AAFP
AMERICAN ACADEMY OF FAMILY PHYSICIANS

FACT SHEET

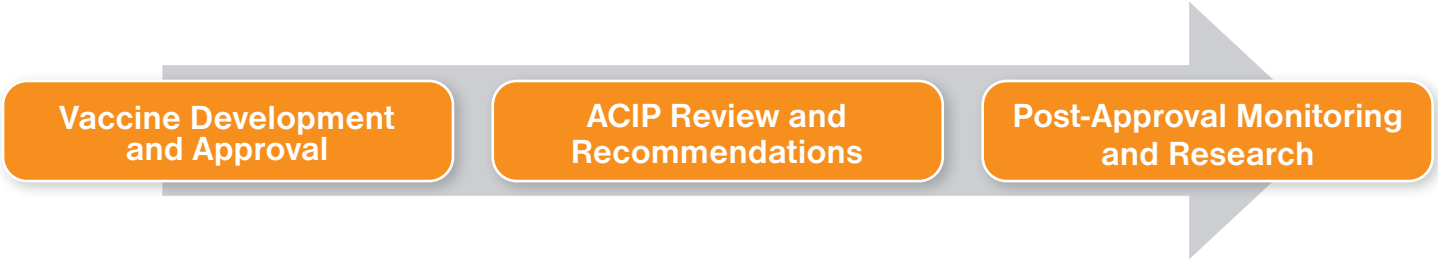
Vaccine Safety System

As a family physician, you are the primary source of information parents and caregivers go to when making health care decisions for their families, including whether or not to get their kids vaccinated. In these ongoing conversations, you probably get a lot of questions, particularly about how vaccines are made, vaccine safety standards, and the review process a vaccine goes through before getting approved.

This fact sheet aims to help you have these conversations by providing an overview of the phases of vaccine development, approval, and safety monitoring.

Stages of Vaccine Development, Approval, and Safety Monitoring

Before vaccines are made available to the public, stages of research, testing, and clinical trials are conducted to ensure their safety and efficacy.[1] Vaccines are tested extensively in the laboratory and with the human subjects during development.



Stage 1: Vaccine Development and Approval

➤ Basic research and Investigational New Drug (IND) application

Researchers conduct basic research and pre-clinical trials and submit an IND application to the U.S. Food and Drug Administration (FDA) for review.[1]

➤ FDA review of IND application

The FDA reviews the IND application to ensure human subjects are not put at unreasonable risk of harm while using the vaccine in clinical studies. This review also ensures that adequate informed consent has been received from the human test subjects and all necessary protections are in place.[1]

➤ Clinical trials

The FDA requires vaccines to undergo three phases of clinical trials with human subjects before they are licensed for public use.[1]

- Phase 1 trials only last a few months and involve between 20 and 100 volunteers.
- Phase 2 trials range in duration from several months up to two years and involve several hundred participants.
- Phase 3 trials are more extensive, involving several hundred to several thousand volunteers and typically lasting for several years.

➤ FDA review of Biologics License Application (BLA)

Once clinical trials have shown a vaccine is safe and effective, the manufacturer submits a BLA in order to request two licenses from the FDA: (1) a product license for the vaccine and (2) an establishment license for the production plant.[1] The FDA reviews the clinical trial data and manufacturing protocols and inspects the plant before licensing the vaccine for use in the general population.

Stage 2: Advisory Committee on Immunization Practices (ACIP) Review and Recommendations

➤ ACIP review

Once the FDA licenses a vaccine, the Centers for Disease Control and Prevention's (CDC's) ACIP makes vaccine recommendations for the United States. The ACIP is comprised of medical and public health experts from all over the country who are assisted by the CDC's many public health researchers.[2] There are 15 experts with voting rights who are formally responsible for making vaccine recommendations. In addition, perspectives and comments for consideration are offered by 30 non-voting representatives from professional organizations and other relevant groups (e.g., the American Academy of Family Physicians [AAFP], the American Academy of Pediatrics [AAP], the U.S. military, the Department of Veterans Affairs, drug manufacturers). ACIP members typically meet three times per year to review information about vaccines. These meetings are open to the public and available online via webcast. Before making recommendations, ACIP members do extensive research, review the scientific evidence, and debate pros and cons thoroughly in order to make sure they recommend a vaccine that is safe and effective.

➤ Publication in *Morbidity and Mortality Weekly Report* (*MMWR*)

Vaccine recommendations made by the ACIP are reviewed by the CDC director and the Department of Health and Human Services (HHS).[2] If adopted, they are published as official CDC/HHS recommendations in the *MMWR*.

Stage 3: Post-Approval Monitoring and Research

- **Phase 4** involves vaccine safety monitoring and research and begins after a vaccine is licensed and recommended for use.[1] The FDA requires manufacturers to submit a sample from each vaccine lot prior to its release for public use. The ACIP continues to monitor vaccine safety and effectiveness data and may change or update recommendations based on new findings from this process.
- **Vaccine Adverse Event Reporting System (VAERS)**, a vaccine surveillance system, monitors any adverse events following vaccination.[3,4] The VAERS relies on individuals to report adverse health events after they are vaccinated, so these data alone cannot determine if the vaccine caused the reported adverse event. Still, the VAERS can act as an early warning system.
- **Vaccine Safety Datalink (VSD)** was created to study rare vaccine adverse events.[3,5] The VSD uses electronic health data from nine participating health care organizations to study questions or concerns raised from the medical literature and then reports its findings to the VAERS. The VSD also monitors the safety of new vaccines and any vaccine for which the recommendation is changed.
- **Clinical Immunization Safety Assessment (CISA)** is a collaboration between the CDC and seven academic medical centers.[3,6] It complements other vaccine safety systems and focuses on conducting studies involving targeted or special populations often excluded from pre-licensure clinical trials.
- **Vaccine Injury Compensation Program (VICP)**[7]: Vaccines do not cause serious problems for most people. But, in very rare cases, a person might have a severe adverse reaction. If this happens, they may be eligible to file a petition for financial compensation from the VICP. This program provides compensation for individuals found to have been injured by a VICP-covered vaccine.

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