

Rapid Public Health Policy Response Project

March 2009

School of Public Health and Health Services

Vaccines and Autism: The Evidence and the Law





URL: www.gwumc.edu/sphhs/about/rapidresponse/index.cfm.

Vaccines and Autism: The Evidence and the Law

About this Paper

A potential link between the measles-mumps-rubella vaccine and autism was dismissed by a federal vaccine court in February 2009. The U.S. Department of Health and Human Services said the findings demonstrate a lack of medical evidence for any association, while Autism Speaks, a patient advocacy group, said questions remain about potential risks for certain subgroups.

Other legal actions are pending as the scientific and patient advocacy communities debate the need to conduct further research on the vaccine-autism link. Meanwhile, public health advocates worry that continuing concerns about the safety of vaccines may depress the population immunization rate. A small rise in reported measles cases may be linked to exemptions that allow families to opt out of vaccine mandates.

This paper reviews the scientific research on vaccines and autism, the legal decisions to date, and the importance of continued attention to vaccine safety and maintaining public confidence in childhood vaccinations.

For more information about the issues raised in this paper, contact:

Alexandra Stewart, JD
Assistant Research Professor, Department of Health Policy
School of Public Health and Health Services
The George Washington University
2021 K Street, N.W., Suite 800
Washington, DC 20006
202-994-4141

E-mail: stewarta@gwu.edu

About the Rapid Health Policy Response Project

The Rapid Health Policy Response Project of the School of Public Health and Health Services at The George Washington University presents data and other background information on breaking public health stories. The goal is to educate the public, policymakers, legislators, health care providers, the media and others in order to promote informed decisionmaking.

Karyn Feiden, an independent consultant who writes about public health and health care, provides editorial support for this project. Financial support comes from the Public Health and Policy Group of Pfizer, Inc., which provides no input into the content of these reports.



On Feb. 12, 2009, the U.S. Court of Federal Claims, acting under the authority of the National Vaccine Injury Compensation Program, unanimously ruled that the plaintiffs had not demonstrated a causal link between autism and the combination of the measles/mumps/rubella (MMR) vaccine and vaccines containing the preservative thimerosal.¹

The U.S. Department of Health and Human Services responded with the following statement: "The medical and scientific communities have carefully and thoroughly reviewed the evidence concerning the vaccine-autism theory and have found no association between vaccines and autism."²

But the decisions did not end the debate. Autism Speaks, a nonprofit advocacy organization that funds biomedical research and raises public awareness about autism, continues to urge further study. Advocates believe questions remain about "whether certain subgroups of individuals with particular underlying medical or genetic conditions may be more vulnerable to adverse effects of vaccines."

In a further development, another case returned to public attention in late February 2009, after a financial settlement was announced with the family of an injured boy. In that decision, issued in 2007, the Court of Claims had concluded that the MMR vaccine had triggered a seizure in a 15-month-old boy, which in turn led a neurological disorder that resulted in "pervasive developmental delay." Pervasive developmental delay "refers to the class of conditions to which autism belongs."

Thus, while the court had dismissed a causal link between vaccines and autism in the three test cases announced in early February, this ruling and others suggests that in very rare cases MMR can trigger conditions that share the features of autism.

This paper reviews several key court decisions, the body of research addressing the question of vaccines and autism, and the implications for broader questions of vaccine safety.

The role of the vaccine court

The National Vaccine Injury Compensation Program, enacted by Congress in 1986, was created to provide a no-fault alternative to traditional fault-based litigation. In establishing a compensation program, the law in essence acknowledges that despite their profound and overwhelming value to society, vaccines, like any medical intervention, carry some level of risk. By establishing a no-fault compensation system, Congress sought to prevent an exit from the vaccine market by manufacturers concerned about their liability exposure, while also promoting greater focus on safety research.

Claimants under the program, which is funded through a special tax on vaccines, are not required to prove negligence. A cause-and-effect relationship is assumed if certain listed injuries or medical conditions occur within a prescribed period of time following vaccination. If other injuries or conditions occur, the injured person must demonstrate that a "preponderance of evidence" proves a relationship between the condition and the immunization.

Vaccines and Autism: The Evidence and the Law

The claims relating to vaccines and autism involved injuries that were not on the formal injury schedule, and thus had to be proved by a preponderance of evidence.

Origins of autism-related vaccine safety concerns

The potential link between the MMR vaccine and autism dates back to 1998, when a *Lancet* study associated symptoms of gastrointestinal disorders with developmental regression. Parents reported that the symptoms seemed to have begun within a month of vaccination, and the British authors hypothesized that intestinal inflammation caused by the vaccine may have unleashed peptides capable of traveling through the bloodstream and into the brain, where they interfered with normal infant development.

The hypothesis linking thimerosal to autism has its roots in a joint recommendation by the American Academy of Pediatrics (AAP) and the U.S. Public Health Service that mercury be removed from vaccines administered to infants. That statement came after the Food and Drug Administration (FDA) determined that immunizations might expose infants to cumulative doses of mercury above some federal safety guidelines. Thimerosal is comprised of about 50 percent mercury by weight, and although the AAP and the Public Health Service took pains to emphasize the significant safety margin built into mercury exposure limits, concerns grew that elevated exposure was somehow linked to autism.

Questions about vaccines generated extensive media attention over the next several years, especially in Great Britain, where the MMR vaccine became "the biggest science story of the year" by 2002, according to a *Guardian* reporter.⁸ Within a few years, MMR vaccination rates in Great Britain fell from 92 percent to below 80 percent.⁹ While the response to the controversy was more subdued in the United States, a small but vocal group of U.S. parents also began to opt out of immunization school entry requirements.

The scientific evidence

In 2004, 10 of the 13 authors on the 1998 *Lancet* paper published a partial retraction: "We wish to make it clear that in this paper no causal link was established between MMR vaccine and autism However, the possibility of such a link was raised We consider now is the appropriate time that we should together formally retract the interpretation placed upon these findings"¹⁰

Over the past decade, the scientific community has conducted substantial research — most of it government-funded — to test the hypothesis that the MMR vaccine has a causal link to autism. The body of evidence is consistent in its failure to demonstrate such a link:

➤ The Immunization Safety Review Committee, part of the Institute of Medicine, reviewed relevant scientific studies, looking both for a plausible biological mechanism that might explain the connection and epidemiological evidence to support it.

The Committee concluded in 2004 "that the body of epidemiological evidence favors rejection of a causal relationship between the MMR vaccine and autism. The committee also concludes that the body of epidemiological evidence favors rejection of a causal relationship



between thimerosal-containing vaccines and autism. The committee further finds that potential biological mechanisms for vaccine-induced autism that have been generated to date are theoretical only."

- ➤ In January 2009, the Centers for Disease Control and Prevention (CDC) summarized ten ongoing or completed studies that it had supported. ¹¹ Among them:
 - > The Danish Medical Research Council, through a cooperative agreement with the CDC, conducted a seven-year retrospective study of more than 500,000 children (all children born in Denmark from 1991 through 1998) and "found no association between the MMR vaccination and autism." ¹²
 - Two groups of Italian infants were given two different versions of the diphtheria/pertussis/tetanus vaccine in 1992–93, one containing thimerosal, one without it, and then followed to ages 10–12. "The weak and inconsistent association found in this study suggests that the association between thimerosal exposure through vaccination in infancy and neuropsychological deficits is unlikely or clinically negligible," according to the authors.¹³
 - > From 2003–05, researchers searched for measles virus in bowel tissue taken from children with autism and gastrointestinal disorders and from children with gastrointestinal disorders alone. The study addressed one of the principal claims raised by plaintiffs in the recent vaccine court cases and echoed the work described in the 1998 *Lancet* paper that first triggered concern. The authors concluded that the results are "inconsistent with a causal role for MMR vaccine as a trigger or exacerbator of either GI [gastrointestinal] difficulties or autism." ¹⁴

Despite this research, a number of advocacy groups assert that a link between vaccines and autism has not been ruled out. In particular, they believe more data are needed to identify potential vaccine safety risks among certain sub-populations of children.

"Fundamental questions have not been addressed, such as whether the use of combination vaccines confers increased risk for adverse events and whether there are subgroups in the general population, such as children with certain genetic or metabolic conditions that are more vulnerable to serious adverse effects of vaccines, including [autism]," said a spokesperson for Autism Speaks. ¹⁵

The Bailey Banks decision and the Hannah Poling settlement

Two vaccine court decisions involving injury claims related to the MMR vaccine generated particular concern about safety.

The case of Bailey Banks, decided in 2007, earned renewed media attention in February 2009 after the government reached a financial settlement with the child's family. In its decision, the court found that 15-month-old Bailey had a seizure following administration of the MMR vaccine, and developed a neurological disorder known as acute disseminated encephalomyelitis. That condition, in turn, led to "pervasive developmental delay not otherwise specified."

Vaccines and Autism: The Evidence and the Law

PDDNOS, according to the court, "is a subthreshold condition in which some — but not all — features of autism ... are identified."⁴

There was no evidence that Bailey Banks had an underlying medical condition prior to being vaccinated. The advocacy group Generation Rescue ran a full-page ad in *USA Today* about the case, quoting the vaccine court decision and calling on the government to tell "the truth about childhood vaccines." ¹⁶

In another case, settled in February 2008, the court had also acknowledged harm done by vaccines, ruling that the family of an injured girl named Hannah Poling was entitled to compensation under the National Vaccine Injury Compensation Program.¹⁷

After receiving five vaccinations during a single doctor's visit, at 19 months of age, Hannah was diagnosed with a mitochondrial enzyme deficiency, characterized in part by regression in a child who had appeared to be developing normally. The court concluded that the case had met "the statutory criteria for demonstrating that the vaccinations [the] CHILD received on July 19, 2000 significantly aggravated an underlying mitochondrial disorder, which predisposed her to deficits in cellular energy metabolism, and manifested as a regressive encephalopathy with features of autism spectrum disorder." The court's observation that vaccines had aggravated an underlying mitrochondrial disorder was significantly different from concluding that vaccines had caused it.

Different parties interpreted the *Poling* settlement substantially differently. The Poling family and many advocacy groups believed it offered clear support for a link between vaccines and autism in vulnerable populations. Hannah's father, Jon S. Poling, who is also a neurologist, wrote "Many in the autism community and their champions believe that the result in this case may well signify a landmark decision as it pertains to children developing autism following vaccinations. This still remains to be seen." He called for "an immunization database for children with metabolic disorders to establish safety guidelines and improve vaccine safety for minority subgroups of children." ¹⁹

Others disagreed, arguing that the basis of the settlement was "poorly reasoned" and that "features of autism spectrum disorder" are evident in most children with profound cognitive impairment and can differ significantly from classic autism. ²⁰

But the bottom line in these cases appears to be that vaccines did cause severe adverse reactions, resulting in conditions with autism-like features.

Vaccine court test cases

Claims that childhood vaccinations had caused, or contributed to, autism mounted through the first decade of the 21st century. By Feb. 1, 2009, more than 5,500 requests for compensation related to autism claims had been filed with the National Vaccine Injury Compensation Program. The Office of Special Masters, established within the U.S. Court of Federal Claims to adjudicate vaccine claims, developed a process for reviewing and judging these claims as a group.²¹ (Special Masters are attorneys appointed by the court to hear complex cases raising voluminous facts.)



The decisions announced Feb. 12, 2009 involved three test cases, heard by three Special Masters, of the theory that MMR vaccines and thimerosal-containing vaccines could combine to cause autism.

The first test case hypothesized the following causation theory: thimerosal-containing vaccines weaken the immune system of certain children, thereby permitting the measles virus contained in the MMR vaccine to persist. The persisting virus thus damaged the digestive system and brain, causing autism, mental retardation and seizures.²² The other two test cases offered variations on this basic theory.

The Special Masters issued their decisions in the three cases after reviewing clinical studies, large epidemiologic studies designed to measure an associational link between autism and child immunization, and the medical records of the children involved. The evidentiary record included almost 5,000 pages of transcripts and more than 700 pages of post-hearing briefs. There were 939 medical articles, 50 expert reports and testimony from 28 experts (by contrast, a typical vaccine case presents about 10 articles and six or fewer experts). To reach their conclusions, the Special Masters had to consider knowledge contained in many subspecialties of biology and medicine, including neurology, gastroenterology, virology, immunology, molecular biology, toxicology, genetics, and epidemiology.²²

The language in the decisions was deeply sympathetic to the families. "[Michelle's] family members clearly have done a wonderful job of coping with Michelle's conditions, and in caring for her with great love. I admire them greatly," wrote one Special Master. "Certainly the mere fact that Michelle's autistic symptoms first became evident to her family during the months after her MMR vaccination might make them wonder about a possible causal connection."

Nonetheless, the final decision was unqualified. As the Special Master wrote, this case "is *not a close case*. The overall weight of the evidence is *overwhelmingly contrary* to the petitioners' causation theories This is a case in which the evidence is so one-sided that any nuances in the interpretation of the causation case law would not make a difference to the outcome of the case."²²

A decision on a second theory, also being examined in three test cases — that thimerosal-containing vaccines alone can cause autism — is expected in late spring or early summer 2009.

Regardless of the conclusion, the autism cases are unlikely to end quickly. Although the Vaccine Injury Compensation Program is intended to be the first place injured parties seek compensation, the law also allows them to claim negligence and pursue traditional avenues of litigation. ²³ All three sets of parents in the three test cases have said they will go to civil court to present their claims as negligence cases. ⁹

The direction of further research

As legal arguments continue, the importance of a robust vaccine safety research agenda comes into sharper focus. Vaccine mandates rank among the most important tools in the public health arsenal, because they create a "herd immunity" for the general population, and particularly for vulnerable children, including children with special health needs who cannot be immunized

Vaccines and Autism: The Evidence and the Law

and infants too young to be immunized. But as Congress recognized when it created the Vaccine Injury Compensation Program, the compulsory nature of immunizations confers a special obligation on society to assure families that vaccines are as safe as possible.

Public trust is the linchpin of effective population-wide immunization, best achieved by more vigorous investments in immunization-safety science and improved communication strategies. "No one claims 'zero risk' for the vaccines against 16 diseases that are currently recommended to protect children in the United States," write the authors of a recent *Pediatrics* article, emphasizing the importance of "research on the short- and longer-term risks and benefits of combinations and timing of multiple vaccines Immunization-safety science requires leadership, infrastructure, facilities and human resources, and appropriate long-range planning and funding."

Further research is also needed into autism, and other conditions that feature the severe developmental delays characteristic of autism.

However, the IOM's Immunization Safety Review Committee has concluded that significant investment into the "theoretical vaccine-autism connection [is not] useful at this time." Recent action by the Interagency Autism Coordinating Committee also seems to support the notion that additional efforts to explore the vaccine-autism link itself are not a priority. Under the Combating Autism Act, the committee was established within the Department of Health and Human Services to guide the nation's autism research agenda. In January 2009, members voted to remove two objectives related to vaccine safety research from its strategic plan.

This action disappointed the advocacy community, which had been consulted as the strategic plan was drafted and had supported those objectives. Protesting both the process by which the decision was made, and the merits of the change itself, Autism Speaks withdrew its support from the plan.²⁷

Duane Alexander, MD, director of the National Institute of Child Health and Human Development, a part of the NIH, was the only federal government member of the Coordinating Committee to abstain from the vote on that decision. In an interview with Autism Speaks, he said, "One question that still remains to be addressed in a study of adequate size and precision is ... whether there is a subgroup in the population that, on a genetic basis, is more susceptible to some vaccine characteristic or component than most of the population, and may develop an ASD [autism-spectrum disorder] in response to something about vaccination." 28

Vaccines and public confidence

As the debate continues, the merits of the vaccine-autism claim, and concerns over vaccine safety more generally, influence the willingness of some parents to vaccinate their children.

The measles/mumps/rubella, diphtheria/pertussis/tetanus, and polio vaccines are almost universally required for school-age American children, and more than 95 percent of them are inoculated.²⁹ But all states allow exemptions to the requirements on medical grounds: 48 states allow religious exemptions, and 21 provide "personal-belief" exemptions, which vary in





their flexibility from state to state.³⁰ A small, but growing, number of "vaccine skeptics" have requested these exemptions for their children.³¹ Public concern is also apparent in the response to a national survey in which almost one-quarter of adults said that a potential link to autism meant it was safer not to vaccinate children.³²

Meanwhile, measles, a highly infectious respiratory disease that can occasionally cause complications that include pneumonia, encephalitis, seizures, and death, is on the rise. From January to July 2008, 131 cases were reported, compared to an average of 63 cases every year from 2000 through 2007, according to the CDC, which warns, "the findings demonstrate that measles outbreaks can occur in communities with a high number of unvaccinated persons." Any lessening of the herd immunity conferred by widespread use of the vaccine puts at risk those individuals who do not respond fully to its protective shield, or can not be vaccinated for medical reasons.

Because measles is one of the first diseases to reappear when vaccination coverage rates fall, it is also something of a "canary in a mine," possibly heralding the return of other preventable childhood diseases. Complications of those diseases, while often avoidable if good health care is readily available, can be significant — mumps can lead to meningitis and permanent deafness, rubella can cause birth defects in pregnant women, untreated diphtheria can lead to coma and death.³⁴

Most public health experts believe any drop in vaccination rates is an unintended consequence of a success story. "Many people don't know what vaccine-preventable childhood diseases even look like, or how dangerous they can be," says Alexandra Stewart, JD, assistant research professor in the Department of Health Policy at The George Washington University's School of Public Health and Health Services. "Vaccines are one of the greatest public advances we have achieved as a society."

Public health can play an important role in sustaining that success. One study, for example, showed that providing in-service training and resource materials to nurses increased the amount of time they spent talking to their patients about vaccines.³⁵ Public health educators can also help to guide Americans to current, science-based information that addresses their legitimate concerns about safety.³⁶

Vaccines are mandatory because they confer vital public health protections. But that mandate also confers special obligations on the government. The Vaccine Injury Compensation Program recognizes the importance of minimizing risk with robust investments in safety research, and compensation for families when injuries associated with vaccines do occur. While the February 2009 decisions find no causal link between MMR vaccines and autism, a strong and transparent safety research agenda and the energetic education of both parents and health care professionals, is essential to sustain and enhance public trust in vaccines.

Vaccines and Autism: The Evidence and the Law

Endnotes

- 1. Office of Special Masters, U.S. Court of Federal Claims. Cedillo v. Secretary of Health and Human Services Case No. 98-916V. Hazlehurst v. Secretary of Health and Human Services Case No. 03-654V. Snyder v. Secretary of Health and Human Services Case No. 01-162V. Feb. 12, 2009.
- "Statement from the Department of Health and Human Services Regarding the Decisions of the U.S. Court of Federal Claims in the Omnibus Autism Proceeding." U.S. Department of Health & Human Services press release: Feb. 12, 2009.
- 3. Autism Speaks. "Statement by Autism Speaks Regarding February 12 Vaccine Court Decision." Web site accessed Feb. 22, 2009.
- 4. Office of Special Masters, U.S. Court of Federal Claims. Banks v. Secretary of Health & Human Services Case no. 02-0738V. July 20, 2007.
- Wakefield AJ, Murch SH, Anthony A., Linnell J., et al. "Ileal-lymphoid-nodular Hyperplasia, Non-specific Colitis, and Pervasive Developmental Disorder in Children." *Lancet* 1998;351 (9103);637–41.
- Immunization Safety Review Committee, Institute of Medicine, Immunization Safety Review: Vaccines and Autism. Washington, DC: The National Academies Press. May 17, 2004.
- 7. Gerber JS, Offit PA. "Vaccines and Autism: A Tale of Shifting Hypotheses." Clinical Infectious Diseases 2009;48:456–61.
- 8. Goldacre B. *Bad Science*. New York: Fourth Estate. May 2008. *The Media's MMR Hoax*, an excerpt from Goldacre's book, appeared in *The Guardian*, Aug. 30, 2008.
- 9. Begley S. "Anatomy of a Scare." Newsweek, March 2, 2009.
- 10. Murch SH, Anthony A, Casson DH, Malik M. "Retraction of an Interpretation." Lancet 2004 March 6;363 (9411):750. Links to individual statements from several of the authors who signed off on the retraction are available on the web page of the Institute for Vaccine Safety, "Majority of Authors Retract Controversial Interpretation of 1998 Lancet Paper Linking MMR Vaccine to a New Syndrome of Bowel Disease and Autism." The lead author of the paper, Andrew Wakefield, who did not sign the retraction, is facing charges of professional misconduct by the British General Medical Council for manipulating data (Deer B., "MMR Doctor Andrew Wakefield Fixed Data on Autism," The Times, Feb. 8, 2009).



- 11. Center for Disease Control and Prevention. "Immunization Safety and Autism: Thimerosal and Autism Research Agenda." Updated Jan. 30, 2009.
- 12. Madsen KM, Hviid A, Vestergaard M., Schendel et al. "A Population-Based Study of Measles, Mumps, and Rubella Vaccination and Autism." *New England Journal of Medicine*, 2002 Nov. 7;347 (19);1477–82.
- Tozzi AE, Bisiacchi P, Tarantino V., De Mei B., et al. "Neuropsychological Performance 10 Years after Immunization in Infancy with Thimerosal-containing Vaccines." *Pediatrics* 2009 Feb.;123 (2);475–82
- Hornig M., Briese T, Buie T, Bauman ML., et al. "Lack of Association Between Measles Virus Vaccine and Autism with Enteropathy: A Case-Control Study." PLoS ONE 2008;3 (9):e3140.
- 15. Statement by Peter Bell, executive vice president for Programs and Services, Autism Speaks. Feb. 4, 2009.
- 16. *USA Today* advertisement, Fe. 25, 2009. See also the Generation Rescue Web site.
- 17. Harris G. "Deal in an Autism Case Fuels Debate on Vaccine." *The New York Times*, March 8, 2008.
- 18. For the text of the Hannah Poling decision, see *artospress.com/misc/autism_vaccine_case.pdf*, Feb. 26, 2008.
- 19. Poling JS. "Vaccines and Autism Revisited." New England Journal of Medicine, 2008 Aug. 7; 359 (6);655.
- 20. Offit PA. "Vaccines and Autism Revisited The Hannah Poling Case." *New England Journal of Medicine*, May 15, 2008;358 (20);2089–91.
- 21. Health Resources and Services Administration. "About the Omnibus Autism Proceeding." Updated Feb. 12, 2009.
- 22. Office of Special Masters, U.S. Court of Federal Claims Cedillo v. Secretary of Health and Human Services Case No. 98-916V. Feb. 12, 2009.
- 23. Sugarman SD. "Cases in Vaccine Court Legal Battles over Vaccines and Autism." New England Journal of Medicine, Sept. 27, 2007;358 (13);1275–7.
- 24. Cooper LZ, Larson HJ, Katz SL. "Protecting Public Trust in Immunization." *Pediatrics* 2008;122;149–53.
- 25. For more information about the DHHS Interagency Autism Coordinating Committee, see its Web site. The guiding statute is public law: Combating



Examining the Health Consequences of the 2008-09 Recession

- Autism Act, Pub L. No 109–416, 120 Stat. 2821 (Dec. 19, 2006). See also the draft strategic plan, "The Interagency Autism Coordinating Committee Strategic Plan for Autism Spectrum Disorder Research." Aug. 15, 2008.
- 26. Kennedy RF, Kirby D. "Autism, Vaccines and the CDC: The Wrong Side of History." *The Huffington Post*, Jan. 27, 2009.
- 27. "Autism Speaks Withdraws Support for Strategic Plan for Autism Research, Decries Unexpected Change in Final Approval Process." Autism Speaks press release: Jan. 15, 2009.
- 28. "NICHD Director Dr. Alexander Discusses the Need for More Research on Environmental Risk Factors for Autism Spectrum." Interview with Autism Speaks. Accessed Feb. 26, 2009.
- Hodge JG. "School Vaccination Requirements: Legal and Social Perspectives."
 National Conference of State Legislatures State Legislative Report August 2002; 27(14).
- 30. Institute for Vaccine Safety. "Vaccine Exemptions." Web page last updated Jan. 7, 2009.
- 31. Almeida M. "Public Health Risk Seen as Parents Reject Vaccines," *The New York Times*, March 21, 2008.
- 32. "Parents Still Fear Autism Could be Linked to Vaccines, Poll Shows." *Science Daily* press release: Oct. 4, 2008.
- 33. "Update: Measles United States, January-July 2008." *Morbidity and Mortality Weekly Report* Aug. 22, 2008;57 (33);893–6.
- 34. See CDC Web page on vaccine-preventable diseases.
- 35. Davis TC. "Vaccines Risk/Benefit Communication: Effect of an Educational Package for Public Health Nurses." Health Education & Behavior Dec. 1, 2006;33 (6);787–801.
- 36. Such materials are available in abundance on the Internet. The National Network for Immunization Information provides an array of scientifically valid information to healthcare professionals, the media, and the public, including Web pages targeted specifically at parents. A Web page of the Open Directory Project provides links to most of the major public and private entities involved with immunizations.