Vaccine Safety

Vaccine safety is a prime concern for manufacturers, immunization providers, and recipients of vaccines. This chapter describes how vaccines licensed for use in the United States are monitored for safety, and presents general information about the provider's role in immunization safety. Further information about contraindications and precautions for individual vaccines, such as pregnancy and immunosuppression, and about potential adverse events associated with the vaccine is contained in Chapter 2, General Recommendations on Immunization, and in the chapters on specific vaccines.

The Importance of Vaccine Safety Programs

Vaccination is among the most significant public health success stories of all time. However, like any pharmaceutical product, no vaccine is completely safe or completely effective. While almost all known vaccine adverse events are minor and self-limited, some vaccines have been associated with very rare but serious health effects. The following key considerations underscore the need for an active and ongoing vaccine safety program.

Decreases in Disease Risks

Today, vaccine-preventable diseases are at or near record lows. By virtue of their absence, these diseases are no longer reminders of the benefits of vaccination. At the same time, approximately 15,000 cases of adverse events following vaccination are reported in the United States each year (these include both true adverse reactions and events that occur coincidentally after vaccination). This number exceeds the current reported incidence of vaccine-preventable childhood diseases. As a result, parents and providers in the United States are more likely to know someone who has experienced an adverse event following immunization than they are to know someone who has experienced a reportable vaccine-preventable disease. Thus, the success of vaccination has led to **increased public attention on health risks associated with vaccines**.

Public Confidence

Maintaining public confidence in immunizations is critical for preventing a decline in vaccination rates that can result in outbreaks of disease. While the majority of parents believe in the benefits of immunization and have their children vaccinated, some have concerns about the safety of vaccines. Public concerns about the safety of whole-cell pertussis vaccine in the 1980s resulted in decreased vaccine coverage levels and the return of epidemic disease in Japan,

Importance of Vaccine Safety

- Decreases in disease risks and increased attention on vaccine risks
- Public confidence in vaccine safety is critical
  - higher standard of safety is expected of vaccines
  - vaccinees generally healthy (vs. ill for drugs)
  - lower risk tolerance = need to search for rare reactions
  - vaccination universally recommended and mandated

Importance of Vaccine Safety

- Ongoing safety monitoring needed for the development of sound policies and recommendations

Sweden, United Kingdom, and several other countries. In the United States, similar concerns led to increases both in the number of lawsuits against manufacturers and the price of vaccines, and to a decrease in the number of manufacturers willing to produce vaccines. Close monitoring and timely assessment of suspected vaccine adverse events can distinguish true vaccine reactions from coincidental unrelated events and help to maintain public confidence in immunizations.

A higher standard of safety is generally expected of vaccines than of other medical interventions because in contrast to most pharmaceutical products, which are administered to ill persons for curative purposes, vaccines are generally given to healthy persons to prevent disease. Public tolerance of adverse reactions related to products given to healthy persons, especially healthy infants and children, is substantially lower than for reactions to products administered to persons who are already sick. This lower risk tolerance for vaccines translates into a need to investigate the possible causes of very rare adverse events following vaccinations.

Adding to public concern about vaccines is the fact that immunization is mandated by many state and local school entry requirements. Because of this widespread use, safety problems with vaccines can have a potential impact on large numbers of persons. The importance of ensuring the safety of a relatively universal human-directed "exposure" like immunizations is the basis for strict regulatory control of vaccines in the United States by the Food and Drug Administration (FDA).

Sound Immunization Recommendations and Policy

Public health recommendations for vaccine programs and practices represent a dynamic balancing of risks and benefits. Vaccine safety monitoring is necessary to accurately weigh this balance and adjust vaccination policy. This was done in the United States with smallpox and oral polio vaccines as these diseases neared global eradication. Complications associated with each vaccine exceeded the risks of the diseases, leading to discontinuation of routine smallpox vaccinations in the United States (prior to actual global eradication) and a shift to a safer inactivated polio vaccine. Sound immunization policies and recommendations affecting the health of the nation depend upon the ongoing monitoring of vaccines and continuous assessment of immunization benefits and risks.

Methods of Monitoring Vaccine Safety

Prelicensure

Vaccines, like other pharmaceutical products, undergo extensive safety and efficacy evaluations in the laboratory, in animals, and in sequentially phased human clinical trials prior to licensure. Phase I human clinical trials usually involve anywhere from 20 to 100 volunteers and focus on detecting serious side effects. Phase II trials generally enroll hundreds of volunteers. These trials might take a few months, or last up to 3 years. Phase II trials determine the best dose for effectiveness and safety and the right number of doses. Next, the vaccine moves into phase III trials, which may last several years. A few hundred to several thousand volunteers may be involved. Some volunteers receive another already-licensed vaccine, allowing researchers to compare one vaccine with another for adverse health effects—anything from a sore arm to a serious reaction. If the vaccine is shown to be safe and effective in Phase III, the manufacturer applies for a license from the FDA. The FDA licenses the vaccine itself (the "product license") and licenses the manufacturing plant where the vaccine will be made (the "establishment license"). During the application, the FDA reviews everything: the clinical trial results, product labeling, the plant itself, and the manufacturing protocols.

FDA licensure occurs only after the vaccine has met rigorous standards of efficacy and safety, and when its potential benefits in preventing disease clearly outweigh any risks. However, while rates of common vaccine reactions, such as injection-site reactions and fever, can be estimated before licensure, the comparatively small number of patients enrolled in these trials generally limits detection of rare side effects or side effects that may occur many months after the vaccine is given. Even the largest prelicensure trials (more than 10,000 persons) are inadequate to assess the vaccine's potential to induce possible rare side effects. Therefore, it is essential to monitor reports of vaccine-associated adverse events once the vaccine has been licensed and released for public use.

Fundamental to preventing safety problems is the assurance that any vaccines for public use are made using Good Manufacturing Practices and undergo lot testing for purity and potency. Manufacturers must submit samples of each vaccine lot and results of their own tests for potency and purity to the FDA before releasing them for public use.

Prelicensure Vaccine Safety Studies

- Laboratory
- Animals
- Humans

Prelicensure Human Studies

- Phases I, II, III trials
- Common reactions are identified
- Vaccines are tested in thousands of persons before being licensed and allowed on the market

Postlicensure Surveillance

- Identify rare reactions
- Monitor increases in known reactions
- Identify risk factors for reactions
- Identify vaccine lots with unusual rates or types of events
- Identify signals

Postlicensure Vaccine Safety Activities

- Phase IV Trials
  - ~10,000 participants
  - better but still limited
- Large-Linked Databases
- Clinical Immunization Safety Assessment Network

Vaccine Adverse Event Reporting System (VAERS)

- National reporting system
- Jointly administered by CDC and FDA
- Passive (depends on healthcare providers and others to report)
- Receives ~15,000 reports per year

Vaccine Adverse Event Reporting System (VAERS)

- Detects
  - new or rare events
  - increases in rates of known side effects
  - patient risk factors
- Additional studies required to confirm VAERS signals
- Not all reports of adverse events are causally related to vaccine

Postlicensure

Because rare reactions, delayed reactions, or reactions within subpopulations may not be detected before vaccines are licensed, postlicensure evaluation of vaccine safety is critical. **The objectives of postlicensure surveillance are to**

- identify rare reactions not detected during prelicensure studies,
- monitor increases in known reactions,
- identify risk factors or preexisting conditions that may promote reactions,
- identify whether there are particular vaccine lots with unusually high rates or certain types of events,
- identify signals of possible adverse reactions that may warrant further study or affect current immunization recommendations.

Historically, postlicensure monitoring of vaccine safety has relied on healthcare providers and the public to report side effects, and on "ad hoc" research studies to investigate possible rare associations between vaccines and identified health conditions of interest to scientists. Today, Phase IV trials and large-linked databases (LLDBs) have been added to improve the capability to study rare risks of specific immunizations. Phase IV studies can be an FDA requirement for licensure. These trials include tens of thousands of volunteers and may address questions of long-term effectiveness and safety or examine unanswered questions identified in Phase III clinical trials. Most recently, a clinical immunization safety assessment network has been established which will increase understanding of vaccine reactions at the individual patient level.

The Vaccine Adverse Event Reporting System

The National Childhood Vaccine Injury Act of 1986 mandated that healthcare workers who administer vaccines, and licensed vaccine manufactures, report certain adverse health events following specific vaccinations. The Vaccine Adverse Event Reporting System (VAERS) is a national reporting system, jointly administered by CDC and FDA. VAERS was created in 1990 to unify the collection of all reports of clinically significant adverse events. VAERS is a passive reporting system and accepts reports from health professionals, vaccine manufacturers, and the general public. Reports are submitted via mail and fax as well as the Internet. All reports, whether submitted directly to VAERS or via state or local public health authorities or manufacturers, are coded and entered into the VAERS database. VAERS receives about 15,000 reports per year (more than 200,000 total to date). Though this seems like a very large number, it is relatively small compared with the approximately 100 million doses of childhood vaccines distributed during the past decade, as well as the millions of additional doses given to adults.

VAERS seeks to capture all clinically significant medical events occurring postvaccination, even if the reporter is not certain that the incident is vaccine related. A review of VAERS from 1991 through 2001 indicated that reports were received from manufacturers (36.2%), healthcare providers (20%), state and local health departments (27.6%), patients or parents (4.2%), others (7.3%), and unknown sources (4.7%).

Data collected on the VAERS reporting form include information about the patient, the vaccination(s) given, the reported health effect (called an adverse event—which may or may not be caused by vaccine), and the person reporting the event. Serious adverse event reports are defined as those involving hospitalization or prolongation of hospitalization, death, or reported life-threatening illness or permanent disability. All reports classified as serious are followed up to obtain additional medical information in order to provide as full a picture of the case as possible. For serious reports, letters to obtain information about recovery status are mailed to the reporters at 60 days and 1 year after vaccination. All records submitted to VAERS directly or as part of follow-up activities are protected by strict confidentiality requirements.

Despite some limitations, VAERS has been able to fulfill its primary purpose of detecting new or rare vaccine adverse events, increases in rates of known side effects, and patient risk factors for particular types of adverse events. Examples include tracking and raising the concern about intussusception after rotavirus vaccine and anaphylactic reaction to measles-mumps-rubella (MMR) vaccine caused by gelatin allergy. Additional studies are always required to confirm "signals" detected by VAERS because not all reported adverse events are causally related to vaccine.
(See "Reporting Suspected Side Effects to VAERS" for detailed information on submitting reports.)

VAERS data with personal identifiers removed are available on the website at http://vaers.hhs.gov, at no cost or through the National Technical Information Service at http://www.ntis.gov or by phone at 800-553-6847 for a fee.

Adverse Event Classifications and Assessment of Causality

Adverse events following vaccination can be classified by frequency (common, rare), extent (local, systemic), severity (hospitalization, disability, death), causality, and preventability (intrinsic to vaccine, faulty production, faulty administration). A recent classification divides vaccine adverse events as follows:

- **Vaccine-induced:** Due to the intrinsic characteristic of the vaccine preparation and the individual response of the

Adverse Event Classification

- Vaccine-induced
- Vaccine-potentiated
- Programmatic error
- Coincidental

vaccinee. These events would not have occurred without vaccination (e.g., vaccine-associated paralytic poliomyelitis).

- **Vaccine-potentiated:** The event would have occurred anyway, but was precipitated by the vaccination (e.g., first febrile seizure in a predisposed child).

- **Programmatic error:** Due to technical errors in vaccine storage, preparation, handling, or administration.

- **Coincidental:** The reported event was not caused by vaccination but happened by chance occurrence or due to underlying illness.

It is natural to suspect a vaccine when a health problem occurs following vaccination, but in reality a causal association may or may not exist. More information would be needed to establish a causal relationship. An adverse health event can be causally attributed to vaccine more readily if 1) the health problem occurs during a plausible time period following vaccination, 2) the adverse event corresponds to those previously associated with a particular vaccine, 3) the event conforms to a specific clinical syndrome whose association with vaccination has strong biologic plausibility (e.g., anaphylaxis) or occurs following the natural disease, 4) a laboratory result confirms the association (e.g., isolation of vaccine strain varicella vaccine from skin lesions of a patient with rash), 5) the event recurs on re-administration of the vaccine ("positive rechallenge"), 6) a controlled clinical trial or epidemiologic study shows greater risk of a specific adverse event among vaccinated versus unvaccinated (control) groups, or 7) a finding linking an adverse event to vaccine has been confirmed by other studies.

Large-Linked Databases

Historically, when a signal of a potential vaccine safety concern was generated from passive surveillance, further ad hoc studies were needed to test the hypothesis. Such studies, while potentially informative about vaccine causality, were costly, time-consuming, and usually limited to assessment of a single event. The need to improve postlicensure monitoring of drug safety became widely recognized in the 1960s following the discovery that thalidomide, a licensed drug commonly used during pregnancy, caused severe birth defects. The inability of passive surveillance systems to determine clear causal relationships, and the lack of timeliness of ad hoc studies to evaluate vaccine adverse events highlighted the need for an active surveillance system using large-linked databases (LLDBs). Pharmacoepidemiologists during the 1980s began to establish and utilize large databases

linking computerized pharmacy prescription (and later, immunization records) and computerized medical records. These LLDBs are derived from defined populations such as members of health maintenance organizations (HMOs), single-provider healthcare systems, and Medicaid programs. Because these databases are usually generated in the routine administration of such programs and do not require completion of a vaccine adverse event reporting form, the problems of underreporting or recall bias, which are sometimes seen with passive surveillance systems like VAERS, are reduced. Therefore, LLDBs can potentially provide an economical and rapid means of conducting postlicensure studies of safety of drugs and vaccines. **CDC's Vaccine Safety Datalink (VSD)** project is one example of such a system. It links the immunization and medical records of members of eight HMOs, comprising more than 5.5 million persons (approximately 2% of the U.S. population) annually, for various vaccine safety studies. Further information about LLDBs is available at http://www.cdc.gov/nip/vacsafe.

Vaccine Safety Datalink (VSD)

- Large-linked database
- Links vaccination and health records
- "Active surveillance"
  - 8 HMOs
  - ~2% of the U.S. population
- Powerful tool for monitoring vaccine safety

Clinical Immunization Safety Assessment Network

The most recent addition to the postlicensure vaccine safety monitoring system is the Clinical Immunization Safety Assessment (CISA) Network, which is **designed to improve scientific understanding of vaccine safety issues at the individual patient level**. The CISA network's goal is to evaluate persons who have experienced certain adverse health events following vaccination. The results of these evaluations will be used to gain a better understanding of how such events might occur and to develop protocols or guidelines for healthcare providers to help them manage similar situations. In addition, the CISA centers will serve as regional information sources to which clinical vaccine safety questions can be referred. Prior to the creation of the CISA network, no coordinated facilities in the United States investigated and managed vaccine side effects on an individual level for the purposes of providing patient care and systematically collecting and evaluating the experiences.

Clinical Immunization Safety Assessment (CISA) Network

- Improve understanding of vaccine safety issues at individual level
- Evaluate persons who experience adverse health events
- Gain better understanding of events
- Develop protocols for healthcare providers

Established in 2001, the CISA network consists of six centers of excellence with vaccine safety expertise working in partnership with CDC. These centers are Johns Hopkins University in Baltimore, Maryland; Boston University Medical Center in Boston, Massachusetts; Columbia Presbyterian Hospital in New York City; Vanderbilt University in Nashville, Tennessee; Northern California Kaiser in Oakland, and Stanford University in Palo Alto, California. For more information about CISA, visit http://www.vaccinesafety.net.

Vaccine Injury Compensation Program (VICP)

- Established by National Childhood Vaccine Injury Act (1986)
- "No fault" program
- Covers all routinely recommended childhood vaccines
- Vaccine Injury Table

Vaccine Injury Compensation

The topic of vaccine safety was prominent during the mid-1970s, with increases in lawsuits filed on behalf of those presumably injured by the whole-cell pertussis component of diphtheria-tetanus-pertussis (DPT) vaccine. Legal decisions were made and damages awarded despite the lack of scientific evidence to support vaccine injury claims. As a result of the liability, prices soared and several manufacturers halted vaccine production. A vaccine shortage resulted, and public health officials became concerned about the return of epidemic disease. To reduce liability and respond to public health concerns, Congress passed the National Childhood Vaccine Injury Act (NCVIA) in 1986.

As a result of the NCVIA, the **National Vaccine Injury Compensation Program (VICP)** was established. This program is intended to compensate individuals who experience certain health events following vaccination on a "no fault" basis. "No fault" means that persons filing claims are not required to prove negligence on the part of either the healthcare provider or manufacturer to receive compensation. The program covers all routinely recommended childhood vaccinations. Settlements are based on a Vaccine Injury Table (Appendix F), which summarizes the adverse events associated with vaccines. This table was developed by a panel of experts who reviewed the medical literature and identified the serious adverse events that are reasonably certain to be caused by vaccines. The Vaccine Injury Table was created to justly compensate those possibly injured by vaccines while separating out unrelated claims. As more information becomes available from research on vaccine side effects, the Vaccine Injury Table is amended.

The VICP has received more than 7,000 claims since its effective date of October 1, 1988. VICP has achieved its policy goals of providing compensation to those injured by rare adverse events and liability protection for vaccine manufacturers and administrators. Further information about the VICP is available at http://www.hrsa.gov/osp/vicp/

The Provider's Role

- Immunization providers can help to ensure the safety and efficacy of vaccines through proper:
  - –vaccine storage and administration
  - –timing and spacing of vaccine doses
  - –observation of contraindications and precautions

The Immunization Provider's Role

Even though federal regulations require vaccines to undergo years of testing before they can be licensed, and vaccines are monitored continually for safety and efficacy, immunization providers still play a key role in helping to ensure the safety and efficacy of vaccines. They do this through proper vaccine storage and administration, timing and spacing of vaccine doses, observation of precautions and contraindications, management of vaccine side effects, reporting of suspected side effects to VAERS, and educating patients and parents about vaccine benefits and risks. Each of these steps

is described only briefly here. Further information is available elsewhere in this book or in resource materials from CDC or other organizations.

Vaccine Storage and Administration

To achieve the best possible results from vaccines, immunization providers should carefully follow the recommendations found in each vaccine's package insert for storage, handling, and administration. Other steps to help ensure vaccine safety include 1) inspecting vaccines upon delivery and monitoring refrigerator and freezer temperatures to ensure maintenance of the cold chain, 2) rotating vaccine stock so the oldest vaccines are used first, 3) never administering a vaccine later than the expiration date, 4) administering vaccines within the prescribed time periods following reconstitution, 5) waiting to draw vaccines into syringes until immediately prior to administration, 6) never mixing vaccines in the same syringe unless they are specifically approved for mixing by the FDA, and 7) recording vaccine and administration information, including lot numbers and injection sites, in the patient's record. If errors in vaccine storage and administration occur, corrective action should be taken immediately to prevent them from happening again and public health authorities should be notified. More information on vaccine storage and handling is available in Appendix C and in CDC's Vaccine Storage and Handling Toolkit, available at http://www2a.cdc.gov/nip/isd/shtoolkit/splash.html.

Timing and Spacing

Timing and spacing of vaccine doses are two of the most important issues in the appropriate use of vaccines. To ensure optimal results from each immunization, providers should follow the currently recommended immunization schedules for children, adolescents, and adults. Decreasing the timing intervals between doses of the same vaccine may interfere with the vaccine's antibody response. For more specific information on timing and spacing of vaccines see Chapter 2, General Recommendations on Immunization. A table showing recommended minimum ages and intervals between vaccine doses is contained in Appendix A.

Providers should also remember the following:

- Administering all needed vaccines during the same visit is important because it increases the likelihood that children will be fully immunized as recommended. Studies have shown that vaccines are as effective when administered simultaneously as they are individually and carry no greater risk for adverse reactions.

The Provider's Role

- **Immunization providers can help to ensure the safety and efficacy of vaccines through proper:**
  - **management of vaccine side effects**
  - **reporting of suspected side effects to VAERS**
  - **vaccine benefit and risk communication**

- There is no medical basis for giving combination vaccines, such as MMR, separately. Administration of separated combination vaccines results in more discomfort and higher risk of disease from delayed protection.

- Some vaccines, such as pediatric diphtheria and tetanus, produce increased rates of side effects when given too frequently. Good recordkeeping, maintaining careful patient histories, and adherence to recommended schedules can decrease the chances that patients receive extra doses of vaccines.

Contraindication

A condition in a recipient that increases the chance of a serious adverse reaction

Precaution

A condition in a recipient that might

- **Increase the chance or severity of an adverse reaction, or**
- **Compromise the ability of the vaccine to produce immunity**

Invalid Contraindications to Vaccination

- Minor illness
- Mild/moderate local reaction or fever following a prior dose
- Antimicrobial therapy
- Disease exposure or convalescence
- Pregnancy or immunosuppression in the household
- Premature birth
- Breastfeeding
- Allergies to products not in vaccine
- Family history (unrelated to immunosuppression)

Contraindications and Precautions

Contraindications and precautions to vaccination are conditions that indicate when vaccines should not be given. A contraindication is a condition in a recipient that increases the chance of a serious adverse reaction. In general, a vaccine should not be administered when a contraindication is present. A precaution is a condition in a recipient that might increase the chance or severity of an adverse reaction or compromise the ability of the vaccine to produce immunity. Normally, vaccination is deferred when a precaution is present. Situations may arise when the benefits of vaccination outweigh the risk of a side effect, and the provider may decide to vaccinate the patient. Most contraindications and precautions are temporary and the vaccine may be given at a later time. More information about contraindications can be found in the Advisory Committee on Immunization Practices (ACIP) statements for individual vaccines. Recommendations for immunizing persons who are immunocompromised can be found in Appendix A. Information on allergic reactions to vaccines can be found in the American Academy of Pediatrics *Red Book*.

Screening for contraindications and precautions is key to preventing serious adverse reactions to vaccines. Every provider who administers vaccines should screen every patient before giving a vaccine dose. Sample screening questionnaires can be found in Chapter 2, General Recommendations on Immunization. Many conditions are often inappropriately regarded as contraindications to vaccination. In most cases, the following are **not** considered contraindications:

- Minor acute illness (e.g., diarrhea and minor upper respiratory tract illnesses, including otitis media) with or without low-grade fever
- Mild to moderate local reactions and/or low-grade or moderate fever following a prior dose of the vaccine
- Current antimicrobial therapy
- Convalescent phase of illness
- Recent exposure to infectious disease

- Premature birth
- Breastfeeding
- Allergies to products not in vaccine
- Family history (unrelated to immunosuppression)

Managing Vaccine Side Effects

Providers should use their best clinical judgment regarding specific management of suspected vaccine side effects. Allergic reactions to vaccines are estimated to occur after vaccination of children and adolescents at a rate of one for every 1.5 million doses of vaccine. All providers who administer vaccines should have procedures in place and be prepared for emergency care of a person who experiences an anaphylactic reaction. Epinephrine and equipment for maintaining an airway should be available for immediate use. All vaccine providers should be familiar with the office emergency plan and should be certified in cardiopulmonary resuscitation.

Reporting Suspected Side Effects to VAERS

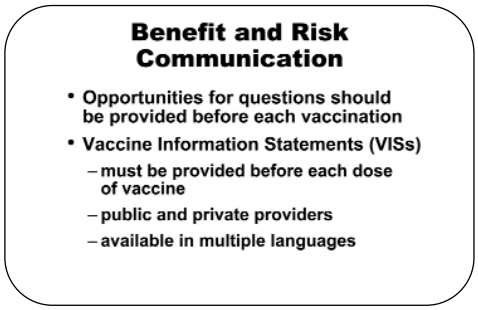
Healthcare providers are required by the National Childhood Vaccine Injury Act of 1986 to report certain events to VAERS and are encouraged to report any adverse event even if they are not sure a vaccine was the cause. A table listing reportable events is available at http://vaers.hhs.gov/reportable.htm. and is contained in Appendix F. Reporting can be done in one of three ways:

- Online through a secure website: https://secure.vaers.org/VaersDataEntryIntro.htm
- Fax a completed VAERS form* to 877-721-0366
- Mail a completed VAERS form* to

  VAERS
  P.O. Box 1100
  Rockville, MD 20849-1100

*A one-page VAERS form can be downloaded from www.vaers.hhs.gov/pdf/vaers_form.pdf or can be requested by telephone at 800-822-7967 or by fax at 877-721-0366. The form is also printed in Appendix F.

When providers report suspected vaccine reactions to VAERS, they provide valuable information that is needed for the ongoing evaluation of vaccine safety. CDC and FDA use VAERS information to ensure the safest strategies of vaccine use and to further reduce the rare risks associated with vaccines.



Benefit and Risk Communication

Parents, guardians, legal representatives, and adolescent and adult patients should be informed of the benefits and risks of vaccines in understandable language. Opportunity for questions should be provided before each vaccination. Discussion of the benefits and risks of vaccination is sound medical practice and is required by law.

The National Childhood Vaccine Injury Act requires that vaccine information materials be developed for each vaccine covered by the Act. These materials, known as "**Vaccine Information Statements (VIS)**," must be provided by all public and private vaccination providers before each dose of vaccine. Copies of VISs are available from state health authorities responsible for immunization, or they can be obtained from CDC's National Immunization Program website at http://www.cdc.gov/nip or from the Immunization Action Coalition at http://www.immunize.org. Translations of VISs into languages other than English are available from certain state immunization programs and from the Immunization Action Coalition website. Further information about VISs and their use is contained in Appendix E.

Healthcare providers should anticipate questions that parents or patients may have regarding the need for or safety of vaccination. A few may refuse certain vaccines, or even reject all vaccinations. Some persons might have religious or personal objections to vaccinations. Having a basic understanding of how patients view vaccine risk and developing effective approaches to dealing with vaccine safety concerns when they arise are imperative for vaccination providers. Healthcare professionals can accomplish this by assessing patients' specific concerns and information needs, providing them with accurate information, and referring them to credible sources for more information. The National Immunization Program's website contains extensive and up-to-date information on vaccine safety issues (http://www.cdc.gov/nip/menus/vacc_safety.htm).

When a parent or patient initiates discussion regarding a vaccine concern, the healthcare professional should discuss the specific concern and provide factual information, using language that is appropriate. Effective, empathetic vaccine risk communication is essential in responding to misinformation and concerns. The Vaccine Information Statements provide an outline for discussing vaccine benefits and risk. Fact sheets, titled, "Vaccines a Safe Choice" and "Helping Parents Who Question Vaccines" (available at http://www.cdc.gov/nip) may also be helpful.

Rather than excluding from their practice those patients who question or refuse vaccination, the more effective public health strategy for providers is to identify common

ground and discuss measures to be followed if the patient's decision is to defer vaccination. Healthcare providers can reinforce key points regarding each vaccine, including safety, and emphasize risks encountered by unimmunized children. Parents should be informed about state laws pertaining to school or child care entry, which might require that unimmunized children stay home from school during outbreaks. Documentation of these discussions in the patient's record, including the refusal to receive certain vaccines (i.e., informed refusal), might reduce any potential liability if a vaccine-preventable disease occurs in the unimmunized patient.

Acknowlegements

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