadette P: "I received the tdap vaccine before I was allowed into my program for college. I passed out after receiving the shot and became super sick for 7 days. Shortly after my health began to rapidly decline. I was diagnosed with an autoimmune disease. Funny thing is my doctors never told me, they just put me on the lowest dosage meds for my 1st pregnancy. After my daughter my autoimmune disease went full blown. I went to specialist who finally told me. They put me on meds. I became pregnant again and was told everything looked good including my levels for my meds. Turns out that was a lie and I lost the baby. I took matters into my own hands, changed my diet, asked for different blood tests and meds (all of which my specialists knew nothing about and said wouldn't help) I've turned my health around almost 80%, got pregnant again and carried the best of my pregancies. I will have this for the rest of my life. If my children are at the same risk of developing an autoimmune disease why would I risk that? I'm at high risk now for diabetes, heart problems, and developing other autoimmune diseases."

Amanda T: "My husband suffered a mini "stroke" 3 years ago. Numerous tests did not show traditional stroke results, but he did show all the initial symptoms (he had the stroke right in front of me, so I know that's what it was). After 2 visits to the ER and being blown off by 2 doctors, we found a doctor that found a major adrenal crash most likely caused by all of the vaccines that he had when he was in the military. Also, when he was in the military, he had an immediate (within hours) reaction to the anthrax vaccine. High fever, vomiting, diarrhea, etc."

Meghan B: " I have nephew labeled "autistic" after receiving the MMR vaccine at age 4 (he was on a delayed schedule) his parents don't believe he is autistic, but vaccine injured, and cannot get a medical exemption."

Rhea K: "My best friend lost ability to walk, see, urinate, and had massive headaches after a flu vaccine in 2009. Symptoms came on the week after she got it. Docs couldn't find any reason for it but when asked if it was related to vaccine it was completely denied (flu vaccine package insert list disorders that have these same symptoms)."

Janice M: "My son Jordan had an anaphylactic reaction to the flu shot at 6 months old. Further testing revealed an egg allergy, which his pediatrician said did not explain the magnitude of his reaction to the shot and there must have been other elements in the vaccine that he was reacting to. His current diagnoses include food allergies, asthma, epilepsy, anxiety, chronic Lyme, and autism. He cannot get a medical exemption."

Melanie M: "My first born (born in '09) was vaccinated on schedule until 7 yrs old. He screamed for days after his 2 month shots and his speach regressed after his mmr. I was under the impression the worst thing that could happen was a fever. He had non stop ear aches until they slowed down around age 8. My second son (born in '16) was vaccinated on schedule up to

4 months then, due to a shortage of vaccines, he only received the DTaP at 6 months. He had a lot of issues before the DTaP including no bowel movements and eczema. The Dr said is all normal, even though these are common listed side effects/adverse reactions of those vaccines. After the DTaP his eczema got worse and he developed tremors where his body would get stiff and his arms would go straight out and he would shake a few seconds then stop. The whole first year of his life he was constantly sick (cough, runny nose, diarrhea, fever) no joke.. Dr still said everything was normal! I started looking for answers since my Dr was of no help and didn't inform me what the possible adverse reactions are and what to look for incase something were to happen. Neither Dr was not interested or able to diagnose adverse reactions or identify that my children are not ideal candidates for vaccinations. I cannot get a medical exemption. I'd like to see a safer vaccination process before continuing and until then we need to keep all 3 exemptions available for parents to choose what's best for their children. Thank you."

 Kaci P: "My son got his 2 month vaccines on November 28 in the afternoon and screamed the whole way home, until he fell asleep- he wouldn't wake to nurse and didn't eat the rest of the day, he just slept. I tried to wake him to eat but he wouldn't wake up. The next morning I woke up to find him with poop everywhere, up his back and front and down his legs. Every time he nursed he screamed and screamed afterwards. He wouldn't lay on his tummy anymore and he just screamed. He would projectile vomit up to 3 feet, every poop was pure liquid and mucousy. I remember one day i had a full load of laundry just from him before lunch. He also had eczema and a horrible raw butt/ diaper rash. After a week I called the Dr's office back and the nurse I spoke to said I needed to take him to the ER right away. Unfortunately that trip was a waste of time, even though the ER doctor watched my son nurse and vomit right in front of her, when she didn't have an answer for me and didn't want to talk about my sons recently received vaccines she tried to tell me he just had a UTI.
For the next 6 weeks we spoke to several nurses over the phone, we went to urgent care, followed up with our pediatrician, and saw another pediatrician in the office as same day appointment. Everyone we saw just kept saying he had a virus. I knew it wasn't a virus because viruses don't last 6 weeks, so I called again and spoke to another nurse, and asked if we could come in and have testing done to see what virus my son had and the nurse told me "No, we don't test for specific viruses because we don't do anything to treat viruses."
I found out, that my son cannot have casein, soy, yeast, or corn. These are all ingredients in the vaccines my son received and I had to change my diet in order to breastfeed my son. This was a listed reaction on the package insert, listed as gastrointestinal: vomiting and diarrhea.
I went to my sons next scheduled appointment, 4 month checkup, and told the Dr I figured out why he had been so sick and he adamantly disagreed and said "That's not how vaccines work." Even though I showed him it was a listed reaction. Then he expected me to give him the next

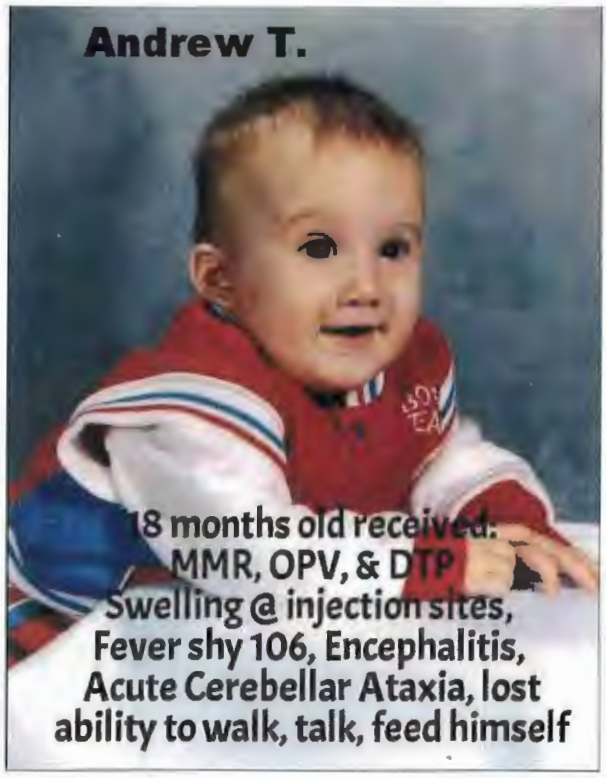
round of vaccines. My son will be 3 in September and still gets sick anytime he has dairy, soy, yeast or corn, and cannot get a medical exemption."

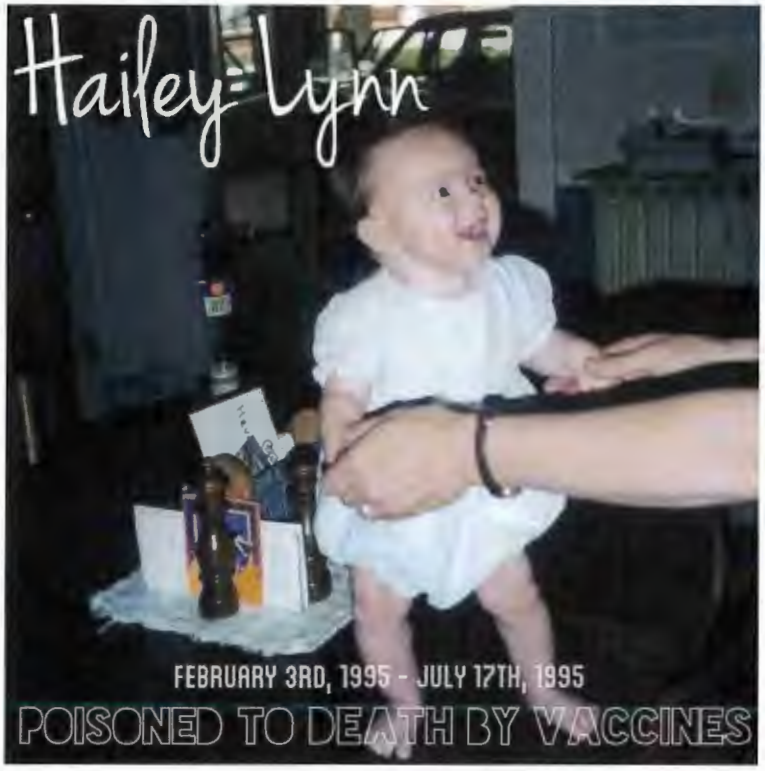
Crystal D: "In 1991 I had an MMR vaccine at school and I went into anaphylactic shock and seizure. When my mother got the call they said to expect the worst. I was in 5th grade (the age recommendation has changed since then) and I remember my brain feeling like it was on fire. I've never been the same since. I struggle to concentrate and have memory issues. My husband is a combat veteran and is vaccine injured from the anthrax vaccine. He had two doses before it was recalled and has battled kidney failure since. He requires daily medication to prevent them from failing. He did not wear his uniform and fight for our freedom just for it to be taken away."

Kellie K: "I had terrible fevers as a child. The kind where my mom would call priests to pray over me & I would lose bodily functions. Now I have some mysterious autoimmune issues. My son suffered the same terrible fevers. He was ALWAYS sick. Asthma, eczema & adhd. I finally put 2 & 2 together. It was the vaccines. We stopped as a tenager. He finally grew out of all those diagnose. My daughter who is vax free got her first cough at 4. Her first ear infection at 5. She'd never thrown up until she was 5. She is healthy. Because she wasn't poisoned."

Foh S: "My first grandchild died of SIDS at three month. He'd recently been vaccinated. My son valiantly tried to give his infant child CPR until the paramedics arrived. They got a heart beat again but no idea how long he had been without oxygen. He was life-flighted down to Children's Hospital in Madison, where we waited for 3 agonizing days for brain swelling to go down to see if there is any brain activity. There wasn't. It was time to disconnect him. It took another several hours for him to pass, all the while watching my young son & his wife age in front of me... my parents grew elderly in those 72 hours as we waited for Dominik, their first great-grandchild to pass away. I died a little bit inside with him. His siblings, now 8 and 4, managed to heal the large gaping hole in our hearts. They are UNvaccinated. Beautiful, healthy, intelligent. Our healing salve. R.I.P. Dominik Michael"

Vaccine Injury Stories





Vaccine Injury Stories

Sarah Yee
6 hrs

These are recent photos of my friend's son before and after the DTaP. On top of the horrific all-over body sores and loss of speech, after this photo was taken his face swelled up and he had 2 seizures. He was totally fine before the shot, yet the doctors are calling all these symptoms a coincidence, and refusing to acknowledge that the vaccine was responsible. Absolutely incredible.

OCTOBER VACCINE INJURY AWARENESS MONTH

Luke was born well connected, hitting all of his developmental milestones and appropriately communicated by the age of one. August 5th, 2005 Luke was injected with 9 vaccines during one well visit; Tripedia's Diphtheria Tetanus Pertussis, Haemophilus Influenza Type B, Measles Mumps Rubella, Vericella, and Pneumococcal PCV 7. Luke ran a fever had a raised migrating rash and soon after became hypothermic, and lethargic. He did not speak again for three years. He is now classified as autistic.

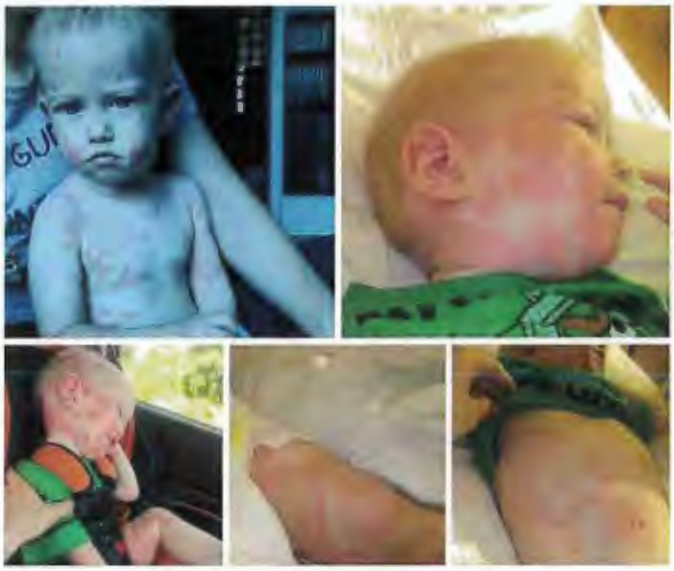
Kari Bundy with **Heather Tate Malone** and **8 others**
13 hours ago

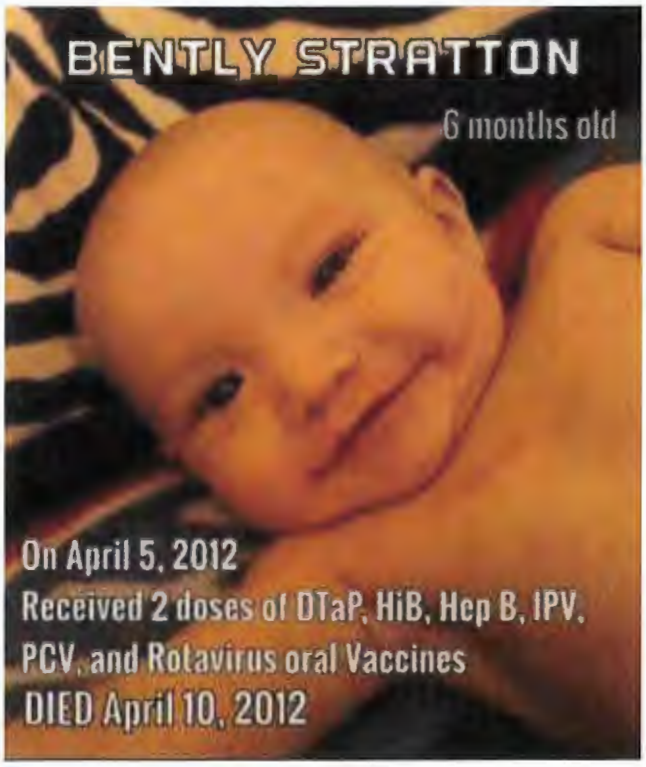
My silly boy. Oliver, sick with Pertussis is pictured on the LEFT. He wasn't vaccinated. My vaccinated son, Mason, is pictured on the RIGHT-- this now I took his remains home with me a few days after he received his dtap vaccine, which I chose for him because I was made to feel terrified of "deadly Pertussis" (Again- Oliver is sick with Pertussis in the photo on the Left) Chance of getting sick and dying from Pertussis-- 0.003832%

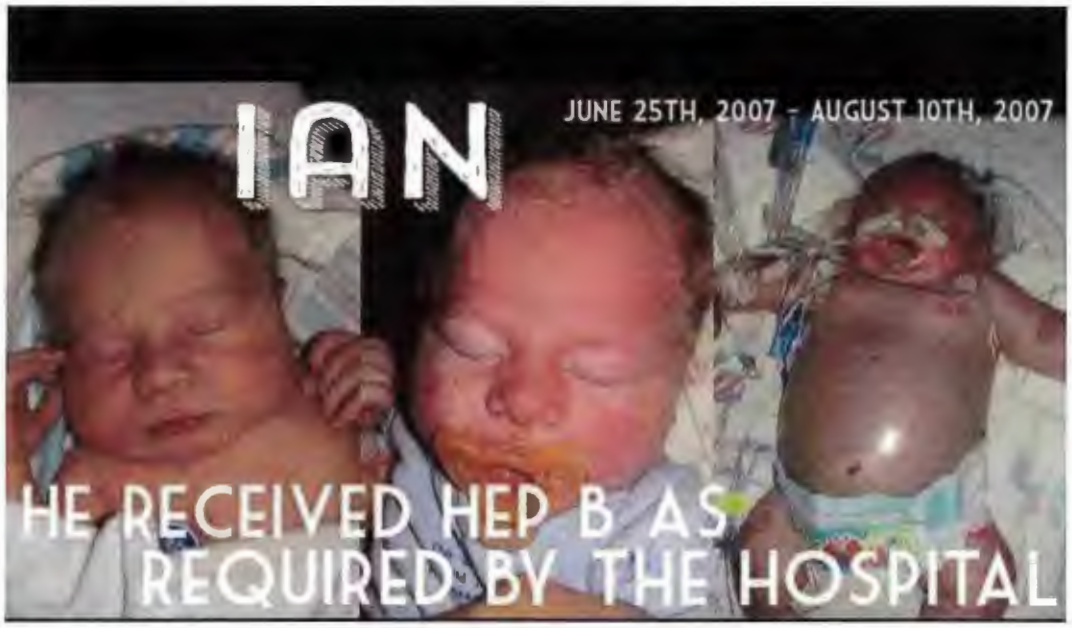
Vaccine Injury Stories

Ariel Fluno
13 mins ·

Heres was MMR did to our son. He suffered for 3 weeks inconsolably. Id take natural measles and IIFE LONG IMMUNITY over this any day. Sorry if me and other parents decide not to get anymore or any at all. But go worship your vaccines. I havent had an mmr since early child hood. Im "unprotected". Dont come near me. Idk how im still alive.






IAN
JUNE 25TH, 2007 - AUGUST 10TH, 2007
HE RECEIVED HEP B AS
REQUIRED BY THE HOSPITAL


Ja'Liyah Cortize Turner
NOVEMBER 29TH, 2013 - APRIL 18TH, 2014
She was 4 months and 20 days when she
Passed away about 4 days after shots

Vaccine Injury Stories

This is a picture of my nephew 2 weeks after receiving the dtap shot and a pic of him healthy the day before vaccation playing with my daughter. I myself do not vaccinate but my little sister did. The greif has been unreal as we lost this sweet boy on july 2, 2014. Can anyone recommend a grief site for her. I urge all parents to research bwfore vaccinating. His death certificate came in and it was ruled as death by vaccination.

Vaccine Injury Stories

My beautiful Angel Johlyn Naval... 01/18/11-01/24/11... stolen from me by the Hep B vaccine.... I can never again hold her in my arms... but I will FOREVER hold her in my heart... ♥ ... Sleep peacefully my love... ♥ Xxxx ♥ oooO ♥

R.I.P. PRECIOUS BABY GIRL
DUE DATE WAS May 4, 2014
She was gone less than 4 days after her mom received the flu vaccine.

Kayla Was 35 Weeks Into A Healthy Pregnancy When Her Doctor Recommended She Get The Flu Vaccine. That Was On Monday March 31, 2014.

That Friday, The Ultrasound Showed Their Baby No Longer Had A Heartbeat.

She Was Born A Still-birth.

Flu Vaccine Package Inserts State They Have Not Been Tested On Pregnant Women For Safety Or Efficacy.

Doctors Stated The Flu Shot Had Nothing To Do With What Happened.

Kayla Says Thank You For Your Prayers. She Was Going To Complete Our Family And We Miss Her So Much.

Vactruth.com

Vaccine Injury Stories

Parents of Saba Button who was victim of flu vaccine debacle receive payout from WA Government

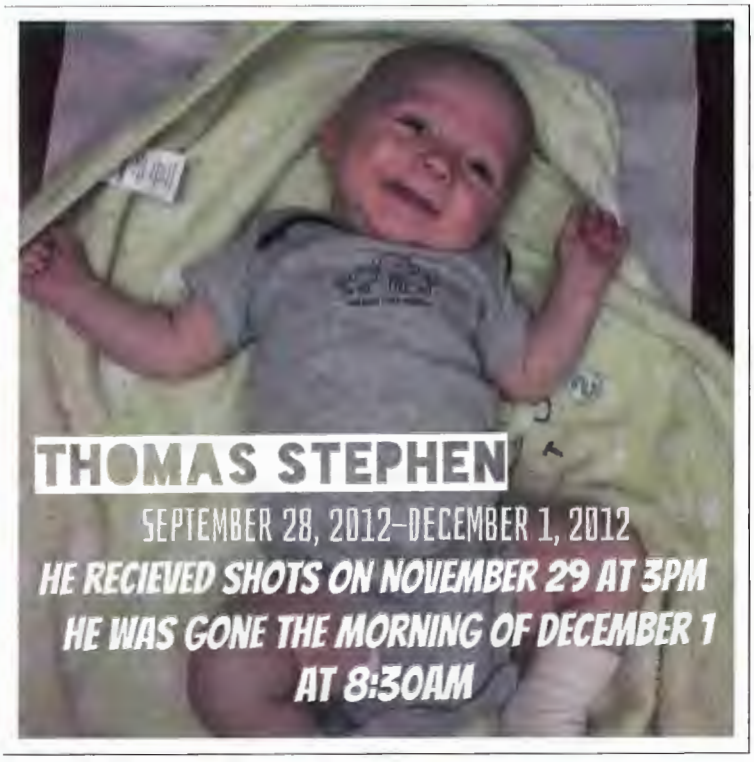
THE parents of a WA girl who has been awarded millions in damages after a defective flu jab left her severely disabled say they it's a "massive relief" the legal...

WWW.PERTHNOW.COM.AU

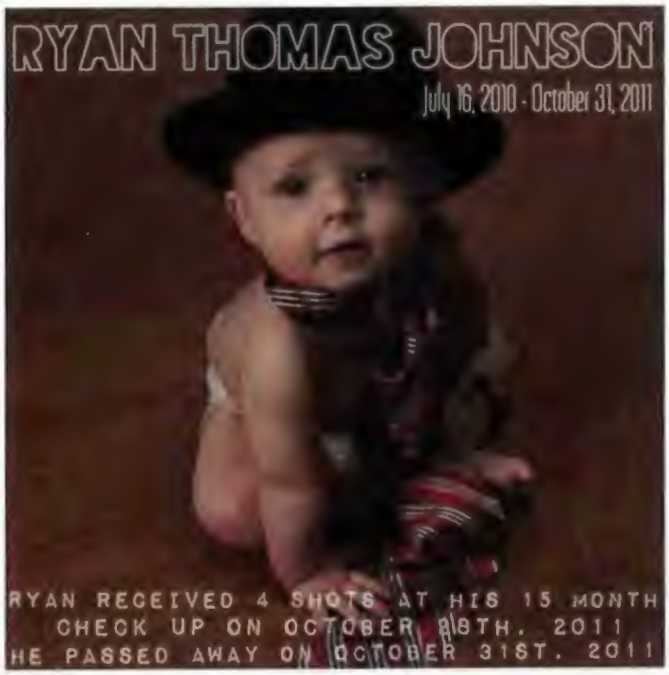
Vaccine Injury Stories

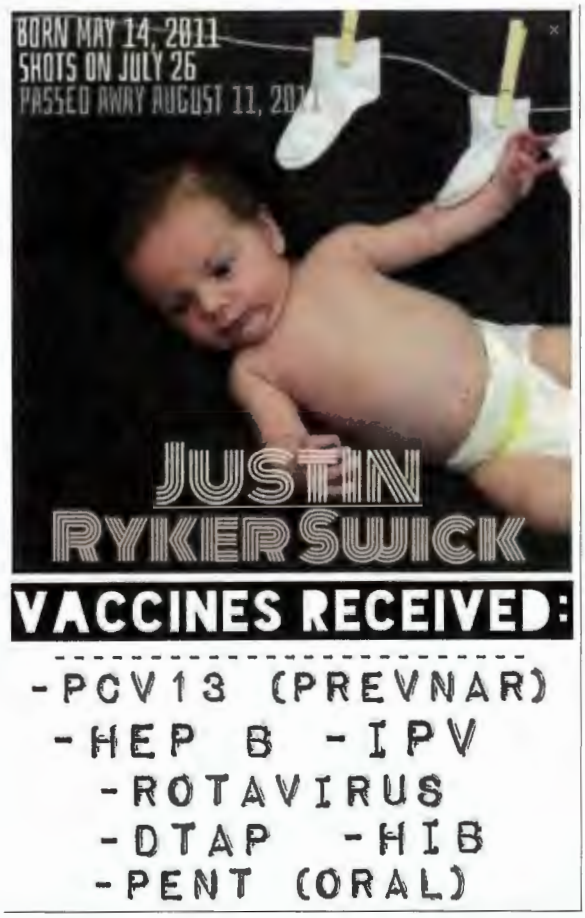
Girl with sore throat gets HPV vaccine, dies hours later
August 8, 2014
http://fox4kc.com/2014/08/08/girl-with-sore-throat-gets-hpv-vaccine-dies-hours-later/

Vaccine Injury Stories

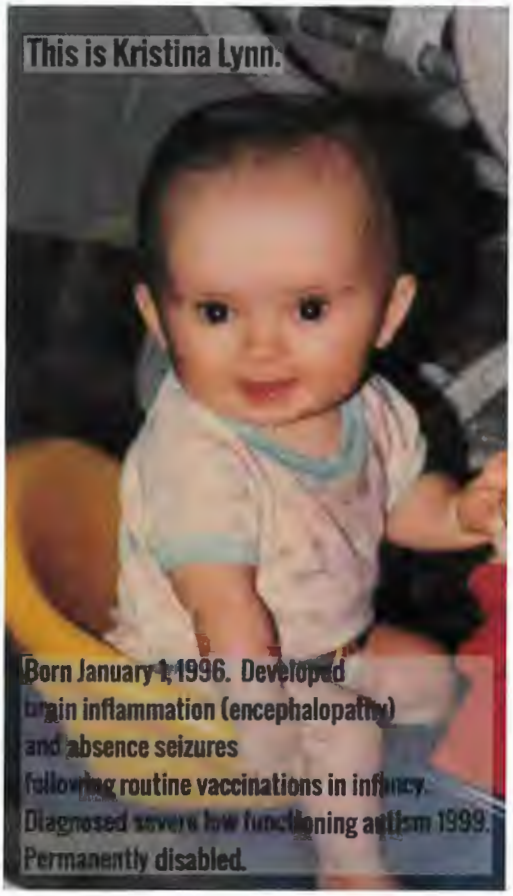


Vaccine Injury Stories





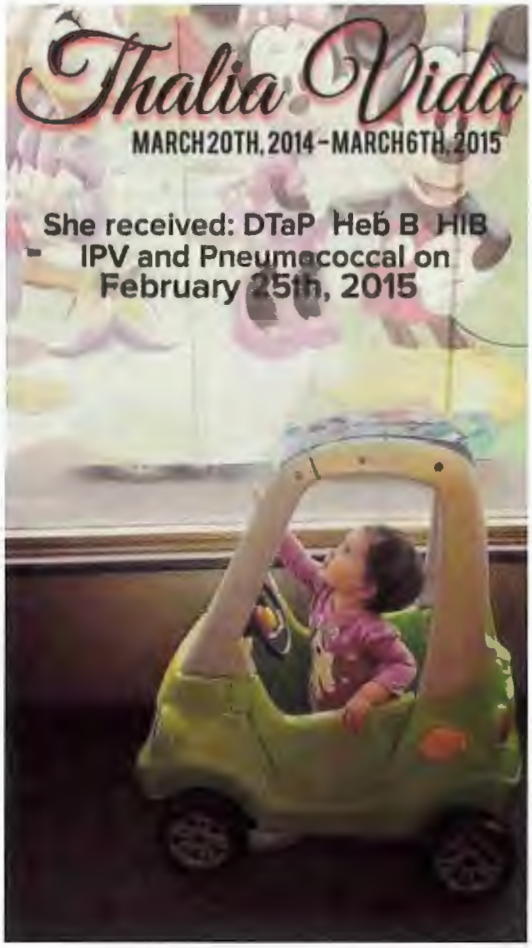
Vaccine Injury Stories



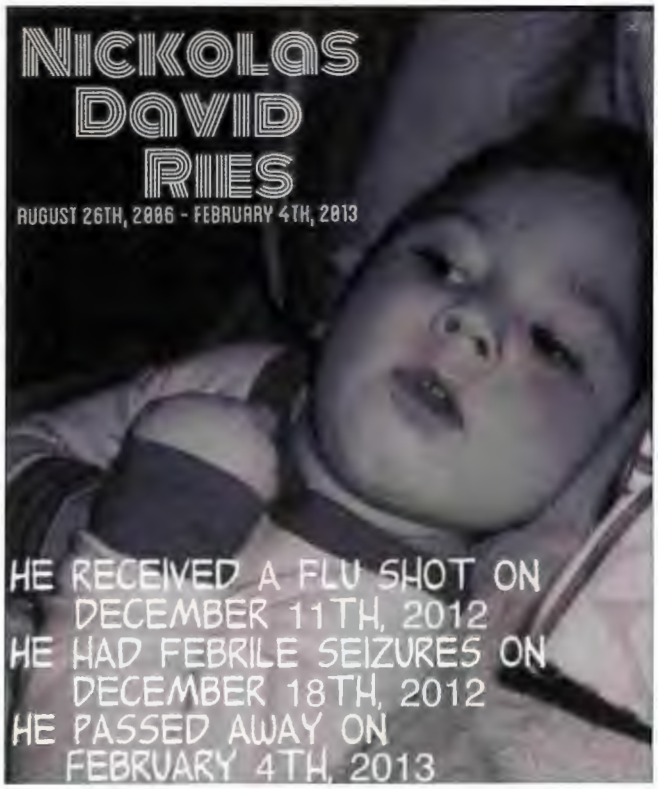
Infant Twins Die Simultaneously After Vaccines, Medical Board Rules 'Just a Coincidence'

Posted by Erin Elizabeth | Feb 1, 2017

Given that the sudden and simultaneous deaths of twins rarely occur, you would think- especially given the fact that they had been recently



Vaccine Injury Stories



YouTube

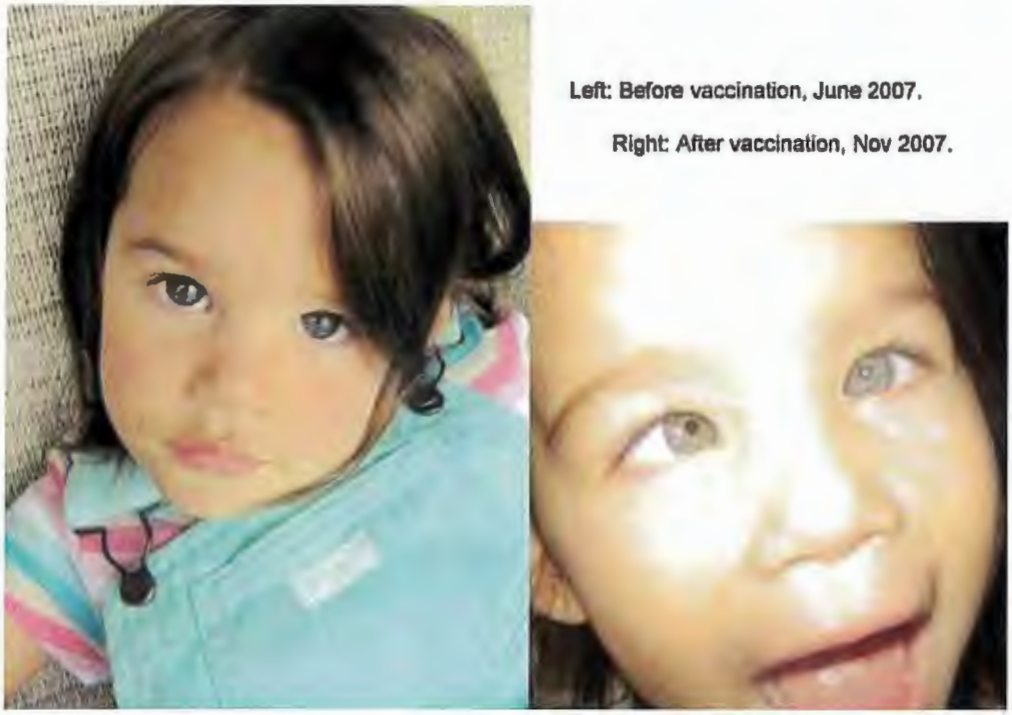
Our Special Angel Was Brain Damaged by a Vaccine!

Vaccine Injury Stories

Http://www.ageofautism.com/2013/11/flu-shot-induced-encephalopathy-chandler-webbs-death-raises-vaccine-safety-questions.html

BUT HEY, AT LEAST HE DIDN'T GET GENITAL WARTS.
#BigPharmaLogic #ProVaxLogic

Vaccine Injury Stories

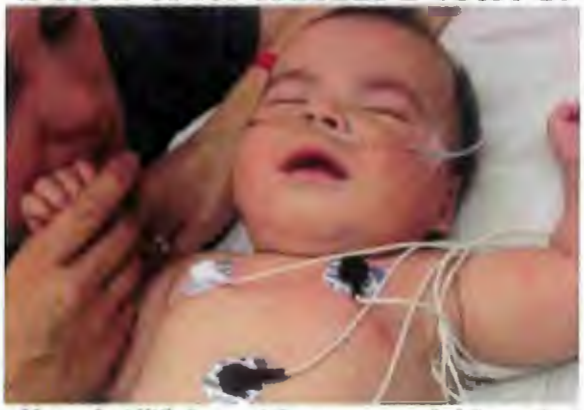


Left: Before vaccination, June 2007.

Right: After vaccination, Nov 2007.

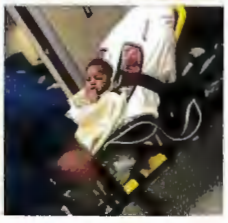
I don't have epilepsy yet,

but I will when I leave.



My perfect little boy got the recommended 4 month vaccines on May 13th...on May 21st he had a status seizure that lasted between 45 minute - 1 hour long.

So my son just got his 4 month shots and not even 24 hrs later his temperature was 102 and he was having seizures right before our eyes. We are still currently in the hospital right now. He hasn't been himself since the shots. No appetite, little cat naps, fever coming and going, and he's just not as happy as usual the picture of him smiling was like a hour before he got his shots. When he came home from the dr he just wouldn't stop crying and I just didn't understand why then about 10 hours later he was seizing. I'm so sad that my baby boy has to go through this. I will not be letting him get vaccinated again.



Tealover
@hornswaggled2

Replying to @bridgtpike

This is why. We DID vax; this was the end result for her.

8:01 AM · 3/30/19 · Twitter Web Client

Vaccine Injury Stories

Baby Dies after Routine Vaccinations

Article from **The Healthy Home Economist**

2

Healthy, full term baby dies after routine vaccinations for Hep B, Polio and DPT.

Published on March 18, 2013

Vaccine Injury Stories

Illinois Teen Dies of ADEM Three Weeks After HPV Vaccination

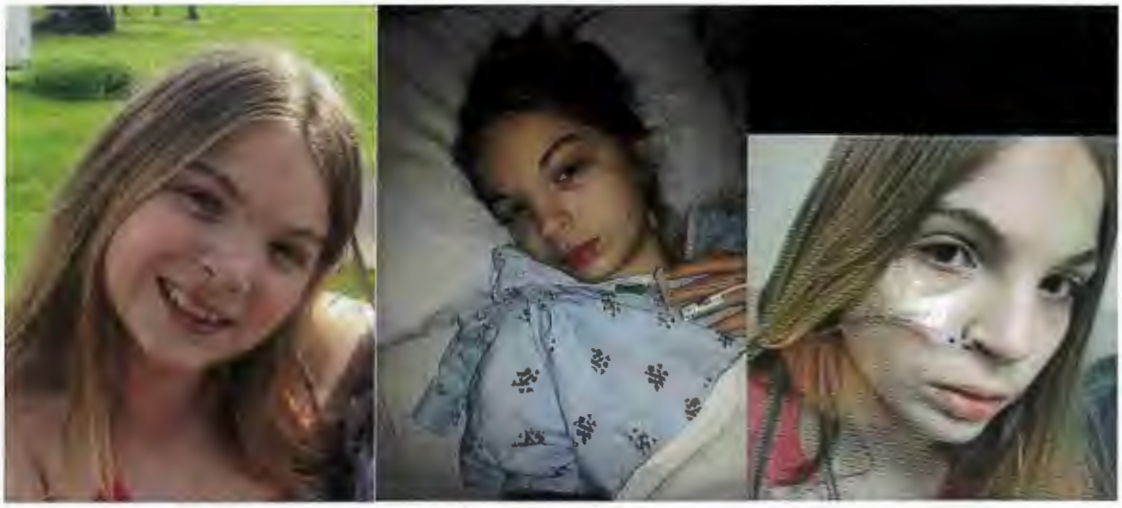
by TVR Staff
Published September 12, 2018 | Vaccination, Risk & Failure Reports

121K
SHARES

Leila
and her family
VICTIMS OF VACCINES
Gone in 3 days after 3 shots.
2/5/10 to 2/20/11

2011

Vaccine Injury Stories



Before Gardasil **After Gardasil**

Vaccine Injury Stories

The following #wedid campaign was in response to the viral photo that you see attached to some of the images. The goal was to help people understand that the majority of those who do not vaccinate were forced to make that choice because their child was harmed. The vast majority of those who don't vaccinate, actually did at one point. The very act of vaccinating is what led them to not continue to do so.

This is a small sampling of the hundreds shared.

Vaccine Injury Stories

Vaccine science is NOT settled

Vaccine Injury Stories

MMR - DTAP - POLIO at 5 yrs old.
Immediately regressed into fevers, absent seizures, chronic body pain, 24/7 head pain, lost language/skills developed autism within months.
Sensory processing disorder, cyclic vomiting and chronic nausea.
No vaccines for 9 yrs remained stable.
MEN C at 14 yrs old.
Same day regressed into chronic pain, chronic exhaustion, collapsing, stopped walking, talking, eating & became bedridden and wheelchair bound. Hospitalized as near to death for 6 months. Diagnosed with CRPS, POTS, CFS. Nasal gastric fed. ACC funded chronic injury rehabilitation home based team.
Acquired brain injury confirmed.

Vaccine Injury Stories

The #saidnomotherever campaign began when people began saying that they would rather have a child with autism instead of getting measles. People effected by vaccine injury responded by trying to show that no mother dealing with a vaccine injured child would say that. The reality is that most people don't understand until it happens to them.

Here are a few of their stories.

Vaccine Injury Stories

Vaccine Injury Stories

My son suffered brain and gut injury from the MMR that I have spent 16 years trying to heal. I'm glad I have dealt with this rather than two weeks with measles, said no mother of a vaccine injured child ever.

Cheryl Peeples
#saidnomother

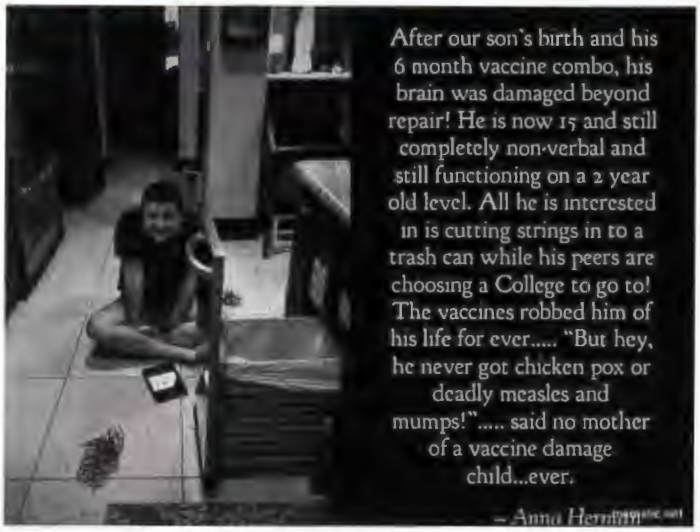
Vaccine Injury Stories

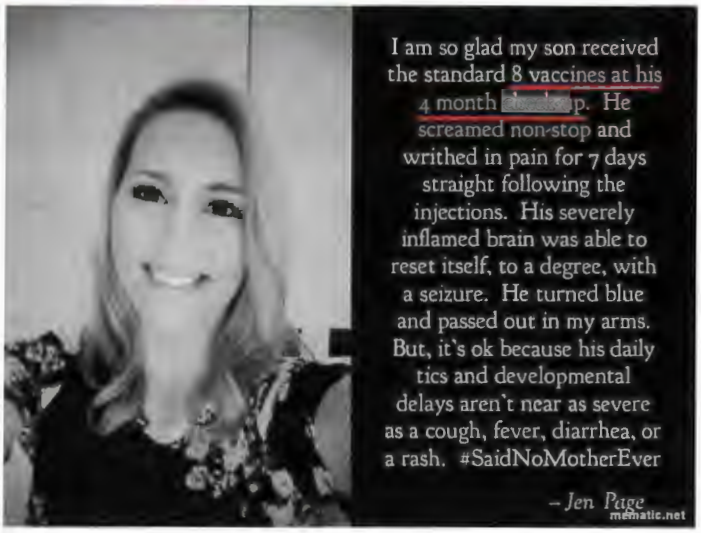
I've enjoyed decades of watching my son falsely labeled "severely autistic and mentally retarded" who really has life-threatening seizures, brain damage, insomnia, and chronic pain from vaccine injury.

His denied services by schools and insurance companies is awesome! Divorce, medical bills, and bullying our entire family has been great!

- Jamie Lynn Melillo, M.S., Licensed MFT

#SAIDNOMOTHER





Vaccine Injury Stories

Vaccine Injury Stories

Vaccine Injury Stories

Vaccine Injury Stories

#saidnomother

I'm really grateful that the NICU staff at Evanston Northshore Hospital never informed me that prospective safety studies on vaccinating premature infants has never been carried out and that post-marketing studies have found increased risk of life-threatening cardiorespiratory events, sepsis and intraventricular hemmorage. I'm so grateful that I wasn't informed that the Hep B vaccine causes liver damage, increases brain aluminum content 50-fold and chronically activates microglia in animal models said no mother ever. -Suzanne Allmart

#saidnomother #ipakNICUchallenge #HepB

Vaccine Injury Stories

MY SON MATTHEW WAS RUSHED TO THE ER THE SAME DAY HE RECEIVED HIS 12 MONTH VACCINATIONS. THE MMR, VARICELLA (CHICKEN POX), HIB, FLU, PCV 7 PNEUMOCOCCAL AND HEPATITIS B, WHICH CAUSED HIS BRAIN TO SWELL WITH ENCEPHALITIS. WE THOUGHT WE WERE GOING TO LOSE OUR CHILD. HE LOST HIS SPEECH AND WOULDN'T ANSWER YOU WHEN YOU CALLED HIS NAME. HE DEVELOPED SENSORY ISSUES AND A LIFELONG DISABILITY OF AUTISM, BUT I SURE AM GLAD HE DIDN'T GET THE MEASLES OR CHICKEN POX.

#SAIDNOMOTHER

~DAPHNE PHILLIPS

I am so glad I subjected my children to vaccines given in untested combinations and which contain aborted fetal DNA fragments. Not only did their shots cause a variety of adverse reactions including wheezing, allergies, eczema, tics, stims, purpura, and night terrors, but my pro-life conscience can live with regret for the rest of my life. It's all worth it though, because they were almost protected against getting whooping cough...said no mother ever.

Jill Wright
#saidnomother

The best decision I have ever made as a mother was to let my son's pediatrician inject my only son with 9 vaccines at one time. The dark circles under his eyes, high fever, and constant nausea after his vaccines had nothing to do with the fact that he fell asleep and never woke up again. I wake up every day with no regret and no guilt that I let this happen to my sunshine. #saidnomotherever

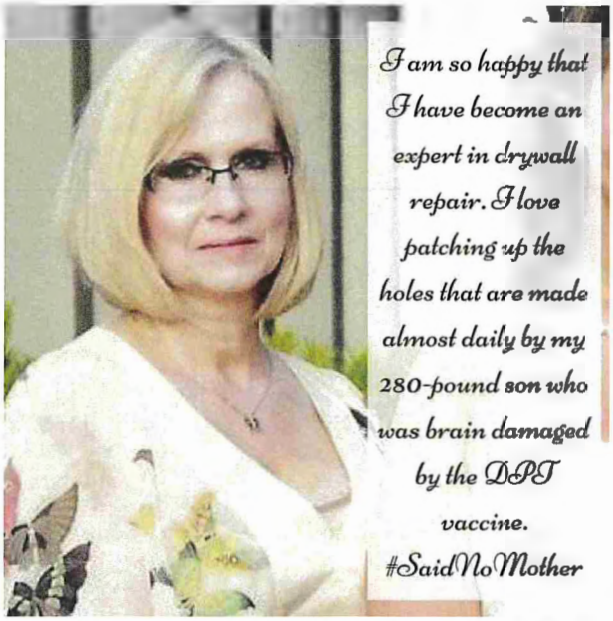
Johnathan M. Wurz
12/19/12-02/25/2017

"I LOVE IT HOW MY 12 YR OLD MUMBLES LOUDLY TO HIMSELF CONSTANTLY, MAKING HIM A TARGET FOR BULLYING."
~SAIDNOMOTHER

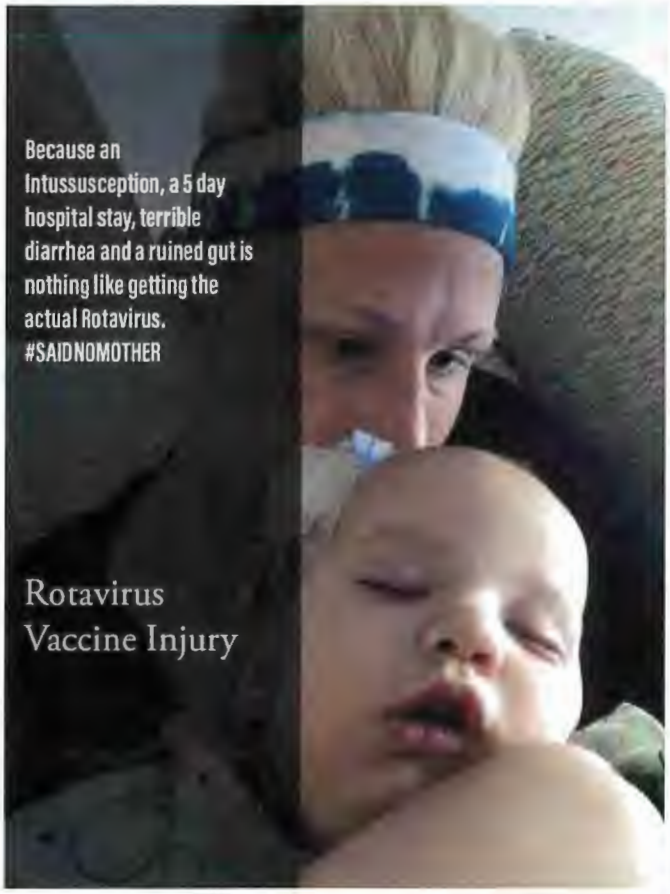
~MADELINE CRIOLLO

Vaccine Injury Stories

Vaccine Injury Stories



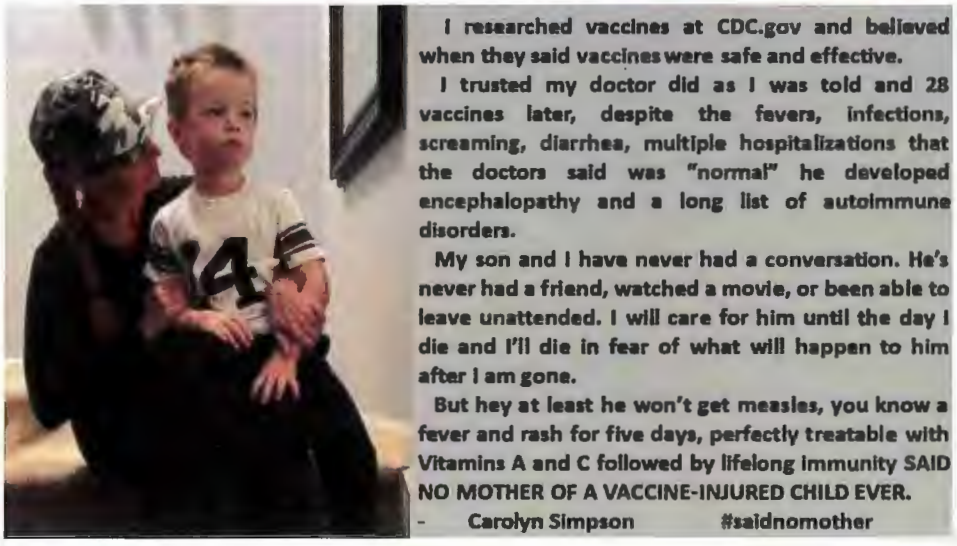
Vaccine Injury Stories



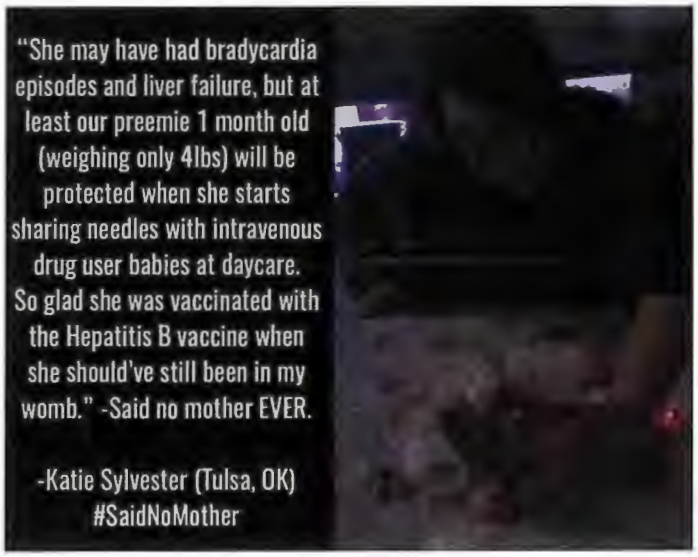
Vaccine Injury Stories

When I was 13 weeks pregnant I got the flu shot and it caused my amniotic sac to rupture and I lost 95% of my amniotic fluid. This led to several doctors insisting that I end my pregnancy. When I chose not to abort, I went on 14 weeks of bed rest only to find out that the rupture of my amniotic sack caused my uterus to collapse on my son dislocating his right knee, which led him to have reconstructive knee surgery at 8 weeks old. We've also spent the last 8 years going to physical therapy to help him walk, run and strengthen his thigh muscles.
But thank God I didn't get sick with the flu while I was pregnant!

-Shannon Kroner
#saidnomother



Vaccine Injury Stories



Following a routine round of vaccines at his 4-month checkup, my son screamed non-stop for SIX DAYS straight! Digestive, behavioral, cognitive, language, sensory, sleep, anxiety and social issues - are just a few that we have dealt with or are still dealing with now... 4 and a half years later! ... But "Go get your DAMN vaccines!"

#SAIDNOMOTHER


I LOOK FORWARD TO DISCRIMINATION
BY PEOPLE CLOSE TO ME
BECAUSE MY SON CANNOT BE
VACCINATED FOR MEDICAL REASONS.
#SAIDNOMOTHER
EVER