



Anthrax Vaccine Adsorbed (AVA) : a Human Reactogenicity and Immunogenicity Clinical Trial

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AVA elicits an antibody response against the protective antigen (PA) of *B. anthracis* when given by subcutaneous (SQ) injection. A multi-site, randomized placebo-controlled clinical trial is underway to compare SQ vs. intramuscular routes of administration and determine the number of priming/boosting doses necessary for protective immunity. The principal immunogenicity endpoints are a 4-fold rise in anti-PA IgG titer and geometric mean concentrations; the principal reactogenicity endpoints are injection site reactions. A total of 1,564 volunteers were enrolled at 5 clinical trial sites between May 2002 and March 2004. Subjects were randomized to 6 regimens of 8 injections over 43 months. Serologic assays were developed and standardized to compare immune responses in humans and animal models with lethal challenge for functional corroboration. The research program also prepared cGMP bulk volume human reference serum. Consistent with prior clinical experience, AVA has been well tolerated in this trial, with 85 Serious Adverse Events reported to FDA, all deemed unrelated or unlikely to be related to study injections. Anti-PA IgG ELISA assays have performed well: lower limit of detection -0.06 $\mu\text{g}/\text{mL}$; lower limit of quantification -3.0 $\mu\text{g}/\text{mL}$; diagnostic sensitivity -97.6%; diagnostic specificity -94.2%; goodness of fit (r^2) -0.99; intra-assay precision -8.5%; and inter-assay precision -17%. The clinical trial will optimize the vaccination regimen, thus enhancing use and acceptability by the military and civilian community. Our laboratory provides standardized and validated serological assays for characterization of human response to anthrax vaccines and serves as a bridge to the development of second generation anthrax vaccines.