

Vaccine Product Approval Process

FDA's Center for Biologics Evaluation and Research (CBER) is responsible for regulating vaccines in the United States. Current authority for the regulation of vaccines resides primarily in Section 351 of the Public Health Service Act and specific sections of the Federal Food, Drug and Cosmetic Act.

Vaccine clinical development follows the same general pathway as for drugs and other biologics. A sponsor who wishes to begin clinical trials with a vaccine must submit an Investigational New Drug application (IND) to FDA. The IND describes the vaccine, its method of manufacture, and quality control tests for release. Also included are information about the vaccine's safety and ability to elicit a protective immune response (immunogenicity) in animal testing, as well as the proposed clinical protocol for studies in humans.

Pre-marketing (pre-licensure) vaccine clinical trials are typically done in three phases, as is the case for any drug or biologic. Initial human studies, referred to as Phase 1, are safety and immunogenicity studies performed in a small number of closely monitored subjects. Phase 2 studies are dose-ranging studies and may enroll hundreds of subjects. Finally, Phase 3 trials typically enroll thousands of individuals and provide the critical documentation of effectiveness and important additional safety data required for licensing. At any stage of the clinical or animal studies, if data raise significant concerns about either safety or effectiveness, FDA may request additional information or studies, or may halt ongoing clinical studies.

If successful, the completion of all three phases of clinical development can be followed by the submission of a Biologics License Application (BLA). To be considered, the license application must provide the multidisciplinary FDA reviewer team (medical officers, microbiologists, chemists, biostatisticians, etc.) with the efficacy and safety information necessary to make a risk/benefit assessment and to recommend or oppose the approval of a vaccine. Also during this stage, the proposed manufacturing facility undergoes a pre-approval inspection during which production of the vaccine as it is in progress is examined in detail.

Following FDA's review of a license application for a new indication, the sponsor and the FDA may present their findings to FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC). This non-FDA expert committee (scientists, physicians, biostatisticians, and a consumer representative) provides advice to the Agency regarding the safety and efficacy of the vaccine for the proposed indication.

Vaccine approval also requires the provision of adequate product labeling to allow health care providers to understand the vaccine's proper use, including its potential benefits and risks, to communicate with patients and parents, and to safely deliver the vaccine to the public.

The FDA continues to oversee the production of vaccines after the vaccine and the manufacturing processes are approved, in order to ensure continuing safety. After licensure, monitoring of the product and of production activities, including periodic facility inspections, must continue as long as the manufacturer holds a license for the product. If requested by the FDA, manufacturers are required to submit to the FDA the results of their own tests for potency, safety, and purity for each vaccine lot. They may also be required to submit samples of each vaccine lot to the FDA for testing. However, if the sponsor describes an alternative procedure which provides continued assurance of safety, purity and potency, CBER may determine that routine submission of lot release protocols (showing results of applicable tests) and samples is not necessary.

Until a vaccine is given to the general population, all potential adverse events cannot be anticipated. Thus, many vaccines undergo Phase 4 studies-formal studies on a vaccine once it is on the market. Also, the government relies on the Vaccine Adverse Event Reporting System (VAERS) to identify problems after marketing begins. The VAERS system and how it works is discussed further on this website.

References

- National Vaccine Advisory Committee. "United States Vaccine Research: A Delicate Fabric of Public and Private Collaboration." *Pediatrics*, Vol 100(6), Dec.1997, pp. 1015-1020.
- Parkman PD, Hardegree MC. "Regulation and Testing of Vaccines." In Plotkin SA, Orenstein WA, [eds.]. *Vaccines*, 3d ed. Philadelphia: Saunders; 1999, pp.1131-1143.
- Stehlin, Isadora. "How FDA Works to Ensure Vaccine Safety." *FDA Consumer Magazine*, March 1996.

Related Links from the Centers for Disease Control and Prevention

- What Would Happen If We Stopped Vaccinations (<http://www.cdc.gov/vaccines/vac-gen/whatifstop.htm>)
- Ten Things You Need To Know About Immunizations (<http://www.cdc.gov/vaccines/vac-gen/10-shouldknow.htm>)
- CDC National Immunization Program (<http://www.cdc.gov/vaccines/>)