

# The US Army's Mission to Develop a Globally Effective HIV Vaccine: History and Progress

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## Summary

HIV continues to threaten global health with 38 million people living with HIV worldwide and over 36 million deaths since 1981. Despite the approval of antiretrovirals for prevention, there were 1.5 million new infections in 2020, and we continue to witness a steady drumbeat of several hundred new infections in US servicemembers annually, which impairs military readiness, imposes a significant cost to military health systems, and threatens blood safety. HIV is a global destabilizing force, impacting partner militaries and challenging public health in strategic geographies such as Ukraine, which has Europe's second largest HIV epidemic. To combat these risks, the US Army has a long-standing mission to develop a globally effective HIV vaccine.

## Methods-Results

In 2009 the landmark RV144 Thai trial, a collaboration between the US Army and Thai Ministry of Public Health, was the first and only demonstration of HIV vaccine efficacy in humans. RV144 evaluated a pox prime and protein boost regimen, which was 60% effective at 1 year but declined to 31% by the end of the study at 3.5 years. Since then, we have learned much about correlates of protection, most notably the importance of antibodies to the V1V2 region of the virus envelope. Subsequent smaller trials have explored ways to improve the potency and durability of key immune responses through boosting strategies, finding that late boosts can improve the level and quality of humoral as well as cellular responses. Key advances also include the development of the Army Liposomal Formulation adjuvants, which have proven safe and immunogenic in phase 1 trials of vaccines against multiple pathogens. Additionally, the HIV field is adopting novel immunogens to mRNA platforms used successfully in COVID-19 vaccines, and the bioproduction facility at the Walter Reed Army Institute of Research is developing the capability to produce next generation HIV mRNA vaccines with mosaic designs to address the global diversity of HIV while optimizing responses shown to protect in the RV144 trial.

## Conclusions

HIV remains a threat to military readiness and global public health and stability. Lessons learned from earlier HIV prevention efficacy trials as well as the COVID-19

vaccine development experience can be leveraged to achieve the ultimate public health tool of an effective HIV vaccine.