Q+A: Understanding the Vaccine Pre-Approval Process

CVEEP
Fighting Infectious Respiratory Disease

In the U.S., long-standing vaccine safety systems are in place to ensure that vaccine safety is closely monitored at every step of vaccine development. These systems include multi-stage clinical trials, safety studies, and regulatory review.

Are vaccines studied for safety before they are available to the public?

Yes! Before a vaccine becomes available in a pharmacy, clinic or provider's office, the FDA follows a gold-standard review process to ensure the safety and efficacy of each vaccine. This process for vaccine development includes multiple stages of **research, clinical trials**, and robust **regulatory reviews**.

1 Research and Development:

During this stage of vaccine development, researchers explore their idea for a potential vaccine. This process often takes 10-15 years of laboratory research. Lab testing identifies antigens that can prevent disease and assesses the antigens' ability to cause a safe immune response. If a vaccine candidate progresses past this stage, the group or organization responsible for developing and testing the vaccine submits an **Investigational New Drug Application** to the FDA. This application describes the proposed clinical trial process.

2 Clinical Trials:

If the application is approved by the FDA, the vaccine then enters the clinical development stage, a three-phase process:

Phase 1:

During this phase, a small group (20-100) of people receive the trial vaccine. Researchers gather information on how safe the vaccine is in people at this time. This includes identifying and learning about side effects and observing how well the vaccine works to create an immune response.

Phase 2:

During Phase 2, the trial expands to hundreds (100-300) of people who have characteristics, like age and physical health, similar to the intended recipients for the vaccine. This phase also includes groups of people from diverse backgrounds to ensure representation across different populations. During this phase additional safety information on side effects, risks, and how well the vaccine works to cause an immune response is gathered.

Phase 3:

The clinical trial expands to thousands (1,000-3,000) of people, often utilizing a randomized control trial (RCT) study design. This phase is used to confirm how well the vaccine works, monitor common and rare side effects, and collect information to support safe usage in people.

The FDA requires clinical trials to include randomized controlled trials (RCT) before a vaccine is approved for all groups including children, adults, and older adults.

RCTs show the protective benefits of a new vaccine before the vaccine is licensed for use. An RCT measures vaccine efficacy by comparing the outcomes of one group who is assigned to get a placebo, and a group that receives the vaccine. A placebo is a "pretend vaccine," or something that looks like a real vaccine but doesn't contain the trial vaccine. In a "double-blind" RCT, neither the researcher nor the participant knows who has received the placebo or the trial vaccine. According to recent research, it is estimated that more than 400 vaccines have been tested using RCTs.[1] Both the initial COVID-19 and flu vaccines were tested using RCTs.[2]

3 Vaccine Manufacturing Process:

During Phase 3 of the clinical trials process, the FDA reviews the company's proposed manufacturing process and inspects the facility where the vaccine will be made. The manufacturer then makes batches of vaccines, which together are called "lots." These lots undergo a series of tests to ensure the vaccine is consistent across lots.

4 Regulatory Review and Approval:

- If the clinical trials are successful, once completed, the vaccine manufacturer submits a **Biological License Application** to the FDA. This application includes data from pre-clinical and clinical trials, details about the manufacturing process, and information about the manufacturing facility.
- Before the FDA grants a license to manufacture the vaccine, the FDA's **Vaccines and Related Biological Products Advisory Committee** (VRBPAC) reviews and evaluates data during a public meeting to make a recommendation on the application status.
- After the FDA approves a vaccine, the Centers for Disease Control and Prevention's (CDC) **Advisory Committee on Immunization Practices** (ACIP) develops recommendations on the use of the vaccine.

After a vaccine is approved, the CDC and the FDA continue monitoring for vaccine safety. Post-approval monitoring ensures that the vaccine's benefits continue to outweigh any risks and backs up demonstrated safety that was seen during clinical trials.

[1] https://www.cidrap.umn.edu/adult-non-flu-vaccines/vaccine-rct-spreadsheet-aims-show-data-dispel-myths-about-vaccines
[2] https://medium.com/@jsteier_29203/randomized-controlled-trials-the-backbone-of-vaccine-safety-017e38125d0d

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