

# Anthrax Vaccine Research Program (AVRP)

Anthrax Vaccine Adsorbed (AVA) is the only US FDA-approved vaccine in the United States for [prevention of anthrax](#) in humans. In 1999, CDC started the Anthrax Vaccine Research Program (AVRP) to study the safety of the vaccine and to measure its ability to provoke an immune response against anthrax.

The first large-scale use of the vaccine to give preexposure protection was in 1991 for US military personnel deployed during the Persian Gulf War. In 1998, the Department of Defense (DoD) began the Anthrax Vaccine Immunization Program (AVIP), a mandatory anthrax vaccination program to protect US forces assigned to areas deemed to be at high risk for weaponized *B. anthracis* attack. Early on, some members of the armed forces expressed concern that the vaccine could have health effects. Facing concerns over both the need to protect military personnel against the threat of biological weapons and the fears about the vaccine, in 1999 the US Congress directed CDC to develop the AVRP to study the safety of the vaccine and its effectiveness.

In the fall of 2001, the intentional release of *B. anthracis* spores resulted in 5 deaths from inhalation anthrax and the possible exposure of more than 30,000 people. The event confirmed the urgency of the research and demonstrated the need for studies related to the possible postexposure treatment use of the vaccine.

## Objectives:

The clinical trial assessed the safety and serological noninferiority of reduced schedules and a comparison of subcutaneous (SC) and intramuscular (IM) routes of administration.

## Key Notes from the AVRP

- The vaccine is safe and effective for the approved indications.
- AVA is the only FDA-approved anthrax vaccine in the United States.
- Administering the vaccine into the muscle mass reduces the common adverse reactions and improves the safety profile.
- Administering the vaccine with the optimized schedule demonstrated effective protection up to 4 years in nonhuman primates.
- Rigorous statistical analysis showed measurable signs of immunity in nonhuman primates.
- Immune system responses to the vaccine in humans are analogous to protective immunity profiles in nonhuman primates.
- Data from human and nonclinical studies indicate the feasibility of preexposure prophylaxis (PrEP) booster schedule reduction.
- Postexposure prophylaxis (PEP) approval of AVA in 2015 demonstrates first use of the 'animal rule' for vaccine approval. The animal rule allows animal efficacy data to be used as a basis for approval when human efficacy studies are not ethical or feasible.
- There is a need for a low-cost, single-dose anthrax vaccine for emergency response.
- Next-generation anthrax vaccines are still in development.

## Summary of AVRP

Jarad M. Schiffer, Michael M. McNeil & Conrad P. Quinn. [Recent developments in the understanding and use of anthrax vaccine adsorbed: achieving more with less](#) [13 pages]. Expert Review of Vaccines. 2016 March.

## More Resources

Quinn et al. [Humoral and Cell-Mediated Immune Responses to Alternate Booster Schedules of Anthrax Vaccine Adsorbed in Humans](#) [13 pages] Clinical and Vaccine Immunology. 2016 April;23 (4). [Humoral and Cell-Mediated Immune Responses – Supplemental Data](#) [28 pages]

Schiffer et al. [Bridging non-human primate correlates of protection to reassess the Anthrax Vaccine Adsorbed booster schedule in humans](#) [8 pages] Vaccine. 2015 May; 33.

- Wright et al. [Effect of reduced dose schedules and intramuscular injection of anthrax vaccine adsorbed on immunological response and safety profile: A randomized trial](#) [10 pages] *Vaccine*. 2014; 32.
- Chen et al. [Comprehensive Analysis and Selection of Anthrax Vaccine Adsorbed Immune Correlates of Protection in Rhesus Macaques](#) [9 pages] *Clinical and Vaccine Immunology*. 2014 November; 21 (11). COP NHP Supplemental [34 pages]
- Ovsyannikova et al. [Human Leukocyte Antigens and Cellular Immune Responses to Anthrax Vaccine Adsorbed](#) [9 pages] *Infection and Immunity*. 2013 July; 81 (7). [HLA homozygosity associations with antibody responses to anthrax protective antigen – Supplemental Table](#) [2 pages]
- Fay et al. [Anthrax Vaccine–Induced Antibodies Provide Cross-Species Prediction of Survival to Aerosol Challenge](#) [12 pages] *Science Translation Medicine*. 2012 September; 4 (151).
- Quinn et al. [A Three-Dose Intramuscular Injection Schedule of Anthrax Vaccine Adsorbed Generates Sustained Humoral and Cellular Immune Responses to Protective Antigen and Provides Long-Term Protection against Inhalation Anthrax in Rhesus Macaques](#) [17 pages] *Clinical and Vaccine Immunology*. 2012 November; 19 (11). [HLA homozygosity associations with antibody responses to anthrax protective antigen – Supplemental Table](#) [2 pages]
- Pajewskia et al. [A genome-wide association study of host genetic determinants of the antibody response to Anthrax Vaccine Adsorbed](#) [7 pages] *Vaccine*. 2012 May; 30.
- Semenova et al. [Validation and long term performance characteristics of a quantitative enzyme linked immunosorbent assay \(ELISA\) for human anti-PA IgG](#) [12 pages] *Journal of Immunological Methods*. 2012; 376.
- Soroka et al. [A two-stage, multilevel quality control system for serological assays in anthrax vaccine clinical trials](#) [9 pages] *Biologicals*. 2010 September.
- Clement et al. [Vaccination of Rhesus Macaques with the Anthrax Vaccine Adsorbed Vaccine Produces a Serum Antibody Response That Effectively Neutralizes Receptor-Bound Protective Antigen In Vitro](#) [10 pages] *Clinical and Vaccine Immunology*, 2010 Nov, 17 (11).
- Marano et al. [Effects of a Reduced Dose Schedule and Intramuscular Administration of Anthrax Vaccine Adsorbed on Immunogenicity and Safety at 7 Months](#) [12 pages] *The Journal of the American Medical Association*. 2008 Oct; 300 (13).
- Li et al. [Standardized, mathematical model-based and validated in vitro analysis of anthrax lethal toxin neutralization](#) [19 pages] *Journal of Immunological Methods*. 2008; 333.
- Semenova et al. [Analysis of anti-protective antigen IgG subclass distribution in recipients of anthrax vaccine adsorbed \(AVA\) and patients with cutaneous and inhalation anthrax](#) [10 pages] *Vaccine*. 2006 Nov; 25.
- Quinn et al. [Immune Responses to Bacillus anthracis Protective Antigen in Patients with Bioterrorism-Related Cutaneous or Inhalation Anthrax](#) [9 pages] *The Journal of Infectious Diseases*. 2004 Oct; 190 (7).
- Semenova et al. [Mass Value Assignment of Total and Subclass Immunoglobulin G in a Human Standard Anthrax Reference Serum](#) [5 pages] *Clinical and Diagnostic Laboratory Immunology*. 2004 April; 11 (5).
- Quinn et al. [Specific, Sensitive, and Quantitative Enzyme-Linked Immunosorbent Assay for Human Immunoglobulin G Antibodies to Anthrax Toxin Protective Antigen](#) [8 pages] *Emerging infectious Diseases*. 2002 Oct; 8 (10)

