

## **GPP Case Study: HVTN 502 (Step)**

### **Trial Background**

- Phase IIb test-of-concept vaccine trial
- Evaluating safety and efficacy
- Conducted by the HIV Vaccine Trials Network (HVTN)
- Sponsored and funded by Merck & Co., Inc. and the National Institute of Allergy and Infectious Disease (NIAID)
- Testing Adenovirus type-5 (Ad5) vector based vaccine
- Enrolled 3000 participants, primarily men who had sex with men (MSM) and women at higher risk of HIV infection
- Conducted in the USA, Australia, South America, and the Caribbean
- Initiated in 2004

### **The Scenario**

In September 2007, after all volunteers had been enrolled, the trial's interim results were reviewed by their independent DSMB. The DSMB concluded that the vaccine did not prevent HIV infection nor reduce the amount of virus in those who became infected with HIV. Data also suggested that the vaccine may have increased the likelihood of HIV acquisition for participants who were uncircumcised or who were previously exposed to Ad5, the common cold virus used to make the vaccine. Concurrently, a sister study known as Phambili was still recruiting volunteers and testing the same candidate vaccine in South Africa. Based on the intermediate Step data and along with early review of data from Phambili itself, its DSMB decided to halt the trial and suspend immunizations in 2007.

### **GPP-Relevant Issues**

**Scientific and ethical challenges.** The potential for vaccine-induced increased susceptibility raised new scientific and ethical issues for the vaccine research field, especially related to the existing vaccine pipeline as well as unanticipated harm for participants.

**Stakeholder dialogue.** Despite these unexpected challenges, the trial results generated unprecedented candid dialogue between researchers and broader stakeholders, including civil society groups and international HIV advocacy organizations such as AVAC.

**Implications for future trials and the research agenda.** A disappointing outcome from one trial can have a significant impact on the entire research endeavour. Step researchers articulated plans to conduct future trials with Step and Phambili cohorts to further investigate the vaccine-induced increased susceptibility. Other vaccine trials were delayed and reconfigured to ensure their design took into account what had been learned from the Step results.

### **GPP-Related Actions**

**Communications planning and coordination.** The Step trial sites were required to develop and implement comprehensive stakeholder engagement plans, which included strategies for communications and issues management. There was ongoing consultation between the central trial network and individual sites, allowing research teams to collaborate and adapt strategies for local relevance.

**Standard and consistent messaging.** Comprehensive messages were developed with the Step protocol team and input from key community stakeholders, trial site community engagement officers, participants, and investigators from participating trial sites to ensure information was

accurate and easily decipherable. These messages helped manage stakeholder expectations and maintain public confidence in the trial.

**Prioritization of trial participants.** The first priority for Step researchers was communicating the trial results clearly to participants. Trial sites used their IRB pre-approved messages and information sheets to guide their communication. They contacted participants by phone, email, and in person, ensuring they received an interpretation of the results directly from the trial site rather than the media.

**Using community expertise.** The intermediate Step results were explained at an open HVTN meeting, where trial investigators and community representatives wrestled with several key issues such as the timing of unblinding the trial and potential concerns about trial participation risks.

**Application of GPP guiding principles in communication.** Trial investigators made themselves broadly available to press, advocacy groups, and other interest groups. Step researchers continued to share information and reach out to stakeholders at various levels, using respectful, transparent, and timely communication. This continuous outreach and engagement created a sense of trust with key stakeholders in the face of this concerning news.

**Media monitoring.** The status of the Step and Phambili trials were widely reported in the international press and online media outlets, and trial sites understood that this could shape public opinion. Researchers actively monitored trial coverage and messages disseminated from local newspapers, social networking sites, and blogs.

### Key Lessons Learned

While infrequent, the premature halting of a biomedical HIV prevention trial due to the lack of efficacy, a concerning safety signal, or other reasons, requires a rapid and effective response. The resulting impact on trial participants, trial site staff, the trial community, and a wide range of stakeholders can be quite profound. In the case of Step, important lessons were learned about how to communicate proactively with key stakeholders, including the media, and in effectively managing potential controversy and fall out:

- **Transparency.** Research teams should be clear with stakeholders about what they know and do not know. In the case of Step, researchers were honest about their uncertainty regarding whether the vaccine truly increased susceptibility. This transparency mitigated the mistrust and negative sentiments that the results could have generated.
  - **Mutual understanding.** CAB members and community stakeholders should be involved in the planning and development of key and supporting messages, and not merely act as recipients of information.
  - **Media engagement.** Ongoing, proactive, and strategic engagement with media throughout the trial is vital for successful trial closures and results dissemination.
- Crisis communication and issues management planning.** An important part of crisis communications planning is to anticipate such possibilities and to plan for them accordingly. Determination of clear roles and responsibilities at the trial network and site level, selection of knowledgeable spokespeople, and development of locally appropriate communication materials were critical in order to avoid confusion and misinterpretations of the trial.