Sample size calculations

Sample size calculations were based on immunogenicity endpoints using variance estimates (anti-PA IgG GMC) from the USAMRIID pilot study (*ref*); a one-sided non-inferiority model for statistical comparisons of the licensed AVA route and regimen to modified AVA route and regimens, and estimated participant attrition during the study period.

Preliminary sample size calculations were also done using proportions of > 4-fold rise in anti-PA IgG antibody titer, reactogenicity endpoints based on data from the USAMRIID pilot study, and risk factors for adverse experiences endpoints, but calculations based on anti-PA IgG GMC yielded the most conservative (i.e., largest) group size and were therefore utilized. For the purposes of this study the Sponsor (CDC) and FDA jointly developed the criteria for the one-sided non-inferiority mode. Estimates for participant attrition were obtained from study sites based on previous vaccine studies of similar duration in adults, although the number of such studies is quite limited.

With this model, the null hypothesis was: study group 2, 3, 4, or 5 will have a significantly lower GMC than the licensed vaccine regimen represented by study group 1. The alternative hypothesis is that study group 2, 3, 4, or 5 are non-inferior to study group 1. If the null hypothesis is rejected then we may conclude, with stated power and level of significance, that study group 2, 3, 4, or 5 are non-inferior to study group 1 in terms of GMC.

The following calculations detail the necessary number of participants needed within each group to have the specified power to reject the null hypothesis of inferiority. In this study we proposed a one-sided, non-inferiority hypothesis. The criterion specified is to consider the ratio of GMCs of the reference group (licensed route and dosage schedule) to a test group (modified route and dosage schedule) to be non-inferior if the upper 97.5% confidence bound for this ratio is less than 1.5. This led to the following hypothesis:

The null hypothesis, H0: GMCr / GMCt >= 1.5 (Inferior)
The alternative hypothesis, H1: GMCr/ GMCt < 1.5 (Non-inferior)
where r = study group 1; t = study group 2,3, 4, or 5.
Reject H0 when the 97.5% upper confidence bound for the ratio (GMCr / GMCt) is < 1.5.

Sample size calculations were based on formulas derived from Schuirmann[1] and further discussed by Phillips.[2] Calculations were made assuming a common $\log_{10}$ standard deviation equaling 0.45 $\log_{10}$ units for each study group. This standard deviation was determined from data collected in the USAMRIID pilot study[3]. Standard deviations were calculated for each time point in the USAMRIID study for the 3 study groups (N = 80). The 75th percentile of standard deviations was 0.45. It is believed this estimate will adequately describe the variability of the $\log_{10}$ anti-PA IgG in the present study, which will enroll a much larger cohort. The sample size has been adjusted to account for two separate analyses.

A 95% one-sided hypothesis test was applied with 80% power; this was adjusted for two analyses. These calculations yielded a group size of 126 participants. The sample size was inflated 100% to 252 and rounded to 260 to account for loss to follow-up and temporary protocol noncompliance.

Sample Size and Power Calculations for Reactogenicity

The primary hypothesis for reactogenicity was: AVA administered by the IM route results in reactogenicity that is decreased compared to that of SQ administration. The reactogenicity power calculations were based on the following endpoint: a dichotomous measurement that refers to the presence or absence of any AE regardless of causality after a given injection as observed during in-clinic evaluations. The sample size and power calculations were for the per-dose analysis comparing the licensed regimen given SQ (study group 1) to the 8-dose regimen given IM (study group 2). The USAMRIID study[3] found that 44% of study participants experienced subcutaneous nodules after the first dose of AVA administered SQ; while no subcutaneous nodules were experienced by participants administered AVA by the IM route. Assuming power = 80% and a two-sided alpha level = 0.05, a minimum of 19 participants in each group would be needed to detect a difference for this study. The 126 per group sample size will therefore be adequate to detect the majority of differences that will be measured in the present study.

Initial data acquired from the USAMRIID pilot study[4] also indicated sample size of 126/group to be adequate to detect the majority of sex-based differences which were reported in that study.

Recruitment of Study Participants

Study centers included Walter Reed Army Institute of Research, Silver Spring, MD; Baylor College of Medicine, Houston, TX; Emory University School of Medicine, Atlanta, GA; Mayo Clinic, Rochester, MN and University of Alabama at Birmingham, Birmingham, AL.

Site investigators and their respective study personnel recruited potential participants in compliance with the International Conference on Harmonization Good Clinical Practices. Recruitment methods included distribution of printed materials about the trial to specifically targeted groups, bulletin board announcements and lectures, or use of appropriate local media such as newspaper advertisements. Upon request potential participants were provided written description of the study and had the opportunity to ask questions about it.

Interested persons were provided the Informed Consent document to review along with the opportunity to ask additional questions generated following review of that document. Upon deciding to enroll they were asked to sign and date the Informed Consent Document and provided a copy. Once Informed Consent was obtained, a relevant medical history was taken to assist the site investigator in determining a potential participant's eligibility.

Potential participants underwent an initial, limited physical examination which included height, weight, blood pressure, temperature, upper extremity and axillary lymph node exam, and other systems, if indicated by the participant's history. Women of childbearing potential underwent a standard urine pregnancy test (which was repeated prior to each vaccination).

Determination of Eligibility

In order to enroll, persons had to meet all appropriate inclusion criteria and be free of all exclusion criteria. The medical history and a baseline physical examination were the basis for determining eligibility, which was confirmed by reviewing an inclusion/exclusion checklist.

Inclusion criteria for this study included: to have read and signed the Informed Consent Document; be female or male, 18 to 61 years old (up to 62nd birthday); females could not be pregnant, not plan to become pregnant for the duration of the study, and agree to exercise adequate birth control from the time of the screening procedures to one month after the last vaccination; be willing and able to return for all follow-up visits and blood collections for the duration of the study; be able to understand and comply with planned study procedures; agree to complete the Participant Diary and to

report concomitant medications and AEs during the study period; and have two intact upper arms with sufficient subcutaneous and intramuscular tissue in the deltoid regions for vaccine administration. Potential participants with a history of the following conditions were eligible for study enrollment: gestational diabetes; treated, controlled, uncomplicated hypertension; history of coronary artery disease who were asymptomatic and on a stable medical regimen, and under the care of a physician; treated hypo- or hyperthyroidism; cured nonmetastatic cancer; disease-free for 5 years (excluding hematologic malignancies); localized skin cancer, resected (including squamous cell and basal cell carcinomas, participants with a history of melanoma must be disease-free for 5 years); exercise-induced bronchospasm; mild asthma, and persons using low to medium doses of inhaled steroids

Exclusion criteria for this study included: prior history of anthrax or immunization against anthrax; known allergy to aluminum hydroxide, formaldehyde, benzethonium chloride, or latex; being pregnant or having or plans to become pregnant for the duration of the study, not agreeing to exercise adequate birth control from the time of the screening procedures to one month after the last vaccination; receipt of experimental products within 30 days prior to study entry or plans to receive experimental products within 60 days after study entry; receipt of a live vaccine outside this trial within 30 days prior to study entry or receipt of an inactivated vaccine outside this trial within 14 days prior to study entry; plans to receive a live vaccine outside this trial within 60 days after study entry or plans to receive an inactivated vaccine outside this trial within 42 days after study entry; received immunosuppressive therapy within 30 days prior to study entry or plans to receive immunosuppressive therapy within 60 days after study entry; used cytotoxic therapy in the previous 5 years or plans to receive cytotoxic therapy within 60 days after study entry; received parenteral immunoglobulin or blood products within three months of study or plans to receive parenteral immunoglobulin or blood products within 60 days after study entry; has an active malignancy or history of metastatic or hematologic malignancy; has current diabetes; has cardiovascular disease with a significant likelihood of progression over 5 years, including any person with a history of cardiomyopathy or congestive heart failure; has moderate to severe asthma, chronic obstructive pulmonary disease, other significant pulmonary disease; was taking high doses of inhaled steroids; had clinically recognized hepatic or renal insufficiency; had inflammatory, vasculitic, or rheumatic disease including systemic lupus erythematosis, polymyalgia rheumatica and rheumatoid arthritis, scleroderma; had known HIV, hepatitis B or hepatitis C infection; had other conditions known to produce or be associated with immune suppression; had neuropathy or other evolving neurologic condition; was nstable and/or had moderate to severe mental illness; had ongoing drug abuse/dependence (including alcohol); and had a seizure disorder.

In addition to the conditions listed above, moderate or severe illness and/or oral temperature >100.4˚F within 3 days of injection or chronic condition that, in the opinion of the investigator, would render injection unsafe or would interfere with evaluations would be considered a temporary exclusion criterion. When participants developed one of the exclusionary criteria after starting the study they were either temporarily suspended or discontinued from receiving further injections; the decision was made based upon the presenting criteria. All suspended or discontinued participants were encouraged to continue AE follow up; however, we did not analyze data from these participants in this analysis.

Randomization and blinding

The Sponsor (CDC) statistician created five separate and non-overlapping lists of sequential four digit study identification numbers; each list was further divided into male and female study identification numbers to facilitate monitoring sex-specific enrollment at each site. The lists were provided to the contract research organization (CRO) for group assignment using a random assignment technique. The master list of site- and sex-specific study identification numbers and group assignments was reviewed by the DSMB Statistician prior to distribution to the unblinded study monitor at the sites. The unblinded study staff member had access to the site assignment list, prepared and labeled syringes, and administered injections. Unblinded staff members did not interact with participants for reactogenicity monitoring and

follow-up; blinded study staff members performed all reactogenicity monitoring and follow-up. The master and site-specific lists of study identification numbers and group assignments were not be shared with the study Sponsor.

Following informed consent document and screening, a candidate began the enrollment process. Participants were sequentially assigned participant IDs, and therefore study group assignments, as they enrolled.

Only unblinded study site and CRO personnel were aware of group assignments; all other study site, CRO and all Sponsor staff were blinded to group assignment until after the final report was submitted to FDA. All analyses were conducted using masked id numbers so that data could be analyzed and reported by study group, but the status of individual participants could remain blinded.

The first injection and blood draw occurred on the day of enrollment.

Reactogenicity

An adverse event (AE) was defined as any reaction, side effect, or untoward event that occurred during the course of the clinical trial, whether or not the event was considered related to the investigational agent or clinically significant. For this study, AEs included events reported by the subject, as well as abnormal findings on clinic examinations, or positive pregnancy tests. A new illness, symptom, sign, or clinically significant clinical laboratory abnormality or worsening of a pre-existing condition or abnormality was considered an AE. Stable chronic conditions such as mild asthma or gestational diabetes where were present prior to entry into the trial and did not worsen were not considered AEs. Each adverse event was classified as serious or non-serious. Based on the seriousness of the AE, appropriate reporting procedures were followed.

Solicited AEs were specific AEs that were expected to occur during a 28-day period following AVA administration. The presence or absence of these AEs was systematically evaluated at both in-clinic evaluations and at home by participants. Solicited AEs included injection site AEs (warmth, tenderness, itching, pain, arm motion limitation, erythema, induration, edema, nodule formation, and bruise) as well as systemic AEs (fatigue, muscle ache, headache, fever, axillary adenopathy).

Two safety datasets were analyzed, in-clinic exam data only, and AE summary data. AE Summary Data included in-clinic, diary and any other reporting sources. In-clinic data is reported in the manuscript with AE summary data comparisons presented in the supplemental material.

AEs were scored by participants as mild (no interference with routine activities, or temperature <102.3°F), moderate (interfered with routine activities, or temperature between 102.3-104°F), or severe (incapacitating, or temperature >104°F). Serious adverse events (SAEs) were classified according to US regulations as those resulting in: death, a life-threatening event, initial inpatient hospitalization or prolongation of hospitalization, significant or persistent disability/incapacity, congenital anomaly/birth defect, and a medical event that required medical or surgical intervention to prevent one of the other outcomes. While remaining blinded to the participant's study status, the DSMB Medical Monitor and site PI assessed the causal relationship using the World Health Organization causality assessment criteria.

Additional analyses: Analyses of AE summary data showed similar results to the in-clinic analyses for injection site AE comparisons between IM and SQ, but the overall AE frequencies were higher for the summary data. Mantel-Haenszel analyses comparing ordinal AE duration data (0, 1-3 and >3 days) using AE summary data demonstrated that injection site AEs in the IM group were generally of shorter duration when compared to SQ (warmth, tenderness, itching, AML, erythema, swelling / lump, bruise, fatigue, and headache, p-values < 0.01) (Table 5). Logistic model analyses of severity

demonstrated that 5.7% of individuals in the IM group experienced fewer moderate and severe injection site AEs compared to 10.7% of SQ recipients (OR=0.53, $p < 0.01$).

Analyses of systemic AE summary data showed similar results to the in-clinic analyses except that muscle ache was not significantly higher among IM recipients (OR=1.13, p=0.17). AE summary data indicated that fever was not significantly affected by route of administration (OR = 0.69, p=0.10)).

Differences in systemic AEs were consistent when AE summary data were analyzed, which also demonstrated that occurrence of fever was not significantly different between males and females (OR=1.26, p=0.24).

References:

1. Schuirmann, D.J. *A comparison of the two one-sided tests procedure and the power approach for assessing the equivalence of average bioavailability.* J Pharmacokinet Biopharm. 1987. **15**: p. 657-80.

2. Phillips, K.F. *Power of the two one-sided tests procedure in bioequivalence.* J Pharmacokinet Biopharm. 1990. **18**: p. 137-44.

3. Pittman, P.R., Kim-Ahn, G., Pifat, D.Y., et al. *Anthrax vaccine: immunogenicity and safety of a dose-reduction, route-change comparison study in humans.* Vaccine. 2002. **20**(9-10): p. 1412-20.

4. Pittman PR, Mangiafico JA, Rossi CA, et al. Anthrax vaccine: increas¬ing intervals between the first two doses enhances antibody response in humans. Vaccine 2000;19(2-3):213–6.

		Serum Anti-PA IgG Responses (95% CI)*			TNA*	Serum Anti-PA IgG Responses (95% CI)*			TNA*
		Month 2				Month 2			
		Male				Female			
Group	Full study vaccination schedule	**GMC, µg/ml**	**GMT**	**4-Fold response in titer Response %**	**TNA ED50 Titer GMT (unadjusted)**	**GMC, µg/ml**	**GMT**	**4-Fold response in titer Response %**	**TNA ED50 Titer GMT (unadjusted)**
		Point estimate (95% CI) *N*¶				**Point estimate (95% CI) *N*¶**			

Supplemental Table 1. Serum anti-PA IgG antibody responses and TNA ED50 Stratified by Sex

Group	Full study vaccination schedule	Serum Anti-PA IgG Responses (95% CI)* Month 7 Male			TNA*	Serum Anti-PA IgG Responses (95% CI)* Month 7 Female			TNA*
		GMC, µg/ml	GMT	4-Fold response in titer Response %	TNA ED50 Titer GMT (unadjusted)	GMC, µg/ml	GMT	4-Fold response in titer Response %	TNA ED50 Titer GMT (unadjusted)
8 SQ	SQ; m 0, 0.5, 1, 6, 12, 18, 30, 42	83.8 (68.6, 102.4) *114*	938.1 (767.9, 1146.0) *114*	94.7 (88.9, 98.0) *114*	214.5 (166.4, 227.6) *54*	101.7 (83.9, 123.4) *121*	1121.4 (925.9, 1358.2) *121*	95.0 (89.5, 98.2) *121*	243.3 (186.6, 317.3) *58*
8 IM	IM; m 0, 0.5, 1, 6, 12, 18, 30, 42	67.0** (54.8, 81.8) *112*	736.2 (602.7, 899.3) *112*	87.5 (79.9, 93.0) *112*	211.5 (154.9, 288.7) *54*	102.5‡,** (85.0, 123.6) *122*	1138.9‡ (945.3, 1372.2) *122*	95.9‡ (90.7, 98.7) *122*	277.9‡ (214.1, 360.9) *49*
7 IM†	IM; m 0, 1, 6, 12, 18, 30, 42	37.3** (32.4, 42.9) *336*	417.3 (363.[illegible], 4[illegible]9.6) *336*	72.9 (67.8, 77.6) *336*	132.3 (110.2, 158.9) *158*	55.5** (48.7, 63.3) *362*	610.2 (535.9, 69[illegible]) *362*	84.3 (80.1, 87.9) *362*	207.4 (176.2, 244.0) *157*
5 IM†	IM; m 0, 1, 6, 18, 42								
4 IM†	IM; m 0, 1, 6, 42								
Placebo IM	IM; m 0, 0.5, 1, 6, 12, 18, 30, 42	1.9 (,)§ *118*	29 (,)§ *118*	0.0 (0.0, 3.1) *118*	18 (,)§ *63*	2.0 (1.9, 2.1) *125*	30.3 (28.5, 32.2) *125*	0.8 (0.0, 4.4) *125*	18 (,)§ *61*
Placebo SQ	SQ; m 0, 0.5, 1, 6, 12, 18, 30, 42								

		Point estimate (95% CI) *N*[¶]				**Point estimate (95% CI) *N*[¶]**			
8 SQ	SQ; m 0, 0.5, 1, 6, 12, 18, 30, 42	197.2 (160.7, 242.0) *103*	2183.5 (1779.2, 2679.5) *103*	100.0 (96.5, 100.0) *103*	1220.9 (942.5, 1581.4) *49*	198.7 (163.6, 241.3) *116*	2165.2 (1784.2, 2627.7) *116*	97.4 (92.6, 99.5) *116*	1341.8 (1046.3, 1720.7) *51*
8 IM	IM; m 0, 0.5, 1, 6, 12, 18, 30, 42	217.8[‡] (177.6, 267.0) *103*	2414.3[‡] (1969.0, 2960.2) *103*	98.1[‡] (93.2, 99.8) *103*	1693.1[‡] (1299.0, 2206.6) *55*	241.9[‡] (199.9, 292.7) *112*	2610.7[‡] (2159.3, 3156.4) *112*	99.1[‡] (95.1, 100.0) *112*	1563.3[‡] (1196.8, 2042.0) *50*
7 IM[†]	IM; m 0, 1, 6, 12, 18, 30, 42	192.7[‡] (167.2, 222.0) *302*	2124.9[‡] (1844.0, 2448.5) *302*	96.7[‡] (94.0, 98.4) *302*	1431.1[‡] (1178.5, 1740.3) *147*	214.8[‡] (188.2, 245.2) *334*	2333.3[‡] (2045.6, 2661.5) *334*	98.8[‡] (97.0, 99.7) *334*	1415.4[‡] (1198.4, 1671.6) *142*
5 IM[†]	IM; m 0, 1, 6, 18, 42								
4 IM[†]	IM; m 0, 1, 6, 42								
Placebo IM	IM; m 0, 0.5, 1, 6, 12, 18, 30, 42	1.9 (1.8, 2.1) *105*	30.0 (28.0, 32.2) *105*	1.00 (0.0, 5.2) *105*	18.3 (17.7, 18.8) *49*	1.93 (1.85, 2.0) *115*	29.5 (28.8, 30.2) *115*	0.0 (0.0, 3.2) *115*	18 (,)[§] *58*
Placebo SQ	SQ; m 0, 0.5, 1, 6, 12, 18, 30, 42								

		Serum Anti-PA IgG Responses (95% CI)[*]			**TNA[*]**	**Serum Anti-PA IgG Responses (95% CI)[*]**			**TNA[*]**
		Month 43				**Month 43**			
		Male				**Female**			
Group	Full study	**GMC, µg/ml**	**GMT**	**4-Fold**	**TNA ED50 Titer**	**GMC,**	**GMT**	**4-Fold**	**TNA ED50**

	vaccination schedule			response in titer Response %	GMT (unadjusted)	µg/ml		response in titer Response %	Titer GMT (unadjusted)
		Point estimate (95% CI) *N*[¶]				Point estimate (95% CI) *N*[¶]			
8 SQ	SQ; m 0, 0.5, 1, 6, 12, 18, 30, 42	217.2 (174.0, 271.2) *71*	2299.2 (1840.7, 2871.7) *71*	100.0 (94.9, 100.0) *71*	1037.7 (782.8, 1375.6) *31*	209.8 (169.2, 260.1) *73*	2190.4 (1768.0, 2713.8) *73*	100.0 (95.1, 100.0) *73*	991.2 (724.7, 1355.7) *29*
8 IM	IM; m 0, 0.5, 1, 6, 12, 18, 30, 42	281.3[‡] (226.5, 349.3) *77*	3019.1[‡] (2430.6, 3750.1) *77*	100.0[‡] (95.3, 100.0) *77*	1528.7[‡] (1142.1, 2046.2) *31*	353.1[‡] (287.3, 434.0) *79*	3756.7[‡] (3058.3, 4614.6) *79*	100.0[‡] (95.4, 100.0) *79*	1549.1[‡] (1194.3, 2009.1) *41*
7 IM[†]	IM; m 0, 1, 6, 12, 18, 30, 42	241.6[‡] (198.7, 293.8) *72*	2648.9[‡] (2176.4, 3224.0) *72*	100.0[‡] (95.0, 100.0) *72*	1522.7[‡] (1093.6, 2120.2) *30*	260.5[‡] (214.7, 316.0) *67*	2788.3[‡] (2298.2, 3383.0) *67*	100.0[‡] (94.6, 100.0) *67*	1372.5[‡] (940.8, 2002.2) *26*
5 IM[†]	IM; m 0, 1, 6, 18, 42	266.8[‡] (218.5, 325.7) *66*	2870.0[‡] (2348.1, 3507.9) *66*	98.5[‡] (91.8, 100.0) *66*	1891.9[‡] (1526.8, 2344.2) *37*	346.7[‡] (287.9, 417.5) *75*	3619.5[‡] (3005.7, 4358.6) *75*	100.0[‡] (95.2, 100.0) *75*	1857.1[‡] (1452.4, 2374.6) *30*
4 IM[†]	IM; m 0, 1, 6, 42	393.4[‡] (326.0, 474.8) *81*	4337.4[‡] (3591.5, 5238.2) *81*	98.8[‡] (93.3, 100.0) *81*	2313.5[‡] (1675.1, 3195.1) *38*	466.1[‡] (387.1, 561.2) *76*	4938.3[‡] (4101.9, 5945.2) *76*	100.0[‡] (95.2, 100.0) *76*	3707.6[‡] (2393.5, 5743.0) *28*
Placebo IM	IM; m 0, 0.5, 1, 6, 12, 18, 30, 42	1.85 (,)[§] *66*	29 (,)[§] *66*	0.0 (0.0, 5.4) *66*	18 (,)[§] *32*	1.87 (1.83, 1.91) *73*	29 (,)[§] *73*	0.0 (0.0, 4.9) *73*	18 (,)[§] *34*
Placebo SQ	SQ; m 0, 0.5, 1, 6, 12, 18, 30, 42								

CI= confidence interval; GMC= geometric mean concentration; GMT= geometric mean titer; IM= intramuscular route; PA= protective antigen; SQ=subcutaneous route; TNA= toxin neutralizing activity; ED50 = Effective Dilution 50%

* Geometric means and CIs were adjusted for study site, age group, sex, race and significant interactions. Geometric means and CIs for the control group, TNA ED50, and titer fold response proportions and CIs were stratified by time period.

† The 7 IM, 5 IM, and 4IM groups were combined for this analysis

‡ Non-inferiority was achieved 4 weeks following study agent injection if the upper bound of the 95% CI for the ratio of the geometric means of the 8-SQ group to that of the test groups was less than 1.5 and if the analogous upper bound for the differences in proportions of 4-fold response was less than 0.10

§ All values were the same (i.e., the lower limit of quantification); as a result the variance is 0 and the confidence intervals are undefined

¶ Number of participants per group at time point

** Statistically significant difference occurred between male and female; see Supplemental Table for full data, including p-value

To calculate geometric mean concentrations and titers, IgG concentrations and titers below the LLOQ (Lower Limit of Quantification) were set to ½ LLOQ, or1.85 µg/ml and 1/29 respectively. 4-fold responses for participants <LLOQ were defined at 4 times the LLOQ. TNA ED50 Titers below the LLOQ were set to ½ LLOQ titer of 18

Thresholds: ELISA - <20 ug/ml vs >= 20 ugs/ml; IgG titer - <240 vs >= 240; TNA ED50 - <160 vs >=160

Less than 3.3% of the ATP data were missing at any one time point; missing data were not imputed.

Supplemental Table 2. Geometric Mean Antibody Concentration (GMC) By Age Categories And Study Arm

Study Arm	<30 years	30-<40 years	40-<50 years	≥50 years
	GMC (mcg/ml) 95% CI *N*			
	Month 2			
8 SQ	125.6 (99.9, 157.9) *74*	110.2 (81.4, 149.3) *39*	81.7 (65.3, 102.3) *76*	73.8 (55.4, 98.2) *46*
8 IM	119.3 (92.8, 153.3) *60*	102.34 (77.9, 134.5) *48*	63.4 (50.6, 79.3) *75*	71.3 (54.3, 93.7) *51*
7 IM 5 IM 4 IM	70.7 (61.0, 82.0) *200*	54.5 (46.8, 63.3) *181*	40.8 (35.1, 47.4) *183*	28.0 (23.5, 33.4) *134*
	Month 7			
8 SQ	243.9 (192.7, 308.8) *66*	228.7 (168.4, 310.5) *38*	190.0 (151.5, 238.3) *73*	160.9 (120.0, 215.6) *42*
8 IM	315.8 (242.8, 410.6) *50*	247.2 (187.5, 326.0) *46*	188.1 (149.8, 236.3) *70*	205.5 (155.9, 270.8) *49*
7 IM 5 IM 4 IM	333.4 (285.9, 388.7) *172*	223.2 (191.3, 260.3) *166*	181.4 (155.8, 211.1) *174*	129.0 (107.7, 154.5) *124*
	Month 43			
8 SQ	270.5 (203.7, 359.3) *33*	238.2 (167.9, 337.9) *23*	195.3 (152.3, 250.3) *50*	181.2 (134.2, 244.8) *38*
8 IM	396.0 (292.1, 536.9) *29*	373.2 (276.8, 503.0) *34*	257.8 (203.1, 327.2) *58*	279.1 (206.8, 376.7) *35*
7 IM	355.4 (273.9, 461.0) *31*	255.0 (201.8, 322.2) *41*	240.5 (189.3, 305.6) *39*	195.9 (147.8, 259.6) *28*
5 IM	422.0 (325.5, 547.2) *31*	395.7 (311.2, 503.1) *38*	282.8 (223.6, 357.7) *40*	188.0 (143.9, 245.6) *32*
4 IM	792.3 (604.6, 1038.3) *28*	449.7 (351.9, 574.6) *36*	429.7 (351.6, 525.0) *63*	197.5 (150.3, 259.7) *30*

Supplemental Table 3. Geometric Mean Antibody Concentration (GMC) By Race Categories And Study Arm

Study Arm	White	Black	Other
	GMC (mcg/ml) 95% CI N		
	Month 2		
8 SQ	107.3 (93.2, 123.6) *184*	77.7 (57.4, 105.1) *40*	109.1 (61.0, 194.9) *11*
8 IM	92.7 (80.2, 107.1) *175*	64.0 (47.6, 86.0) *43*	131.7 (81.3, 213.2) *16*
7 IM 5 IM 4 IM	53.7 (49.4, 58.4) *524*	40.1 (34.0, 47.2) *141*	48.5 (34.8, 67.6) *33*
	Month 7		
8 SQ	216.5 (187.5, 249.9) *172*	211.6 (154.8, 289.1) *36*	252.7 (141.4, 451.5) *11*
8 IM	248.3 (214.3, 287.7) *163*	212.6 (156.5, 288.9) *37*	298.1 (182.8, 486.0) *15*
7 IM 5 IM 4 IM	232.7 (213.6, 253.6) *483*	188.3 (158.7, 223.5) *121*	238.7 (170.6, 334.0) *32*
	Month 43		
8 SQ	233.2 (199.2, 273.0) *120*	253.4 (174.7, 367.6) *19*	202.7 (98.7, 416.0) *5*
8 IM	320.1 (272.6, 375.8) *117*	394.6 (284.0, 548.5) *28*	382.1 (225.3, 648.0) *11*
7 IM	270.9 (235.6, 311.5) *108*	282.9 (211.9, 377.6) *25*	393.6 (219.7, 705.3) *6*
5 IM	320.9 (279.1, 369.0) *107*	381.9 (287.8, 506.7) *26*	414.1 (246.2, 696.6) *8*
4 IM	482.4 (422.7, 550.6) *123*	441.7 (339.2, 575.2) *31*	283.0 (129.5, 618.6) *3*