U.S. Vaccine Safety: A Four-Prong Approach to Post-Licensure Monitoring

VAERS, the Vaccine Adverse Event Reporting System, is the most commonly known vaccine monitoring system in the U.S. It is, however, just one part of a multi-layered process to ensure vaccines administered in the U.S. are as safe as possible.

- **VAERS** collects adverse event reports, but it relies on individuals to report injuries and is therefore not meant to form a comprehensive database of possible vaccine side effects.
    - VAERS is a *passive reporting system*, which means it waits for individuals to report an adverse event after vaccination. Anyone can report a reaction or injury, including health care providers, patients and patients' representatives, such as caregivers or attorneys.[i]
    - The system is co-managed by the U.S. Food and Drug Administration (FDA) and the CDC. It is not meant to identify whether health problems were caused by vaccines, but rather if unexpected or unusual patterns are emerging in reports that could indicate a safety issue that needs to be researched further.[ii]
    - Because VAERS relies on individuals reporting, it only represents a small proportion of potential vaccine side effects. VAERS data alone therefore cannot be used to answer the question "Does a certain vaccine cause a certain side effect?" There are reports in VAERS of common conditions that may occur by chance alone that are found shortly after vaccination. Further investigation may find no medical link between vaccination and these conditions.
    - The National Childhood Vaccine Injury Act (NCVIA) requires health care providers to report "Any adverse event listed by the vaccine manufacturer as a contraindication to further doses of the vaccine; or Any adverse event listed in the VAERS Table of Reportable Events Following Vaccination that occurs within the specified time period after vaccination." In addition, the CDC encourages providers to report any clinically significant adverse event that occurs in a patient following a vaccination, even if they are unsure whether a vaccine caused the event.

VAERS is just one of four monitoring systems. The other three offer a more complete picture of possible vaccine adverse events by proactively collecting and analyzing data.

- **The Vaccine Safety Datalink (VSD)** has been a continuing collaboration since 1990 between the CDC's Immunization Safety Office and eight health care organizations including:[iii]
    - Several Kaiser Permanente sites (Washington, Oregon, California, and Colorado)
    - Marshfield Clinic Research Foundation (Wisconsin)
    - Harvard Pilgrim Health (Massachusetts)
    - HealthPartners Research Foundation (Minnesota)
    - Group Health Cooperative of Puget Sound (Washington)
        - Each of these sites share all vaccine-related information with the CDC and pairs it with general patient information, including doctor office, urgent care facility, emergency room and hospital visits and diagnoses. Included in the data is the name

of each vaccine and dates of administration. The CDC can then identify potential patterns between vaccination and illnesses. Any pattern is then investigated to determine whether there is a link between a vaccine and an illness.

- VSD conducts studies based on questions or concerns raised from the medical literature and reports to VAERS. In addition, when new vaccines are recommended or if changes are made in how a vaccine is recommended, VSD will monitor the safety of these vaccines.
- VSD has developed several pivotal reports as a result of their monitoring including:
  - Establishing the safety of thimerosal in vaccines.[iv]
  - A comprehensive white paper establishing the safety of the childhood immunization schedule in the U.S.[v]
  - Fourteen studies demonstrating the safety of vaccines during pregnancy. It is currently studying the safety of Tdap vaccination, inadvertent HPV vaccination, and influenza vaccination during pregnancy.

- **The Clinical Immunization Safety Assessment (CISA) Project** was established in 2001 to better understand individual risk for adverse events following immunization. CISA addresses vaccine safety issues, conducts high quality clinical research and assesses complex clinical adverse events following vaccination. The CDC's Immunization Safety Office works with the following national network of partners to connect clinicians with experts who can help consult on vaccine safety questions related to individual patients:[vi]
  - Boston Medical Center
  - Cincinnati Children's Hospital Medical Center
  - Columbia University
  - Duke University
  - Johns Hopkins University
  - Kaiser Permanente Northern California
  - Vanderbilt University

- **The Post-Licensure Rapid Immunization Safety Monitoring System (PRISM)** is a partnership between the FDA's Center for Biologics Evaluation and Research and Aetna, HealthCore (Wellpoint), Humana, and OptumInsight (United Healthcare). Scientists use PRISM to actively monitor and analyze data from a representative subset of the general population. PRISM links data from health plans with data from state and city immunization information systems (IIS). The system has access to information for over 190 million people allowing it to identify and analyze rare health outcomes that would otherwise be difficult to assess.[vii] Just a few of PRISM's investigations since 2010 have already yielded important results:[viii]
  - A PRISM study looked at more than 1.4 million doses of Gardasil® (a vaccine to prevent HPV) and found no connection between the vaccine and venous thromboembolism in females 9 to 26 years of age.
  - Another PRISM study was able to identify a link between a rotavirus vaccine (RotaTeq®) and an increased risk of intussusception in infants, which led to its withdrawal from the market.

All four vaccine safety monitoring systems are equally important to identifying and understanding potential links between vaccination and possible side effects.

[i] U.S. Department of Health and Human Services. "About VAERS: Background and Public Health Importance." Accessed 6 April 2018. https://vaers.hhs.gov/about.html.
[ii] U.S. Department of Health and Human Services. "About VAERS: Background and Public Health Importance." Accessed 6 April 2018. https://vaers.hhs.gov/about.html.
[iii] Centers for Disease Control and Prevention. "Vaccine Safety Datalink (VSD)." Accessed 5 July 2018. https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vsd/index.html.
[iv] Centers for Disease Control and Prevention. "Frequently Asked Questions about Thimerosal." Accessed 5 July 2017. https://www.cdc.gov/vaccinesafety/concerns/thimerosal/faqs.html.
[v] National Center for Emerging and Zoonotic Infectious Diseases. "White Paper Studying the Safety of the Childhood Immunization Schedule for the Vaccine Safety Datalink." U.S. Centers for Disease Control and Prevention. Accessed 5 July 2018. https://www.cdc.gov/vaccinesafety/pdf/WhitePaperSafety_WEB.pdf.
[vi] Centers for Disease Control and Prevention. "Clinical Immunization Safety Assessment (CISA) Project." Accessed 5 July 2018. https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html.
[vii] Centers for Disease Control and Prevention. "Ensuring the Safety of Vaccines in the United States." Accessed 27 July 2018. https://www.cdc.gov/vaccines/hcp/conversations/downloads/vacsafe-ensuring-color-office.pdf.
[viii] Shoaibi, Azadeh. "PRISM Identifies Vaccine Safety Issues." *FDA Voice*. 7 April 2017. Accessed 5 July 2018. https://blogs.fda.gov/fdavoice/index.php/2017/04/prism-identifies-vaccine-safety-issues/.