Vaccination.

Your health. Your family. Your choice.

Is the Childhood Vaccine Schedule Safe?

An epidemic of chronic disease and disability is plaguing America's children, who are the most highly vaccinated children in the world and also among the most chronically ill and disabled. Today, the Centers for Disease Control (CDC) states that 1 child in 6 in America suffers with learning and behavior disorders while millions more suffer with asthma, diabetes and other chronic allergic and autoimmune diseases. The epidemic of chronic disease and disability among children has increased dramatically in the past five decades.

U.S. CHILD CHRONIC DISEASE INCREASES

1976: 1 child in 30 was learning disabled	→	***2013:*** 1 child in 6 is learning disabled.
1980: 1 child in 27 had asthma	→	***2013:*** 1 child in 9 has asthma.
1992: 1 child in 500 developed autism	→	***2013:*** 1 child in 50 develops autism.
2001: 1 child in 555 had diabetes	→	***2013:*** 1 child in 400 has diabetes.

THREE TIMES AS MANY VACCINATIONS FOR CHILDREN

1953: CDC recommended 16 doses of 4 vaccines (smallpox, DPT) between two months and age six.

1983: CDC recommended 23 doses of 7 vaccines (DPT, MMR, polio) between two months and age six.

2013: CDC recommended 50 doses of 14 vaccines between day of birth and age six and 69 doses of 16 vaccines between day of birth and age 18.

MULTIPLE VACCINATIONS GIVEN SIMULTANEOUSLY

In 1983, the CDC directed doctors to give a child no more than 4 vaccines (DPT, polio) simultaneously. By 2013, the CDC directed that a child can receive 8 or more vaccines at once.

The Institute of Medicine published a report in 2013 stating that *"key elements of the entire [CDC recommended childhood vaccine] schedule – the number, frequency, timing, order and age of administration of vaccines – have not been systematically examined in research studies."*

VACCINATIONS DURING PREGNANCY

A new CDC policy directs doctors to give pregnant women one dose of influenza vaccine in any trimester and one dose of pertussis containing Tdap vaccine after 20 weeks during every pregnancy. The Food and Drug Administration (FDA) has determined that large, well controlled long term studies have not been conducted to confirm that influenza and Tdap vaccination during pregnancy is safe.

National Vaccine Information Center

50 DOSES OF 14 VACC
69 DOSES OF 16 VA

Before you take the r

Based on the CDC's 2017 Recomm

BIRTH (12 hours)	2 MONTHS	4 MONTHS	6 MONTHS
Hepatitis B	Diphtheria	Diphtheria	Diphtheria
	Tetanus	Tetanus	Tetanus
	Pertussis	Pertussis	Pertussis
	Polio	Polio	Polio
	Haemophilus Influenzae Type B (HIB)	HIB	HIB
	Rotavirus	Rotavirus	Rotavirus
	Hepatitis B	PCV	Hepatitis B
	Pneumococcal (PCV)		PCV
			Influenza

VACCINE INGREDIENTS: Different vaccines contain different ingredients including lab al proteins, antibiotics and human, animal and insect DNA and RNA. Learn more at NVIC.org.

National Vaccine Information Center | 21525 R

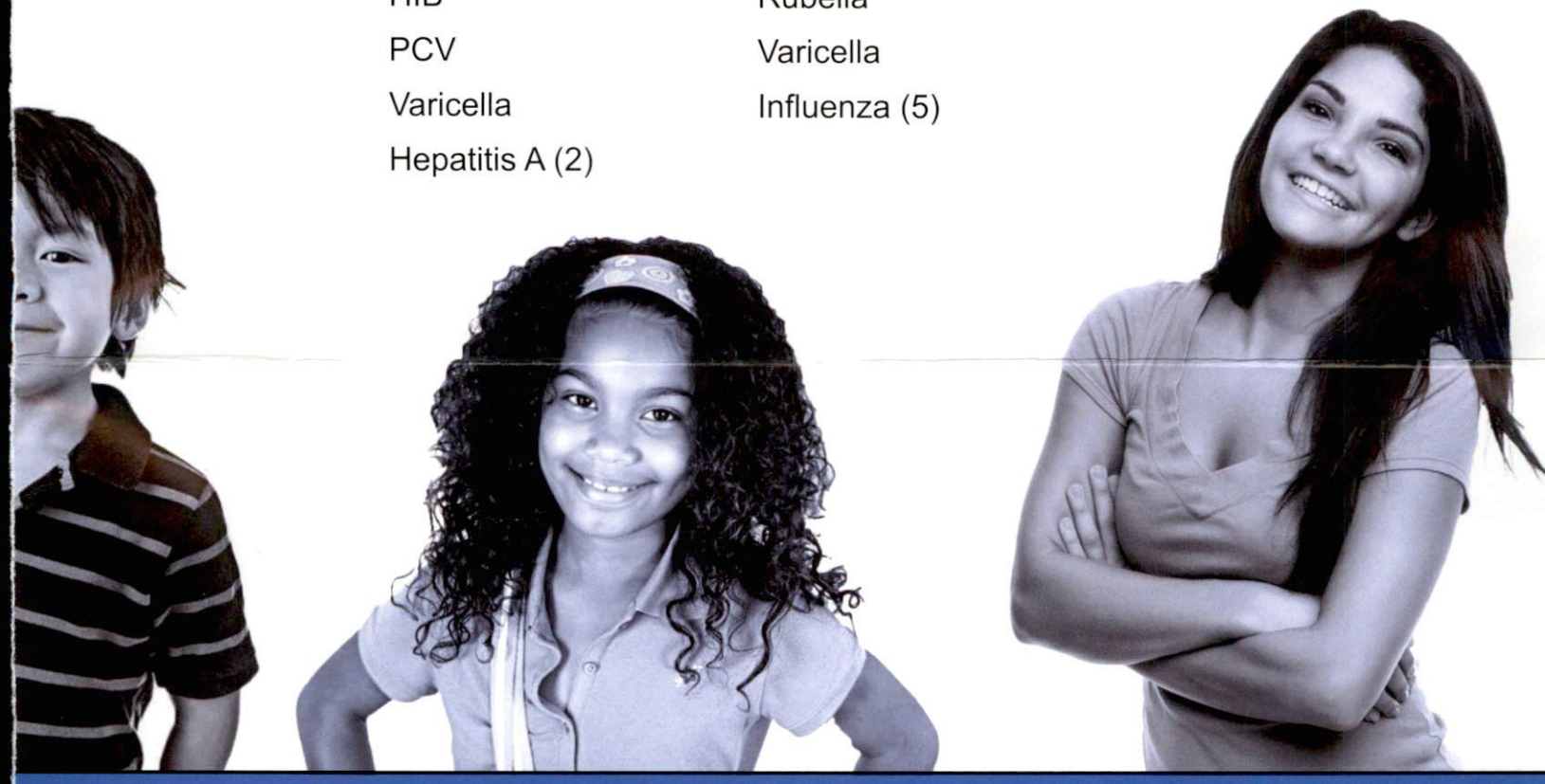
Revised 12/2017

CINES BEFORE AGE 6?
CCINES BY AGE 18?

isk, find out what it is.

ended Childhood Vaccine Schedule

7 MONTHS	12 - 18 MONTHS	2 - 6 YEARS	7-18 YEARS
Influenza	Diphtheria	Diphtheria	Diphtheria
	Tetanus	Tetanus	Tetanus
	Pertussis	Pertussis	Pertussis
	Measles	Polio	Influenza (12)
	Mumps	Measles	Human Papillovirus [HPV] (2)
	Rubella	Mumps	Meningococcal (2)
	HIB	Rubella	
	PCV	Varicella	
	Varicella	Influenza (5)	
	Hepatitis A (2)		



tered live or inactivated viruses and bacteria, chemicals, metals,

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National Vaccine Information Center

www.NVIC.org

If You Vaccinate Your Child,

Learn How to Recognize the Signs and Symptoms of Vaccine Reactions*

VACCINE REACTIONS	MOTHER'S DESCRIPTIONS
High Fever (over 103° F)	"His temperature was 105 degrees. I had to put cool towels on him to bring the fever down."
Skin (hives, rashes, swelling)	"There was a big, hot swollen lump at the site of the shot that stayed for weeks."
High Pitched Screaming	"It was a pain cry, a shrill scream and lasted for hours and nothing would help."
Collapse/Shock	"She turned white with a blue tinge around her mouth and went completely limp."
Excessive Sleepiness	"He passed out and we couldn't wake him to feed or do anything for over 12 hours."
Convulsion	"Her eyes twitched, her chin trembled, her body went rigid and then would shake."
Brain Inflammation	"He just laid in his crib with his eyes wide open then would arch his back and scream and go un conscious. Now he has seizures."
Behavior Changes	"She won't sleep or eat. She throws herself down and screams for no reason. She was sweet and happy and is now out of control. She changed into a totally different child."
Mental/Physical Regression	"My 18 month old son stopped talking and walking after those shots. He developed severe allergies, constant diarrhea, ear infections and was sick all the time."

Other reported vaccine reactions include: loss of muscle control, paralysis, regressive autism, asthma, arthritis, blood disorders, diabetes, Guillain Barre syndrome, sudden death.

Call a doctor immediately or go to an emergency room if symptoms of serious vaccine reaction complications or dramatic changes in physical, mental, or emotional behavior after vaccination.

NATIONAL CHILDHOOD VACCINE INJURY ACT OF 1986

By June 2016, over $3.3 billion had been awarded for vaccine injuries and deaths suffered by more than 4,500 children and adults.

REPORT VACCINE REACTIONS

Serious health problems following vaccination should be documented in medical records and promptly reported to the federal Vaccine Adverse Events Reporting System (VAERS). You can also make vaccine reaction reports to NVIC's Vaccine Reaction Registry, which has operated since 1982 and serves as a watchdog on reports submitted to VAERS.

LEARN MORE

Go to NVIC.org and learn more about signs and symptoms of infectious diseases and vaccine reactions; how to report vaccine reactions; how to meet deadlines for applying for federal vaccine injury compensation and how to protect your legal right to informed consent to vaccination in America.

DID YOU KNOW...

Vaccines are pharmaceutical products, which carry risks for injury and death that can be greater for some people than others. NVIC encourages everyone to become fully informed about both the risks and complications of diseases and vaccines before making a vaccine decision.

REPORTING VACCINE REACTIONS

Recognizing a vaccine reaction is critical for seeking appropriate medical attention. All vaccine providers are legally required to report serious adverse events (hospitalization, injury, death, etc.) experienced by children or adults after vaccination to the federal Vaccine Adverse Event Reporting System (VAERS). Vaccine providers are also required to record adverse events following vaccination in an individual's permanent medical record. Consumers may also directly report any serious health problem that occurs after vaccination to VAERS for all vaccines.

For more information on vaccine reaction symptoms and reporting, **www.NVIC.org.**

Ask 8 If You Vaccinate!

1. Am I or my child sick right now?
2. Have I or my child had a bad reaction to a vaccination before?
3. Do I or my child have a personal or family history of vaccine reactions, neurological disorders, severe allergies or immune system problems?
4. Do I know the disease and vaccine risks for myself or my child?
5. Do I have full information about the vaccine's side effects?
6. Do I know how to identify and report a vaccine reaction?
7. Do I know I need to keep a written record, including the vaccine manufacturer's name and lot number, for all vaccinations?
8. Do I know I have the right to make an informed choice?

If you answered yes to questions 1, 2, and 3, or no to questions 4, 5, 6, 7 and 8 and do not understand the significance of your answers, please visit NVIC.org for more information.

Informed consent to medical risk-taking is a human right!

VACCINE INJURY

Not all symptoms that occur following vaccination are caused by the vaccine(s) recently received. However, it cannot be automatically concluded that symptoms which do occur are not caused by a vaccine. There are also many reported vaccine reactions that have not been adequately studied before new vaccines are licensed and given to millions of people.

It is important for your vaccine provider to record ALL serious health problems, symptoms or dramatic changes in physical, mental or emotional behavior that occur following vaccination. This information should be recorded in permanent medical records and reported to VAERS.

Until it has been determined that any serious health problem, which developed after vaccination was not causally related to the vaccination(s), further vaccination may significantly increase risks for more serious health problems.

IDENTIFYING VACCINE REACTIONS

If you or your child experiences any of the symptoms listed below in the hours, days or weeks following vaccination, it should be reported to VAERS. Some vaccine reaction symptoms include:

- Pronounced swelling, redness, heat or hardness at injection site;
- Body rash or hives;
- Shock/collapse followed by unresponsiveness, deep sleep;
- High pitched screaming or hours of persistent crying;
- Changes in sleep/wake pattern, and dramatic personality changes;
- High fever (over 103 F);
- Twitching or jerking of the body, arm, leg or head;
- Weakness/paralysis of any part of the body;
- Crossing of eyes, loss of eye contact, awareness or social withdrawal;
- Loss of ability to roll over, sit up or stand up;
- Head banging or unusual flapping, rubbing, rocking, spinning;
- Joint pain or muscle weakness;
- Disabling fatigue;
- Loss of memory;
- Onset of chronic ear or respiratory infections, breathing problems (including asthma);
- Severe/persistent diarrhea, or chronic constipation;
- Excessive bruising, bleeding or anemia.

ABOUT THE NATIONAL CHILDHOOD VACCINE INJURY ACT OF 1986

NVIC's co-founders worked with Congress to secure vaccine safety informing, recording and reporting provisions in the National Childhood Vaccine Injury Act of 1986, which created the federal vaccine injury compensation program (VICP) as an alternative to a civil lawsuit against vaccine manufacturers and doctors. By June 2016, over $3.3 billion had been awarded for vaccine injuries and deaths suffered by more than 4,500 children and adults.

This historic law acknowledged that vaccine injuries and deaths are real; that the vaccine injured and their families should be financially compensated; and that vaccine safety and informed consent protections were needed in the mass vaccination system.

The 1986 law required vaccine providers to provide parents of minor children and adults with written Vaccine Information Statements (VIS) before vaccination; keep written records of vaccine manufacturer names and lot numbers for each vaccine given; enter serious health problems following vaccination into the permanent medical record; and report serious health problems following vaccination to the federal Vaccine Adverse Events Reporting System (VAERS).

After decades of abuse by federal health agencies and neglect by Congress, the VICP had become far too adversarial with a history of denying two out of three vaccine injured plaintiffs compensation and failing to adequately implement vaccine safety provisions. In 2015, NVIC publicly called for an end to the partial civil product liability shield that Congress gave to vaccine manufacturers in 1986 and the total liability shield given by the U.S. Supreme Court in 2011 when the Court affirmed that government licensed and recommended vaccines are "unavoidably unsafe."

Visit www.NVIC.org for more information on vaccine reactions and how to meet deadlines for filing a compensation claim in the VICP.

ABOUT US

The National Vaccine Information Center (NVIC) is a charitable non-profit organization founded in 1982 by parents of vaccine-injured children. NVIC is dedicated to preventing vaccine injuries and deaths through public education and to securing and defending informed consent protections in U.S. vaccine policies and laws.

NVIC does not make vaccine use recommendations or give legal or medical advice. We support the availability of all preventive health care options and the right of consumers to make educated, voluntary health care choices without penalty.

OUR WORK

NVIC provides the following programs and services to the public.

- ✓ Public education about vaccines and diseases;
- ✓ Analysis and monitoring of vaccine research, regulation, policymaking, and legislation;
- ✓ Health choice advocacy to secure informed consent protections in vaccine policies and laws;
- ✓ Promotion of quality scientific research into vaccine safety questions and identification of high risk factors for vaccine injury;
- ✓ Counseling, information and resource referral for the vaccine injured.

PROTECT VACCINE CHOICES IN YOUR STATE

Go to NVICAdvocacy.org and learn how you can take action to protect medical, religious and conscientious belief vaccine exemptions in vaccine policies and laws.

National Vaccine Information Center

www.NVIC.org

If You Vaccinate

Ask 8 Questions

Your Health.
Your Family.
Your Choice.

HB 1312 – NVIC (National Vaccine Information Center) Concerns:

http://leg.colorado.gov/sites/default/files/documents/2019A/bills/2019a_1312_01.pdf

- Requires anyone using a religious or personal belief exemption to submit the exemption in person to CDPHE (Colorado Department of Public Health and Environment) or county, district or municipal health agency on a form developed by CDPHE. The form has to be signed by a representative of the dept. (Page 6 line 22 through Page 7 line 10)
- Requires CDPHE to develop educational materials regarding only the benefits of immunizations and update those annually. (Page 5 lines 4-9)
- Requires physicians and PAs who write medical exemptions to submit that medical exemption to the tracking system. (Page 6 lines 10-13)
- Subsequent renewals of exemptions would have to be submitted online or in person to CDPHE. (Page 7 lines 10-19)
- Requires CDPHE or the county, district, or municipal health agency to submit religious or personal belief exemption data to the tracking system. (Page 8 lines 4-8)
- Requires CDPHE to adopt rules for medical exemptions based on contraindications described by ACIP (Advisory Committee on Immunization Practices). (Page 8 lines 9-15)
- Requires CDPHE to report exemption information annually as part of the "State Measurement for Accountable, Responsive and Transparent Government Act" (SMART). (Page 8 lines 16-22)
- Requires CDPHE to adopt the immunization recommendations from ACIP. This means the health department would be forced to adopt the full ACIP Recommended Schedule and mandate those vaccines in Colorado. (Page 9 lines 10-14)
- Allows CDPHE to go even further than ACIP recommendations giving them authority to mandate vaccines in addition to those recommended by ACIP. (Page 9 lines 16-21)
- Allows CDPHE to adopt rules to establish the timing by which schools, parents and students must comply with the vaccine requirements. (Page 9 lines 21 - 25)
- Requires medical practitioners to submit vaccine and medical exemption data to the tracking system, but also states that they are not subject to a regulatory sanction for not complying. (Page 10 lines 11-19)
- No fiscal note

Supporting and additional information, Cindy Loveland testimony in opposition to HB 1312:

Spinning immunization and exemption rates:

Letter explaining why Colorado was not DEAD LAST vaccinating, dated Jan. 7, 2004. (Page 1-4)

National Immunization Survey selected Vaccination Series all states for 2002. (Page 5-6)

Three things to know from the Colorado Health Institute White Paper on Colorado immunization rates, published May 2005. (Page 7)

CDPHE chart showing statewide fully Immunized and exemption rates by vaccine, 95.4% for MMR (Measles, Mumps and Rubella Vaccine) 92.9 percent in compliance, meaning 7.1% of students were not compliant with either a certificate of immunization showing vaccines given or a medical, religious or personal belief exemption on file. (Page 8)

Rate spinning in Washington and Oregon. (Page 9-11)

Graph showing Colorado in the middle of the county for multi-vaccine category for children 19-35 months using NIS numbers. (Page 15)

Graph showing NIS numbers for MMR for 19-35 months compared to US 1995 to 2017. (Page 16)

ADDITIONAL INFORMATION:

1978 personal exemption added to Colorado State Law. HB 1089. (Page 12-14)

Policy perspective from CCIC (Colorado Children's Immunization Coalition) policy perspective – Addressing the barriers to vaccination. (Page 17)

Copy of certificate of immunization from 1992, front and back, included both immunizations and exemptions. (Page 18)

Current Non-Medical (Religious and Personal Belief) exemption form. (Page 19-20)

CDPHE Immunization Program workgroup draft forms from 2011 showing compelled speech and requiring the signature of a religious leader. (Page 21-22)

Association of American Physicians and Surgeons letter of opposition to HB 1312 dated April 9, 2019.

Cindy Loveland
State Contact for NVIC
mrssnappy@aol.com

Jan. 7, 2004

Colorado is **NOT DEAD LAST** in vaccinating toddlers.

A recent article in the Rocky Mountain News stated – the *$500,000 for immunization is aimed at getting children the full range of shots they need. State health officials told lawmakers earlier this month that Colorado ranks 50th in the nation with a 62.7 percent immunization rate.* (1)

From another article, *top health officials told lawmakers they're embarrassed the state ranks dead last in the nation in childhood immunizations* (2)

As the state contact for NVIC (National Vaccine Information Center), I have serious concerns about the way this immunization survey is being interpreted and used.

There are several things that public and elected officials should take into consideration before using the 2002 National Immunization Survey as justification for any policy changes or funding.

First, Colorado is **NOT** last in vaccinating toddlers for most vaccines according to this study. If you look at the estimated individual vaccine coverage levels for children 19 to 35 months for 3 DTP, 3 Polio, 1 MMR, 3 Hib (Haemophilus influenzae type b) and 3 hepatitis b, they are all over 90%. In each of these categories there are states that rank below CO. (3) (see attached)

Cont.

Second, the category used by the CDC to rank Colorado last included a 4th DTP shot by the age of 35 months. (4) In Colorado, the 4th dose of DTP can be given up until the age of 48 months. (5) The low ranking does not take this factor into account.

Third, and more importantly, in Colorado the 4th and 5th dose of DTP has been suspended since April 2001 because of shortages. More funding will not change vaccination coverage rates if there are long-term shortages or differences between CDC recommendations and the actual Colorado immunization schedule. (6)

Fourth, the estimates for states should *be interpreted with caution* according to the CDC publication MMWR, (Morbidity and Mortality Weekly Report). (7)

Finally, Colorado meets the target set by the Health and Human Services *Healthy People 2010* document for vaccination coverage of toddlers of 90%. According to this document, *vaccination coverage levels of 90 percent are, in general, sufficient to prevent circulation of viruses and bacteria-causing vaccine-preventable diseases.* (8)

Colorado does **NOT** have a crisis in vaccinating toddlers. Colorado is only last when using a category that includes the suspended 4th DTP shot that can be given up to the age of 48 months.

I would like to know if Governor Owens and elected officials are getting all pertinent details of this study.

I would also like to know how state health officials plan to use the $500,000.00 that is "aimed at getting children the full range of shots they need".

NVIC and their Colorado members are opposed to any efforts to increase immunization rates or provide "outreach" that would include; parents being coerced to get all shots by using the immunization tracking system; limiting rights of parents to exempt their children from vaccines for medical, religious or personal reasons; or giving parents inaccurate or incomplete information regarding the risks vs. the benefits of vaccines. (9)

Colorado parents are already experiencing serious challenges to their rights to exemption. The number of calls I receive from parents having trouble with exemptions has gone up significantly in recent months. One outrageous example was a newborn baby in Grand Junction forced by court order to receive hepatitis b vaccine against the parents' objection for religious reasons despite the fact that the mother did not have hepatitis b. (10)

Parents choose not to vaccinate their children according to the "one size fits all" schedule for many different reasons. Most parents that I deal with who are exempting their children from vaccines are doing so for religious reasons, because they have a child who was damaged or killed by a vaccine reaction or because of legitimate safety and efficacy concerns. Many Coloradoans also choose to take an alternative or natural approach to health care and wellness.

Cont.

Parents, like myself, are doing their own research into vaccines are discovering that there is much more to consider than what they are getting from physicians, the media and local health officials.

The recent flu outbreak and how information was disseminated is an example of this. People getting a vaccine at the local King Soopers or Kmart are not going to be able to get all the information they need about the vaccine or contraindications, let alone have a chance to read the package insert to see what's in the shot. No one in public health or the media ever mentioned the fact that most flu vaccine still contains the mercury preservative thimerosal. (11) (See attached) Several childhood vaccines still contain mercury. (12)

The controversy over what role mercury in childhood vaccines has in the increase of autism and learning disabilities is ongoing. One recent study concluded - ***strong epidemiological evidence for a link between increasing mercury from thimerosal containing childhood vaccines and neurodevelopment disorders***. (13)

Another concern that has been overlooked is the fact that The Institute of Medicine study, *Multiple Immunizations and Immune Dysfunction*, concluded that *epidemiological evidence regarding risk for allergic disease, particularly asthma, was inadequate to accept or reject a causal relationship.* Further studies are needed. (14)

Two of my four children have reactive airways. Asthma and reactive airways in children is a growing problem and I think it's irresponsible to add flu vaccine for children to the already crowded vaccination schedule when the issue of multiple vaccines causing or contributing to asthma is still being investigated.

It is vital that when public health and elected officials look at vaccination issues, they respect and enforce parental rights and exemption rights. It is also vital that public health officials and elected officials have access to information from all sides of controversial vaccine issues before making any policy decisions.

Many of the ongoing vaccine controversies were addressed at the NVIC *Third International Public Conference on Vaccination*. I have enclosed a copy of the program from this conference. Please take a look at the number of distinguished speakers who spoke at this conference. I attended this conference and have a full set of audiotapes that I would like to make available to any public health, elected official or staff member that would like more information on some of these controversial issues. These tapes can also be ordered through the NVIC website, www.nvic.org. (15)

Sincerely,

Cindy Loveland

Cont.

References:

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(2) Funding sought to lift state from 50th spot for kid shots, By John J. Sanko, Rocky Mountain News, December 3, 2003
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(3) Estimated Vaccination Coverage^ with Individual Vaccines and Selected Vaccination Series Among Children 19-35 Months of Age by State US, National Immunization Survey, Q1/2002-Q4/2002
http://www2a.cdc.gov/nip/coverage/nis/nis_iap.asp?fmt=v&rpt=tab3_antigen_state&qtr=Q1/2002-Q4/2002
(4) Estimated Vaccination Coverage* with 4:3:1:3:3† Among Children 19-35 Months of Age by Race/Ethnicity‡ and by State and Immunization Action Plan Area -- US, National Immunization Survey, Q1/2002-Q4/2002§
http://www2a.cdc.gov/nip/coverage/nis/nis_iap.asp?fmt=r&rpt=tab29_43133_race_iap&qtr=Q1/2002-Q4/2002
(5) Colorado certificate of immunization- CDPHE – PSD-IMM 67375B14-RC10 7/02 and CO immunization manual
http://www.cdphe.state.co.us/dc//////Immunization/immunmanual/sec15.pdf
(6) CDPHE news release, August 7, 2002
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(7) Morbidity and Mortality Weekly Report, Aug. 8, 2003, Vol. 52/No. 31 pg. 729 -
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(8) Healthy people 2010 Section 14-22
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(13) Journal of American Physicians and Surgeons, Vol. 8, Spring 2003
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Estimated Vaccination Coverage[A] with Individual Vaccines and Selected Vaccination Series Among Children 19-35 Months of Age by State US, National Immunization Survey, Q1/2002-Q4/2002*

	3+DTP[†]	4+DTP[‡]	3+Polio[§]	1+MMR[‖]	3+Hib[¶]	3+HepB[**]	1+Var[††]	3+PCV[‡‡]	4:3:1[§§]	4:3:1:3[‖‖]
US National	94.9±0.6	81.6±0.9	90.2±0.7	91.6±0.7	93.1±0.6	89.9±0.7	80.6±0.9	40.8±1.1	78.5±1.0	77.5±1.0
Alabama	96.8±2.4	86.5±4.3	89.0±4.0	91.6±3.6	96.1±2.1	91.7±3.2	89.3±3.8	32.2±5.7	80.8±5.1	79.5±5.1
Alaska	95.7±2.9	82.3±5.3	86.6±4.9	88.7±4.5	94.8±3.1	88.8±4.7	63.6±6.5	29.8±5.8	78.3±5.6	78.3±5.6
Arizona	92.8±3.0	74.8±4.4	86.5±3.7	88.9±3.1	91.6±3.0	89.2±3.3	78.6±3.9	28.1±4.2	70.0±4.7	69.5±4.7
Arkansas	95.7±2.1	76.4±5.8	92.9±2.8	92.8±3.3	95.3±2.2	91.6±3.0	88.7±4.1	24.9±6.2	74.6±5.9	74.4±5.9
California	93.5±2.6	81.4±3.5	90.3±2.6	90.4±2.9	90.1±2.9	88.2±3.0	85.1±3.2	41.9±4.2	77.5±3.7	75.8±3.8
Colorado	91.1±4.2	66.2±6.5	90.1±3.9	90.7±4.0	92.1±3.5	92.4±3.3	79.8±5.5	36.8±6.4	64.7±6.6	64.3±6.6
Connecticut	95.7±2.9	87.1±4.7	93.8±3.7	95.3±2.7	97.1±2.7	91.4±3.8	86.5±4.6	46.4±6.5	86.1±4.8	85.7±4.9
Delaware	96.8±2.4	88.4±4.2	91.6±3.6	95.2±2.7	91.5±4.4	92.4±4.1	86.0±4.2	46.9±6.6	84.8±4.6	81.1±5.3
District of Columbia	94.2±3.5	77.9±7.2	92.6±3.3	91.2±4.9	90.4±4.6	91.0±3.9	91.1±4.8	36.2±7.4	73.8±7.4	72.2±7.4
Florida	95.3±2.5	80.6±4.3	90.2±3.3	91.1±3.2	92.8±2.9	89.9±3.5	80.8±4.4	36.0±5.3	78.0±4.4	77.2±4.4
Georgia	96.8±1.7	86.2±3.7	92.9±2.4	93.0±3.0	93.9±2.5	92.4±2.6	89.2±3.4	42.6±5.5	83.4±3.9	82.0±4.1
Hawaii	94.4±3.8	83.0±5.3	91.3±4.2	96.4±2.5	93.5±3.4	90.7±4.3	81.6±5.2	62.7±6.4	81.3±5.4	80.9±5.4
Idaho	94.8±3.0	78.5±5.5	88.5±4.4	86.9±4.6	93.6±3.2	89.5±4.0	65.9±6.0	29.2±5.7	73.9±5.7	73.3±5.8
Illinois	96.9±1.6	84.4±4.0	91.8±2.7	94.4±2.2	95.8±1.8	92.5±2.7	69.9±5.1	38.4±5.1	80.4±4.2	79.6±4.3
Indiana	95.2±2.3	81.7±4.3	90.5±3.3	91.1±3.2	91.7±3.5	93.2±2.7	70.0±5.3	40.7±5.9	79.2±4.5	77.9±4.6
Iowa	96.5±2.5	83.3±5.1	91.4±3.6	92.3±3.5	92.7±4.0	90.6±4.2	66.5±6.2	43.3±6.6	80.7±5.4	79.7±5.4
Kansas	93.5±4.3	76.2±6.5	89.9±4.8	93.9±2.8	92.1±4.4	86.9±5.5	76.2±5.5	39.7±6.6	74.0±6.6	72.9±6.6
Kentucky	93.5±4.1	76.3±6.2	89.3±4.9	88.0±5.0	93.1±4.4	90.5±4.7	78.3±6.0	47.7±7.0	74.4±6.3	74.4±6.3
Louisiana	95.7±2.3	74.2±5.4	87.5±3.9	87.4±3.9	92.8±3.2	90.7±3.4	83.4±4.0	26.7±5.1	69.8±5.5	69.3±5.5
Maine	97.0±2.3	87.3±4.5	94.6±3.1	92.3±3.5	93.8±3.1	93.7±2.9	73.0±6.0	39.0±6.4	83.7±4.9	82.8±4.9
Maryland	98.0±1.3	84.6±5.0	92.5±3.7	95.4±3.2	96.4±2.0	93.0±2.8	87.7±4.8	42.5±6.3	81.8±5.5	80.8±5.6
Massachusetts	97.0±2.3	92.3±3.0	94.8±2.7	95.5±2.5	97.7±2.2	93.7±3.0	87.0±3.9	62.0±5.5	89.5±3.4	89.2±3.4
Michigan	97.9±1.0	87.4±3.7	92.9±2.4	93.3±2.9	96.6±1.9	93.1±2.4	83.0±5.0	34.0±5.7	84.3±4.1	83.8±4.2
Minnesota	98.7±1.2	85.1±5.2	94.8±2.7	92.2±3.9	89.8±5.4	87.9±4.6	73.6±6.2	48.2±6.8	82.2±5.6	78.9±6.5
Mississippi	95.3±3.2	79.9±6.0	91.0±4.2	91.1±4.0	90.3±4.5	88.3±5.0	77.5±5.9	24.5±6.7	77.8±6.2	77.8±6.2
Missouri	94.7±3.8	81.2±6.0	86.5±5.2	94.8±3.2	94.2±3.6	87.7±5.1	77.1±5.8	49.1±6.8	77.7±6.3	77.3±6.4
Montana	88.2±5.0	72.9±6.6	83.6±5.7	85.3±4.8	86.5±5.3	82.0±5.7	59.2±6.9	39.6±6.6	71.5±6.6	70.9±6.7
Nebraska	95.9±2.7	82.4±5.3	92.1±3.9	93.2±3.7	92.2±4.1	91.2±4.2	74.8±5.8	44.8±6.6	80.6±5.4	79.2±5.5
Nevada	90.4±4.6	79.0±5.9	88.5±4.8	89.4±4.6	89.8±4.6	90.1±4.6	74.7±6.1	13.1±4.4	78.4±5.9	77.8±6.0
New Hampshire	99.0±1.0	93.5±2.8	96.7±2.2	93.9±3.6	97.9±1.7	93.7±3.1	73.9±6.2	47.8±6.6	88.1±4.4	87.3±4.5
New Jersey	95.7±2.8	84.9±4.6	90.6±3.7	92.8±3.3	95.5±2.4	90.5±3.7	80.2±5.4	55.6±6.2	81.9±4.9	80.4±5.0
New Mexico	92.9±3.7	70.2±6.5	85.9±5.2	92.5±3.6	91.3±3.7	85.9±5.2	80.5±5.9	28.0±6.3	68.1±6.6	67.4±6.6
New York	96.2±1.8	85.4±3.8	91.0±2.9	94.4±2.4	96.2±2.1	92.3±2.7	81.0±4.1	48.0±5.2	81.8±4.0	81.3±4.0
North Carolina	95.7±3.3	88.2±4.8	93.9±3.3	94.9±3.1	97.4±2.3	91.4±4.1	81.8±5.9	42.9±7.2	86.9±4.9	86.5±4.9
North Dakota	93.0±5.5	81.4±6.6	90.7±5.6	90.7±5.7	94.9±5.3	93.5±5.5	67.4±6.7	29.5±6.0	78.8±6.7	78.8±6.7
Ohio	94.0±2.7	81.7±4.2	87.1±3.7	91.3±3.1	91.8±3.3	88.0±3.7	75.4±4.4	42.6±4.8	77.9±4.4	77.1±4.4
Oklahoma	90.3±4.9	71.3±7.0	86.6±5.4	86.4±5.3	86.1±6.0	86.5±5.4	81.0±5.8	31.1±6.5	69.6±7.1	66.7±7.4
Oregon	93.3±3.2	78.7±5.3	86.3±4.5	86.6±4.4	92.0±3.5	85.5±4.6	73.7±5.6	37.3±5.9	74.8±5.6	74.5±5.6
Pennsylvania	92.8±4.0	83.0±4.8	89.9±4.3	92.2±4.0	93.7±3.9	92.1±4.1	84.7±4.9	54.4±6.1	78.7±5.2	77.1±5.3
Rhode Island	99.7±0.5	92.9±3.7	94.2±3.6	96.0±2.7	93.9±4.3	97.0±2.0	88.9±4.9	66.8±6.5	90.1±4.1	85.8±5.5
South Carolina	96.8±3.3	82.2±6.1	92.8±4.5	92.6±4.7	95.2±4.0	93.8±3.8	86.0±5.4	42.8±6.7	80.5±6.4	80.2±6.4
South Dakota	94.4±4.0	84.3±6.0	90.1±5.2	95.5±3.4	93.4±4.0	90.6±4.5	71.2±6.5	15.7±5.1	82.0±6.3	81.2±6.3
Tennessee	95.5±2.0	83.0±3.8	93.2±2.3	92.5±2.4	94.6±2.1	93.0±2.4	81.1±4.1	41.8±4.9	80.5±3.9	79.7±4.0
Texas	93.1±2.9	74.6±5.0	87.2±3.7	87.7±3.9	91.4±3.0	86.2±3.8	82.9±4.1	33.9±4.7	71.3±5.0	70.9±5.0
Utah	96.3±2.1	82.6±5.3	88.2±4.3	94.0±3.2	93.1±3.6	92.1±3.4	78.1±5.5	29.7±5.8	79.9±5.6	79.1±5.6
Vermont	99.0±1.4	91.0±3.5	94.5±2.8	94.7±2.6	97.5±1.9	89.8±3.7	66.5±6.0	41.3±6.2	87.7±3.9	87.0±4.0
Virginia	93.7±3.8	81.3±5.5	88.4±4.8	90.3±4.2	90.9±4.4	83.2±5.4	83.0±5.4	54.4±6.6	77.7±5.8	76.6±5.9
Washington	93.2±2.6	77.4±4.6	87.1±3.5	89.6±3.1	89.4±3.6	84.9±4.0	65.1±5.1	25.2±4.1	74.7±4.7	73.1±4.9
West Virginia	96.1±2.5	82.9±5.9	93.8±3.1	93.6±3.0	94.4±4.5	89.9±4.9	81.8±4.8	35.4±6.9	79.0±6.1	78.5±6.2
Wisconsin	96.2±1.9	86.2±4.0	92.1±3.2	92.9±2.9	94.5±2.2	93.3±2.2	79.8±4.0	44.3±5.2	83.4±4.2	81.8±4.3
Wyoming	92.2±4.2	78.4±6.0	85.7±5.4	89.7±4.4	92.8±4.1	88.8±4.8	65.2±6.5	27.7±5.8	76.5±6.1	76.5±6.1

Oregon	93.3±3.2	78.7±5.3	86.3±4.5	86.6±4.4	92.0±3.5	85.5±4.6	73.7±5.6	37.3±5.9	74.8±5.6	74.5±5.6	70.0±5.9	60.3±6.1
Pennsylvania	92.8±4.0	83.0±4.8	89.9±4.3	92.2±4.0	93.7±3.9	92.1±4.1	84.7±4.9	54.4±6.1	78.7±5.2	77.1±5.3	74.7±5.5	67.6±5.8
Rhode Island	99.7±0.5	92.9±3.7	94.2±3.6	96.0±2.7	93.9±4.3	97.0±2.0	88.9±4.9	66.8±6.5	90.1±4.1	85.8±5.5	84.5±5.6	80.7±5.9
South Carolina	96.8±3.3	82.2±6.1	92.8±4.5	92.6±4.7	95.2±4.0	93.8±3.8	86.0±5.4	42.8±6.7	80.5±6.4	80.2±6.4	78.8±6.5	73.8±6.7
South Dakota	94.4±4.0	84.3±6.0	90.1±5.2	95.5±3.4	93.4±4.0	90.6±4.5	71.2±6.5	15.7±5.1	82.0±6.3	81.2±6.3	79.9±6.4	62.0±7.0
Tennessee	95.5±2.0	83.0±3.8	93.2±2.3	92.5±2.4	94.6±2.1	93.0±2.4	81.1±4.1	41.8±4.9	80.5±3.9	79.7±4.0	78.2±4.1	67.3±4.8
Texas	93.1±2.9	74.6±5.0	87.2±3.7	87.7±3.9	91.4±3.0	86.2±3.8	82.9±4.1	33.9±4.7	71.3±5.0	70.9±5.0	67.9±5.1	65.0±5.1
Utah	96.3±2.1	82.6±5.3	88.2±4.3	94.0±3.2	93.1±3.6	92.1±3.4	78.1±5.5	29.7±5.8	79.9±5.6	79.1±5.6	75.7±5.9	61.4±6.5
Vermont	99.0±1.4	91.0±3.5	94.5±2.8	94.7±2.6	97.5±1.9	89.8±3.7	66.5±6.0	41.3±6.2	87.7±3.9	87.0±4.0	80.9±4.7	57.7±6.3
Virginia	93.7±3.8	81.3±5.5	88.4±4.8	90.3±4.2	90.9±4.4	83.2±5.4	83.0±5.4	54.4±6.6	77.7±5.8	76.6±5.9	72.0±6.2	64.8±6.5
Washington	93.2±2.6	77.4±4.6	87.1±3.5	89.6±3.1	89.4±3.6	84.9±4.0	65.1±5.1	25.2±4.1	74.7±4.7	73.1±4.9	69.2±5.0	51.9±5.1
West Virginia	96.1±2.5	82.9±5.9	93.8±3.1	93.6±3.0	94.4±4.5	89.9±4.9	81.8±4.8	35.4±6.9	79.0±6.1	78.5±6.2	76.9±6.3	65.8±6.8
Wisconsin	96.2±1.9	86.2±4.0	92.1±3.2	92.9±2.9	94.5±2.2	93.3±2.2	79.8±4.0	44.3±5.2	83.4±4.2	81.8±4.3	80.3±4.3	67.5±5.0
Wyoming	92.2±4.2	78.4±6.0	85.7±5.4	89.7±4.4	92.8±4.1	88.8±4.8	65.2±6.5	27.7±5.8	76.5±6.1	76.5±6.1	73.3±6.4	54.1±6.8

^ Estimate=NA (Not Available) if the unweighted sample size for the numerator was <30 or (CI half width)/Estimate > 0.5 or (CI half width) >10.
* Children in the Q1/2002-Q4/2002 National Immunization Survey were born between February 1999 and May 2001.
† Three or more doses of any diphtheria and tetanus toxoids and pertussis vaccines including diphtheria and tetanus toxoids, and any acellular pertussis vaccine (DTP/DTaP/DT)
‡ Four or more doses of any diphtheria and tetanus toxoids and pertussis vaccines including diphtheria and tetanus toxoids, and any acellular pertussis vaccine (DTP/DTaP/DT)
§ Three or more doses of any poliovirus vaccine
ll One or more doses of measles-mumps-rubella vaccine; previous reports of vaccination coverage were for measles-containing vaccine (MCV)
¶ Three or more doses of Haemophilus influenzae type b (Hib) vaccine
** Three or more doses of hepatitis B vaccine
†† One or more doses of varicella at or after child's first birthday, unadjusted for history of varicella illness
‡‡ Three or more doses of pneumococcal conjugate vaccine
§§ Four or more doses of DTP, three or more doses of poliovirus vaccine, and one or more doses of any MCV.
llll Four or more doses of DTP, three or more doses of poliovirus vaccine, one or more doses of any MCV, and three or more doses of Hib
¶¶ Four or more doses of DTP, three or more doses of poliovirus vaccine, one or more doses of any MCV, three or more doses of Hib, and three or more doses of HepB
***Four or more doses of DTP, three or more doses of poliovirus vaccine, one or more doses of any MCV, three or more doses of Hib, three or more doses of HepB, and one or more doses of varicella
††† % ± 95% Confidence Interval

tab3_antigen_state

Three things to know ...

- Colorado enjoys 2-year old immunization rates that approach Healthy People 2010 objectives for all recommended vaccines except the fourth dose of diphtheria, tetanus and pertussis (DTaP).
- To the extent that under-immunized children reside in geographic, cultural or economic pockets of need, the risk associated with a vaccine-preventable outbreak is heightened.
- Childhood poverty is the most frequently cited risk factor for under-immunization.

www.coloradohealthinstitute.org/research/colorado-childhood-immunization-rates-policy-and-practice

May2005

COLORADO
Department of Public Health & Environment

Questions and answers about Colorado's 2017-2018 school and child care immunization data

Colorado's 2017-2018 School and Child Care Immunization Data website is a resource for families, schools, local public health agencies, health care providers and other partners. The site requires one of the following browsers:

- Chrome on Windows, Mac, and Android 4.4 or later.
- Apple Safari on Mac and iOS 8.x or later.
- Internet Explorer 11 or newer.
- Mozilla Firefox 3.x or later on Windows and Mac.

How/where did the Colorado Department of Public Health and Environment get the data?

A Colorado Board of Health rule requires most schools and licensed child cares to report aggregate immunization and exemption data to the department annually. Schools and child care/preschool facilities reported the data directly to the department through an online data collection tool or by sending data directly to the department between October 2017 and December 2017.

Who must report: Public, private and parochial schools with grades K - 12, as well as child care centers, preschools and Head Start programs licensed by the Colorado Department of Human Services to provide care for 10 or more children.

Who does not need to report: School-age child care centers, family child care homes, drop-in centers, day treatment centers, foster care homes, day camps, resident camps and online only K - 12 schools - though these facilities are still required to collect immunization or exemption forms for their students.

What do the data show?

For the 2017-2018 school year, the Colorado Department of Public Health and Environment collected de-identified immunization and exemption data from 1,860 K-12 schools (▫ 59) representing more than 880,000 students (▫ 30,000). 92.9 percent of students were in compliance with school immunization rules.

Statewide school fully immunized and exemption rates by vaccine

Vaccine	Fully immunized rate	Exemption rate
DTaP	94.35% (▫ .43)	2.64% (▫ .26)
Hep B	94.68% (▫ .47)	2.88% (▫ .24)
MMR	94.53% (▫ .25)	2.87% (▫ .25)
Polio	94.32% (▫ .31)	2.83% (▫ .25)
Varicella	92.89% (▫ 1.27)	3.53% (▫ .25)
Tdap (6th grade and up)	90.50% (▫ .65)	2.80% (▫ .33)

Washington HB 1638

Department of Health [US] https://www.doh.wa.gov/DataandStatisticalReports/HealthBehaviors/Immunization/SchoolReports/DataTables

"22% of Clark County Students Are NOT MISSING MMR"

Clark CO MMR Exempt 5.3%
WA State MMR Exempt 2.9%

Clark Co. is citing the IIS, which is the wrong survey- IIS does not measure school rates or exemptions.

Washington State Department of Health

School Immunization Data Tables

Historical School Immunization and Exemption Rates by State and County

Use these data when comparing Washington to other states, publishing state-level immunization rates, or comparing state-level data across years.

- Historical immunization data for state and county, 1998-2018 (Excel) Ap

WA DOH tracks every student to the individual injection and exemption. It is the only proper data for considering school attendance legislation.

Data by School Year and Grade Level

These tables include immunization rates by regional service area, county, educational service district, school district, school type (public and private) and school facility.

WA K-12 ALL TYPE MMR EXEMPTION RATE ONLY 2.9%

CLARK CO ALL TYPE MMR EXEMPTION RATE ONLY 5.3%

Raw Excel data captures

School Year 2017-2018

- Kindergarten data, 2017-2018 school year (Excel) April 2018
- 6th grade data, 2017-2018 school year (Excel) April 2018
- All students, kindergarten through 12th grade, 2017-2018 school year (Excel) April 2018

K-12 School_year	Reported_enrolment	Percent_complete_for_all_immunizations	Percent_with_any_exemption	Percent_with_medical_exemption	Percent_with_personal_exemption	Percent_with_religious_exemption	Percent_with_religious_membership_exemption	Percent_exempt_for_diphtheria_tetanus	Percent_exempt_for_pertussis	Percent_exempt_for_measles_mumps_rubella	Percent_exempt_for_polio	Percent_exempt_for_Hepatitis B	Percent_exempt_for_varicella
2017-18	1,082,689	88.5%	4.8%	0.9%	3.7%	0.3%	0.1%	3.0%	2.9%	2.9%	2.9%	3.0%	3.7%

County	School_year	Reported_enrollment	Percent_complete_for_all_immunizations	Percent_with_any_exemption	Percent_with_medical_exemption	Percent_with_personal_exemption	Percent_with_religious_exemption	Percent_with_religious_membership_exemption	Percent_exempt_for_diphtheria_tetanus	Percent_exempt_for_pertussis	Percent_exempt_for_measles_mumps_rubella	Percent_exempt_for_polio	Percent_exempt_for_Hepatitis B	Percent_exempt_for_varicella
CLARK	2017-18	73,849	76.3%	7.3%	0.8%	5.8%	0.6%	0.2%	5.5%	5.2%	5.3%	5.2%	5.0%	5.9%

What is the Washington State Immunization Information System?

The Washington State Immunization Information System (IIS) is a secure, web-based tool that helps healthcare providers keep track of their patients' immunizations. The immunization records in the system remain available when families move or change providers. The system helps providers:

IIS does not survey all students or measure school exemptions.

Who uses the System?

About 2,100 partner health organizations participate and exchange data with the IIS. This includes most of Washington's major health plans, the state Medicaid program, local health departments, community and migrant health centers, and many private healthcare provide

https://www.doh.wa.gov/ForPublicHealthandHealthcareProviders/HealthcareProfessionsandFacilities/DataReportingandRetrieval/ImmunizationInformationSystem/ForProviders

Oregon

2018 K-12 County and State Immunization and Exemption Rates

County	Adjusted Enrollment[c]	% Measles 2[d]	% Complete[e]	% Any Medical Exemption[f]	% Any Nonmedical Exemption[g]	% Nonmedical Exemption: Measles[h]	% NME: All[i]
Baker	2127	94.6%	91.5%	0.2%	5.5%	4.2%	2.9%
Benton	11354	96.0%	93.7%	0.1%	5.5%	3.9%	2.5%
Clackamas	61100	95.4%	93.1%	0.1%	5.9%	4.5%	3.3%
Clatsop	5095	95.8%	92.6%	0.1%	4.7%	3.7%	2.7%
Columbia	7604	96.4%	94.5%	0.1%	4.5%	3.4%	2.0%
Coos	7925	97.0%	94.9%	0.2%	3.7%	2.5%	1.4%
Crook	3001	96.5%	95.2%	0.1%	3.8%	3.2%	1.9%
Curry	2346	93.9%	92.0%	0.3%	7.0%	5.6%	3.8%
Deschutes	27408	94.4%	91.7%	0.1%	7.5%	5.5%	3.5%
Douglas	14529	95.7%	93.6%	0.1%	5.2%	3.9%	2.6%
Grant	863	93.5%	90.6%	0.2%	8.3%	6.4%	3.7%
Harney	1101	97.1%	96.0%	0.0%	3.1%	2.5%	1.9%
Hood River	4279	96.5%	94.7%	0.0%	4.5%	3.4%	1.9%
Jackson	32006	92.9%	89.4%	0.2%	8.2%	6.5%	4.2%
Jefferson	3653	97.9%	96.9%	0.0%	2.5%	1.9%	1.0%
Josephine	11341	91.3%	89.1%	0.1%	10.1%	8.5%	7.2%
Klamath	10028	96.9%	95.1%	0.1%	3.1%	2.4%	1.3%
Lake	1103	97.6%	95.6%	0.2%	3.4%	2.3%	1.4%
Lane	46466	95.6%	93.7%	0.1%	5.5%	4.3%	3.0%
Lincoln	5546	97.4%	95.0%	0.1%	3.5%	2.4%	1.4%
Linn	18859	97.2%	95.5%	0.2%	3.5%	2.6%	1.6%
Malheur	5459	98.6%	97.9%	0.1%	1.8%	1.3%	1.0%
Marion	57228	97.0%	95.4%	0.1%	3.7%	2.9%	2.0%
Morrow	2454	98.9%	96.7%	0.1%	1.1%	0.8%	0.4%
Multnomah	101777	95.4%	92.2%	0.1%	6.1%	4.3%	2.7%
North Central[a]	4224	97.2%	95.2%	0.1%	3.7%	2.6%	1.6%
Polk	12754	96.1%	94.6%	0.1%	4.6%	3.6%	2.2%
Tillamook	3655	96.0%	93.5%	0.1%	5.0%	3.9%	2.5%
Umatilla	13945	98.2%	97.0%	0.1%	1.8%	1.4%	1.0%
Union	4166	95.9%	92.7%	0.2%	5.6%	3.8%	2.7%
Wallowa	831	92.2%	88.3%	0.1%	4.8%	2.5%	0.8%
Washington	94085	97.4%	95.4%	0.2%	3.3%	2.3%	1.3%
Wheeler	149	97.3%	97.3%	0.7%	2.0%	2.0%	2.0%
Yamhill	16847	95.6%	93.9%	0.1%	5.2%	4.2%	2.8%
Oregon[b]	605276	95.8%	93.5%	0.1%	5.2%	3.9%	2.6%

[a] Includes Gillam, Sherman and Wasco counties

[b] State-level rates include public, private and online schools, while county rates include only public and private

[c] Number of students adjusted to avoid double counting of students enrolled in multiple sites

[d] Percent of students with at least two doses of Measles containing vaccine

[e] Percent of students complete for all vaccines required for their grade

[f] Percent of students with a medical exemption for one or more required vaccines

[g] Percent of students with a nonmedical exemption for one or more required vaccine

[h] Percent of students with a nonmedical exemption for Measles vaccine

[i] Percent of students with a nonmedical exemption for all vaccines required for their grade

Oregon HB 3063

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By Fedor Zarkhin | The Oregonian/OregonLive

Thousands of Oregon children would have to get vaccinated or stay out of school under a bill being prepared by Rep. Mitch Greenlick, D-Portland.

The proposal comes amid a measles outbreak that has infected 52 children in Clark County and has spread to Oregon, where four people have been infected.

Greenlick's bill, which is still being finalized, would eliminate non-medical exemptions for unvaccinated school children. The goal, Greenlick said, is to protect those children who can't get vaccinated for medical reasons.

"People have a right to make bad decisions about the healthcare of their children," Greenlick said. "But that does not give them the right to send unprotected children into their school."

At least 93 percent of children must be vaccinated to prevent outbreaks. One in five Oregon schools have measles vaccination rates below that threshold, according Oregon Health Authority data, with rates at some schools as low as 30 percent.

About 15,500 Oregon school children have non-medical exemptions for all vaccines, according to state data. Under the lawmaker's proposal, those kids would have to either get vaccinated or be home-schooled, Greenlick said.

Opposition could be stiff. A similar proposal in 2015 was abandoned following pressure from opponents. In Washington on Friday, hundreds protested a bill that would eliminate personal and philosophical exemptions to vaccines. And Greenlick has already received many calls from people accusing him of trying to restrict their freedoms, he said. Greenlick blamed the opposition on scientific illiteracy and said it would not stop him from pursuing the bill. And he said he hoped his colleagues in the legislature would be on board.

"I'll just ask them to think carefully about it and to think about Vancouver," he said. "We'll try rationality."

-- Fedor Zarkhin

https://www.oregonlive.com/health/2019/02/proposal-would-eliminate-personal-vaccine-exemption-for-oregon-school-kids.html

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1978 -
HB -1089

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CHAPTER 90

HEALTH

SCHOOL ENTRY IMMUNIZATION

HOUSE BILL NO. 1089. BY REPRESENTATIVES Traylor, Dittemore, Smith, Valdez, Wayland, DeHerrera, DeMoulin, Dick, Herzberger, Hume, Jones, Lucero, Marks, Massari, McElderry, Sears, Showalter, Taylor, Trimble, Valdez, Wayland, Witherspoon, and Zakhem; also SENATORS Hughes, Kogovsek, Phelps, Stockton, Allshouse, and D. Sandoval.

AN ACT

CONCERNING REQUIRED EVIDENCE OF IMMUNIZATION FOR SCHOOL ENROLLMENT.

Be it enacted by the General Assembly of the State of Colorado:

Section 1. Part 9 of article 4 of title 25, Colorado Revised Statutes 1973, as amended, is REPEALED AND REENACTED, WITH AMENDMENTS, to read:

PART 9

SCHOOL ENTRY IMMUNIZATION

25-4-901. Definitions. As used in this part 9, unless the context otherwise requires:

(1) "School" means a public, private, or parochial nursery school, day care center, child care facility, family care home, head start program, kindergarten, or elementary or secondary school through grade twelve.

25-4-902. Immunization prior to attending school. Except as provided in section 25-4-903, no child shall attend any school in the state of Colorado on or after the dates specified in section 25-4-906 (4) unless such child can present to the appropriate official of the school a certificate of immunization from a licensed physician or authorized representative of the department of health or local health department stating that such child has received immunization against communicable diseases as specified by the state board of health or a written authorization signed by one parent or guardian or the emancipated child requesting that local health officials administer the immunizations or a plan signed by one parent or guardian or the emancipated child for receipt by the child of the required

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Capital letters indicate new material added to existing statutes; dashes through words indicate deletions from existing statutes and such material not part of act.

inoculation or the first or the next required of a series of inoculations within thirty days.

25-4-903. Exceptions from immunization. (1) A child who transfers into a school may enter school provisionally and shall have sixty days in which to submit a certificate of immunization. Any child for whom a certificate of immunization is not submitted within sixty days shall be suspended or expelled from school until a certificate of immunization is provided.

(2) A child shall be exempted from receiving the required immunizations:

(a) Upon submitting certification from a licensed physician that the physical condition of the child is such that one or more specified immunizations would endanger his life or health;

(b) Upon submitting a statement signed by one parent or guardian or the emancipated child that the parent, guardian, or child is an adherent to a religious belief whose teachings are opposed to immunizations or that the parent or guardian or the emancipated child has a personal belief that is opposed to immunizations.

(3) The state board of health may provide, by regulation, for further exemptions to immunization based upon sound medical practice.

25-4-904. Immunization rules and regulations. (1) The state board of health shall establish rules and regulations for administering this part 9. Such rules and regulations shall establish which immunizations shall be required and the manner and frequency of their administration and shall conform to recognized standard medical practices. Such rules and regulations may also require the reporting of statistical information and names of noncompliers by the schools. The department of health shall administer and enforce the immunization requirements.

(2) All rule-making authority granted to the board of health under the provisions of this article is granted on the condition that the general assembly reserves the power to amend or rescind any rule of the board. In addition to the recourse provided by section 24-4-103 (8) (d), C.R.S. 1973, the general assembly may amend or rescind a rule of the board by passage of a joint resolution.

25-4-905. Immunization of indigent children. The local health department, a public health or school nurse (under the supervision of a licensed physician), or the department of health in the absence of a local health department or public health nurse shall provide, at public expense to the extent that funds are available, immunizations required by this part 9 to each child whose parents or guardians cannot afford to have the child immunized or, if emancipated, who cannot himself afford immunization and who has not been exempted. The department of health shall provide all vaccines necessary to comply with this section as far as funds will permit. Nothing in this section shall preclude the department of health from distributing vaccines to physicians or others as required by law or the regulations of the department. No indigent child shall be excluded, suspended, or expelled from school unless the immunizations have been available and readily accessible to the child at public expense.

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25-4-906. Certificate of immunization - forms. (1) The department of health shall provide official certificate of immunization forms to the schools, private physicians, and local health departments. Any immunization record provided by a licensed physician, registered nurse, or public health official may be accepted by the school official as certification of immunization if the information is transferred to the official certificate of immunization and verified by the school official.

(2) Each school shall maintain on file an official certificate of immunization for every child enrolled as a student. The certificate shall be returned to the parent or guardian or the emancipated child when a child withdraws, transfers, is promoted, or otherwise leaves the school or the school shall transfer the certificate with the child's school record to the new school.

(3) The department of health may examine, audit, and verify the records of immunizations maintained by each school.

(4) All children enrolled in any school in Colorado on and after August 15, 1979, shall furnish the required certificate of immunization or shall be suspended or expelled from school. Children enrolling in school in Colorado for the first time on and after July 1, 1978, shall provide a certificate of immunization or shall be excluded from school except as provided in section 25-4-903.

25-4-907. Noncompliance. The board of education of each school district shall suspend or expel from school, pursuant to the provisions of section 22-33-105, C.R.S. 1973, any child enrolled as a student not otherwise exempted under this part 9 who fails to comply with the provisions of this part 9. No child shall be suspended or expelled for failure to comply with the provisions of this part 9 unless there has been a direct personal notification by the appropriate school authority to the child's parent or guardian or to the emancipated child of the noncompliance with this part 9, and of their rights under sections 25-4-902 and 25-4-903. In the event of suspension or explusion, school officials shall notify the state or local department of health. An agent of the department shall then contact the parent or guardian or the emancipated child in an effort to secure compliance with this part 9 in order that the child may be reenrolled in school.

25-4-908. When exemption from immunization not recognized. If at any time there is, in the opinion of the state or local health department, danger of an epidemic from any of the communicable diseases for which an immunization is required pursuant to the rules and regulations promulgated pursuant to section 25-4-904, no exemption or exception from immunization against such disease shall be recognized. Quarantine by the state or local health department is hereby authorized as a legal alternative to immunization.

Section 2. 22-33-106 (3), Colorado Revised Statutes 1973, is amended BY THE ADDITION OF A NEW PARAGRAPH to read:

22-33-106. Grounds for suspension, expulsion, and denial of admission. (3) (e) Failure to comply with the provisions of part 9 of article 4 of title 25, C.R.S. 1973. Any suspension, expulsion, or denial of admission for

Overview | **National Immunization Rates** | State Immunization Rates | National VFC Immunization Rates | State VFC Immunization Rates | National Poverty Immunization Rates | State Poverty Immunization Rates | National WIC Immunization Rates | State WIC Immunization Rates

2017 National NIS Vaccination Rates for 4:3:1:3:3:1:4 at 19 - 35 Months of Age

Vaccine/Series	Age	Year	Confidence Intervals	Zoom (If Applicable)
4:3:1:3:3:1:4	19 - 35 Months	2017	Show	0

For questions, feedback, or more information contact us at cdphe.dcdimmunization@state.co.us or (303) 692-2700

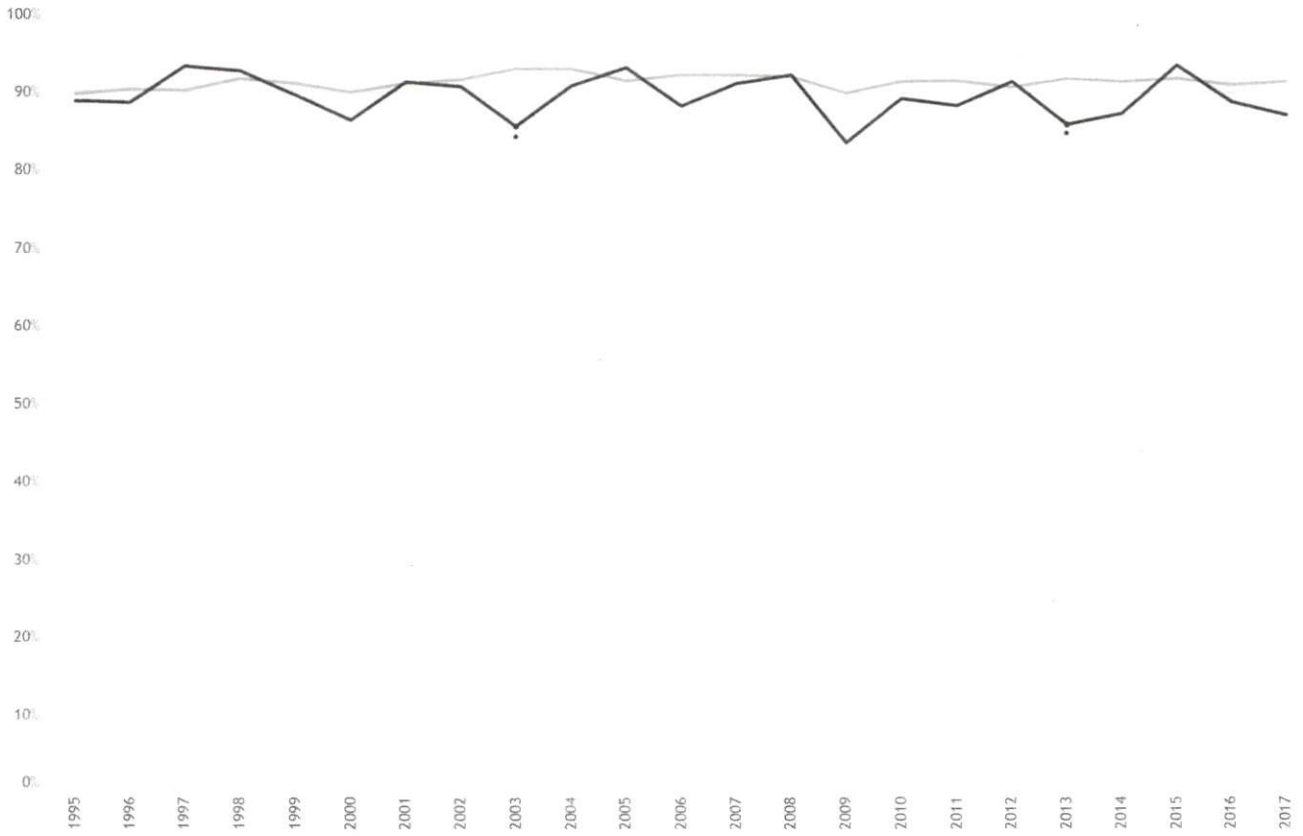
COLORADO Department of Public Health & Environment

Source: CDC, NCIRD (2017), 2017 National Immunization Survey-Child.

Colorado Not Dead Last in 2017 multi-dose series

Colorado NIS Vaccination Rate for 1+ MMR at 19 - 35 Months of Age

Vaccine/Series: 1+ MMR | Age: 19 - 35 Months | State: Colorado | Colorado | United States | * significant difference | Confidence Intervals Show 0 | Zoom (If Applicable)



For questions, feedback, or more information contact us at cdphe.dcdimmunization@state.co.us or (303) 692-2700

COLORADO Department of Public Health & Environment

Source: CDC, NCIRD (2017), 2017 National Immunization Survey-Child

Policy Perspective: *Addressing the barriers to vaccination that some Colorado families face*

Stephanie Wasserman, MSPH, Colorado Children's Immunization Coalition

Colorado parents who refuse or delay vaccinating their children are a growing concern for our state because this trend leaves pockets of under- and unvaccinated kids in our schools, childcares and communities, making us all vulnerable to outbreaks of vaccine-preventable diseases. However, many families in Colorado want to vaccinate but continue to face barriers to accessing services. For these Coloradans, low immunization rates reflect ongoing challenges in insurance coverage, geography and other issues. While the Affordable Care Act (ACA) has increased the number of insured Coloradans covered on private health insurance or through Medicaid, many are still not able to easily and conveniently access immunization services and are missing out on the public health benefits and protections of vaccines. For example, fewer than 600 Colorado health care sites (including community health centers, pediatric and family practices, hospitals, Indian Health Service, local public health agencies, rural health centers, school-based health centers and youth services) participate in the Vaccines for Children (VFC) program, the federal program that allows healthcare providers to administer free vaccines to uninsured, Medicaid-eligible, and Alaska Native or American Indian children. One Colorado county (Gilpin) lacks a single healthcare provider site that participates in the VFC program. Another seven rural counties (Custer, Dolores, Elbert, Jackson, Mineral, Pitkin and San Juan), offer only a single location where VFC vaccine is available. Of these seven sites, more than half are small, rural local public health agencies, many staffed with a single public health nurse providing immunizations at limited times, or by appointment only. This means that some families are expected to travel many miles to get vaccinated at times that may not be feasible or convenient for them. Transportation challenges, inability to take time off of work, childcare issues and other barriers result in missed opportunities to vaccinate and lower immunization rates. Colorado must do more to provide funding, capacity and resources to support core public health infrastructure, especially in rural communities, and to encourage increased participation among health care providers in the VFC program.

If you wish to receive this publication, please provide us with your E-mail address below.

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E-mail Address: _____
(Print clearly please)

The Vaccine Preventable Diseases Report publications are always posted on Children's Hospital Colorado website at:
https://www.childrenscolorado.org/health-professionals/stay-informed/

Please return your E-mail address to: Emily Falco, Children's Hospital Colorado, Epidemiology – Box B276, 13123 E. 16th Avenue, Aurora, CO 80045
or E-mail address: emily.falco@childrenscolorado.org

Thank you for your interest in our publication.

The Vaccine Preventable Diseases Report
Department of Epidemiology©
Children's Hospital Colorado, Dept. of Epidemiology, B-276
13123 E. 16th Avenue, Aurora, CO 80045
Phone: (720) 777-6412; FAX: (720) 777-7295
emily.falco@childrenscolorado.org
www.ChildrensColorado.org

Name _____ Date of Birth _____

STATEMENT OF EXEMPTION TO IMMUNIZATION LAW

IN THE EVENT OF AN OUTBREAK, EXEMPTED PERSONS WILL BE SUBJECT TO EXCLUSION FROM SCHOOL AND QUARANTINE.

MEDICAL EXEMPTION

THE PHYSICAL CONDITION OF THE ABOVE NAMED PERSON IS SUCH THAT IMMUNIZATION WOULD ENDANGER LIFE OR HEALTH, OR IS MEDICALLY CONTRAINDICATED DUE TO OTHER MEDICAL CONDITIONS.

SIGNED _____ DATE _____
(PHYSICIAN)

RELIGIOUS EXEMPTION

PARENT OR GUARDIAN OF THE ABOVE NAMED PERSON OR THE PERSON HIMSELF/HERSELF ADHERES TO A RELIGIOUS BELIEF OPPOSED TO IMMUNIZATIONS.

SIGNED _____ DATE _____
(PARENT OR GUARDIAN OR EMANCIPATED STUDENT/CONSENTING MINOR)

PERSONAL EXEMPTION

PARENT OR GUARDIAN OF THE ABOVE NAMED PERSON OR THE PERSON HIMSELF/HERSELF ADHERES TO A PERSONAL BELIEF OPPOSED TO IMMUNIZATIONS.

SIGNED _____ DATE _____
(PARENT OR GUARDIAN OR EMANCIPATED STUDENT/CONSENTING MINOR)

COLORADO LAW REQUIRES THIS FORM BE COMPLETED AND PROVIDED TO THE SCHOOL

Name _____ **Date of Birth** _____

Parent/Guardian _____

COLORADO DEPARTMENT OF HEALTH — CERTIFICATE OF IMMUNIZATION

MINIMUM DOSES REQUIRED

VACCINE	Preschool (15mo-4yrs)	Grades K-6 (5-11yrs)	Grades 7-12 (12-18yrs)	College
DTP/Td/DT	3	4	4	
Polio	2	3	3	
Measles*	1	1	2	2
Mumps*	1	1	2	2
Rubella*	1	1	2	2
Hib**	1			

Any student starting or completing the vaccine series within 6 months of first enrollment in a Colorado school may be certified with:

VACCINE	Preschool (15mo-4yrs)	Grades K-6 (5-11yrs)	Grades 7-12 (12-18yrs)
DTP/DT OR	3	3	
Td (Age 7+)		2	2
Polio	2	2	2
Measles*	1	1	2
Mumps*	1	1	2
Rubella*	1	1	2
Hib**	1		

* Students enrolling in child care facilities or schools through grade 6 for the first time on or after July 1, 1992, must have had an MMR dose which was administered at age 15 months or older.

Beginning July 1, 1992, 7th graders and college freshmen born since January 1, 1957 must have had 2 measles doses, 2 mumps doses and 2 rubella doses;if the student received a 2nd measles dose prior to July 1, 1992, the 2nd rubella and mumps doses are **not** required. The measles, mumps and rubella doses must have been administered on or after the first birthday and at least one month apart. By July 1, 1995 all college students born since January 1, 1957 must comply. By July 1, 1997 all students in grades 7–12 must comply.

** One Hib vaccine dose must have been administered at age 15 months or older. Children age 5 and older are exempt from Hib requirements.

Your doctor or clinic may recommend additional doses.

VACCINE	ENTER DATE EACH IMMUNIZATION WAS GIVEN				
DIPHTHERIA - TETANUS - PERTUSSIS (DTP)					
- OR - TETANUS - DIPHTHERIA (Td, DT)					
POLIO					
HAEMOPHILUS INFLUENZAE TYPE b** (ENTER MONTH, DAY, YEAR)					
MEASLES* (ENTER MONTH, DAY, YEAR)					
MUMPS* (ENTER MONTH, DAY, YEAR)					
RUBELLA* (ENTER MONTH, DAY, YEAR)					

Written evidence of laboratory tests showing immunity to measles, mumps, and rubella is acceptable.

Attach written proof to this Certificate or record test results and dates in the boxes at left.

TO THE BEST OF MY KNOWLEDGE, THIS PERSON HAS RECEIVED THE ABOVE IMMUNIZATIONS.

SIGNED _____
(PHYSICIAN, NURSE OR SCHOOL HEALTH AUTHORITY)

TITLE _____ DATE _____

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Immunization

Non-Medical Exemption Form (Religious and Personal Belief)

Vaccines are one of the greatest public health achievements of the past century and save an estimated 3 million children's lives every year. The Colorado Department of Public Health and Environment strongly supports vaccination as one of the easiest and most effective tools in preventing diseases that can cause serious illness and even death. For nearly all children, the benefits of preventing disease with a vaccine far outweigh the risks. Declining to follow the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) immunization schedule for number, space and timing of doses, may endanger an unvaccinated child's health and others who come into contact with him/her. Some vaccine-preventable diseases are common in other countries and unvaccinated children could easily get one of these diseases while traveling or from a traveler.

Colorado law C.R.S. § 25-4-902 requires all students attending any school in the state of Colorado to be vaccinated against certain vaccine-preventable diseases as established by Colorado Board of Health rule 6 CCR 1009-2, unless an exemption is filed. This law applies to students attending public, private and parochial kindergarten, elementary and secondary schools through 12th grade, colleges or universities, and child care facilities licensed by the Colorado Department of Human Services including child care centers, school-age child care centers, preschools, day camps, resident camps, day treatment centers, family child care homes, foster care homes, and Head Start programs. Prior to kindergarten, a non-medical exemption must be filed each time a student is due for vaccines according to the schedule developed by the ACIP.[1,2] From kindergarten through 12th grade, a non-medical exemption must be filed every year during the student's school enrollment/registration process.[1] Students with a recorded immunization exemption may be kept out of a child care facility or school during a disease outbreak; the length of time will vary depending on the type of the disease and the circumstances of the outbreak.

Please complete all required fields below; incomplete forms will not be accepted. *All fields are required unless noted optional.*

Type of Non-Medical Exemption Claimed: □ Personal Belief □ Religious

Student Information:

Last Name:	First Name:	(optional) Middle Name:
Gender: □ Female □ Male	Date of Birth:	
Street #:	Street Name:	Street Type (e.g. Ave.):
Unit #:	P.O. Box:	
City:	State:	Zip Code:
Email Address:		County:
Phone Number:		□ Home □ Cell

Parent/Guardian Completing This Form: □ Check if an emancipated student or student over 18 years old

Last Name:	First Name:	(optional) Middle Name:
Relationship to student: □ Mother □ Father □ Guardian		
Street #:	Street Name:	Street Type (e.g. Ave.):
Unit #:	P.O. Box:	
City:	State:	Zip Code:
Email Address:		County:
Phone Number:		□ Home □ Cell

School/Licensed Child Care Facility Information:

School Name/Licensed Child Care Facility:		
School District:		□ Check if Not Applicable
Address:		
City:	State:	Zip Code:
Phone Number:		Grade of Student:

[1] Colorado Board of Health rule 6 CCR 1009-2: https://www.sos.state.co.us/CCR/GenerateRulePdf.do?ruleVersionId=7698&fileName=6%20CCR%201009-2.

[2] 2018 Recommended Immunizations from Birth through 6 Years Old: www.cdc.gov/vaccines/parents/downloads/parent-ver-sch-0-6yrs.pdf. Based on this schedule, a non-medical exemption would be submitted at 2 months, 4 months, 6 months, 12 months and 18 months of age.

Vaccine Preventable Disease Information

The information provided below is to ensure parents/guardians/students are informed about the risks of not vaccinating.

Diphtheria, tetanus, pertussis (DTaP, Tdap) - Unvaccinated children may be at increased risk of developing diphtheria, tetanus and/or pertussis if exposed to these diseases. Serious symptoms and effects of diphtheria include heart failure, paralysis, breathing problems, coma, and death. Serious symptoms and effects of tetanus include "locking" of the jaw, difficulty swallowing and breathing, seizures, painful tightening of muscles in the head and neck, and death. Serious symptoms and effects of pertussis (whooping cough) include severe coughing fits that can cause vomiting and exhaustion, pneumonia, seizures, brain damage, and death. For more information: http://www.cdc.gov/vaccines/hcp/vis/vis-statements/dtap.pdf and http://www.cdc.gov/vaccines/hcp/vis/vis-statements/tdap.pdf

Haemophilus influenzae type b (Hib) - Unvaccinated children may be at increased risk of developing invasive Hib disease if exposed to this disease. Serious symptoms and effects include bacterial meningitis, pneumonia, severe swelling in the throat, brain damage, deafness, infections of the blood, joints, bones, and covering of the heart, and death. For more information: http://www.cdc.gov/vaccines/hcp/vis/vis-statements/hib.pdf

Hepatitis B - Unvaccinated children may be at increased risk of developing hepatitis B if exposed to this disease. Serious symptoms and effects include jaundice, life-long liver problems such as liver damage, scarring, liver cancer, and death. For more information: http://www.cdc.gov/vaccines/hcp/vis/vis-statements/hep-b.pdf

Inactivated poliovirus (IPV) - Unvaccinated children may be at increased risk of developing polio if exposed to this disease. Serious symptoms and effects include paralysis of muscles that control breathing, meningitis, permanent disability, and death. For more information: http://www.cdc.gov/vaccines/hcp/vis/vis-statements/ipv.pdf

Measles, mumps, rubella (MMR) - Unvaccinated children may be at increased risk of developing measles, mumps, and/or rubella if exposed to these diseases. Serious symptoms and effects of measles include pneumonia, seizures, brain damage, and death. Serious symptoms and effects of mumps include meningitis, painful swelling of the testicles or ovaries, sterility, deafness, and death. Serious symptoms and effects of rubella include rash, arthritis, and muscle or joint pain. If a pregnant woman gets rubella, she could have a miscarriage or her baby could be born with serious birth defects such as deafness, heart problems, and mental retardation. For more information: http://www.cdc.gov/vaccines/hcp/vis/vis-statements/mmr.pdf

Pneumococcal conjugate (PCV13) - Unvaccinated children may be at increased risk of developing pneumococcal disease if exposed to this disease. Serious symptoms and effects include pneumonia, lung infections, blood infections, meningitis and death. For more information: http://www.cdc.gov/vaccines/hcp/vis/vis-statements/pcv13.pdf.

Varicella (chickenpox) - Unvaccinated children may be at increased risk of developing varicella if exposed to this disease. Serious symptoms and effects include severe skin infections, pneumonia, brain damage, and death. For more information: http://www.cdc.gov/vaccines/hcp/vis/vis-statements/varicella.pdf

Required Vaccines for School Entry - Place an "X" next to each vaccine you are declining.

	Diphtheria, tetanus, pertussis (DTaP)		Inactivated poliovirus (IPV)
	Tetanus, diptheria, pertussis (Tdap)		Measles, mumps, rubella (MMR)
	Haemophilus influenzae type b (Hib)		Pneumococcal conjugate (PCV13)
	Hepatitis B		Varicella (chickenpox)

Statement of Exemption

I am the parent/guardian of the above-named student or am the student himself/herself (emancipated or over 18 years of age) and am declining the vaccine(s) indicated above due to a religious or personal belief that is opposed to vaccines. The information I have provided on this form is complete and accurate.

- I may change my mind at any time and accept vaccination(s) for my child/myself in the future.
- I can review evidence-based vaccine information at www.colorado.gov/cdphe/immunization-education, or www.ImmunizeforGood.com for additional information on the benefits and risks of vaccines and the diseases they prevent.
- I can contact the Colorado Immunization Information System (CIIS) at www.ColoradoIIS.com or my health care provider to locate my child's/my immunization record.[3]

I acknowledge that I have read this document in its entirety.

Parent/Guardian/Student (emancipated or over 18 yrs old) signature: _____ Date: _____

(Optional) I authorize my/my student's school to share my/my student's immunization records with state/local public health agencies and the Colorado Immunization Information System, the state's secure, confidential immunization registry.

Parent/Guardian/Student (emancipated or over 18 yrs old) signature: _____ Date: _____

[3] Under Colorado law, you have the option to exclude your child's/your information from CIIS at any time. To opt out of CIIS, go to www.colorado.gov/cdphe/ciis-opt-out-procedures. Please be advised you will be responsible for maintaining your child's/your immunization records to ensure school compliance.

2011 BOH Workgroup Proposed: 21

DRAFT

Colorado Personal Exemption Form

Child's Name: _____ Birth Date: _____

Parent's/Guardian's Name: _____

	Declined (Please initial each vaccine)
Required	
☐ Hepatitis B Vaccine	_____
☐ Diphtheria, tetanus, acellular pertussis (DTaP or Tdap) vaccine	_____
☐ Diphtheria tetanus (DT or Td) vaccine	_____
☐ *Haemophilus influenza* type b (Hib) vaccine	_____
☐ Inactivated poliovirus (IPV) vaccine	_____
☐ Pneumococcal conjugate (PCV13) or polysaccharide vaccine	_____
☐ Measles-mumps-rubella (MMR) vaccine	_____
☐ Varicella (chickenpox) vaccine	_____
Recommended	
☐ Human papillomavirus (HPV) vaccine	_____
☐ Rotavirus vaccine	_____
☐ Hepatitis A vaccine	_____
☐ Meningococcal conjugate or polysaccharide vaccine	_____
☐ Influenza (flu) vaccine	_____
☐ Other	_____

I have read the Vaccine Information Statement from the Centers for Disease Control and Prevention (CDC) explaining the vaccine(s) and the disease(s) it prevents. I have had the opportunity to discuss with my child's Physician/Nurse/PA or Public Health Official about the purpose of the need for vaccine(s) and the risks and benefits of the listed vaccine(s). I understand the following:

- The **purpose** of, and the need for, required and recommended vaccine(s)
- The **risks and benefits** of the required and recommended vaccine(s)
- If my child does not receive the vaccine(s) according to the medically accepted schedule, the consequences could include contracting the illness the vaccine(s) should prevent, possibly causing:
  - certain types of cancer
  - death
  - meningitis
  - pneumonia
  - brain damage
  - seizures
  - illness requiring hospitalization
  - paralysis
  - deafness
  - possible other severe and permanent effects
  - transmittal of the disease to others in the community
  - my child to be restricted from attending child care or school during disease outbreaks
- I have decided at this time to decline the vaccine(s) recommended for my child as indicated above, by initialing the appropriate box under the column titled "Declined."
- I know that failure to follow the advice of the Physician, Nurse, PA, or Public Health Official may endanger the health or life of my child and others who come into contact with my child.
- I know that I may change my mind and talk to my child's physician, nurse, PA, or Public Health Official at any time and accept vaccination(s) for my child anytime in the future.
- I know that I can review the website www.ImmunizeforGood.com to learn about vaccines and the diseases they prevent.
- I know that I can contact the Colorado Immunization Information System (CIIS) or my medical provider to locate my child's immunization record at www.ColoradoIIS.com
- I acknowledge that I have read this document in its entirety and fully understand it.
- I am signing this document as a Personal Exemption.

Compelled speech

Physician/Nurse/PA /Public Health signature: _____ Date: _____

Parent/Guardian Statement (optional): _____

_____

2011 BOH workgroup

Colorado Religious Exemption Form

Child's Name: _____ Birth Date: _____

Parent's/Guardian's Name: _____

	Declined (Please initial each vaccine)
Required	
☐ Hepatitis B Vaccine	_____
☐ Diphtheria, tetanus, acellular pertussis (DTaP or Tdap) vaccine	_____
☐ Diphtheria tetanus (DT or Td) vaccine	_____
☐ *Haemophilus influenza* type b (Hib) vaccine	_____
☐ Inactivated poliovirus (IPV) vaccine	_____
☐ Pneumococcal conjugate (PCV13) or polysaccharide vaccine	_____
☐ Measles-mumps-rubella (MMR) vaccine	_____
☐ Varicella (chickenpox) vaccine	_____
Recommended	
☐ Human papillomavirus (HPV) vaccine	_____
☐ Rotavirus vaccine	_____
☐ Hepatitis A vaccine	_____
☐ Meningococcal conjugate or polysaccharide vaccine	_____
☐ Influenza (flu) vaccine	_____
☐ Other	_____

Religious Leader signature: _____ Date: _____

Parent/Guardian Statement (optional): _____

_____

Colorado Medical Exemption Form

Child's Name: _____ Birth Date: _____

Parent's/Guardian's Name: _____

	Declined (Please initial each vaccine)
Required	
☐ Hepatitis B Vaccine	_____
☐ Diphtheria, tetanus, acellular pertussis (DTaP or Tdap) vaccine	_____
☐ Diphtheria tetanus (DT or Td) vaccine	_____
☐ *Haemophilus influenza* type b (Hib) vaccine	_____
☐ Inactivated poliovirus (IPV) vaccine	_____
☐ Pneumococcal conjugate (PCV13) or polysaccharide vaccine	_____
☐ Measles-mumps-rubella (MMR) vaccine	_____
☐ Varicella (chickenpox) vaccine	_____
Recommended	
☐ Human papillomavirus (HPV) vaccine	_____
☐ Rotavirus vaccine	_____
☐ Hepatitis A vaccine	_____
☐ Meningococcal conjugate or polysaccharide vaccine	_____
☐ Influenza (flu) vaccine	_____
☐ Other	_____

Physician/Nurse/PA/Public Health signature: _____ Date: _____

Parent/Guardian Statement (optional): _____

_____

I have had the opportunity to discuss again my decision not to vaccinate my child and still decline the required and recommended vaccines. Check the box for the age you are currently exempting your child from receiving vaccine. You will be asked to review this document again at the next age level.

Parent/Guardian Signature: _____

			4 mo.	6 mo.	12-15 mos.	4 yrs	11-12 yrs
Parent/Guardian Initials: _____	Date: _____	Valid for:	☐	☐	☐	☐	☐
Parent/Guardian Initials: _____	Date: _____	Valid for:	☐	☐	☐	☐	☐
Parent/Guardian Initials: _____	Date: _____	Valid for:	☐	☐	☐	☐	☐
Parent/Guardian Initials: _____	Date: _____	Valid for:	☐	☐	☐	☐	☐

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Association of American Physicians and Surgeons, Inc.
A Voice for Private Physicians Since 1943
Omnia pro aegroto

To: Colorado legislators

Re: Vaccine exemptions

April 9, 2019

The Association of American Physicians and Surgeons (AAPS) strongly opposes H.B. 1312 or other measures that violate patient privacy, place bureaucratic burdens on parents trying to exercise their right to withhold informed consent for a medical procedure, or override individualized medical decision-making.

Patient autonomy is a key foundation of the charter for Medical Professionalism, and informed consent is required by the Nuremberg code. The patient's or parent's choice to receive a particular vaccine at a particular time should be between the patient or parent and the patient's chosen physician.

Like all medical interventions, vaccines have risks and benefits that vary with frequency and severity of disease, vaccine safety, and individual patient factors. A national bureaucratic committee cannot consider patient individuality, and may be slow to recognize newly identified contraindications.

Vaccines are necessarily risky, as recognized by the U.S. Supreme Court and by Congress. The Vaccine Injury Compensation Program has paid some $4 billion in damages, and high hurdles must be surmounted to collect compensation. The damage may be so devastating that most people would prefer restored function to a multimillion-dollar damage award.

Safety studies are generally not of sufficient power to rule out serious adverse reactions (e.g. encephalopathy, epilepsy, autoimmune disease, or death) that may be more common (say 1 in 10,000) than death or serious complication from the disease to be prevented. For most vaccines, the risk is not precisely known, but may be higher than is acceptable for some voluntary, occupational risks, or for some environmental risks. Most choose to take the risk of a complication that is so infrequent that most pediatricians have not observed it, in order to reduce the risk of a disease. But others should be free to opt out.

It is fundamentally unfair to *force* children to take a risk that might be higher than a worker would be *allowed* to take, such as exposure to a toxic chemical in the workplace, in order to attend school, or to place burdens on parents who decline.

To rule out serious but infrequent serious complications, a study would require an adequate number of subjects, a long duration (years, not days), an unvaccinated control group ("placebo" must be truly inactive such as saline, not the adjuvant or everything-but

-the-intended-antigen), and consideration of all adverse health events, including neurodevelopment disorders, not just those already recognized by a bureaucratic committee. Most vaccine safety studies fall far short of this.

Note that many vaccines contain live viruses, with the ability to cause atypical infections or to mutate in unpredictable ways, so some level of uncertainty is inevitable.

Some parents, even if they believe the benefits of a vaccine exceed the risks, have a moral objection. In this country, individual conscience is sacrosanct, even without a seal of approval from an organized, government-recognized religious group. Most often, this concerns the use of aborted human fetuses. Consider that such vaccines may contain human DNA, which might also pose risks.

The current nationwide rush to limit vaccine exemptions is fueled by outbreaks of measles, several hundred cases to date. The last recorded death from measles in the U.S. occurred in 2015, according to the Centers for Disease Control and Prevention (CDC, https://www.cdc.gov/measles/downloads/measlesdataandstatsslideset.pdf). More than a hundred deaths in association with the MMR vaccine have been reported to the Vaccine Adverse Event Reporting System (VAERS). While a causal relationship is not proved, it also has not been ruled out.

Much wider outbreaks would change the risk: benefit ratio, and many would voluntarily reconsider their decision. Even for those who did not, governmental overriding of the medical decisions of patients and physicians is a serious intrusion into individual liberty, autonomy, and parental decisions about child-rearing.

AAPS believes that liberty rights are unalienable. Patients and parents have the right to refuse vaccination, although potentially contagious persons can be restricted in their movements (e.g. as with Ebola), as needed to protect others against a clear and present danger. Unvaccinated persons with no exposure to a disease and no evidence of a disease are not a clear or present danger.

AAPS represents thousands of physicians in all specialties nationwide. It was founded in 1943 to protect private medicine and the patient-physician relationship.

Please oppose H.B. 1312 and all other governmental intrusions into medical decision-making.

Respectfully yours,

Jane M Orient

Jane M. Orient, M.D.
Executive Director

Esteemed members of the committee,

In this packet is the following;

1: A care guide on how to care for the immune compromised at home. I drew a red arrow at the live vaccine statement.

2: The vaccine list that is on the market and who makes them what they do and if they are inactivated, live or recombinant. Date January 2019

3: Acellular Persussis vaccine study, however I find it interesting that DTaP is a inactivated vaccine yet it is spreading perstussis, makes one wonder what other ones if not all may do this?

4: DTaP VIS, Vaccine Information Statement, this they will happily give to you at the doctors office it is 2 pages long

5: DTaP vaccine insert, this one I have had to fight to get and be told I can have it after I vaccinate, I declined. It is 18 pages long, quite a bit more info than the VIS. Note on page 12 at the bottom Sudden Infant Death Syndrome!!
The 2 combined is what Informed Consent Really looks like at a minimum.

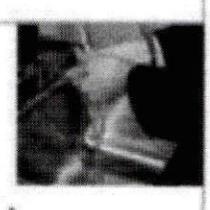
6: Vaccine Excipient & Media Summary
This is the ingredient list for each vaccine on the market as of October 2018. There are a lot of children and adults with allergies and or sensitivities which can be mild to severe to the ingredients.

7: Hot lot document, shows that vaccine makers have been aware for a long time that vaccines cause SIDS. It is dated 1979. sadly this is just the tip of the ice berg, who knows what other information they are hiding from us???!!!

The Johns Hopkins Hospital Patient Information

Original Date 9/05
Oncology
Revised / Reviewed 6/12

Care at Home for the Immunocompromised Patient

What can I do to prevent infection?	 • Hand washing is the **best way** to prevent infection. • Carry hand sanitizer with you at all times. • Wash with soap and water or hand sanitizer -before and after you use the bathroom -before and after preparing or eating food -after touching pets or animals -after contact with someone who has an infection such as a cold or the flu -after touching surfaces in public areas (such as elevator buttons, handrails and gas pumps)
Do I need to wear a mask?	• Wear an N95 respirator mask when you travel to and from the hospital, when you are in the hospital, within two football fields of construction or digging, and in any public place. • Close all car windows and turn on the re-circulate button of your ventilation system. • Avoid crowds if possible. An area is crowded if you are within an arm's length of other people. • Avoid closed spaces if possible.
Can I have visitors?	• Tell friends and family who are sick, or have recently had a live vaccine (such as chicken pox, measles, rubella, intranasal influenza, polio or smallpox) not to visit. • It may be a good idea to have visitors call first. • Avoid contact with children who were recently vaccinated.
Are there any precautions I should follow about my medicine?	• Do not take aspirin or aspirin-like products (such as Advil™, Motrin™ or Excedrin™) unless told by your doctor. • You should wear a medical alert bracelet that identifies you as a cancer patient or bone marrow transplant patient at risk for bleeding or infection. • **Keep a current medication list with you at all times.** • Do not take any herbal products. • Avoid grapefruit juice, which interacts with many medications.

U.S. Vaccines: Table 1

(For Combination Vaccines, See Table 2)

Vaccine	Trade Name	Abbreviation	Manufacturer	Route	Doses in Routine Series	Approved Ages	Comments
Adenovirus	Adenovirus Type 4 & Type 7		Barr Labs Inc.	Oral (2 Tablets)	1	17-50 years	Live: Approved for military populations
Anthrax	BioThrax®	AVA	Emergent BioSolutions	IM	3	18-65 years	Inactivated, Adj.
Cholera	Vaxchora®		PaxVax	Oral (Liquid)	1	18-64 years	Live Attenuated
DTaP	Daptacel®	DTaP	sanofi	IM	5	6 weeks-6 years	Inactivated, Adj.
	Infanrix®	DTaP	GlaxoSmithKline	IM	5	6 weeks-6 years	Inactivated, Adj.
DT	Generic	DT	sanofi	IM	5	6 weeks-6 years	Inactivated, Adj.: Use when pertussis is contraindicated
Haemophilus influenzae type b (Hib)	ActHIB®	Hib (PRP-T)	sanofi	IM	4	2 months-5 years	Inactivated, Adj. (Tetanus toxoid conjugate)
	Hiberix®	Hib (PRP-T)	GlaxoSmithKline	IM	4	6 weeks-4 years	Inactivated, Adj. (Tetanus toxoid conjugate)
	PedvaxHIB®	Hib (PRP-OMP)	Merck	IM	3	2-71 months	Inactivated, Adj. (Meningococcal conjugate)
Hepatitis A	Havrix®	HepA	GlaxoSmithKline	IM	2	Pediatric: 12 months-18 years Adult: ≥19 years	Inactivated, Adj.
	Vaqta®	HepA	Merck	IM	2	Pediatric: 12 months-18 years Adult: ≥19 years	Inactivated, Adj.
Hepatitis B	Engerix-B®	HepB	GlaxoSmithKline	IM	3	Pediatric: Birth-19 years Adult: ≥20 years	Recombinant, Adj.
	Recombivax HB®	HepB	Merck	IM	3	Pediatric: Birth-19 years Adult: ≥20 years	Recombinant, Adj.
	Heplisav-B®	HepB	Dynavax Technologies	IM	2	≥18 years	Recombinant, Adj.
Herpes Zoster (Shingles)	Zostavax®	ZVL	Merck	SC	1	≥50 years	Live Attenuated ACIP recommends ≥60 years
	Shingrix®	RZV	GlaxoSmithKline	IM	2	≥50 years	Recombinant, Adj.

Vaccine	Trade Name	Abbreviation	Manufacturer	Route	Doses in Routine Series	Approved Ages	Comments
Human Papillomavirus (HPV)	Gardasil®9	9vHPV	Merck	IM	2 or 3	9-45 years	Recombinant, Adj. ACIP recommends 9-26 years
Influenza	Afluria®	IIV3 IIV4	Seqirus	IM	1 or 2	≥5 years	Inactivated
	Fluad®	IIV3	Seqirus	IM	1	≥65 years	Inactivated, Adj.
	Fluarix®	IIV4	GlaxoSmithKline	IM	1 or 2	≥6 months	Inactivated
	Flublok®	RIV4	sanofi	IM	1	≥18 years	Recombinant, Egg-Free
	Flucelvax®	ccIIV4	Seqirus	IM	1 or 2	≥4 years	Cell-Culture
	FluLaval®	IIV4	GlaxoSmithKline	IM	1 or 2	≥6 months	Inactivated
	FluMist®	LAIV4	Medimmune	Intranasal	1 or 2	2-49 years	Live Attenuated
	Fluzone®	IIV3 IIV4	sanofi	IM	1 or 2	≥6 months	Inactivated
	Fluzone® High-Dose	IIV3	sanofi	IM	1	≥65 years	Inactivated
Japanese encephalitis	Ixiaro®	JE	Valneva	IM	2	≥2 months	Inactivated, Adj.
Measles, Mumps, Rubella	M-M-R®II	MMR	Merck	SC	2	≥12 months	Live Attenuated
Meningococcal	Menactra®	MCV4 MenACWY-D	sanofi	IM	2	9 months-55 years	Inactivated (Diphtheria toxoid conjugate)
	Menveo®	MCV4 MenACWY-CRM	GlaxoSmithKline	IM	2	2 months-55 years	Inactivated (CRM_{197} conjugate)
	Trumenba®	MenB-FHbp	Pfizer	IM	2 or 3	10-25 years	Recombinant, Adj.
	Bexsero®	MenB-4C	GlaxoSmithKline	IM	2	10-25 years	Recombinant, Adj.
Pneumococcal	Pneumovax® 23	PPSV23	Merck	IM or SC	1	≥2 years	Inactivated Polysaccharide
	Prevnar 13®	PCV13	Pfizer	IM	4	≥6 months	Inactivated, Adj. (CRM_{197} conjugate)
Polio	Ipol®	IPV	sanofi	IM or SC	4	≥6 months	Inactivated
Rabies	Imovax® Rabies		sanofi	IM	3 (pre-exposure) 5 (post-exposure)	All ages	Inactivated
	RabAvert®		GlaxoSmithKline	IM	3 (pre-exposure) 5 (post-exposure)	All ages	Inactivated
Rotavirus	RotaTeq®	RV5	Merck	Oral (Liquid)	3	6-32 weeks	Live, Pentavalent
	Rotarix®	RV1	GlaxoSmithKline	Oral (Liquid)	2	6-24 weeks	Live, Monovalent

Vaccine	Trade Name	Abbreviation	Manufacturer	Route	Doses in Routine Series	Approved Ages	Comments
Tetanus, (reduced) Diphtheria	Tenivac®	Td	sanofi	IM	1 (Every 10 years)	≥7 years	Inactivated, Adj.
	(Generic)	Td	Massachusetts Biological Labs	IM	1 (Every 10 years)	≥7 years	Inactivated, Adj.
Tetanus, (reduced) Diphtheria, (reduced) Pertussis	Boostrix®	Tdap	GlaxoSmithKline	IM	1	≥10 years	Inactivated, Adj.
	Adacel®	Tdap	sanofi	IM	1	10-64 years	Inactivated, Adj.
Typhoid	Typhim Vi®		sanofi	IM	1	≥2 years	Inactivated, Polysaccharide
	Vivotif®		PaxVax	Oral (Capsules)	4	≥6 years	Live Attenuated
Varicella	Varivax®	VAR	Merck	SC	2	≥12 months	Live Attenuated
Vaccinia (Smallpox)	ACAM2000®		sanofi	Percutaneous	1	All ages	Live Attenuated
Yellow Fever	YF-Vax®	YF	sanofi	SC	1	≥9 months	Live Attenuated

U.S. Vaccines: Table 2

(Combination Vaccines)

Vaccine	Trade Name	Abbreviation	Manufacturer	Route	Doses in Routine Series	Approved Ages	Comments
DTaP, Polio	Kinrix®	DTaP-IPV	GlaxoSmithKline	IM	1	4-6 years	Inactivated, Adj.: Approved as 5th DTaP and 4th IPV.
	Quadracel™	DTaP-IPV	sanofi	IM	1	4-6 years	Inactivated, Adj.: Approved as 5th DTaP and 4th IPV.
DTaP, hepatitis B, Polio	Pediarix®	DTaP-HepB-IPV	GlaxoSmithKline	IM	3	6 weeks-6 years	Inactivated, Adj.: Approved for 2, 4, 6 month doses.
DTaP, Polio, Haemophilus influenzae type b	Pentacel®	DTaP-IPV/Hib	sanofi	IM	4	6 weeks-4 years	Inactivated, Adj.: Approved for 2, 4, 6, 15-18 month doses.
Hepatitis A, Hepatitis B	Twinrix®	HepA-HepB	GlaxoSmithKline	IM	3	≥18 years	Inactivated/Recombinant, Adj. Pediatric HepA + Adult HepB
Measles, Mumps, Rubella, Varicella	ProQuad®	MMRV	Merck	SC	2	12 months-12 years	Live Attenuated

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

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

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

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

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

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

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

Significance

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

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

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

See Commentary on page 575.

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This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1314688110/-/DCSupplemental.

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

Results

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

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

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

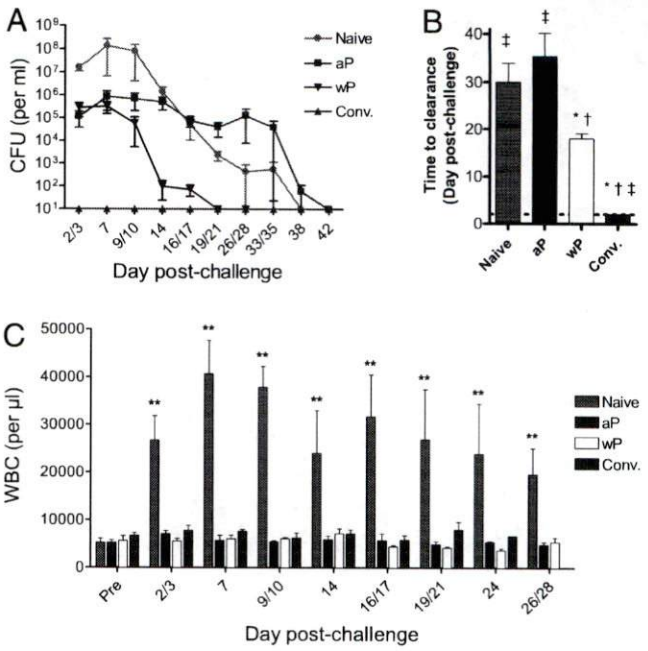

Fig. 1. The effect of vaccination or convalescence on colonization and leukocytosis. Naïve animals, aP-vaccinated animals, wP-vaccinated animals, and previously infected [convalescent conv.)] animals were directly challenged with *B. pertussis* (n = 3–4 per group). (*A*) Colonization was monitored by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

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

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

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

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

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

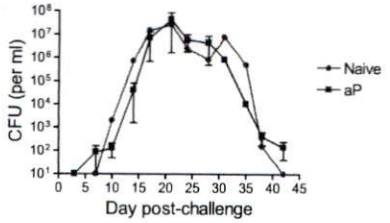

Fig. 2. aP does not protect against colonization following natural transmission. A naïve animal was directly challenged. After 24 h, a naïve animal and two aP-vaccinated animals were placed in the same cage as the directly challenged animal and followed for colonization as in Fig. 1.

pertussis toxin (PT), filamentous hemagglutinin (FHA), pertactin (PRN), and fimbriae types 2 and 3 (FIM). We show that wP, aP, and natural infection induce high-antibody titers to all antigens, and the aP group generally possessed equivalent or greater pre-challenge titers, suggesting that the differences in colonization between the groups do not correlate with levels of circulating antipertussis antibodies (Fig. 4). Following challenge, the titers for vaccinated animals were essentially unchanged, whereas boosting was observed for some antigens in convalescent animals (Fig. S1).

T-Cell Memory Response Elicited by Acellular Pertussis Vaccination Is Mismatched Compared with Natural Infection. Although a large number of clinical studies have characterized the antibody response to pertussis infection and vaccination, key deficiencies remain in our understanding of pertussis-induced helper T-cell immune responses in humans and primates. Importantly, no clinical studies have investigated whether the primary series of pertussis vaccines induce Th17 memory, a recently identified T cell that specializes in controlling extracellular bacterial infections at mucosal surfaces through stimulating neutrophil recruitment (24). To assess *B. pertussis*-specific T-cell memory responses in naïve, aP-vaccinated, wP-vaccinated, and convalescent animals, peripheral blood mononucleated cells (PBMCs) were collected 1 wk before infection. Total PBMC were incubated either with medium alone or with heat-killed *B. pertussis* as an ex vivo simulation of the memory responses recalled during the ensuing challenge. Following an overnight incubation, nonadherent PBMC, including T cells, were collected and separated using magnetic beads into the following fractions: CD4−, CD4+, CD95−CD4+, or left unseparated (total nonadherent cells). Memory helper T cells in primates are characterized by surface expression of CD4 and CD95 (25, 26). After further culture of all fractions, the supernatants were analyzed for secretion of IL-17, IFN-γ, and IL-5; cytokines that are characteristic of Th17, Th1, and Th2 cells, respectively. Very low background cytokine secretion was observed from nonstimulated cells isolated from naïve, vaccinated, or convalescent animals or from stimulated cells from naïve animals (Figs. S2 and S3). When stimulated with heat-killed *B. pertussis*, both total nonadherent cells and CD4+ cells from convalescent animals secreted high levels of IL-17, some IFN-γ, and no IL-5. When the CD95+ memory cells were depleted, the CD95−CD4+ cells did not secrete IL-17 or IFN-γ, consistent with induction of *B. pertussis*-specific Th17 and Th1 memory cells (Fig. 5). Stimulated total nonadherent cells and CD4+ cells from aP-vaccinated animals secreted significant IFN-γ, but the response was weaker than convalescent cells ($P = 0.01$), and there was no significant increase in IL-17 secretion. However, there was a significant IL-5 response, consistent with skewing toward Th2 and Th1 memory (Fig. 5). Total nonadherent cells and CD4+ cells from wP-vaccinated animals secreted similar IFN-γ compared with aP cells, but no IL-5. IL-17 secretion was between levels for naïve and convalescent cells, suggesting that T-cell memory induced by wP vaccination is similar to natural infection, but the Th17 and Th1 memory responses were weaker.

Discussion

The introduction of whole-cell vaccines consisting of inactivated *Bordetella pertussis* organisms in the United States in the 1940s caused a precipitous decrease in pertussis incidence (27). However, over the past 30 y, pertussis has resurged in the United States. The resurgence began during the wP vaccine era, but the pace has quickened since aP vaccines were recommended for all primary and booster doses (11). This correlation has led many to hypothesize that aP vaccines are less effective on a population scale than the wP vaccines they replaced (10, 12, 13). Consistent with this notion, several recent observational studies concluded that children primed with aP vaccine had a twofold to fivefold greater risk of pertussis diagnosis compared with wP-primed children (19–22). Our results in nonhuman primates add to these findings by showing that animals vaccinated with wP cleared infection by a direct challenge twice as fast as animals vaccinated with aP. However, neither vaccine was able to prevent colonization as well as immunity from a previous infection.

Another hypothesis as to why pertussis is reemerging is that the duration of immunity in aP-vaccinated children is shorter than anticipated. Although some first-generation acellular vaccines had poor immunity and efficacy, double-blinded clinical trials and field-efficacy studies for the US-licensed acellular vaccines estimated the short-term efficacy to be excellent: ~85% after three doses and 98% after five doses (28–30). However, recent cohort and case-control studies concluded that 5 y following the fifth aP dose, children are fourfold to 15-fold more likely to acquire pertussis compared with within the first year, consistent with waning aP immunity (30–33).

We hypothesized an additional explanation for pertussis resurgence is that aP-vaccinated individuals can act as asymptomatic or mildly symptomatic carriers and contribute significantly to transmission in the population. Observational studies suggest that asymptomatic pertussis can occur in vaccinated children and adults based on PCR or serological data (34, 35). However, during the aP vaccine trials, participants were not screened for *B. pertussis* infection unless they presented with pertussis-like symptoms and at least 7–21 d cough (12). Therefore, no experimental data exist on whether vaccination prevents *B. pertussis* colonization or transmission in humans. In the present study we show that aP-vaccinated primates were heavily infected following direct challenge, and the time to clearance was not different compared with naïve animals. Similarly, there was no difference in the kinetics or peak level of colonization between aP-vaccinated and naïve animals that were infected by natural transmission. Importantly, we also show in two experiments that aP-vaccinated animals transmitted *B. pertussis* to naïve cage mates. Together these data form the key finding of this study: aP vaccines do not prevent infection or

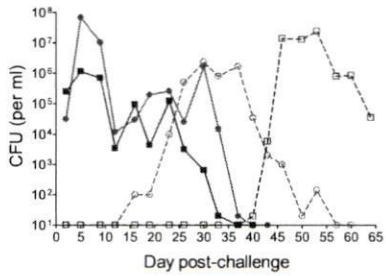

Fig. 3. Infected aP vaccinees can transmit pertussis to naïve contacts. Two animals vaccinated with aP were housed in separate cages, and each was directly challenged. Twenty four hours after challenge, an unchallenged naïve animal was placed in each cage. All animals were followed for colonization as in Fig. 1. One cage pairing is shown with turquoise lines with circles, and the other is shown with maroon lines with squares. Solid lines with closed symbols indicate the aP-vaccinated, directly challenged animals, and open symbols with dashed lines are used for the unchallenged, naïve contacts.

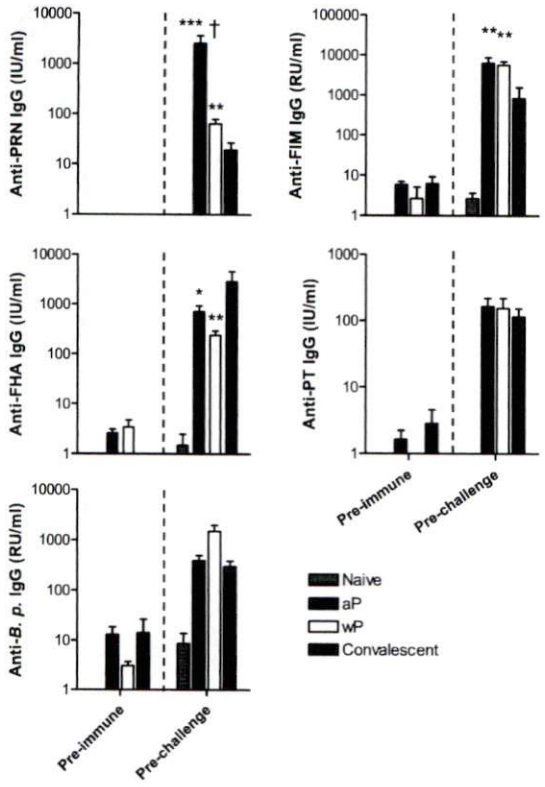

Fig. 4. Vaccination and previous infection induce robust serum antibody responses. Antibody responses to the four vaccine antigens—PRN, FIM, FHA, and PT—and to heat-killed *B. pertussis* (*B. p.*) were measured by ELISA. Preimmune sera were collected from vaccinated animals before immunization and from conv. animals before initial infection (n = 3–4 per group). Because Infanrix does not contain FIM, four Daptacel-vaccinated animals were included in the anti-FIM ELISA. Prechallenge sera were collected from all animals 1 wk before challenge. International Units (IU) or relative units (RU) in each sample were determined by comparing the responses to the WHO international standard pertussis antiserum on each plate. ***P < 0.001, **P < 0.01, *P < 0.05 vs. Convalescent. †P < 0.001 vs. wP.

transmission of *Bordetella pertussis* even 1 mo after completing the primary vaccination series.

We show that wP, aP, and natural infection all induce high-antibody titers. The prechallenge titers in aP-vaccinated animals were generally equivalent or higher than those observed in convalescent and wP-vaccinated animals, suggesting that aP is immunogenic in baboons and that the inability to prevent infection was not due to low-antibody titers. Compared with the large number of clinical studies that have characterized the antibody response to pertussis infection and vaccination, very few have investigated pertussis-induced helper T-cell immune responses in humans. Taken as a whole, these limited data suggest that aP vaccination induces Th2 or mixed Th2/Th1 responses, whereas wP vaccination and natural infection induce a Th1 response (13). However, none of these studies tested for Th17 memory, a recently identified T cell that specializes in controlling extracellular bacterial infections at mucosal surfaces (24). Our data show that natural infection induced robust Th17 and Th1 immunity. Animals vaccinated with wP, which cleared infection faster than naïve and aP-vaccinated animals, showed similar but weaker T-cell responses. wP vaccination is generally believed to induce strong Th1 responses, but what we observed here was relatively weak. This observation might be explained by heterogeneity in the manufacturing of different wP vaccines. Future studies will compare the immune response induced by wP vaccines produced by three different manufacturers. In comparison with natural infection and wP, aP-induced immunity was mismatched, showing a Th2 response with a weaker Th1 response and no significant Th17 response.

Together, the cytokine and T-cell immunological data observed in baboons are generally consistent with those observed in mice (13). We previously showed that pertussis infection in baboons induces a mucosal immune response characterized by production of IL-17 and a variety of chemokines and cytokines associated with IL-17 signaling, including IL-6 and IL-8. This primary immune response correlated with long-lived Th17 and Th1 memory responses that lasted >2 y (36). Mice infected with *B. pertussis* also express mucosal IL-17, IL-6, and IL-8 homologs and induce Th17 and Th1 memory (37–40). Mice vaccinated with wP also develop Th17 and Th1 memory that results in partial protective immunity, similar to what we observed in the baboon model (41, 42). A recent report by Ross et al. (42) concluded that an aP containing PT, FHA, and PRN induces Th1, Th2, and Th17 immune responses in C57BL/6 mice (42). However, a previous study from the same group found Th1 and Th2 but no

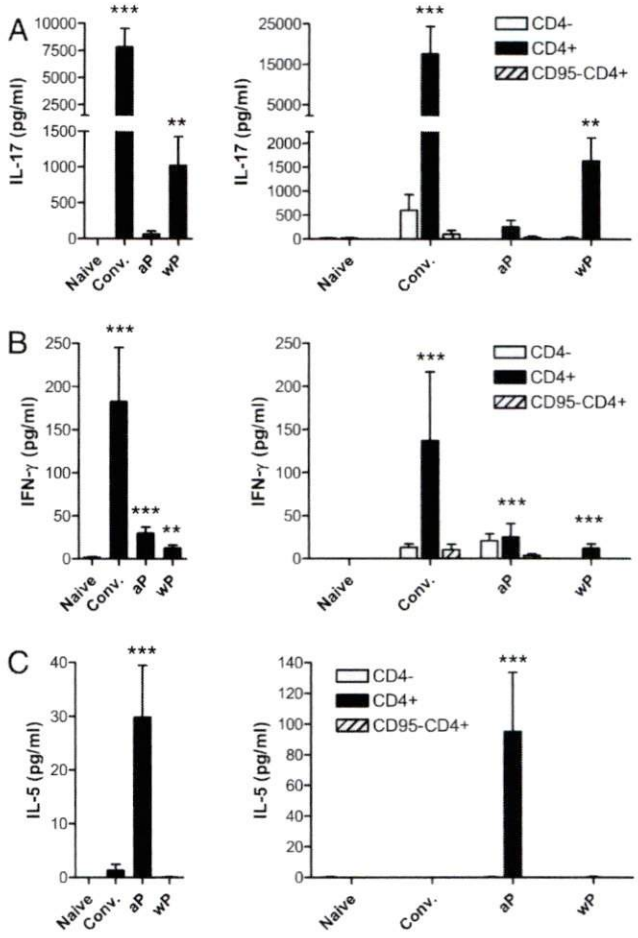

Fig. 5. Helper T-cell responses induced by vaccination and infection. PBMC collected from naïve, aP-vaccinated, wP-vaccinated, and conv. animals 1 wk before infection were incubated overnight with either medium alone or medium containing heat-killed *B. pertussis* (n = 3–4 per group). For each growth condition, nonadherent cells were collected and either left unseparated (total nonadherent cells) or separated using anti-CD4 and anti-CD95 magnetic particles. Total nonadherent, CD4−, CD4+, and CD95−CD4+ cells were then cultured under the same conditions as before (with medium alone or stimulated with heat-killed *B. pertussis*). After 36 h, supernatants were collected and analyzed for IL-17 (*A*), IFN-γ (*B*), and IL-5 (*C*). Cytokine secretion in response to *B. pertussis* stimulation is presented for total nonadherent cells (*Left*) and separated cells (*Right*). ***P < 0.001, **P < 0.01, *P < 0.05 vs. same fraction from naïve animals.

significant Th17 responses in C3H/HeJ and C3H/HeN mouse strains vaccinated with an aP containing PT and FHA (41). Nevertheless, data from two clinical studies recently showed negligible Th17 recall responses (~10 pg/mL) in PBMC isolated from aP-vaccinated 4-y-old children before and after booster, suggesting aP does not induce Th17 memory in humans (43, 44).

Taken as a whole, the data presented in this study suggest that antibodies induced by aP vaccination are sufficient for preventing severe pertussis symptoms but do not mitigate colonization. Inhibition of leukocytosis likely occurs through antibody-mediated neutralization of PT, a toxin which interferes with leukocyte extravasation by blocking chemokine receptor signaling (1). The mechanism by which aP prevents coughing despite heavy bacterial colonization is not known but deserves further attention. On the other hand, induction of Th17/Th1 memory responses correlated with the ability to clear infection: convalescent and wP-vaccinated animals possessed strong Th17 responses and Th1 responses and cleared infection more quickly than aP-vaccinated animals which lacked Th17 responses but possessed Th1/ Th2 memory. Although we have not definitively shown that Th17 cells are required for *B. pertussis* clearance, this correlation is consistent with the role these cells play in fighting extracellular bacterial infections at mucosal surfaces by inducing neutrophil chemotaxis. The current studies were not designed to look at immune cell recruitment to the respiratory tract, but additional experiments are underway to determine the role of neutrophils in the immune response to pertussis infection and vaccination in baboons. We are also investigating other possible mechanisms that could prevent mucosal colonization; for example, a possible role for IgA and IgD which are secreted in primate lower and upper respiratory tracts, respectively (45, 46).

The baboon model offers many advantages, chiefly the ability to investigate pertussis pathogenesis, transmission, and host immune responses to infection and vaccination in a primate species that is >96% genetically similar to humans (47). However, there are also several limitations associated with this model. There are far fewer animals available for research compared with smaller-animal models. In addition, there is a paucity of immunological reagents that are validated for baboons compared with mice and humans. Although antibodies against cell surface markers are generally cross-reactive, anti-cytokine antibodies tend to be much more species-specific. For this reason we have so far been unable to assess T-cell responses using intracellular cytokine staining and flow cytometry. This led us to develop the cell separation assay as an alternative method for phenotyping the memory T-cell responses induced by pertussis infection and vaccination (36). One limitation of our assay is that during the CD4+ cell purification, antigen-presenting cells such as macrophages and dendritic cells are removed after an overnight incubation. This likely explains the low IFN-γ secretion observed in all groups because antigen-presenting cells increase IFN-γ secretion by antigen-specific CD4+ T cells through a positive feedback loop (48). In line with this hypothesis, our previous data showed that restimulated whole PBMC from convalescent animals secreted much higher levels of IFN-γ. In addition, restimulation assays using human PBMC or murine splenocytes after infection or vaccination also show higher levels of secreted IFN-γ (42, 49). Together these observations suggest that although our assay is valuable for phenotyping T-cell memory, it likely underrepresents the magnitude of Th1 memory responses. We used heat-killed *B. pertussis* as an antigen for our restimulation assays because we believe this is the most relevant method for ex vivo simulation of T-cell memory recalled during infection. However, it is possible that this assay underdetects immune responses that would be observed had we used purified vaccine antigens. Another disadvantage of primate models is that it is not feasible to directly link an immune response to protection. Although protection from pertussis has been shown to be mediated by IFN-γ and, to a lesser extent, IL-17 signaling using knockout mouse strains lacking specific gene products (13), the relative protection afforded by Th17 or Th1 responses in vaccinated or convalescent baboons or humans is not known.

Currently, a major focus of public health agencies is the prevention of pertussis infection in young infants who have not completed their primary aP series and have considerable morbidity and mortality to pertussis infection (1). One recommendation to reduce transmission of pertussis to infants is by "cocooning," or vaccinating people who have contact with infants (11). Our data show that aP-vaccinated animals are infected and transmit pertussis to naïve contacts. Consistent with these findings, seroepidemiological studies have concluded that *B. pertussis* circulation is still high in countries with excellent aP uptake (27, 50), and a cross-sectional study showed that postpartum aP vaccination of mothers did not reduce pertussis illness in young infants (51). These data suggest that cocooning is unlikely to be an effective strategy to reduce the burden of pertussis in infants. However, it is important to note that our data in combination with human data show that vaccination with aP provides excellent protection from severe pertussis (52). Therefore, any short-term plan for addressing the resurgence of pertussis should include continued efforts to enhance aP immunization. However, to protect the most vulnerable members of the population and achieve optimal herd immunity, it will be necessary to develop a vaccination strategy that effectively blocks pertussis infection and transmission.

Materials and Methods

Ethics Statement. All animal procedures were performed in a facility accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International in accordance with protocols approved by the Center for Biologics Evaluation and Research Animal Care and Use Committee and the principles outlined in the *Guide for the Care and Use of Laboratory Animals* by the Institute for Laboratory Animal Resources, National Research Council (53).

Bacterial Strains and Media. *B. pertussis* strain D420 was grown on Bordet–Gengou and Regan–Lowe plates prepared as described previously (17). Heat-killed *B. pertussis* was prepared by resuspending to an OD_{600} of 0.90 (5×10^9 cfu/mL) in PBS and heating at 65 °C for 30 min.

Vaccination, Infection, and Evaluation of Baboons. Baboons obtained from the Oklahoma Baboon Research Resource at the University of Oklahoma Health Sciences Center were inoculated with human doses of aP or wP administered intramuscularly at 2, 4, and 6 mo of age. For studies using aP, equal numbers of animals were vaccinated with Daptacel (Sanofi Pasteur Ltd.) and Infanrix (GlaxoSmithKline). For wP, animals were vaccinated with Triple Antigen (Serum Institute of India Ltd.), which meets the World Health Organization (WHO) recommendations for potency. Naïve animals were age-matched but not vaccinated. Previously infected animals were clear of *B. pertussis* infection for 1 to 2 mo before reinfection. Direct challenge and transmission studies were performed as described previously (17, 18). The inoculum for each direct challenge was between 10^9–10^{10} cfu as determined by measurement of optical density and confirmed by serial dilution and plating to determine the number of cfu per mL of inoculum. Baboons were evaluated twice weekly as described previously for enumeration of circulating white blood cells and serum separation (17). Nasopharyngeal washes were diluted and plated on Regan–Lowe plates to quantify bacterial cell counts.

Isolation of PBMC and Cell Separation. Baboons were anesthetized, and PBMC were isolated from peripheral blood as described previously (36) and cryopreserved in RPMI-1640 medium supplemented with 10% (vol/vol) DMSO and 12.5% (wt/vol) BSA using Mr. Frosty containers (Nalgene). After thawing, cells were washed twice and nonadherent cells were collected as described previously. For each growth condition, cells were incubated overnight with either medium alone or medium containing heat-killed *B. pertussis* (50 bacteria:1 PBMC). Nonadherent cells were collected, and 2×10^6 cells were left unseparated (total nonadherent cells). Using the method previously described, 4×10^6 cells were separated using anti-CD4 magnetic particles, and another 4×10^6 cells were depleted of CD95+ cells and then separated with anti-CD4 magnetic particles (36). The following fractions were collected: Total nonadherent, CD4–, CD4+, and CD95–CD4+. After incubation with or without heat-killed *B. pertussis*, cells were pelleted and supernatants were collected for IL-17A quantitation by ELISA (Aniara) and quantitation of IFN-γ and IL-5 using the Milliplex MAP nonhuman primate kit according to the manufacturer's instructions (Millipore). Data are presented as

the cytokine concentration secreted by *B. pertussis*-stimulated cells minus the basal concentration secreted by cells incubated with medium alone.

Detection of Serum Antibodies to Pertussis Antigens. Nunc Maxisorp 96-well plates were coated overnight with 0.2 μg/mL PT, 0.5 μg/mL FHA, 2 μg/mL PRN, or 0.2 μg/mL FIM (List Biologicals) as described previously (17, 54). For whole-bacteria ELISA, plates were coated overnight at 37 °C with heat-killed *B. pertussis* prepared as described above. Serum IgG for each antigen was measured as described previously (17). Each plate contained a standard curve from the WHO international standard pertussis antiserum (National Institute for Biological Standards and Control) used to assign international units for PT, FHA, and PRN and relative units for FIM and heat-killed *B. pertussis* by comparison with the linear portion of the standard curve. Because Infanrix does not contain FIM, only Daptacel-vaccinated animals were included in the anti-FIM ELISA.

Statistics. All data are reported as mean ± SEM. Statistical analyses were performed by ANOVA with post hoc *t* test using JMP (version 9) software (SAS Institute, Inc.). Antibody and cytokine data were normalized by log transformation before analysis.

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DTaP (Diphtheria, Tetanus, Pertussis) Vaccine: *What You Need to Know*

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

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

1 Why get vaccinated?

DTaP vaccine can help protect your child from **diphtheria**, **tetanus**, and **pertussis**.

- **DIPHTHERIA (D)** can cause breathing problems, paralysis, and heart failure. Before vaccines, diphtheria killed tens of thousands of children every year in the United States.
- **TETANUS (T)** causes painful tightening of the muscles. It can cause "locking" of the jaw so you cannot open your mouth or swallow. About 1 person out of 5 who get tetanus dies.
- **PERTUSSIS (aP)**, also known as Whooping Cough, causes coughing spells so bad that it is hard for infants and children to eat, drink, or breathe. It can cause pneumonia, seizures, brain damage, or death.

Most children who are vaccinated with DTaP will be protected throughout childhood. Many more children would get these diseases if we stopped vaccinating.

2 DTaP vaccine

Children should usually get 5 doses of DTaP vaccine, one dose at each of the following ages:

- 2 months
- 4 months
- 6 months
- 15–18 months
- 4–6 years

DTaP may be given at the same time as other vaccines. Also, sometimes a child can receive DTaP together with one or more other vaccines in a single shot.

3 Some children should not get DTaP vaccine or should wait

DTaP is only for children younger than 7 years old. DTaP vaccine is not appropriate for everyone—a small number of children should receive a different vaccine that contains only diphtheria and tetanus instead of DTaP.

Tell your health care provider if your child:

- Has had an **allergic reaction after a previous dose of DTaP**, or has any **severe, life-threatening allergies**.
- Has had a **coma or long repeated seizures within 7 days after a dose of DTaP**.
- Has **seizures or another nervous system problem**.
- Has had a condition called **Guillain-Barré Syndrome (GBS)**.
- Has had **severe pain or swelling after a previous dose** of DTaP or DT vaccine.

In some cases, your health care provider may decide to postpone your child's DTaP vaccination to a future visit.

Children with minor illnesses, such as a cold, may be vaccinated. Children who are moderately or severely ill should usually wait until they recover before getting DTaP vaccine.

Your health care provider can give you more information.

CDC

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

4 Risks of a vaccine reaction

- Redness, soreness, swelling, and tenderness where the shot is given are common after DTaP.
- Fever, fussiness, tiredness, poor appetite, and vomiting sometimes happen 1 to 3 days after DTaP vaccination.
- More serious reactions, such as seizures, non-stop crying for 3 hours or more, or high fever (over 105°F) after DTaP vaccination happen much less often. Rarely, the vaccine is followed by swelling of the entire arm or leg, especially in older children when they receive their fourth or fifth dose.
- Long-term seizures, coma, lowered consciousness, or permanent brain damage happen extremely rarely after DTaP vaccination.

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

5 What if there is a serious problem?

An allergic reaction could occur after the child leaves the clinic. If you see signs of a severe allergic reaction (hives, swelling of the face and throat, difficulty breathing, a fast heartbeat, dizziness, or weakness), call 9-1-1 and get the child to the nearest hospital.

For other signs that concern you, call your child's health care provider.

Serious reactions should be reported to the Vaccine Adverse Event Reporting System (VAERS). Your doctor will usually file this report, or you can do it yourself. Visit **www.vaers.hhs.gov** or call **1-800-822-7967**. *VAERS is only for reporting reactions, it does not give medical advice.*

6 The National Vaccine Injury Compensation Program

The National Vaccine Injury Compensation Program (VICP) is a federal program that was created to compensate people who may have been injured by certain vaccines. Visit **www.hrsa.gov/vaccinecompensation** or call **1-800-338-2382** to learn about the program and about filing a claim. There is a time limit to file a claim for compensation.

7 How can I learn more?

- Ask your healthcare provider.
- Call your local or state health department.
- Contact the Centers for Disease Control and Prevention (CDC):
  - Call **1-800-232-4636** (**1-800-CDC-INFO**) or
  - Visit **www.cdc.gov/vaccines**

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

INFANRIX (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed)
Suspension for Intramuscular Injection
Initial U.S. Approval: 1997

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

INFANRIX is a vaccine indicated for active immunization against diphtheria, tetanus, and pertussis as a 5-dose series in infants and children 6 weeks to 7 years of age. (1)

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

A 0.5-mL intramuscular injection given as a 5-dose series: (2.2)

- One dose each at 2, 4, and 6 months of age.
- One booster dose at 15 to 20 months of age and another booster dose at 4 to 6 years of age.

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

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

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

- Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any diphtheria toxoid-, tetanus toxoid-, or pertussis-containing vaccine, or to any component of INFANRIX. (4.1)
- Encephalopathy within 7 days of administration of a previous pertussis-containing vaccine. (4.2)
- Progressive neurologic disorders. (4.3)

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

- If Guillain-Barré syndrome occurs within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the decision to give INFANRIX should be based on potential benefits and risks. (5.1)
- The tip caps of the prefilled syringes contain natural rubber latex which may cause allergic reactions. (5.2)
- Syncope (fainting) can occur in association with administration of injectable vaccines, including INFANRIX. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope. (5.3)
- If temperature ≥105°F, collapse or shock-like state, or persistent, inconsolable crying lasting ≥3 hours have occurred within 48 hours after receipt of a pertussis-containing vaccine, or if seizures have occurred within 3 days after receipt of a pertussis-containing vaccine, the decision to give INFANRIX should be based on potential benefits and risks. (5.4)
- For children at higher risk for seizures, an antipyretic may be administered at the time of vaccination with INFANRIX. (5.5)
- Apnea following intramuscular vaccination has been observed in some infants born prematurely. Decisions about when to administer an intramuscular vaccine, including INFANRIX, to infants born prematurely should be based on consideration of the individual infant's medical status, and the potential benefits and possible risks of vaccination. (5.6)

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

Rates of injection site reactions (pain, redness, swelling) ranged from 10% to 53%, depending on reaction and dose number, and were highest following Doses 4 and 5. Fever was common (20% to 30%) following Doses 1-3. Other common solicited adverse events were drowsiness, irritability/fussiness, and loss of appetite, reported in approximately 15% to 60% of subjects, depending on event and dose number. (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.

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

Do not mix INFANRIX with any other vaccine in the same syringe or vial. (7.1)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: /xxxx

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

INFANRIX® is indicated for active immunization against diphtheria, tetanus, and pertussis as a 5-dose series in infants and children 6 weeks to 7 years of age (prior to seventh birthday).

2 DOSAGE AND ADMINISTRATION

2.1 Preparation for Administration

Shake vigorously to obtain a homogeneous, turbid, white suspension. Do not use if resuspension does not occur with vigorous shaking. 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.

For the prefilled syringes, attach a sterile needle and administer intramuscularly.

For the vials, use a sterile needle and sterile syringe to withdraw the 0.5-mL dose and administer intramuscularly. Changing needles between drawing vaccine from a vial and injecting it into a recipient is not necessary unless the needle has been damaged or contaminated. Use a separate sterile needle and syringe for each individual.

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

2.2 Dose and Schedule

A 0.5-mL dose of INFANRIX is approved for intramuscular administration in infants and children 6 weeks to 7 years of age (prior to the seventh birthday) as a 5-dose series. The series consists of a primary immunization course of 3 doses administered at 2, 4, and 6 months of age (at intervals of 4 to 8 weeks), followed by 2 booster doses, administered at 15 to 20 months of age and at 4 to 6 years of age. The first dose may be given as early as 6 weeks of age.

The preferred administration site is the anterolateral aspect of the thigh for most infants younger than 12 months of age and the deltoid muscle of the upper arm for most children 12 months of age to 7 years of age.

2.3 Use of INFANRIX with Other DTaP Vaccines

Sufficient data are not available on the safety and effectiveness of interchanging INFANRIX and Diphtheria and Tetanus Toxoids and Acellular Pertussis (DTaP) vaccines from different manufacturers for successive doses of the DTaP vaccination series. Because the pertussis antigen components of INFANRIX and PEDIARIX® [Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Hepatitis B (Recombinant) and Inactivated Poliovirus Vaccine] are the same, INFANRIX may be used to complete a DTaP vaccination series initiated with PEDIARIX.

2.4 Additional Dosing Information

If any recommended dose of pertussis vaccine cannot be given *[see Contraindications (4.2, 4.3), Warnings and Precautions (5.5)]*, Diphtheria and Tetanus Toxoids Adsorbed (DT) For Pediatric Use should be given according to its prescribing information.

3 DOSAGE FORMS AND STRENGTHS

INFANRIX is a suspension for injection available in 0.5-mL single-dose vials and prefilled TIP-LOK® syringes.

4 CONTRAINDICATIONS

4.1 Hypersensitivity

Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any diphtheria toxoid-, tetanus toxoid-, or pertussis-containing vaccine, or to any component of INFANRIX is a contraindication *[see Description (11)]*. Because of the uncertainty as to which component of the vaccine might be responsible, no further vaccination with any of these components should be given. Alternatively, such individuals may be referred to an allergist for evaluation if immunization with any of these components is being considered.

4.2 Encephalopathy

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

4.3 Progressive Neurologic Disorder

Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, or progressive encephalopathy is a contraindication to administration of any pertussis-containing vaccine, including INFANRIX. Pertussis vaccine should not be administered to individuals with these conditions until a treatment regimen has been established and the condition has stabilized.

5 WARNINGS AND PRECAUTIONS

5.1 Guillain-Barré Syndrome

If Guillain-Barré syndrome occurs within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the decision to give any tetanus toxoid-containing vaccine, including INFANRIX, should be based on careful consideration of the potential benefits and possible risks. When a decision is made to withhold tetanus toxoid, other available vaccines should be given, as indicated.

5.2 Latex

The tip caps of the prefilled syringes contain natural rubber latex which may cause allergic

reactions.

5.3 Syncope

Syncope (fainting) can occur in association with administration of injectable vaccines, including INFANRIX. 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.

5.4 Adverse Events following Prior Pertussis Vaccination

If any of the following events occur in temporal relation to receipt of a pertussis-containing vaccine, the decision to give any pertussis-containing vaccine, including INFANRIX, should be based on careful consideration of the potential benefits and possible risks:

- Temperature of ≥40.5°C (105°F) within 48 hours not due to another identifiable cause;
- Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours;
- Persistent, inconsolable crying lasting ≥3 hours, occurring within 48 hours;
- Seizures with or without fever occurring within 3 days.

5.5 Children at Risk for Seizures

For children at higher risk for seizures than the general population, an appropriate antipyretic may be administered at the time of vaccination with a pertussis-containing vaccine, including INFANRIX, and for the ensuing 24 hours to reduce the possibility of post-vaccination fever.

5.6 Apnea in Premature Infants

Apnea following intramuscular vaccination has been observed in some infants born prematurely. Decisions about when to administer an intramuscular vaccine, including INFANRIX, to infants born prematurely should be based on consideration of the individual infant's medical status, and the potential benefits and possible risks of vaccination.

5.7 Preventing and Managing Allergic Vaccine Reactions

Prior to administration, the healthcare provider should review the patient's immunization history for possible vaccine hypersensitivity. Epinephrine and other appropriate agents used for the control of immediate allergic reactions must be immediately available should an acute anaphylactic reaction occur.

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 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 INFANRIX could reveal adverse reactions not observed in clinical

trials.

Approximately 95,000 doses of INFANRIX have been administered in clinical studies. In these studies, 29,243 infants have received INFANRIX in primary series studies, 6,081 children have received a fourth consecutive dose of INFANRIX, 1,764 children have received a fifth consecutive dose of INFANRIX, and 559 children have received a dose of INFANRIX following 3 doses of PEDIARIX.

Solicited Adverse Events

In a US study, 335 infants received INFANRIX, ENGERIX-B® [Hepatitis B Vaccine (Recombinant)], inactivated poliovirus vaccine (IPV, Sanofi Pasteur SA), Haemophilus b (Hib) conjugate vaccine (Wyeth Pharmaceuticals Inc.), and pneumococcal 7-valent conjugate (PCV7) vaccine (Wyeth Pharmaceuticals Inc.) concomitantly at separate sites. All vaccines were administered at 2, 4, and 6 months of age. Data on solicited local reactions and general adverse events were collected by parents using standardized diary cards for 4 consecutive days following each vaccine dose (i.e., day of vaccination and the next 3 days) (Table 1). Among subjects, 69% were white, 16% were Hispanic, 8% were black, 4% were Asian, and 2% were of other racial/ethnic groups.

Table 1. Solicited Local Reactions and General Adverse Events (%) Occurring within 4 Days of Vaccination[a] with Separate Concomitant Administration of INFANRIX, ENGERIX-B, IPV, Haemophilus b (Hib) Conjugate Vaccine, and Pneumococcal Conjugate Vaccine (PCV7) (Modified Intent-to-Treat Cohort)

	INFANRIX, ENGERIX-B, IPV, Hib Vaccine, & PCV7		
	Dose 1	**Dose 2**	**Dose 3**
Local[b]			
N	335	323	315
Pain, any	31.9	30.0	29.8
Pain, Grade 2 or 3	9.0	8.7	8.9
Pain, Grade 3	2.7	1.5	1.3
Redness, any	18.2	32.8	39.0
Redness, >20 mm	0.3	0.0	1.9
Swelling, any	9.6	20.4	24.8
Swelling, >20 mm	0.6	0.0	1.3
General			
N	333	321	311
Fever[c] (≥100.4°F)	19.8	30.2	23.8
Fever[c] (>101.3°F)	4.5	9.7	5.8
Fever[c] (>102.2°F)	0.3	3.1	2.3
Fever[c] (>103.1°F)	0.0	0.3	0.3
N	335	323	315
Drowsiness, any	54.0	48.3	38.4
Drowsiness, Grade 2 or 3	17.6	12.4	11.1
Drowsiness, Grade 3	3.6	0.6	1.9
Irritability/Fussiness, any	61.5	61.6	56.5
Irritability/Fussiness, Grade 2 or 3	19.4	21.1	19.4
Irritability/Fussiness, Grade 3	3.9	3.4	3.2
Loss of appetite, any	27.8	26.6	23.8
Loss of appetite, Grade 2 or 3	5.1	3.4	5.4
Loss of appetite, Grade 3	0.6	0.3	0.0

Hib conjugate vaccine and PCV7 manufactured by Wyeth Pharmaceuticals Inc. IPV manufactured by Sanofi Pasteur SA.

Modified intent-to-treat cohort = All vaccinated subjects for whom safety data were available.

N = Number of infants for whom at least one symptom sheet was completed; for fever, numbers exclude missing temperature recordings or tympanic measurements.

Grade 2: Pain defined as cried/protested on touch; drowsiness defined as interfered with normal daily activities; irritability/fussiness defined as crying more than usual/interfered with normal daily activities; loss of appetite defined as eating less than usual/interfered with normal daily activities.

Grade 3: Pain defined as cried when limb was moved/spontaneously painful; drowsiness defined as prevented normal daily activities; irritability/fussiness defined as crying that could not be comforted/prevented normal daily activities; loss of appetite defined as no eating at all.

[a] Within 4 days of vaccination defined as day of vaccination and the next 3 days.

[b] Local reactions at the injection site for INFANRIX.

[c] Axillary temperatures increased by 1°C and oral temperatures increased by 0.5°C to derive equivalent rectal temperature.

In a US study, the safety of a booster dose of INFANRIX was evaluated in children 15 to 18 months of age whose previous 3 DTaP doses were with INFANRIX (N = 251) or PEDIARIX (N = 559). Vaccines administered concurrently with the fourth dose of INFANRIX included measles, mumps, and rubella (MMR) vaccine (Merck & Co., Inc.), varicella vaccine (Merck & Co., Inc.), pneumococcal 7-valent conjugate (PCV7) vaccine (Wyeth Pharmaceuticals Inc.), and any US-licensed Hib conjugate vaccine; these were given concomitantly in 13.2%, 6.3%, 37.4%, and 41.2% of subjects, respectively. Data on solicited adverse events were collected by parents using standardized diary cards for 4 consecutive days following each vaccine dose (i.e., day of vaccination and the next 3 days) (Table 2). Among subjects, 85% were white, 6% were Hispanic, 6% were black, 1% were Asian, and 2% were of other racial/ethnic groups.

Table 2. Solicited Local Reactions and General Adverse Events (%) Occurring within 4 Days of Vaccination[a] with INFANRIX Administered as the Fourth Dose following 3 Previous Doses of INFANRIX or PEDIARIX (Total Vaccinated Cohort)

	Group Primed with INFANRIX[b] N = 247	Group Primed with PEDIARIX[c] N = 553
Local[d]		
Pain, any	44.5	48.3
Pain, Grade 2 or 3	19.0	18.6
Pain, Grade 3	3.6	3.4
Redness, any	48.2	49.9
Redness, >20 mm	6.1	6.0
Swelling, any	32.8	32.7
Swelling, >20 mm	3.6	5.2
Increase in mid-thigh circumference, any	33.2	26.2
Increase in mid-thigh circumference, >40 mm	0.0	1.3
General		
Fever[e] (>99.5°F)	8.9	15.4
Fever[e] (>100.4°F)	4.5	6.7
Fever[e] (>101.3°F)	2.0	2.0
Drowsiness, any	35.6	31.3
Drowsiness, Grade 2 or 3	9.3	6.7
Drowsiness, Grade 3	2.4	1.3
Irritability, any	52.2	53.9
Irritability, Grade 2 or 3	18.2	19.7
Irritability, Grade 3	3.2	1.4
Loss of appetite, any	24.7	23.3
Loss of appetite, Grade 2 or 3	5.3	4.9
Loss of appetite, Grade 3	2.4	0.5

Total Vaccinated Cohort = All subjects who received a dose of study vaccine.

N = Number of subjects for whom at least one symptom sheet was completed.

Grade 2: Pain defined as cried/protested on touch; drowsiness defined as interfered with normal daily activities; irritability defined as crying more than usual/interfered with normal daily activities; loss of appetite defined as eating less than usual/no effect on normal daily activities.

Grade 3: Pain defined as cried when limb was moved/spontaneously painful; drowsiness defined as prevented normal daily activities; irritability defined as crying that could not be comforted/prevented normal daily activities; loss of appetite defined as eating less than usual/interfered with normal daily activities.

[a] Within 4 days of vaccination defined as day of vaccination and the next 3 days.

[b] Received INFANRIX, ENGERIX-B, IPV (Sanofi Pasteur SA), PCV7 vaccine (Wyeth

Pharmaceuticals Inc.), and Hib conjugate vaccine (Wyeth Pharmaceuticals Inc.) at 2, 4, and 6 months of age.

[c] Received PEDIARIX, PCV7 vaccine (Wyeth Pharmaceuticals Inc.), and Hib conjugate vaccine (Wyeth Pharmaceuticals Inc.) at 2, 4, and 6 months of age or PCV7 vaccine 2 weeks later.

[d] Local reactions at the injection site for INFANRIX.

[e] Axillary temperatures.

In a US study, the safety of a fifth consecutive dose of INFANRIX coadministered at separate sites with a fourth dose of IPV (Sanofi Pasteur SA) and a second dose of MMR vaccine (Merck & Co., Inc.) was evaluated in 1,053 children 4 to 6 years of age. Data on solicited adverse events were collected by parents using standardized diary cards for 4 consecutive days following each vaccine dose (i.e., day of vaccination and the next 3 days) (Table 3). Among subjects, 43% were white, 18% Hispanic, 15% Asian, 7% black, and 17% were of other racial/ethnic groups.

Table 3. Solicited Local Reactions and General Adverse Events (%) Occurring within 4 Days of Vaccination[a] with a Fifth Consecutive Dose of INFANRIX When Coadministered with IPV and MMR Vaccine (Total Vaccinated Cohort)

Local[b]	**N = 1,039-1,043**
Pain, any	53.3
Pain, Grade 2 or 3[c]	12.0
Pain, Grade 3[c]	0.6
Redness, any	36.6
Redness, ≥50 mm	20.0
Redness, ≥110 mm	4.1
Arm circumference increase, any	37.8
Arm circumference increase, >20 mm	7.4
Arm circumference increase, >30 mm	3.2
Swelling, any	27.0
Swelling, ≥50 mm	11.5
Swelling, ≥110 mm	1.8
General	**N = 993-1,036**
Drowsiness, any	17.5
Drowsiness, Grade 3[d]	0.8
Fever, ≥99.5°F	14.8
Fever, >100.4°F	4.4
Fever, >102.2°F	1.1
Fever, >104°F	0.0
Loss of appetite, any	16.0
Loss of appetite, Grade 3[e]	0.6

IPV manufactured by Sanofi Pasteur SA. MMR vaccine manufactured by Merck & Co., Inc.
Total Vaccinated Cohort = All vaccinated subjects for whom safety data were available.
N = Number of children with evaluable data for the events listed.
[a] Within 4 days of vaccination defined as day of vaccination and the next 3 days.
[b] Local reactions at the injection site for INFANRIX.
[c] Grade 2 defined as painful when the limb was moved; Grade 3 defined as preventing normal daily activities.
[d] Grade 3 defined as preventing normal daily activities.
[e] Grade 3 defined as not eating at all.

In the US booster immunization studies in which INFANRIX was administered as the fourth or fifth dose in the DTaP series following previous doses with INFANRIX or PEDIARIX, large swelling reactions of the limb injected with INFANRIX were assessed.

In the fourth-dose study, a large swelling reaction was defined as injection site swelling with a diameter of >50 mm, a >50 mm increase in the mid-thigh circumference compared with the pre-

vaccination measurement, and/or any diffuse swelling that interfered with or prevented daily activities. The overall incidence of large swelling reactions occurring within 4 days (Day 0-Day 3) following INFANRIX was 2.3%.

In the fifth-dose study, a large swelling reaction was defined as swelling that involved >50% of the injected upper arm length and that was associated with a >30 mm increase in mid-upper arm circumference within 4 days following vaccination. The incidence of large swelling reactions following the fifth consecutive dose of INFANRIX was 1.0%.

Less Common and Serious General Adverse Events

Selected adverse events reported from a double-blind, randomized Italian clinical efficacy trial involving 4,696 children administered INFANRIX or 4,678 children administered whole-cell DTP vaccine (DTwP) (manufactured by Connaught Laboratories, Inc.) as a 3-dose primary series are shown in Table 4. The incidence of rectal temperature ≥104°F, hypotonic-hyporesponsive episodes, and persistent crying ≥3 hours following administration of INFANRIX was significantly less than that following administration of whole-cell DTP vaccine.

Table 4. Selected Adverse Events Occurring within 48 Hours following Vaccination with INFANRIX or Whole-Cell DTP in Italian Infants at 2, 4, or 6 Months of Age

	INFANRIX (N = 13,761 Doses)		Whole-Cell DTP Vaccine (N = 13,520 Doses)	
Event	Number	Rate/1,000 Doses	Number	Rate/1,000 Doses
Fever (≥104°F)[ab]	5	0.36	32	2.4
Hypotonic-hyporesponsive episode[c]	0	0	9	0.67
Persistent crying ≥3 hours[a]	6	0.44	54	4.0
Seizures[d]	1[e]	0.07	3[f]	0.22

[a] $P < 0.001$.

[b] Rectal temperatures.

[c] $P = 0.002$.

[d] Not statistically significant at $P < 0.05$.

[e] Maximum rectal temperature within 72 hours of vaccination = 103.1°F.

[f] Maximum rectal temperature within 72 hours of vaccination = 99.5°F, 101.3°F, and 102.2°F.

In a German safety study that enrolled 22,505 infants (66,867 doses of INFANRIX administered as a 3-dose primary series at 3, 4, and 5 months of age), all subjects were monitored for unsolicited adverse events that occurred within 28 days following vaccination using report cards. In a subset of subjects (N = 2,457), these cards were standardized diaries which solicited specific adverse events that occurred within 8 days of each vaccination in addition to unsolicited adverse events which occurred from enrollment until approximately 30 days following the third vaccination. Cards from the whole cohort were returned at subsequent visits and were

supplemented by spontaneous reporting by parents and a medical history after the first and second doses of vaccine. In the subset of 2,457, adverse events following the third dose of vaccine were reported via standardized diaries and spontaneous reporting at a follow-up visit. Adverse events in the remainder of the cohort were reported via report cards which were returned by mail approximately 28 days after the third dose of vaccine. Adverse events (rates per 1,000 doses) occurring within 7 days following any of the first 3 doses included: unusual crying (0.09), febrile seizure (0.0), afebrile seizure (0.13), and hypotonic-hyporesponsive episodes (0.01).

6.2 Postmarketing Experience

In addition to reports in clinical trials, worldwide voluntary reports of adverse events received for INFANRIX since market introduction are listed below. This list includes serious events and events that have a plausible causal connection to INFANRIX. These adverse events were reported voluntarily from a population of uncertain size; therefore, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccination.

Infections and Infestations

Bronchitis, cellulitis, respiratory tract infection.

Blood and Lymphatic System Disorders

Lymphadenopathy, thrombocytopenia.

Immune System Disorders

Anaphylactic reaction, hypersensitivity.

Nervous System Disorders

Encephalopathy, headache, hypotonia, syncope.

Ear and Labyrinth Disorders

Ear pain.

Cardiac Disorders

Cyanosis.

Respiratory, Thoracic, and Mediastinal Disorders

Apnea, cough.

Skin and Subcutaneous Tissue Disorders

Angioedema, erythema, pruritus, rash, urticaria.

General Disorders and Administration Site Conditions

Fatigue, injection site induration, injection site reaction, Sudden Infant Death Syndrome.

7 DRUG INTERACTIONS

7.1 Concomitant Vaccine Administration

In clinical trials, INFANRIX was given concomitantly with Hib conjugate vaccine, pneumococcal 7-valent conjugate vaccine, hepatitis B vaccine, IPV, and the second dose of MMR vaccine *[see Adverse Reactions (6.1), Clinical Studies (14.3)]*.

When INFANRIX is administered concomitantly with other injectable vaccines, they should be given with separate syringes. INFANRIX should not be mixed with any other vaccine in the same syringe or vial.

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 INFANRIX.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Animal reproduction studies have not been conducted with INFANRIX. It is also not known whether INFANRIX can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.

8.4 Pediatric Use

Safety and effectiveness of INFANRIX in infants younger than 6 weeks of age and children 7 to 16 years of age have not been established. INFANRIX is not approved for use in these age groups.

11 DESCRIPTION

INFANRIX (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed) is a noninfectious, sterile vaccine for intramuscular administration. Each 0.5-mL dose is formulated to contain 25 Lf of diphtheria toxoid, 10 Lf of tetanus toxoid, 25 mcg of inactivated pertussis toxin (PT), 25 mcg of filamentous hemagglutinin (FHA), and 8 mcg of pertactin (69 kiloDalton outer membrane protein).

The diphtheria toxin is produced by growing *Corynebacterium diphtheriae* in Fenton medium containing a bovine extract. Tetanus toxin is produced by growing *Clostridium tetani* in a modified Latham medium derived from bovine casein. The bovine materials used in these extracts are sourced from countries which the United States Department of Agriculture (USDA) has determined neither have nor present an undue risk for bovine spongiform encephalopathy (BSE). Both toxins are detoxified with formaldehyde, concentrated by ultrafiltration, and

purified by precipitation, dialysis, and sterile filtration.

The acellular pertussis antigens (PT, FHA, and pertactin) are isolated from *Bordetella pertussis* culture grown in modified Stainer-Scholte liquid medium. PT and FHA are isolated from the fermentation broth; pertactin is extracted from the cells by heat treatment and flocculation. The antigens are purified in successive chromatographic and precipitation steps. PT is detoxified using glutaraldehyde and formaldehyde. FHA and pertactin are treated with formaldehyde.

Diphtheria and tetanus toxoids and pertussis antigens (PT, FHA, and pertactin) are individually adsorbed onto aluminum hydroxide.

Diphtheria and tetanus toxoid potency is determined by measuring the amount of neutralizing antitoxin in previously immunized guinea pigs. The potency of the acellular pertussis components (PT, FHA, and pertactin) is determined by enzyme-linked immunosorbent assay (ELISA) on sera from previously immunized mice.

Each 0.5-mL dose contains aluminum hydroxide as adjuvant (not more than 0.625 mg aluminum by assay) and 4.5 mg of sodium chloride. Each dose also contains ≤100 mcg of residual formaldehyde and ≤100 mcg of polysorbate 80 (Tween 80).

INFANRIX is available in vials and prefilled syringes. The tip caps of the prefilled syringes contain natural rubber latex; the plungers are not made with natural rubber latex. The vial stoppers are not made with natural rubber latex.

INFANRIX is formulated without preservatives.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Diphtheria

Diphtheria is an acute toxin-mediated infectious disease caused by toxigenic strains of *C. diphtheriae*. Protection against disease is due to the development of neutralizing antibodies to the diphtheria toxin. A serum diphtheria antitoxin level of 0.01 IU/mL is the lowest level giving some degree of protection; a level of 0.1 IU/mL is regarded as protective.[1]

Tetanus

Tetanus is an acute toxin-mediated infectious disease caused by a potent exotoxin released by *C. tetani*. Protection against disease is due to the development of neutralizing antibodies to the tetanus toxin. A serum tetanus antitoxin level of at least 0.01 IU/mL, measured by neutralization assays, is considered the minimum protective level.[2,3] A level of 0.1 IU/mL is considered protective.[4]

Pertussis

Pertussis (whooping cough) is a disease of the respiratory tract caused by *B. pertussis*. The role

of the different components produced by *B. pertussis* in either the pathogenesis of, or the immunity to, pertussis is not well understood. There is no well established serological correlate of protection for pertussis.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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

14 CLINICAL STUDIES

14.1 Diphtheria and Tetanus

Efficacy of diphtheria toxoid used in INFANRIX was determined on the basis of immunogenicity studies. A VERO cell toxin neutralizing test confirmed the ability of infant sera (N = 45), obtained one month after a 3-dose primary series, to neutralize diphtheria toxin. Levels of diphtheria antitoxin ≥0.01 IU/mL were achieved in 100% of the sera tested.

Efficacy of tetanus toxoid used in INFANRIX was determined on the basis of immunogenicity studies. An in vivo mouse neutralization assay confirmed the ability of infant sera (N = 45), obtained one month after a 3-dose primary series, to neutralize tetanus toxin. Levels of tetanus antitoxin ≥0.01 IU/mL were achieved in 100% of the sera tested.

14.2 Pertussis

Efficacy of a 3-dose primary series of INFANRIX has been assessed in 2 clinical studies.

A double-blind, randomized, active Diphtheria and Tetanus Toxoids (DT)-controlled trial conducted in Italy assessed the absolute protective efficacy of INFANRIX when administered at 2, 4, and 6 months of age. The population used in the primary analysis of the efficacy of INFANRIX included 4,481 infants vaccinated with INFANRIX and 1,470 DT vaccinees. The mean length of follow-up was 17 months, beginning 30 days after the third dose of vaccine. After 3 doses, the absolute protective efficacy of INFANRIX against WHO-defined typical pertussis (21 days or more of paroxysmal cough with infection confirmed by culture and/or serologic testing) was 84% (95% CI: 76, 89). When the definition of pertussis was expanded to include clinically milder disease with respect to type and duration of cough, with infection confirmed by culture and/or serologic testing, the efficacy of INFANRIX was calculated to be 71% (95% CI: 60, 78) against >7 days of any cough and 73% (95% CI: 63, 80) against ≥14 days of any cough. Vaccine efficacy after 3 doses and with no booster dose in the second year of life was assessed in 2 subsequent follow-up periods. A follow-up period from 24 months to a mean age of 33 months was conducted in a partially unblinded cohort (children who received DT were offered pertussis vaccine and those who declined were retained in the study cohort). During this period, the efficacy of INFANRIX against WHO-defined pertussis was 78% (95% CI: 62, 87). During the third follow-up period which was conducted in an unblinded manner among children

from 3 to 6 years of age, the efficacy of INFANRIX against WHO-defined pertussis was 86% (95% CI: 79, 91). Thus, protection against pertussis in children administered 3 doses of INFANRIX in infancy was sustained to 6 years of age.

A prospective efficacy trial was also conducted in Germany employing a household contact study design. In preparation for this study, 3 doses of INFANRIX were administered at 3, 4, and 5 months of age to more than 22,000 children living in 6 areas of Germany in a safety and immunogenicity study. Infants who did not participate in the safety and immunogenicity study could have received a DTwP vaccine or DT vaccine. Index cases were identified by spontaneous presentation to a physician. Households with at least one other member (i.e., besides index case) aged 6 through 47 months were enrolled. Household contacts of index cases were monitored for incidence of pertussis by a physician who was blinded to the vaccination status of the household. Calculation of vaccine efficacy was based on attack rates of pertussis in household contacts classified by vaccination status. Of the 173 household contacts who had not received a pertussis vaccine, 96 developed WHO-defined pertussis, as compared with 7 of 112 contacts vaccinated with INFANRIX. The protective efficacy of INFANRIX was calculated to be 89% (95% CI: 77, 95), with no indication of waning of protection up until the time of the booster vaccination. The average age of infants vaccinated with INFANRIX at the end of follow-up in this trial was 13 months (range: 6 to 25 months). When the definition of pertussis was expanded to include clinically milder disease, with infection confirmed by culture and/or serologic testing, the efficacy of INFANRIX against ≥7 days of any cough was 67% (95% CI: 52, 78) and against ≥7 days of paroxysmal cough was 81% (95% CI: 68, 89). The corresponding efficacy of INFANRIX against ≥14 days of any cough or paroxysmal cough were 73% (95% CI: 59, 82) and 84% (95% CI: 71, 91), respectively.

Pertussis Immune Response to INFANRIX Administered as a 3-Dose Primary Series

The immune responses to each of the 3 pertussis antigens contained in INFANRIX were evaluated in sera obtained 1 month after the third dose of vaccine in each of 3 studies (schedule of administration: 2, 4, and 6 months of age in the Italian efficacy study and one US study; 3, 4, and 5 months of age in the German efficacy study). One month after the third dose of INFANRIX, the response rates to each pertussis antigen were similar in all 3 studies. Thus, although a serologic correlate of protection for pertussis has not been established, the antibody responses to these 3 pertussis antigens (PT, FHA, and pertactin) in a US population were similar to those achieved in 2 populations in which efficacy of INFANRIX was demonstrated.

14.3 Immune Response to Concomitantly Administered Vaccines

In a US study, INFANRIX was given concomitantly, at separate sites, with Hib conjugate vaccine (Sanofi Pasteur SA) at 2, 4, and 6 months of age. Subjects also received ENGERIX-B and oral poliovirus vaccine (OPV). One month after the third dose of Hib conjugate vaccine, 90% of 72 infants had anti-PRP (polyribosyl-ribitol-phosphate) ≥1.0 mcg/mL.

In a US study, INFANRIX was given concomitantly, at separate sites, with ENGERIX-B, IPV

(Sanofi Pasteur SA), pneumococcal 7-valent conjugate (PCV7), and Hib conjugate vaccines (Wyeth Pharmaceuticals Inc.) at 2, 4, and 6 months of age. Immune responses were measured in sera obtained approximately one month after the third dose of vaccines. Among 121 subjects who had not received a birth dose of hepatitis B vaccine, 99.2% had anti-HBsAg (hepatitis B surface antigen) ≥10 mIU/mL following the third dose of ENGERIX-B. Among 153 subjects, 100% had anti-poliovirus 1, 2, and 3, ≥1:8 following the third dose of IPV. Although serological correlates for protection have not been established for the pneumococcal serotypes, a threshold level of ≥0.3 mcg/mL was evaluated. Following the third dose of PCV7 vaccine, 91.8% to 99.4% of subjects (N = 146-156) had anti-pneumococcal polysaccharide ≥0.3 mcg/mL for serotypes 4, 9V, 14, 18C, 19F, and 23F, and 73.0% had a level ≥0.3 mcg/mL for serotype 6B.

15 REFERENCES

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2. Wassilak SGF, Roper MH, Kretsinger K, and Orenstein WA. Tetanus Toxoid. In: Plotkin SA, Orenstein WA, and Offit PA, eds. *Vaccines.* 5th ed. Saunders; 2008:805-839.
3. Department of Health and Human Services, Food and Drug Administration. Biological products; Bacterial vaccines and toxoids; Implementation of efficacy review; Proposed rule. *Federal Register* December 13, 1985;50(240):51002-51117.
4. Centers for Disease Control and Prevention. General Recommendations on Immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2006;55(RR-15):1-48.

16 HOW SUPPLIED/STORAGE AND HANDLING

INFANRIX is available in 0.5-mL single-dose vials and disposable prefilled TIP-LOK syringes (packaged without needles):

NDC 58160-810-01 Vial in Package of 10: NDC 58160-810-11

NDC 58160-810-43 Syringe in Package of 10: NDC 58160-810-52

Store refrigerated between 2° and 8°C (36° and 46°F). Do not freeze. Discard if the vaccine has been frozen.

17 PATIENT COUNSELING INFORMATION

The parent or guardian should be:

- informed of the potential benefits and risks of immunization with INFANRIX, and of the importance of completing the immunization series.
- informed about the potential for adverse reactions that have been temporally associated with administration of INFANRIX or other vaccines containing similar components.

- instructed to report any adverse events to their healthcare provider.
- given the Vaccine Information Statements, which are required by the National Childhood Vaccine Injury Act of 1986 to be given prior to immunization. These materials are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines).

Manufactured by **GlaxoSmithKline Biologicals**

Rixensart, Belgium, US License 1617

Novartis Vaccines and Diagnostics GmbH

Marburg, Germany, US License 1754

Distributed by **GlaxoSmithKline**

Research Triangle Park, NC 27709

INF:XXPI

INTERNAL CORRESPONDENCE

Wyeth

Mr. Larry Hewlett	from Alan Bernstein
WLD located Radnor	company WLI located Marietta
DTP Vaccine	date August 27, 1979

After the reporting of the SID cases in Tennessee, we discussed the merits of limiting distribution of a large number of vials from a single lot to a single state, county or city health department and obtained agreement from the senior management staff to proceed with such a plan.

This subject has been discussed with Charlie Young and the following guidelines were developed by FSRD. I would appreciate your comments concerning this procedure and the advisability of formalizing these guidelines.

Interim Measures in Affect

1. Allocation of stock to Distribution Centers is designated by lot number in a manner designed to leave the maximum variety of lot numbers in Great Valley and Marietta to service substantial orders.

2. Managers in D.C.'s carrying average inventories of over 3000 packages (approximate) have been requested to advise FSRD of any orders exceeding 2000 vials. FSRD will then designate shipment by lot number, furnishing additional stock as needed.

Permanent Policy Proposal

1. A D.C. will not fill any order with stock exceeding 2000 packages of one lot number before clearing with FSRD.

2. When additional stock is needed for compliance, FSRD will make necessary arrangements.

3. In the event that the national inventory does not permit compliance, FSRD will clear exception with Marietta management, or make arrangements for split delivery.

WYE FF

Alan Bernstein

Mr. Gray

Dr. McCarthy

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.
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	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, 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
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, 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, glutaraldehyde, 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. 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
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 B (Heplisav-B)	vitamins and mineral salts, yeast protein, yeast DNA, deoxycholate, phosphorothioate linked oligodeoxynucleotide, phosphate buffered saline, sodium phosphate, dibasic dodecahydrate, 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
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, 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, lipids, vitamins, amino acids, mineral salts
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)

Vaccine	Contains
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, 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 (MenB – Bexsero)	aluminum hydroxide, *E. coli*, histidine, sucrose, deoxycholate, kanamycin
Meningococcal (MenB – Trumenba)	defined fermentation growth media, polysorbate 80, aluminum phosphate, 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)	Vero cells, 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-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, 2% human serum albumin, 0.7% sodium chloride USP, 5% Mannitol USP, neomycin, polymyxin B, 50% Glycerin USP, 0.25% phenol USP
Td (Tenivac)	aluminum phosphate, formaldehyde, modified Mueller-Miller casamino acid medium without beef heart infusion, ammonium sulfate, sodium chloride, water

Vaccine	Contains
Td (Mass Biologics)	aluminum phosphate, formaldehyde, thimerosal, modified Mueller's media which contains bovine extracts, ammonium sulfate
Tdap (Adacel)	aluminum phosphate, formaldehyde, 2-phenoxyethanol, Stainer-Scholte medium, casamino acids, dimethyl-beta-cyclodextrin, glutaraldehyde, modified Mueller-Miller casamino acid medium without beef heart infusion, ammonium sulfate, modified Mueller's growth medium
Tdap (Boostrix)	modified Latham medium derived from bovine casein, Fenton medium containing a bovine extract, formaldehyde, modified Stainer-Scholte liquid medium, glutaraldehyde, aluminum hydroxide, sodium chloride, polysorbate 80
Typhoid (Typhim Vi)	hexadecyltrimethylammonium bromide, formaldehyde, phenol, polydimethylsiloxane, disodium phosphate, monosodium phosphate, semi-synthetic medium, sodium chloride, sterile water
Typhoid (Vivotif Ty21a)	yeast extract, casein, dextrose, galactose, 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

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.

Updates:

Trumenba: (added Aluminum phosphate)
RotaTeq: PI dated 2/2017
Rotarix: 6/11/18 (PI dated xx/xxxx)
Smallpox: 3/2018
Td (Tenivac): April 2013
Td (Mass Biologics): April 2009 (no change)
Tdap (Adacel): xxx/2017 (no change)
Tdap (Boostrix): 6/12/2018 (PI dated xx/xxxx) (no change)
Typhim Vi: March 2014 (added sodium chloride & buffered saline)
Ty21a: September 2013
Varicella Frozen: 2/2017
Varicella Refrigerator Stable: 2/2017
YF Vax: June 2016
Zostivax Frozen: xx/2018
Zostivax Refrigerator Stable: xx/2018
Shingrix: 10/2017

ITEMS THAT DO NOT QUALIFY FOR A MEDICAL EXEMPTION BASED ON ACIP

Anemias
Platelet Disorders
Spleen and Lymphatic Disorders
Cardiac Arrhythmias
Grand mal Seizures
Guillain-Barre Syndrome
Neurological Disorders
Diabetes
Chemical Injury or Poisoning
Pneumonia
Malabsorption Issues
Respiratory Arrest
Clonic Convulsions
Metabolic Disorders
Thyroid Disorders
Bacterial Infections
Petite mal Seizures
Encephalitis
Transverse Myelitis
Severe Eczema
White Blood Cell Disorders
CNS Inflammation
Vision Loss
Vaccine Related Death of a Sibling
Atonic Seizures
Cerebral Atrophy
Extreme Restlessness
Depressed Mood Disorder
Complex Partial Seizures
Sensory Processing Disorder
Unresponsive to Stimuli
Rapid weight loss/loss of appetite
Heart Failure
Gastrointestinal Inflammatory Conditions
Speech regression/loss of speech
Sepsis/ Sepsis Shock
Organ Failure
Extreme Swelling
Allergies
Halted Cognitive Development
Kawasaki Disease
Gaze Palsy
Acute Flaccid Myelitis
Muscular Weakness
Memory Impairment
Immune System Dysfunction

Is Aluminum in Vaccines Safe?

If a premature baby receives more than 10 mcg of aluminum in an IV, it can accumulate in the bones and brain, and can be toxic. The FDA maximum limit for aluminum received in an IV is 25 mcg per day. The suggested aluminum per kg of weight to give to a person is up to 5 mcg (a 5 pound baby should get no more than 11 mcg of aluminum). Anything that has more than 25 mcg of aluminum is "supposed" to have a Warning label "This product contains aluminum that may be toxic..."

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

• 8 pound healthy baby	18.2 mcg
• 15 pound healthy baby	34.1 mcg
• 30 pound healthy toddler	68.1 mcg
• 50 pound healthy child	113.0 mcg
• 150 pound adult	340.5 mcg
• 300 pound adult	794.5 mcg

So how much aluminum is in the vaccines that are routinely given to children?

• Hib (PedVaxHib brand only)	225 mcg
• Hepatitis B	250 mcg
• DTaP (varies with manufacturer)	170 – 625 mcg
• Pneumococcus	125 mcg
• Hepatitis A	250 mcg
• HPV	225 mcg
• Pentacel (DTaP, HIB & Polio combo vaccine)	330 mcg
• Pediarix (DTaP, Hep B & Polio combo vaccine)	850 mcg

Hepatitis B vaccine is recommended for all infants at birth and contains 250 mcg aluminum. This one vaccine alone is **±14 TIMES THE AMOUNT OF ALUMINUM THAT IS FDA-APPROVED.**

CDC recommends up to 8 vaccinations at 2, 4 & 6 months for a total of >1,000 mcg of aluminum. This amount is above the minimum for a 350 pound adult.

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=201.323

http://vaxtruth.org/2011/08/vaccine-ingredients/

journeyboost.com

FDA

CFR - Code of Federal Regulations Title 21

The information on this page is current as of April 1 2018.

For the most up-to-date version of CFR Title 21, go to the Electronic Code of Federal Regulations (eCFR).[6]

[Code of Federal Regulations]
[Title 21, Volume 4]
[Revised as of April 1, 2018]
[CITE: 21CFR201.323]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER C--DRUGS: GENERAL
PART 201 -- LABELING
Subpart G--Specific Labeling Requirements for Specific Drug Products

Sec. 201.323 Aluminum in large and small volume parenterals used in total parenteral nutrition.

(a) The aluminum content of large volume parenteral (LVP) drug products used in total parenteral nutrition (TPN) therapy must not exceed 25 micrograms per liter ([micro]g/L).

(b) The package insert of LVP's used in TPN therapy must state that the drug product contains no more than 25 [micro]g/L of aluminum. This information must be contained in the "Precautions" section of the labeling of all large volume parenterals used in TPN therapy.

(c) Except as provided in paragraph (d) of this section, the maximum level of aluminum present at expiry must be stated on the immediate container label of all small volume parenteral (SVP) drug products and pharmacy bulk packages (PBPs) used in the preparation of TPN solutions. The aluminum content must be stated as follows: "Contains no more than __ [micro]g/L of aluminum." The immediate container label of all SVP's and PBP's that are lyophilized powders used in the preparation of TPN solutions must contain the following statement: "When reconstituted in accordance with the package insert instructions, the concentration of aluminum will be no more than __ [micro]g/L." This maximum level of aluminum must be stated as the highest of:

(1) The highest level for the batches produced during the last 3 years;

(2) The highest level for the latest five batches, or

(3) The maximum historical level, but only until completion of production of the first five batches after July 26, 2004.

(d) If the maximum level of aluminum is 25 [micro]g/L or less, instead of stating the exact amount of aluminum as required in paragraph (c) of this section, the immediate container label may state: "Contains no more than 25 [micro]g/L of aluminum." If the SVP or PBP is a lyophilized powder, the immediate container label may

state: "When reconstituted in accordance with the package insert instructions, the concentration of aluminum will be no more than 25 [micro]g/L".

(e) The package insert for all LVP's, all SVP's, and PBP's used in TPN must contain a warning statement. This warning must be contained in the "Warnings" section of the labeling. The warning must state:

WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 [micro]g/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

(f) Applicants and manufacturers must use validated assay methods to determine the aluminum content in parenteral drug products. The assay methods must comply with current good manufacturing practice requirements. Applicants must submit to the Food and Drug Administration validation of the method used and release data for several batches. Manufacturers of parenteral drug products not subject to an approved application must make assay methodology available to FDA during inspections. Holders of pending applications must submit an amendment under 314.60 or 314.96 of this chapter.

[65 FR 4110, Jan. 26, 2000, as amended at 67 FR 70691, Nov. 26, 2002; 68 FR 32981, June 3, 2003]

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