Ensuring the Safety of Vaccines in the United States

For more information on vaccines, vaccine-preventable diseases, and vaccine safety:

https://www.cdc.gov/vaccines/conversations

Last reviewed January 2018

- Currently, the United States has the safest vaccine supply in its history.
- The United States' long-standing vaccine safety system ensures that vaccines are as safe as possible. It detects problems rapidly and allows us to respond. As new information and science become available, this system is, and will continue to be, updated and improved.
- The U.S. Food and Drug Administration (FDA) ensures the safety, effectiveness, and availability of vaccines for the United States. Before the FDA licenses (approves) a vaccine, the vaccine is tested extensively by its manufacturer. FDA scientists and medical professionals carefully evaluate all the available information about the vaccine to determine its safety and effectiveness.
- Most common side effects of a vaccine are identified in studies before the vaccine is licensed. Some adverse events are so rare, however, that they may not be detected in these studies. Therefore, the U.S. vaccine safety monitoring system continuously monitors for adverse events (possible side effects) after a vaccine is licensed. When millions of people receive a vaccine, less common side effects that were not identified earlier may show up.

Adverse Events and Side Effects Adverse events reported to the Vaccine Adverse Event Reporting System (VAERS) are not necessarily side effects caused by vaccination. An **adverse event** is a health problem that happens after vaccination that may or may not be caused by a vaccine. By definition, a **side effect** has been shown to be linked to a vaccine by scientific studies.

| Prelicensure: Vaccine Safety Testing |

The U.S. Food and Drug Administration (FDA) must license (approve) a vaccine before it can be used in the United States. FDA regulations for the development of vaccines help to ensure their safety, purity, potency, and effectiveness. Before a vaccine is approved by FDA for use by the public, results of studies on safety and effectiveness of the vaccine are evaluated by highly trained FDA scientists and doctors. FDA also inspects the vaccine manufacturing sites to make sure they comply with current Good Manufacturing Practice regulations.

Vaccine Development

Vaccine development begins in the laboratory before any tests in animals or humans are done. If laboratory tests show that a vaccine has potential, it is usually tested in animals. If a vaccine is safe in animals, and studies suggest that it will be safe in people, clinical trials with volunteers are next.

Clinical Trials

Typically, there are three phases of clinical trials. Vaccines that are being developed for children are first tested in adults. FDA sets guidelines for the three phases of clinical trials to ensure the safety of the volunteers.

Phase 1 clinical trials focus on safety and include 20–100 healthy volunteers. In Phase 1, scientists begin to learn how the size of the dose may be related to side effects. If possible at this early stage, scientists also try to learn how effective the vaccine may be.

If no serious side effects are found in Phase 1, next is Phase 2, which involves several hundred volunteers. This phase includes studies that may provide additional information on common short-term side effects and how the size of the dose relates to immune response.

In Phase 3 studies, hundreds or thousands of volunteers participate. Vaccinated people are compared with people who have received a placebo or another vaccine so researchers can learn more about the test vaccine's safety and effectiveness and identify common side effects.

Clinical trials are conducted according to plans that FDA reviews to ensure the highest scientific and ethical standards. The results of the clinical trials are a part of FDA's evaluation to assess the safety and effectiveness of each vaccine. In addition to evaluating the results of the clinical trials, FDA scientists and medical professionals carefully evaluate a wide range of information including results of studies on the vaccine's physical, chemical, and biological properties, as well as how it is manufactured, to ensure that it can be made consistently safe, pure, and potent.

CS HCVG15-CHD-148 02/26/2018

The trials and all other data must show that the vaccine's benefits outweigh the potential risks (side effects) for people who will be recommended to receive the vaccine. Only if a vaccine's benefits are found to outweigh its potential risks does the FDA grant a license for the vaccine, allowing it to be used by the public.

| Postlicensure: Vaccine Safety Monitoring |

After vaccines are licensed, they are monitored closely as people begin using them. The purpose of monitoring is to watch for adverse events (possible side effects). Monitoring a vaccine after it is licensed helps ensure that the benefits continue to outweigh the risks for people who receive the vaccine.

Monitoring is essential for two reasons. First, even large clinical trials may not be big enough to reveal side effects that do not happen very often. For example, some side effects may only happen in 1 in 100,000 or 1 in 500,000 people.

Second, vaccine trials may not include groups who might have different types of side effects or who might have a higher risk of side effects than the volunteers who got the vaccine during clinical trials. Examples of these groups include people with chronic medical conditions and pregnant women.

If a link is found between a possible side effect and a vaccine, public health officials take appropriate action by first weighing the benefits of the vaccine against its risks to determine if recommendations for using the vaccine should change.

The Advisory Committee on Immunization Practices (ACIP), a group of medical and public health experts, carefully reviews safety and effectiveness data on vaccines as a part of its work to make recommendations for the use of vaccines. The ACIP modifies recommendations, if needed, based on safety monitoring.

VAERS

Postlicensure monitoring begins with the Vaccine Adverse Event Reporting System (VAERS), a national system used by scientists at FDA and the Centers for Disease Control and Prevention (CDC) to collect reports of adverse events (possible side effects) that happen after vaccination. Health care professionals, vaccine manufacturers, vaccine recipients, and parents or family members of people who have received a vaccine are encouraged to submit reports to VAERS if they experience any adverse events after getting any vaccine.

Scientists monitor VAERS reports to identify adverse events that need to be studied further. All serious reports are reviewed by medical professionals on a daily basis. VAERS data provide medical professionals at CDC and FDA with a signal of a potential adverse event. Experience has shown that VAERS is an excellent tool for detecting potential adverse events. Reports of adverse events that are unexpected, appear to happen more often than expected, or have unusual patterns are followed up with specific studies.

VAERS data alone usually cannot be used to answer the question, "Does a certain vaccine cause a certain side effect?" This is mainly because adverse events reported to VAERS may or may not be caused by vaccines. There are reports in VAERS of common conditions that may occur by chance alone that are found shortly after vaccination. Investigation may find no medical link between vaccination and these conditions.

VSD

Scientists use CDC's Vaccine Safety Datalink (VSD) to do studies that help determine if possible side effects identified using VAERS are actually related to vaccination. VSD is a network of 8 managed care organizations across the United States. The combined population of these organizations is more than 24 million people.

PRISM

To further monitor for possible vaccine side effects, FDA utilizes Post-Licensure Rapid Immunization Safety Monitoring (PRISM). PRISM is the largest vaccine safety surveillance system in the United States. 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 registries. Because PRISM has access to information for over 190 million people, FDA is able to identify and analyze rare health outcomes that would otherwise be difficult to assess.

CISA

The Clinical Immunization Safety Assessment (CISA) Project is a collaboration between CDC and 7 medical research centers. Vaccine safety experts conduct individual case reviews and clinical research studies about vaccine safety.

Vaccine Manufacturing

Once a vaccine is licensed, FDA regularly inspects vaccine manufacturing facilities to make sure they are following strict regulations. Vaccines are manufactured in batches called lots, and vaccine manufacturers must test all lots of a vaccine to make sure they are safe, pure, and potent. Vaccine lots cannot be distributed until released by FDA.

| the science |

Food and Drug Administration regulation and evaluation of vaccines by V. Marshal and NW Baylor. Pediatrics. 2011 May;127 Suppl 1:S23-30. *http://pediatrics.aappublications.org/content/127/Supplement_1/S23.long*

Vaccine Safety: Current Systems and Recent Findings by Melinda Wharton. Current Opinion in Pediatrics. February 2010. Vol 22: pages 88-93. https://*www.cdc.gov/vaccines/hcp/patient-ed/conversations/downloads/vacsafe-wharton.pdf*

Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS) by TT Shimabukuro, M Nguyen, D Martin, F DeStefano. Vaccine. 2015 Aug 26;33(36):4398-405. *http://www.sciencedirect.com/science/article/pii/S0264410X15009822?via%3Dihub*

The Vaccine Safety Datalink: successes and challenges monitoring vaccine safety. MM McNeil, J Gee, ES Weintraub, EA Belongia, GM Lee, JM Glanz, JD Nordin, NP Klein, R Baxter, AL Naleway, LA Jackson, SB Omer, SJ Jacobsen, F DeStefano. Vaccine. 2014 Sep 22;32(42):5390-8. *http://www.sciencedirect.com/science/article/pii/S0264410X14010251?via%3Dihub*

For more information on vaccines call 800-CDC-INFO (800-232-4636) or visit https://www.cdc.gov/vaccines.