

**HIV VACCINE
AWARENESS DAY**

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Experimental Medicine Vaccine Trials (EMVTs) Opportunities and Challenges

HIV vaccine trials to date have answered some scientific questions, but raised many others that must be answered if the world is ever to develop an effective HIV vaccine. The lack of efficacy in the Imbokodo, Uhambo and AMP trials, all large, late-phase efficacy trials, have prompted researchers to look for trial designs that can quickly ask and answer key questions, inform decisions about which vaccine candidates to advance into larger trials and, hopefully, increase the probability of demonstrating efficacy. Recently, various researchers, funders and vaccine developers have focused on experimental medicine vaccine trials (EMVTs) to build on current knowledge and help to advance the field.

What are Experimental Vaccine Trials (EMVTs)?

EMVTs are clinical investigations undertaken to test or generate a scientific hypothesis that advances vaccine discovery and development. They do not provide direct prevention or treatment benefits to the participant, rather, they are designed to answer a scientific question.

Why Might EMVTs Be Important?

EMVTs may speed the investigative process, resulting in more rapid iterations, testing hypotheses and generating faster findings to inform the next round of trials.

EMVTs differ from product development trials where vaccine candidates progress through Phase 1 to 3 trials with the hopes of product licensure. Designed as small Phase 1 trials, but setting aside the necessity for a licensable product, EMVTs aim to quickly and safely answer if an experimental agent induces a potentially protective response, and may offer researchers a more viable way to sift through the many variables that may contribute to successful HIV vaccine design. The focus of EMVTs is **to accelerate vaccine science rather than progress individual products**. They are iterative by nature and offer a path to quickly investigate the potential of vaccine candidates. Faster findings then inform the next round of trials.

The EMVT approach would address questions that cannot be resolved in animal testing, providing a method for an early validation that innovative vaccine strategies show promise in humans. EMVTs do not compromise safety protocols or standards, nor do they increase the risk to participants. EMVTs may involve more intense biological sampling such as biopsies or blood draws to collect as much information as possible.

EMVTs could bring savings and efficiency in a number of ways: small teams could test candidates on shorter timelines, using standardized manufacture, toxicology and regulatory procedures; and multiple candidates could be tested in parallel.

Why This Approach?

EMVTs have been discussed as a promising strategy for a number of years in the HIV vaccine field. Interest in EMVTs is growing as the field recognizes the need to accelerate the pace of research, on the heels of disappointing results from recent efficacy trials.

| | Traditional Phase I | Experimental Medicine Phase I |
|---|--|---|
| Purpose of the trial | Product development | Scientific information |
| Next step | Hopefully Phase II | Improve Vx design / Phase I |
| Number of Volunteers | ~20-100 | Defined by scientific question |
| Use of Controls / Placebo | Yes | Potentially No |
| Duration (months) | ~12-18 months | Usually <12 months |
| Laboratory monitoring of volunteer | Safety / mostly regular immunogenicity | Safety / mostly special assays |
| Preclinical (animal) evaluation | Extensive (up to protection) | Limited / generic for platform (safety) |
| Vaccine Manufacturing | Scalable product (reproducibility) | Pilot / small scale lot |
| Product characterization | Suitable for Ph3 trials; long term stability | Description of product (qualified assays); purity, potency, stability |
| Regulatory | IND / IMPD | IND / IMPD |
| Ethics | IRB approval; involves large communities | IRB approval; involves individuals |
| Industrial partner | Highly desirable | Desirable, but not essential |

Challenges for EMVTs

To move forward at scale, some challenges must be confronted.

- Some regulatory bodies provide greater flexibility for EMVTs, but there is much complexity around communicating highly adaptable trial designs to regulatory and ethics bodies. A global standard is needed.
- Currently, there is no commercial incentive for the private sector to manufacture small batch vaccine candidates.
- It will be ethically imperative and complex to communicate the lack of a direct benefit to participants. This, coupled with more intensive biological sampling, may justify increased incentives for volunteers, within strictly observed ethical boundaries.
- While the US FDA has provisions to reduce the risk of investment in drug development and late-stage failure, no specific provision exists to mitigate the risk of investment in vaccine development.

ADDITIONAL RESOURCES

- Experimental Medicine Vaccines for Advocates—Recording of a session with Imperial College London’s, Robin Shattock: <https://www.youtube.com/watch?v=0Hj93ApieE0>

For more on HIV vaccines go to avac.org/prevention-option/hiv-vaccine and avac.org/hvad.