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## U.S. Childhood Vaccine Availability: Legal, Regulatory, and Economic Complexities

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**OVERVIEW** — *Despite the vital role they play in public health, childhood vaccines travel a complicated road from laboratory to provider and patient. From the fall of 2000 until well into 2002, a combination of factors, including market dynamics, legal challenges, and regulatory hurdles, led to a shortage of some childhood vaccines. This paper examines each of these factors, focusing on the important roles of both the public and the private sectors.*

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# U.S. Childhood Vaccine Availability: Legal, Regulatory, and Economic Complexities

Vaccines have been heralded as one of the most cost-effective public health and biomedical success stories. Protecting against once-dreaded diseases ranging from polio to diphtheria, they are a staple of most U.S. children's routine medical care.<sup>1</sup> In the past two years, however, "unique and unprecedented" shortages of vaccines for children<sup>2</sup> have left health professionals frustrated and legislative leaders demanding explanations. And the post-September 11 environment, in which the specter of potential bioterror agents such as anthrax and smallpox looms large, has expanded concerns over the nation's vaccine infrastructure from the largely pediatric arena to the realm of homeland security.

Eleven childhood diseases are currently vaccine-preventable. As of June 2002, five vaccines that provide protection against eight of these diseases—diphtheria, tetanus, pertussis (DTaP and Td vaccine), pneumococcal infection (PCV-7 vaccine), measles, mumps, rubella (MMR vaccine), and varicella—were in short supply.<sup>3</sup> Although, with the exception of PCV-7, these vaccines are again widely available,<sup>4</sup> the research obstacles, development and manufacturing complexities, regulatory and legislative challenges, and production and distribution difficulties that led to the shortages are all potential harbingers of 21st century public health and medical challenges.

With commercial pharmaceutical and biotechnology companies, health plans, and providers integral partners in vaccine policy and delivery, the private sector as well as the federal and state governments are critical to ensuring that vaccines are available and safe. The recent and ongoing efforts to meet childhood immunization goals can provide critical insights for policymakers and public health officials monitoring the dual threats of bioterrorism and naturally emerging and reemerging infectious diseases that may be prevented by vaccines.

## PUBLIC HEALTH IMPLICATIONS AND TENSIONS

The public health implications of childhood immunization and vaccine policy are considerable. They reach far beyond individual children and families into society as a whole and contribute to tensions between the public and the private sectors over the research, development, and manufacture of vaccines. These tensions are over and above those surrounding prescription drugs, because of the different role that vaccines play

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in public health. For example, unlike prescription drugs, vaccines are administered to healthy people, most often infants and children. Also unlike prescription drugs, they are (with some exceptions) compulsory—children cannot enter or attend school or day care in most states without documentation showing receipt of the minimum vaccine dose required by the state.

Despite vaccines' wide acceptance and use after the initial controversy that surrounded them,<sup>5</sup> over the last several years there has been evidence of a shift in public attitudes concerning their use in children. This rising concern has been fueled in part by fears about vaccine safety as well as by religious objections and resentment of government-mandated vaccine policy by "parents' rights" advocates. Nevertheless, most recognize that, as the public health community often notes, dangerous infectious diseases that are largely under control in this country are "only a plane ride away" and that, consequently, immunization is important to everyone.

Immunizing a child not only protects him or her, but also helps to protect the community at large, particularly those with chronic diseases and suppressed immune systems. Immunization can also reduce disease outbreaks. Ironically, many health officials are concerned that the very success of vaccine programs actually may contribute to their downfall. For example, most parents have never seen an active case of measles, whooping cough, polio, or lockjaw (an effect of tetanus infection). Some who do not want their own children exposed to the potential risks associated with vaccines argue that, since the majority of other children have been inoculated, chances of a disease outbreak are slim.

The dangers inherent in relying on community immunity—or "herd immunity," as it is sometimes called—are numerous. Children run the risk of contracting a communicable disease while traveling outside the country. Even if they do not leave the United States, they may be exposed to an unimmunized person carrying disease: immunization levels among U.S. residents are not 100 percent, and the United States is visited by nearly 1 million people each day whose immunization status is not checked and who may therefore carry vaccine-preventable disease. Experience has shown that, when the childhood immunization rate, or "coverage level," drops, epidemics ensue, and at that point it may be too late to protect the youngest and most vulnerable children. A recent paper put out by the PATH (Program for Appropriate Technology in Health) Children's Vaccine Program underscored this point:

Many people in North America and Europe have become complacent about vaccines, assuming that since certain diseases rarely appear, they are no longer a threat. Others fear that the vaccine itself is more dangerous than the disease. These misperceptions have caused underimmunization rates that have led to a resurgence of highly contagious diseases such as measles, diphtheria, and pertussis. A measles outbreak in the United States in 1989 led to 123 deaths—ninety percent of those who died had not been vaccinated.<sup>6</sup>

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In the United States, outstanding progress has been made in immunizing children by the time they are two years of age. According to Walter A. Orenstein, M.D., director of the National Immunization Program of the Centers for Disease Control and Prevention:

Coverage for most vaccines is 90 percent or higher....[E]very day in the U.S., 11,000 babies are born who must be vaccinated. To be protected against 11 vaccine-preventable diseases, they require 16-20 doses or injections by 2 years of age, a challenge for any health care delivery system. Recent small, but significant, decreases in coverage for some vaccines indicate we cannot take for granted that past successes will automatically translate into future successes.<sup>7</sup>

Recent shortages have made it particularly difficult for physicians and other health providers to keep track of who has been vaccinated and who requires follow-up. They have also placed added burdens on parents to ensure that their children are adequately immunized.

The shortages have also exacerbated the tensions that exist between the public and the private sectors over vaccines. While the government plays an early role in vaccine research, through the National Institutes of Health (NIH) and other agencies, most of the research, development, and manufacturing takes place in the private sector. On the one hand, while vaccines represent an individual medical intervention, they are also considered by most to be a social good. Therefore, it has been argued, society has an obligation to make vaccines available at the lowest possible price to ensure widespread access. But the vaccine development system is grounded principally in the private sector, which must earn a profit in order to satisfy Wall Street and shareholders. Vaccine companies share society's goals but also must balance them with the commercial viability, product liability, and market potential of the products they research, develop, and manufacture.

It is unlikely that these tensions can ever be completely resolved, but vaccine shortages undermine the nation's ability to protect the health of its citizens in the face of threats such as bioterrorism, and both the public and the private sectors have critical roles to play in ensuring that vaccines are available when needed. In an Institute of Medicine (IOM) report entitled *Setting the Course: A Strategic Vision for Immunization—Part 2*, Bernard Guyer, M.D., highlighted the connection between childhood vaccine shortages and public health in times of crisis:

The quality of the immunization system can be seen as an indicator of the strength of the public health infrastructure. If the nation cannot ensure that the 11,000 children born each day receive the routine immunizations that they need, it may not be able to adequately protect the health of all 280 million Americans in times of crisis. Although crisis can stimulate action, sustained efforts are necessary to maintain the public health infrastructure and achieve immunization goals.<sup>8</sup>

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## VACCINES: WHAT THEY ARE AND HOW THEY WORK

The last century has witnessed the spectacular reduction of horrific diseases. Many can remember (or recall seeing pictures of) children in iron lungs, the result of succumbing to paralytic polio. With the launch of the universal Salk vaccination effort in April 1955, millions of people were spared. While, only 50 years ago, polio was the leading cause of paralysis in the world, the polio vaccine has raised the expectation that the world will soon be free from the disease.<sup>9</sup> Similarly, naturally occurring smallpox was eradicated in 1980 through global vaccination. Other success stories abound.<sup>10</sup>

Vaccines are administered via injection, oral administration, or through inhalation by aerosol and powder and can be either a “live” weakened (attenuated) or dead (inactivated) disease germ. Vaccines create immunity—protection against a disease. The primary purpose of the immune system is to identify foreign substances often referred to as antigens. In response to a vaccine, the body produces antibodies (protein molecules) or immune system cells (producing what is known as cell-mediated immunity). These responses assist with the elimination of the antigens and remain in the body, safeguarding the vaccinated person from future disease germs.

## GETTING SAFE VACCINES TO CHILDREN: SOME FEDERAL ROLES

The federal government has an expansive commitment to vaccines. More than 20 different agencies have a role in vaccine research.<sup>11</sup> A number of agencies and programs within the Department of Health and Human Services (DHHS) play a role in national, state and local immunization efforts. The National Vaccine Program Office within the Office of the Assistant Secretary for Health, for example, has the responsibility to coordinate all federal, state, provider, industry, and other stakeholder efforts around vaccines. In addition to its involvement in research and coordination, the federal government plays an integral role in (a) licensing and regulating vaccines to ensure that they are safe and (b) financing and purchasing childhood vaccines. This section focuses on these last two areas of federal involvement.

### Regulation and Licensure of Vaccine Products

Vaccines are biologic agents, that is, complex products derived from living sources. Unlike the structure of most drugs, which are chemically synthesized, that of biologics is not well characterized. Biologic products such as vaccines are subject to licensure (approval for marketing) under provisions of the Public Health Service Act. The Food and Drug Administration (FDA) has the responsibility to regulate vaccines in the United States.

Vaccine clinical development follows the same general pathway as that for drugs. Vaccine licensure is a lengthy process that may take ten years or more. Before a vaccine is licensed by the FDA, it is extensively tested in the laboratory, in animals, and in human beings to ensure its safety. Prelicensure clinical trials are done in three phases: Phase 1 (safety and immunogenicity studies), Phase 2 (dose-ranging studies), and Phase 3 (effectiveness and additional large-scale safety studies). If successful, the completion of all three phases of clinical development can be followed by the submission of a biologics license application, or BLA. During this stage the manufacturing facility undergoes a pre-approval inspection during which vaccine production is examined in detail. Vaccine licensing also requires the provision and FDA approval of adequate labeling information.

Once a vaccine is approved and licensed, the FDA continues to oversee its production to ensure continuing safety. This oversight involves periodic facility inspections. In addition, as part of the manufacturing process, both the manufacturer and the FDA are required to perform certain tests twice on each lot of the product before it is released for distribution.<sup>12</sup>

As part of the post-licensure monitoring, the federal government's passive surveillance system, VAERS (the Vaccine Adverse Event Reporting System), is designed to capture information on rare side-effects and delayed reactions that may not be evident until the vaccine is administered to millions of people.<sup>13</sup> Another post-marketing surveillance system established by the federal government is the Vaccine Safety Datalink Project (VSD), a collaborative project involving the Centers for Disease Control and Prevention (CDC) and several large managed-care organizations. A "large-linked" database, the VSD contains medical and immunization information on more than 7 million people. In addition to these systems, individual vaccine companies invest significant resources in developing their own surveillance systems. Merck, for example, has used its own funding to set up quality-control reporting systems, in addition to the government systems already in place. Other vaccine manufacturers have implemented similar programs.

**Vaccine Safety Issues and Responses** — Among the goals of the federal government in the regulation of vaccines, ensuring that they are safe is paramount. It is expected that the safety of a product administered to healthy children and adults will be continuously scrutinized and questioned. Both Congress and the FDA have responded vigorously to concerns about vaccine safety to maintain public confidence and thereby ensure the health of the public.

Although vaccines are among the safest of all medical interventions, in the mid-1980s, the number of lawsuits related to potential vaccine injuries began to rise. As litigation costs soared, prices escalated and several vaccine manufacturers halted production. The number of vaccine manufacturers plummeted and shortages occurred. Public health officials were concerned about the potential return of disease epidemics. In response

**Both Congress and the FDA have responded vigorously to concerns about vaccine safety.**

to the situation, Congress passed the National Childhood Vaccine Injury Act (NCVIA) of 1986. Key among the many provisions of the NCVIA were the establishment within DHHS of the National Vaccine Program Office, the creation of the National Vaccine Injury Compensation Program within the Health Resources and Services Administration (to compensate those injured by vaccines on a “no fault” basis), and the requirement that all health care providers report certain adverse events following inoculation to the secretary of health and human services.

Since the mid-1990s, accusations about the safety of vaccines have proliferated in some circles, largely through the use of the Internet. Increased attention to vaccine safety issues, coupled with the widespread use of childhood vaccines, resulted in a request by the CDC and the NIH to have the Institute of Medicine “convene an independent committee that could provide timely and objective assistance to the Department of Health and Human Services in reviewing emerging immunization-safety hypotheses.”<sup>14</sup> The first report specifically reviewed the alleged relationship between the measles, mumps, rubella vaccine and autistic spectrum disorders (ASDs). At the end of their analyses, the IOM committee members concluded:

although...the evidence favors rejection of the causal relationship at the population level between MMR vaccine and autistic spectrum disorders, the committee nevertheless recommends that this issue receive continued attention. It does so in the recognition that its conclusion does not exclude the possibility that MMR vaccine could contribute to ASD in a small number of children, as well as the following factors: the identified limitations of the evidence, the burden of ASD, the burden of the diseases prevented by the vaccine, the immense concern of parents, and the prominence of the issue in public debate.<sup>15</sup>

Another prominent issue regarding vaccine safety in recent years has been the use of preservatives, particularly thimerosal, a mercury-containing organic compound (an organomercurial). Since the 1930s, thimerosal has been used as a preservative in many biological and drug products, including vaccines, to prevent potentially life-threatening contamination from microbes such as staphylococci. Because of the “theoretical potential for neurotoxicity of even low levels of organomercurials and because of the increased number of thimerosal containing vaccines that have been added to the infant immunization schedule,”<sup>16</sup> concerns about its use have been brought center stage. As a result, the FDA has worked with vaccine manufacturers to reduce or eliminate thimerosal from most vaccines.<sup>17</sup>

In addition to regulating the manufacture of vaccines, the U.S. government has a strong interest in efforts being made by other governments and by vaccine companies to improve the safety of vaccine delivery systems. Among the technologies that hold the promise of increasing vaccine safety, both in developing countries and in the United States, are auto-disposable syringes and safety boxes, monodose prefilled injection devices, needle-free injections, and thermostable vaccines that

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eliminate the need for refrigerated equipment and its associated maintenance.<sup>18</sup> Table 1 highlights the impact of such technology change on immunization services.

### The Federal Government as Purchaser: Vaccines for Children Program and Section 317 Grants

A number of federal funding streams provide assistance to the states for vaccine purchases and immunization programs. While states use their own funds (as well as in-kind support) to varying degrees, most rely significantly on federal monies. Some states have virtually no state funds devoted to vaccine purchase and depend almost entirely on federal monies. Grants are provided to the states, primarily through the Vaccines for Children (VFC) program and Section 317 immunization categorical

**TABLE 1**  
**Impact of Technology Change on Immunization Services**

Aspect of Services Impacted	Technology Change		
	Safer Multidose Vaccine Delivery	Monodose Prefilled Injection Devices	Thermostable Vaccines Delivered with Drugs
<b>Equity of Access to New Vaccines</b>	Safe injection devices and disposal technology assured for mass immunization. Lowest cost per delivered multivalent dose of new vaccine.	Ease of administration, permitting community care providers to immunize. A single dose available to a single child always.	Vaccines carried to people wherever they live, with no refrigeration impediment. Potency of vaccine assured for every child, wherever he/she lives.
<b>Safety of Vaccine Administration</b>	No reuse of syringes possible. Reduced needle-stick risks. Sterilization assured by monitoring—or eliminated.	No reuse of injection devices possible. Vaccine dose integrity and sterility guaranteed to the point of use. No possibility of manual manipulation of vaccine.	Elimination of needle and consequent elimination of needle-stick hazard.
<b>Simplicity and Efficiency of Vaccine Delivery</b>	Progressive elimination of complex and risky sterilization procedures. Progressive improvement in waste management systems. Higher cost for improved safety.	Elimination of administrative vaccine wastage, resulting in lower costs. Reduced reliance on refrigeration and ice-making at the peripheral level, where 75% of distribution costs are concentrated. Less equipment maintenance. Easier stock control.	Reformed health systems able to integrate drugs fully with vaccines. Complete elimination of refrigeration in the distribution system, leading to reduced costs and managerial burden. Easier stock control.

Source: J. Lloyd, Technologies for Vaccine Delivery in the 21st Century.

grants. In its 2002 report *Calling the Shots: Immunization Finance Policies and Practices*, the IOM noted that “in FY 1999, the federal government supplied more than \$600 million in (primarily childhood) vaccines to the states through the Section 317 and [VFC] programs.”<sup>19</sup>

In an effort to improve vaccine availability nationwide, Congress created the VFC program as part of the Omnibus Budget Reconciliation Act of 1993. The program, which is funded through Medicaid and administered by the CDC, provides publicly purchased vaccine, for eligible children, at no charge to public and private health care providers in all states and U.S. territories. To be eligible, children must fall into one of the following four categories: Medicaid-eligible, uninsured, Native American or Alaska Native origin, or underinsured (that is, covered by insurance that does not cover vaccines). VFC will cover the immunization in this last eligibility category only if it is received in a federally qualified health center or in a rural health center.<sup>20</sup>

Coordinating eligibility for children in Medicaid, the State Children’s Health Insurance Program (SCHIP), and the VFC program has been a thorny issue for the states. Most troublesome is the fact that children previously eligible for VFC lose their eligibility if they are enrolled in a non-Medicaid expansion SCHIP plan. In these cases, the state has to pay the cost of the vaccine for those SCHIP children who are considered by the state to be privately insured. The issue now is who pays for the vaccine. This is frustrating for these states because, instead of being purchased wholly with federal dollars, the vaccines are bought with a combination of state and federal dollars. In addition to the associated administrative headaches, the vaccines purchased under this arrangement are more expensive because states do not typically purchase vaccines at the discounted federal price.

Section 317 of the Public Health Service Act provides for grants administered by the CDC and awarded annually based on proposals submitted by states and territories. These grants not only are used to purchase vaccines but also can be used to support immunization infrastructure improvements in such areas as outreach, data collection, and surveillance of coverage levels and vaccine safety, as well as professional education. While these grant monies increased significantly during the mid-1990s—rising from a total of \$37 million awarded for 1990 to \$261 million for 1995—by 1999, the grants had declined to \$111 million.<sup>21</sup> Since then, however, the funding has increased substantially. “Overall, state and local governments are expected to receive \$427 million in 2002 Section 317 funding, an increase of 57 percent over levels received in 2000.” (See table on Section 317 support for state and local immunization, provided by Federal Funds Information for States, appended to this document.)<sup>22</sup>

Further complicating state childhood vaccine fiscal matters is the fact that the appropriations cycles of many states are out of sync with the Section 317 funding cycle. They can also be out of sync with recommendations of

**Coordinating eligibility for children in Medicaid, SCHIP, and the VFC program has been a thorny issue for the states.**

the CDC Advisory Committee on Immunization Practices. The result is that states are vulnerable to unforeseen costs, such as those arising from changes in childhood vaccine schedules or the introduction of new vaccines. For example, even though states can use Section 317 funding for new as well as existing vaccines, when Prevnar, an important new pneumococcal conjugate vaccine was introduced, many states choosing to offer the vaccine were faced with a budgetary short-fall.

## **PUBLIC- AND PRIVATE-SECTOR COOPERATION: PROVIDERS, REGISTRIES, AND EDUCATION**

Providers in both the public and private sectors are the key to a successful vaccine program. Until recently, immunization providers in the United States had not been well defined. A February 2002 article published in the *American Journal of Public Health* attempted to provide such a characterization, specifically seeking answers to the following questions: How many practices and clinics provide vaccinations to children? How many children are served in the public and the private sectors? What is the overall capacity of the system to deliver vaccinations to the birth cohort? How evenly is this capacity distributed? Relying upon 1997 data from the National Immunization Survey<sup>23</sup> and the VFC programs, the researchers concluded that "U.S. childhood vaccination provider capacity is adequate. Efforts to raise coverage rates should focus on increasing preventive care use among children, improving the vaccination performance of providers, and ensuring continuity of care."<sup>24</sup>

Traditionally, individual health care providers have been required to report vaccine-related adverse events as well as disease outbreaks. Some argue, however, that there is room for improvement and are calling for greater private-sector assistance in monitoring patterns of vaccine coverage and disease outbreaks within a community. Bruce Gellin, M.D., executive director of the National Network for Immunization Information, for example, has underscored the need for systematic tracking of vaccine delivery. "There is a practical issue here. If the vaccine is not available when you need it, someone needs to keep track and reschedule doctor visits. The confusion and chaos is substantial."<sup>25</sup>

Increasingly, states are relying upon registries to keep track of immunizations—identifying areas of need and monitoring adverse effects.<sup>26</sup> For a registry to be successful, however, it must have the support of parents and the providers administering the vaccines. These systems must be compatible with the operations of the private physician office and have the backing of health professionals. Similarly, health officials stress that parents need to recognize the value of having access to immunization registries and have confidence that their child's privacy will be protected.

Aware of the difficulties in reaching all children, some officials are calling for the creation of a national educational campaign, designed to explain the merits of childhood vaccine policy. Such a campaign, they stress, will

**Increasingly, states are relying upon registries to keep track of immunizations.**

need to address the broad constellation of concerns raised by parents and others. The direct support and involvement of the private sector are critical to its success.

Highlighting the success of one state's efforts to improve immunization rates, via registries and education campaigns, the National Conference of State Legislatures's Kristine Goodwin gave the following example:

In Utah, which has one of the highest birth rates in the nation and a history of ranking at the bottom of states in immunization levels, officials have had impressive success in boosting vaccination rates, doubling the percentage of immunized two-year olds, from 37 percent in 1991 to 82 percent in 1999. Linda Abel, immunization program manager in the Department of Health, said the state turned a corner in 1994, when First Lady Jacalyn Leavitt championed an aggressive "Immunize by Two: It's Up To You" campaign. Since then, she said, there's been a "consistent message" and tenacity and coordination on the part of public- and private-sector partners, including the state's largest HMO, the Utah PTA and corporations like McDonald's, Wal-Mart and Krogers. Accomplishments include: a statewide registry, a media promotion, a home visiting program and a high profile "Care-A-Van" that brings the campaign to local stores and schools. While the van dispenses vaccines, Abel said its more important contribution is "getting the message out" about the value of immunizations.<sup>27</sup>

## VACCINE MANUFACTURER CONCERNS AND CHALLENGES

Beginning in the 1980s, with the rise in childhood vaccine safety lawsuits, a number of companies dropped out of the vaccine market. The passage of the NCVIA and the no-fault compensation it provided under the National Vaccine Injury Compensation Program created what many believed was a win-win situation for patients and companies, although parents and providers remain concerned about the cumbersome process and low payouts. Recently, a proliferation of class-action suits, the great majority of which are related to thimerosal, has companies concerned.

### Manufacturing and Production

As noted earlier, companies producing biologic agents such as vaccines face significant manufacturing and production challenges.<sup>28</sup> Because vaccines require the use of biologic organisms, each vaccine is unique in terms of its manufacturing. In addition, production time is long, and purity and potency tests are strict.

Commenting in a March 4, 2002, *American Medical News* cover story on vaccine shortages, Wayne Pisano, an executive vice president at Aventis Pasteur explained:

It takes Aventis Pasteur between 27 and 32 weeks to produce a purified bulk lot of Td [tetanus and diphtheria] vaccine. Production is followed

**Beginning in the 1980s, a number of companies dropped out of the vaccine market.**

by eight to ten weeks of testing and four to six weeks of packaging and final approvals. All in all, it takes about 11 months to produce a lot of Td vaccine.<sup>29</sup>

Pisano went on to explain that additional manufacturing challenges have involved the voluntary removal of the preservative thimerosal from all childhood vaccines in order to address concerns that thimerosal potentially posed health risks, since such concerns could lead to a decline in the number of children being vaccinated. Aventis accomplished this by repackaging its diphtheria, tetanus, and acellular pertussis (DtaP) from multidose to single-dose vials to avoid the risk of contamination. This process necessitated additional licensing work with the FDA. According to Pisano, "the net effect is that we invested approximately two years' development effort to replace an existing product." Other experts note that the time spent creating thimerosal-free vaccines (for existing products) had a direct impact on supply. That is, creating single-dose vials decreased the yield of vaccine produced and thus contributed to the vaccine shortage.

Other production difficulties exist and, given the extremely limited number of vaccine manufacturers, even planned renovations to manufacturing plants can disrupt supply. When Merck & Co., Inc., the nation's only MMR and chickenpox vaccine manufacturer experienced production delays from a shutdown of its operations twice in two months, there was no other company to step in and fill the gap.

Many of these circumstances have led manufacturers to withdraw from the vaccine market, increasing the levels of shortages. Recent vaccine shortages began in November 2000 when supplies of the Td booster declined. Then, in January 2001, Wyeth Pharmaceuticals, after 50 years of producing tetanus and diphtheria vaccines, announced plans to halt production. That left only two companies, Aventis Pasteur and Glaxo SmithKline for DtaP production and Aventis as the sole manufacturer of the Td booster. Today, only four manufacturers produce vaccine for the nation's children.

In addition to the manufacturing and production challenges, companies have expressed frustration in trying to pin down demand, which often exceeds their projections. To some extent, it is a very expensive guessing game—the price of which is measured not only in cost but also in vaccine availability.

## **CHILDHOOD VACCINE SHORTAGES: PROPOSED SOLUTIONS AND POLICY CHANGES**

In the short term, recent vaccine shortages have caused the federal government temporarily to scale back recommendations regarding the timing of immunizations and to advise directing the available supply of vaccines to those children at higher risk of contracting vaccine-preventable diseases. They have also led many states to suspend some immunization

requirements related to day care and school attendance and ration the amount of vaccines distributed to providers.<sup>30</sup>

For the long term, a number of possible solutions have been suggested as health officials, manufacturers, and the government have sought to resolve the complex issues that have contributed to the shortages and to prevent their recurrence. Experts readily acknowledge that these solutions have implications for the country's emergency preparedness capabilities.

In addition to their day-to-day vaccine-related responsibilities, several federal committees and agencies function to address vaccine shortages, as summarized in Table 2.

**TABLE 2**  
**Federal Agency and Committee Functions**  
**Related to Averting or Mitigating Vaccine Shortages**

Agency/Committee	Function
Advisory Committee on Immunization Practices (ACIP)	Evaluate and recommend changes in the immunization schedule to accommodate reduced supplies.
Centers for Disease Control and Prevention (CDC)	Monitor production, monitor inventories of state immunization programs, manage distribution of public supplies, administer stockpiles, track back orders, and work with ACIP to modify immunization schedules in order to respond to vaccine shortages.
Food and Drug Administration (FDA)	Accelerate review of revisions to existing licenses and vaccine lots submitted for release. Work with manufacturers to correct violations of good manufacturing practices that could disrupt production.
National Vaccine Program Office (NVPO)	Facilitate development of contingency plans, identify the reasons for shortages and options to address them, and identify strategies to prevent future shortages.
National Vaccine Advisory Committee (NVAC)	Study and make recommendations to the DHHS assistant secretary for health on ways to achieve an adequate supply of safe and effective vaccines.

*Source: U.S. General Accounting Office, Childhood Vaccines: Ensuring an Adequate Supply Poses Continuing Challenges (GAO-02-987), September 2002.*

A number of steps have been taken in an effort to understand better the dynamics of childhood vaccine availability and to prevent future shortages. Most recently, Congress requested that the General Accounting Office (GAO) study the matter. The report, *Childhood Vaccines: Ensuring an Adequate Supply Poses Continuing Challenges*, released in September 2002, made several recommendations to the DHHS secretary to help

promote the availability of vaccine products. These included “adding vaccines to the types of products that can be considered under FDA’s authority to expedite the approval of products in development trials and directing CDC to address several operational and strategic issues in expanding childhood vaccine stockpiles.”<sup>31</sup>

In February 2002, the DHHS National Vaccine Advisory Committee convened a group consisting of vaccine companies, physicians, insurers, and federal agency personnel to articulate the problems and develop solutions. Among the group’s recommendations were the following:

- Stabilize the supply by creating additional stockpiles of vaccines that could be used during shortages.
- Increase liability protection for manufacturers and physicians.
- Streamline the regulatory process.
- Require manufacturers to provide adequate notice before they voluntarily stop production.
- Create a national education outreach and advertising campaign on the importance and real value of vaccines.

Sen. Bill Frist (R-Tenn.), along with cosponsors Sens. Kay Bailey Hutchison (R-Tex.), Jim Bunning (R-Ky.), Zell Miller (D-Ga.), Jim Jeffords (I-Vt.) and Gordon Smith (R-Ore.) have introduced legislation, S. 2053, the “Improved Vaccine Affordability and Availability Act,” which would require the federal government to establish and maintain a six-month stockpile of prioritized (childhood and adult) vaccines. In addition, the legislation would expand the funding available for state and local efforts to raise immunization rates among adults and children who are underserved or at a high risk for vaccine-preventable diseases. Lastly, the bill would “restore balance” to the National Vaccine Injury Compensation Program.<sup>32</sup> Other provisions of the bill would ensure that claimants, including third parties, file timely claims through the vaccine injury compensation process before suing in court and ensure predictability for manufacturers by clarifying that ingredients in the FDA-approved vaccine may not be considered to be adulterants or contaminants in that vaccine.

In addition to the recommended solutions listed above, other experts have suggested providing additional market incentives, including tax incentives for manufacturers. Pediatricians are calling for increased reimbursement, urging the Centers for Medicare and Medicaid Services to recognize the physician work associated with administering vaccines. “It would be unreasonable to expect that pediatricians can afford to continue to administer vaccines if the costs to the practice are more than the reimbursement.”<sup>33</sup> Increasing FDA funding in the area of vaccine testing research has also been suggested as a necessary step toward strengthening childhood vaccine supplies.

Others, including the Institute of Medicine, have called for a National Vaccine Authority to carry out a number of functions, such as defining

the need and assessing the market for vaccines, helping establish and oversee a government-owned factory, spurring private vaccine development by guaranteeing prices for immunizations, financing vaccine research, and assisting companies in the production of pilot vaccine lots. There appears to be little agreement at this point, however, that a new federal entity is the answer. Critics of this approach point out, for example, that any government-owned or operated vaccine facility would experience the same good manufacturing practice challenges and liability challenges that private companies face.

Despite some differences of opinion over some of the recommendations, there is overwhelming agreement that forging stronger public-private partnerships is critical. It is generally recognized and acknowledged that the challenges are too broad for either the private or the public sector to tackle alone. The costs and risks associated with vaccine research, development, and manufacturing are, according to most experts, too high for the private sector to shoulder alone. Similarly, most agree that the patchwork system of federal and state vaccine programs creates confusion and obfuscates the roles and responsibilities of all parties.

The unpredictability of demand and the fluctuations in federal financing urgently point to the need for what the IOM's *Calling the Shots* referred to as a "national strategic vision," one that calls for a strengthening of the federal and state immunization partnership. The IOM identified six fundamental roles for such a system: "to assure the purchase of vaccines, to assure service delivery, to prevent and control infectious disease, to monitor and survey levels of immunization coverage and vaccine safety concern, especially within high-risk settings, to sustain and improve vaccine coverage rates for child and adult populations, and to use primary care and public health resources efficiently in achieving national immunization goals."

According to the IOM and other experts, long-term vaccine supply and safety issues can be resolved only by a robust public-private partnership and an enhanced public health infrastructure. Ultimately, the answer to the question of what the government's role in ensuring an adequate childhood vaccine supply should be must be answered in a way that addresses both today's shortages and tomorrow's as-yet-unknown shortages and risks.

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## ENDNOTES

1. The focus of this paper is on childhood immunizations. While many of the issues raised in the context of childhood vaccines have relevance to adult vaccines, there are significant differences and are beyond the scope of this issue brief.
2. Walter A. Orenstein, "Protecting our Kids: What Is Causing the Current Shortage in Childhood Vaccines?" testimony before the Committee on Governmental Affairs, U.S. Senate, Washington, D.C., June 12, 2002; accessed October 16, 2002, at <http://www.cdc.gov/nip/news/testimonies/vac-shortages-walt-6-12-2002.htm>.

3. Orenstein, "Protecting."
4. National Immunization Program, "Current Vaccine Shortages," updated November 8, 2002, Centers for Disease Control and Prevention; accessed November 18, 2002, at <http://www.cdc.gov/nip/news/shortages/#Which>.
5. Right from the start, Edward Jenner, who in 1796 developed the smallpox vaccine, faced opposition. Safety, efficacy, availability and willingness of people to be immunized have been issues in the past, just as they continue to be debated today.
6. Mark Kane and Heidi Lasher, "The Case for Childhood Immunization," Occasional Paper #5, Children's Vaccine Program at PATH, March 2002, 7; available November 4, 2002, at [http://www.childre vaccine.org/files/CVP\\_Occ\\_Paper5.pdf](http://www.childre vaccine.org/files/CVP_Occ_Paper5.pdf).
7. Walter A. Orenstein, "Responding to the Challenges of the 21st Century: CDC's National Immunization Program," testimony before the Committee on Health, Education, Labor and Pensions, U.S. Senate, November 27, 2001; available November 4, 2002, at <http://www.hhs.gov/asl/testify/t011127.html>.
8. Bernard Guyer, *Setting the Course: A Strategic Vision for Immunization, Part 2, Summary of the Austin Workshop* (Washington, D.C.: National Academies Press, 2002), 38; available October 24, 2002, at <http://books.nap.edu/books/0309085179/html/index.html>.
9. Kane and Lasher, "Case for Childhood Immunization," 3.
10. While the majority of children in the United States have been inoculated, this is not the case world-wide. Global vaccination policy is not addressed in this paper.
11. Anthony S. Fauci, National Institute of Allergy and Infectious Diseases, National Institutes of Health, "Responding to the Challenges of the 21st Century: NIH's Role in Vaccine Research and Development," testimony before the Committee on Health, Education, Labor and Pensions, U.S. Senate, November 29, 2001; available November 4, 2002, at <http://www.niaid.nih.gov/director/congress/2001/112901.htm>.
12. There is a test at the "bulk" stage and then there is another test at the "filled vial" stage.
13. VAERS is a passive system in that parents and providers can initiate reports on possible adverse events.
14. Immunization Safety Review Committee, "Immunization Safety Review: Measles, Mumps, Rubella Vaccine and Autism," foreword, Institute of Medicine, Washington D.C., 2001, ix; available November 4, 2002, at [http://www.iom.edu/iom/iomhome.nsf/WFiles/ISR-MMR-4Pager/\\$file/ISR-MMR-4Pager.pdf](http://www.iom.edu/iom/iomhome.nsf/WFiles/ISR-MMR-4Pager/$file/ISR-MMR-4Pager.pdf).
15. Immunization Safety Review Committee, "Immunization Safety Review," executive summary, 7.
16. Center for Biologics Evaluation and Research, "Thimerosal in Vaccines," Food and Drug Administration; accessed March 27, 2002, at <http://www.fda.gov/cber/vaccine/thimerosal.htm>.
17. Thimerosal is still present in influenza vaccines.
18. J. Lloyd, *Technologies for Vaccine Delivery in the 21st Century* (Geneva: World Health Organization, 2000); available October 15, 2002, at <http://www.childre vaccine.org/files/Vaccine-tech-21st-century.pdf/>.
19. Additionally, the IOM reported that the Centers for Medicare and Medicaid Services paid providers serving Medicare beneficiaries, whose benefits include preventive adult vaccines, \$114 million for influenza and pneumococcal immunizations. See Institute of Medicine (IOM), *Calling the Shots: Immunization Finance Policies and Practices* (Washington, D.C.: National Academy Press, 2000).
20. The issue of insurance coverage for vaccines, particularly in the case of a suggested, rather than a mandated, vaccine, is an important issue but one that this paper does not cover in depth.

21. IOM, *Calling the Shots*, 3.
22. Vic Miller, "Growth in Federal Grants for Immunization," *Federal Funds Information for States*, Issue Brief No. 02-58, November 7, 2002.
23. The National Immunization Survey furnishes annual population-based estimates of provider-verified immunization rates for children aged 19 to 35 months.
24. Charles W. LeBaron et al., "Childhood Vaccination Providers in the United States," *American Journal of Public Health*, 92, no. 2 (February 2002): 266-270.
25. Rhonda Rowland, "Childhood Vaccines in Short Supply," CNN.com, February 18, 2002; accessed February 18, 2002, at <http://www.cnn.com/2002/HEALTH/parenting/02/18/vaccine.shortages>.
26. Registries are "confidential, population-based, computerized information systems that attempt to collect vaccination data about all children within a geographic area. Registries are an important tool to increase and sustain high vaccination coverage by consolidating vaccination records of children from multiple providers, generating reminder and recall vaccination notices for each child, and providing official vaccination forms and vaccination coverage assessments." See National Immunization Program, "What Are Immunization Registries?" Centers for Disease Control and Prevention; available November 4, 2002, at <http://www.cdc.gov/nip/registry/ir.htm>.
27. Kristine Goodwin, "Childhood Immunizations: States Tackle Costs, Education, Disparities," *NCSL State Health Notes*, 21, no. 335, October 23, 2000; available November 4, 2002, at <http://www.ncsl.org/programs/health/childimm.htm>.
28. Unlike prescription drugs, vaccines are not typically patented. Despite that, there are no generic vaccine products on the market. The barriers to generic production in the vaccine field are not patents; rather, they are the expertise necessary, the significant capital investment required, the stringent regulatory process, and the unique production challenges.
29. Susan J. Landers, "Vaccine Shortages Frustrate Everyone," *American Medical News*, March 4, 2002.
30. U.S. General Accounting Office (GAO), *Childhood Vaccines: Ensuring an Adequate Supply Poses Continuing Challenges* (GAO-02-987), U.S. General Accounting Office, Washington, D.C., 2002; available November 8, 2002, at <http://www.gao.gov/new.items/d02987.pdf>.
31. GAO, *Childhood Vaccines*, 4.
32. Office of Sen. Bill Frist, "Frist Urges Action to Alleviate Nation's Vaccine Shortage," press release, June 24, 2002; available November 4, 2002, at <http://frist.senate.gov/press-item.cfm/hurl/id=184112>.
33. American Academy of Pediatrics, *Pediatrician Testifies about Fragile Vaccine Delivery System: Vaccine Shortage Leaves Children Vulnerable to Diseases*, press release, May 12, 2002; available November 4, 2002, at [http://www.aap.org/advocacy/washing/vaccine\\_supply.htm](http://www.aap.org/advocacy/washing/vaccine_supply.htm).

## Glossary\*

**Acellular vaccine** — A vaccine containing partial cellular material as opposed to complete cells.

**Active immunity** — The production of antibodies against a specific disease by the immune system. Active immunity can be acquired in two ways, either by contracting the disease or through vaccination. Active immunity is usually permanent, meaning individuals are protected from the disease for the duration of their lives.

**Adjuvant** — A substance (for example, aluminum salt) that is added during production to increase the body's immune response to a vaccine.

**Adverse events** — Undesirable experiences occurring after immunization that may or may not be related to the vaccine.

**Advisory Committee on Immunization Practices (ACIP)** — A panel of 15 experts who make recommendations on the use of vaccines in the United States. The panel is advised on current issues by representatives from the Centers for Disease Control and Prevention, Food and Drug Administration, National Institutes of Health, American Academy of Pediatrics, American Academy of Family Physicians, American Medical Association, and others. The recommendations of the ACIP guide immunization practice at the federal, state, and local level.

**Attenuated vaccine** — A vaccine in which live virus is weakened through chemical or physical processes in order to produce an immune response without causing the severe effects of the disease. Attenuated vaccines currently licensed in the United States include measles, mumps, rubella, polio, yellow fever, and varicella. Also known as live vaccine.

**Booster shots** — Additional doses of a vaccine needed periodically to "boost" the immune system. For example, the tetanus and diphtheria (Td) vaccine which is recommended for adults every ten years.

**Brachial neuritis** — Development of a disease despite a person's having responded to a vaccine.

**Combination vaccine** — Two or more vaccines administered at once in order to reduce the number of shots given. For example, the MMR (measles, mumps, rubella) vaccine.

**Community immunity** — Having a large percentage of the population vaccinated in order to prevent the spread of certain infectious diseases. Even individuals not vaccinated (such as newborns and those with chronic illnesses) are offered some protection because the disease has little opportunity to spread within the community. Also known as herd immunity.

**Conjugate vaccine** — The joining together of two compounds (usually a protein and polysaccharide) to increase a vaccine's effectiveness.

**Epidemic** — The occurrence of disease within a specific geographical area or population that is in excess of what is normally expected.

**Etiology** — The cause of.

**Herd immunity** — See *community immunity*.

**Immune system** — The complex system in the body responsible for fighting disease. Its primary function is to identify foreign substances in the body (bacteria, viruses, fungi or parasites) and develop a defense against them. This defense is known as the immune response. It involves production of protein molecules called antibodies to eliminate foreign organisms that invade the body.

**Immunity** — Protection against a disease. There are two types of immunity, passive and active. Immunity is indicated by the presence of antibodies in the blood and can usually be determined with a laboratory test. See *active immunity* and *passive immunity*.

**Immunization** — The process by which a person or animal becomes protected against a disease. This term is often used interchangeably with vaccination or inoculation.

**Inactive vaccine** — A vaccine made from viruses and bacteria that have been killed through physical or chemical processes. These killed organisms cannot cause disease.

**Incubation period** — The time from contact with the infectious agents (bacteria or viruses) to onset of disease.

**Infectious agents** — Organisms capable of spreading disease (for example, bacteria or viruses).

**Investigational vaccine** — A vaccine that has been approved by the Food and Drug Administration (FDA) for use in clinical trials on humans. However, investigational vaccines are still in the testing and evaluation phase and are not licensed for use in the general public.

**Live vaccine** — See *attenuated vaccine*.

**Microbes** — Tiny organisms (including viruses and bacteria) that can be seen only with a microscope.

**Outbreak** — Sudden appearance of a disease in a specific geographic area (such as a neighborhood or community) or population (for example, adolescents).

**Pandemic** — An epidemic occurring over a very large area.

**Passive immunity** — Protection against disease through antibodies produced by another human being or animal. Passive immunity is effective, but protection is generally limited and diminishes over time (usually a few weeks or months). For example, the maternal antibodies are passed to the infant prior to birth. These antibodies temporarily protect the baby for the first 4 to 6 months of life.

**Pathogens** — Organisms (for example, bacteria, viruses, parasites, and fungi) that cause disease in human beings.

**Prevalence** — The number of disease cases (new and existing) within a population over a given time period.

**Quarantine** — The isolation of a person or animal who has or is suspected of having a disease, in order to prevent further spread of the disease.

**Smallpox** — An acute, highly infectious, often fatal disease caused by a poxvirus and characterized by high fever and aches with subsequent widespread eruption of pimples that blister, produce pus, and form pock marks, also called variolae.

**Strain** — A specific version of an organism. Many diseases, including HIV/AIDS and hepatitis, have multiple strains.

**Vaccination** — Injection of a killed or weakened infectious organism in order to prevent the disease.

**Vaccine** — A product that produces immunity, therefore protecting the body from the disease. Vaccines are administered through needle injections, by mouth, and by aerosol.

**Vaccine Adverse Event Reporting System (VAERS)** — A database managed by the Centers for Disease Control and Prevention and the Food and Drug Administration. VAERS provides a mechanism for the collection and analysis of adverse events associated with vaccines currently licensed in the United States. Reports to VAERS can be made by the vaccine manufacturer, recipient, recipient's parent/guardian, or health care provider. For more information on VAERS call (800) 822-7967.

**Vaccine Safety Datalink Project (VSD)** — In order to increase knowledge about vaccine adverse events, the Centers for Disease Control and Prevention have formed partnerships with eight large health maintenance organizations (HMOs) to continually evaluate vaccine safety. The project contains data on more than 6 million people. Medical records are monitored for potential adverse events following immunization. The VSD project allows for planned vaccine safety studies as well as timely investigations of a hypothesis.

**Waning immunity** — The loss of protective antibodies over time.

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*\*Adapted from "Glossary," National Immunization Program, Centers for Disease Control and Prevention, <http://www.cdc.gov/nip/webuti/terms/glossary.htm>.*

Table 1

## Section 317 Support for State and Local Immunization

(calendar years; dollars in thousands)

	2002			Vaccine Share	2000 Awards	Change 2000-2002	
	Operations	Vaccines	Total			Amount	Percent
Alabama	\$3,621	\$3,129	\$6,750	46%	\$4,045	\$2,705	67%
Alaska	2,198	2,022	4,220	48%	2,576	1,644	64%
Arizona	3,687	3,865	7,552	51%	4,086	3,466	85%
Arkansas	2,148	3,561	5,709	62%	3,334	2,375	71%
California	23,373	11,314	34,687	33%	24,627	10,060	41%
Colorado	2,978	3,891	6,870	57%	3,094	3,776	122%
Connecticut	2,742	2,653	5,394	49%	5,056	338	7%
Delaware	1,073	292	1,365	21%	608	757	124%
District of Columbia	1,502	1,363	2,865	48%	1,227	1,638	134%
Florida	8,623	5,424	14,047	39%	5,606	8,441	151%
Georgia	5,314	2,184	7,497	29%	3,423	4,074	119%
Hawaii	1,696	1,583	3,279	48%	1,376	1,903	138%
Idaho	1,525	2,213	3,738	59%	2,152	1,586	74%
Illinois	8,709	12,213	20,922	58%	11,455	9,467	83%
Indiana	3,694	6,644	10,338	64%	4,707	5,631	120%
Iowa	1,789	2,526	4,316	59%	2,718	1,598	59%
Kansas	1,825	2,821	4,647	61%	2,820	1,827	65%
Kentucky	2,447	1,692	4,138	41%	3,423	715	21%
Louisiana	2,130	5,197	7,327	71%	4,306	3,021	70%
Maine	1,962	2,687	4,649	58%	2,374	2,275	96%
Maryland	4,125	2,987	7,113	42%	5,452	1,661	30%
Massachusetts	6,368	6,750	13,118	51%	18,014	-4,896	-27%
Michigan	6,447	11,205	17,652	63%	17,131	521	3%
Minnesota	3,204	2,747	5,952	46%	4,658	1,294	28%
Mississippi	2,697	2,169	4,866	45%	4,500	366	8%
Missouri	3,619	4,036	7,655	53%	6,092	1,563	26%
Montana	543	736	1,279	58%	896	383	43%
Nebraska	1,627	1,370	2,996	46%	1,812	1,184	65%
Nevada	1,849	2,608	4,456	59%	4,715	-259	-5%
New Hampshire	1,772	1,375	3,146	44%	2,624	522	20%
New Jersey	4,324	4,655	8,979	52%	5,221	3,758	72%
New Mexico	1,715	1,687	3,402	50%	1,798	1,604	89%
New York State	15,986	8,020	24,006	33%	12,771	11,235	88%
North Carolina	5,234	8,669	13,902	62%	7,251	6,651	92%
North Dakota	772	1,307	2,080	63%	1,566	514	33%
Ohio	6,347	12,330	18,678	66%	6,744	11,934	177%
Oklahoma	3,424	4,804	8,228	58%	3,981	4,247	107%
Oregon	2,597	2,103	4,699	45%	2,972	1,727	58%
Pennsylvania	7,336	4,226	11,562	37%	6,692	4,870	73%
Rhode Island	1,603	1,239	2,842	44%	1,883	959	51%
South Carolina	3,022	5,012	8,034	62%	3,275	4,759	145%
South Dakota	776	1,782	2,558	70%	1,474	1,084	74%
Tennessee	2,744	6,152	8,896	69%	5,914	2,982	50%
Texas	15,246	21,281	36,527	58%	22,342	14,185	63%
Utah	2,259	2,275	4,534	50%	1,325	3,209	242%
Vermont	1,216	1,080	2,296	47%	1,484	812	55%
Virginia	4,166	2,795	6,961	40%	5,619	1,342	24%
Washington	4,081	4,846	8,927	54%	5,714	3,213	56%
West Virginia	1,989	921	2,911	32%	1,941	970	50%
Wisconsin	4,280	2,585	6,865	38%	4,703	2,162	46%
Wyoming	867	1,112	1,979	56%	969	1,010	104%
Puerto Rico	3,225	1,961	5,185	38%	5,732	-547	-10%
Virgin Islands	752	39	791	5%	480	311	65%
Pacific Territories	1,135	2,321	3,456	67%	1,763	1,693	96%
<b>TOTAL</b>	<b>\$210,385</b>	<b>\$216,454</b>	<b>\$426,839</b>	<b>51%</b>	<b>\$272,520</b>	<b>\$154,319</b>	<b>57%</b>

Note: For Illinois, New York, Pennsylvania and Texas, includes awards directly to selected cities.

Source: CDC administrative tables.

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