BEHIND VACCINE DEVELOPMENT: THE CLINICAL TRIAL PROCESS

Why Clinical Trials Matter

Clinical trials are research studies involving human volunteers that test the **safety and efficacy** of preventative measures or treatment products such as vaccines, medicines or medical devices[1,2]

For vaccine candidates, clinical trials:[1]

- Provide important insight into diseases vaccines can help prevent
- Are a critical step to support the approval of vaccines by regulatory bodies

How Are New Vaccines Developed?

The development cycle of a vaccine includes:[3]

- Exploratory stage
- Pre-clinical stage
- Clinical development
- Regulatory review and approval
- Manufacturing
- Quality control

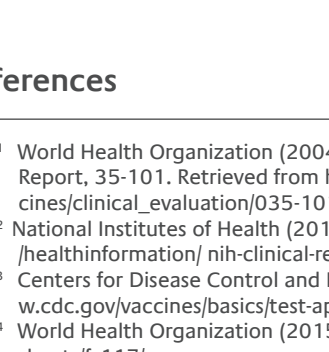
Clinical development, in general, is a **three-phase** process:[3]

Phase 1: Preliminary safety studies are done in small groups of healthy volunteers

Phase 2: Study size is expanded and vaccine is tested for safety and immunogenicity in people with characteristics (such as age and physical health) similar to those for whom the vaccine is intended

Phase 3: Vaccine is given to large number of people and tested for safety and efficacy

Many vaccines also undergo long-term studies after the vaccine is licensed for ongoing monitoring of safety and efficacy[3]



The process of vaccine development can be challenging and requires special consideration because vaccines:[1]

- Are given to healthy individuals to prevent disease and help contribute to the health and well-being of society as a whole
- Demand a high safety threshold to achieve approval
- Are highly complex substances derived from living materials that require specific manufacturing processes
- Require specialized testing to assure quality and safety in all vaccines distributed

Advancing Takeda's Dengue Vaccine Candidate

Takeda has a long-standing history of conducting clinical trials and bringing products to market across the globe, and for more than 70 years, Takeda has produced **vaccines to prevent infectious diseases**

One vaccine candidate in Takeda's late-stage pipeline is a **dengue vaccine**

An estimated

390 million

dengue infections occur globally on an annual basis, and there are more than 20,000 dengue-related deaths each year around the world[4,5]

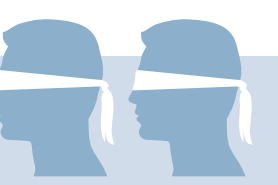
Based on Phase 1 and Phase 2 trials, which provided data that suggest that Takeda's vaccine candidate is generally safe, well tolerated and immunogenic, the vaccine has progressed into Phase 3 trials in dengue-endemic Latin American and Asian countries. This marks an important milestone on the journey toward regulatory approval [6,7,8]

Phase 3 Trial Is Underway

The **double-blind, randomized** and placebo-controlled Phase 3 trial has been designed to:[9]

- Investigate the efficacy, safety and immunogenicity of two doses of vaccine against cases of dengue caused by **all four virus strains**
- Evaluate the vaccine candidate's ability to protect individuals at risk for symptomatic dengue across geographies, **whether or not they have had previous exposure** to dengue virus, including: **children and adults,** travelers and those living in endemic areas

Takeda is working to provide the necessary evidence to support the safe and effective use of its dengue vaccine candidate in people who need it as soon as possible



Double-blinding:

A clinical trial design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug and which are receiving a placebo or another therapy[10]

Randomization:

A method based on chance by which study participants are assigned to different treatment groups. Randomization allows for researchers to comparably test different treatments in similar groups[10]

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