



## Robust infrastructure ensures vaccine safety after licensure



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Several steps must occur before a vaccine becomes part of routine clinical practice, including licensure by the Food and Drug Administration (FDA) and establishment of recommendations for its use by the Advisory Committee on Immunization Practices (ACIP) of the Centers

for Disease Control and Prevention (CDC) and the AAP Committee on Infectious Diseases (COID).

Safety issues are of paramount consideration in each step. Pre-licensure phases 1-3 clinical trials will detect common adverse events. After vaccine licensure, monitoring for rare adverse events continues for some vaccines through formal phase 4 trials conducted by the FDA and manufacturer.

To help ensure safety of all vaccines following licensure, a robust vaccine safety infrastructure is in place. This multi-system infrastructure was stimulated by passage of the National Childhood Vaccine Injury Act of 1986. The act also created a compensation program for families affected by childhood vaccine-associated adverse events.

Within the Department of Health and Human Services, the Immunization Safety Office (ISO) of the CDC leads most of the agency's risk assessment research and surveillance activities for vaccines. Many other governmental agencies play important roles in vaccine safety, including the National Vaccine Program Office.

In the ISO, the following four research and surveillance components work together to assess the safety of vaccines used in children, adolescents and adults in the U.S. population. Additional information about each of these four components can be found in the 2006 *Red Book*.

### Vaccine Adverse Event Reporting System (VAERS)

This vaccine safety component has been operated jointly by the FDA and CDC since its inception in 1990. VAERS is a national passive reporting system used to detect early warning signals and generate hypotheses about possible new vaccine events or changes in frequency of recognized events associated with vaccines licensed in the United States. Vaccine providers are required by law to report significant events that occur post-immunization to VAERS. VAERS data

cannot be used to prove an hypothesis but can be used to generate one. VAERS data are monitored continuously to detect previously unknown adverse events or increases in recognized adverse events.

### Vaccine Safety Datalink (VSD)

This component was established in 1990 as a collaborative effort between the ISO and eight large managed care organizations. The VSD project includes a large linked database containing data on vaccination, medical outcomes, birthdate and census data. This project allows for planned immunization safety studies as well as investigation of hypotheses arising from review of medical literature, VAERS reports, changes in immunization schedules or introduction of new vaccines.

### Clinical Immunization Safety Assessment (CISA)

This component was established in 2001 as a joint effort of CDC, six medical research centers and America's Health Insurance Plans. Goals of CISA are to study pathophysiologic basis of adverse events following immunizations, study risk factors associated with developing an adverse event and to provide clinicians with evidence-based guidelines when evaluating adverse events.

### Brighton Collaboration

This component represents an international voluntary collaboration that aims to facilitate development, evaluation and dissemination of high-quality information about safety of human vaccines.

In addition, vaccine safety issues pertaining to each newly licensed vaccine are reviewed at each meeting of the COID and the ACIP to determine if evidence-based changes in recommendations for vaccine use are needed based on newly gathered data. Examples of changes in recommendations made based on data include:

- switch from recommending oral poliovirus (OPV) vaccine to recommending inactivated poliovirus (IPV) vaccine;
- switch from recommending diphtheria and tetanus toxoids and pertussis (DTP) vaccine to recommending diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine;
- rescinding rotavirus vaccine recommendations due to intussusception and establishment of recommendations for use of second generation rotavirus vaccines; and
- removal of priority recommendation for combined measles-mumps-rubella-varicella (MMRV) vaccine over measles-mumps-rubella (MMR) or varicella vaccines administered separately during the same visit.



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As a response to the 2005 recommendations made by the Institute of Medicine, the CDC initiated a process of developing an ISO scientific safety research agenda. On April 11, this scientific agenda was presented to the Vaccine Safety Working Group of the National Vaccine Advisory Committee. Discussion included content of the draft scientific agenda, prioritization of topics and methods of implementing the agenda. Additional information can be found at [www.cdc.gov/vaccinesafety/agenda.htm](http://www.cdc.gov/vaccinesafety/agenda.htm).

Until the 20th century, approximately half of U.S. children died as a result of childhood illness. The current immunization program has resulted in control of many serious childhood illnesses and has

saved thousands of lives annually.

As the recommended childhood and adolescent immunization schedule continues to expand, the U.S. immunization program will be challenged to integrate novel immunization strategies, including enhancement of the vaccine safety infrastructure, which will require commitment of resources.

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*Dr. Pickering is editor of the 2006 Red Book: Report of the Committee on Infectious Diseases. Dr. Bocchini is chair of the AAP Committee on Infectious Diseases.*