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## Report Title

Final Report on ACCELERATE ANTHRAX: CpG 7909 Vaccine Adjuvant Program

### ABSTRACT

A clinical study “Phase 1/2, Proof-of-Concept, Double-Blind, Randomized, Controlled Trial Assessing the Immunogenicity and Safety of Anthrax Vaccine Adsorbed (BioThrax?) Combined with CPG 7909 in Normal Volunteers” was completed and presented at the 2005 Interscience Conference on Antimicrobial Agents and Chemotherapy in a poster entitled “Marked Enhancement Of Antibody Response To Anthrax Vaccine Adsorbed With CPG 7909 In Healthy Volunteers“. The conclusions from this study included:

1. AVA plus CPG 7909 was reasonably well tolerated
2. There was a trend to greater frequency and severity of adverse events in the AVA plus CPG 7909 group compared to the AVA alone and CPG 7909 alone groups but this was not statistically significant
3. AVA plus CPG 7909 elicited a heightened (6 to 8-fold increase) and accelerated (21 to 24 days) antibody response ( $p < 0.001$ ) compared to AVA alone
4. AVA plus CPG 7909 elicited a positive anti-PA antibody response in  $>50\%$  of subjects within 14 days of a single immunization

A robust, large scale manufacturing process of CPG 7909 has been developed and is judged suitable for the supply of drug for further clinical studies and product commercialization.

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**List of papers submitted or published that acknowledge ARO support during this reporting period. List the papers, including journal references, in the following categories:**

**(a) Papers published in peer-reviewed journals (N/A for none)**

**Number of Papers published in peer-reviewed journals:** 0.00

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**(b) Papers published in non-peer-reviewed journals or in conference proceedings (N/A for none)**

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MARKED ENHANCEMENT OF ANTIBODY RESPONSE TO ANTHRAX VACCINE ADSORBED WITH CPG 7909 IN HEALTHY VOLUNTEERS

D. RYNKIEWICZ<sup>1</sup>, M. RATHKOPF<sup>2</sup>, J. RANSOM<sup>3</sup>, I. SIM<sup>4</sup>, L. GIRI<sup>5</sup>, J. QUINN<sup>2</sup>, T. WAYTES<sup>5</sup>, M. AL-ADHAMI<sup>4</sup>, W. JOHNSON<sup>6</sup>, C. NIELSEN<sup>7</sup> <sup>1</sup>V.A. & U. of Texas Health Science Center, San Antonio, TX; <sup>2</sup>Wilford Hall Medical Ctr, San Antonio, TX; <sup>3</sup>Fast Track Drugs & Biologics, Potomac, MD; <sup>4</sup>Coley Pharmaceutical Group, Wellesley, MA; <sup>5</sup>Emergent BioSolutions, Gaithersburg, MD; <sup>6</sup>USAMRIID, Ft. Detrick, MD; <sup>7</sup>Consultant to DARPA, Arlington, VA

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**Number of Manuscripts:** 0.00

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**Number of Inventions:**

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**Graduate Students**

NAME

PERCENT SUPPORTED

**FTE Equivalent:**

**Total Number:**

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**Names of Post Doctorates**

NAME

PERCENT SUPPORTED

**FTE Equivalent:**

**Total Number:**

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**Names of Faculty Supported**

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PERCENT SUPPORTED

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**Names of Under Graduate students supported**

NAME

PERCENT SUPPORTED

**FTE Equivalent:**

**Total Number:**

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**Names of Personnel receiving masters degrees**

NAME

**Total Number:**

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**Names of personnel receiving PHDs**

NAME

**Total Number:**

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**Names of other research staff**

NAME

PERCENT SUPPORTED

**FTE Equivalent:**

**Total Number:**

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**Sub Contractors (DD882)**

## **Inventions (DD882)**



# MARKED ENHANCEMENT OF ANTIBODY RESPONSE TO ANTHRAX VACCINE ADSORBED WITH CPG 7909 IN HEALTHY VOLUNTEERS

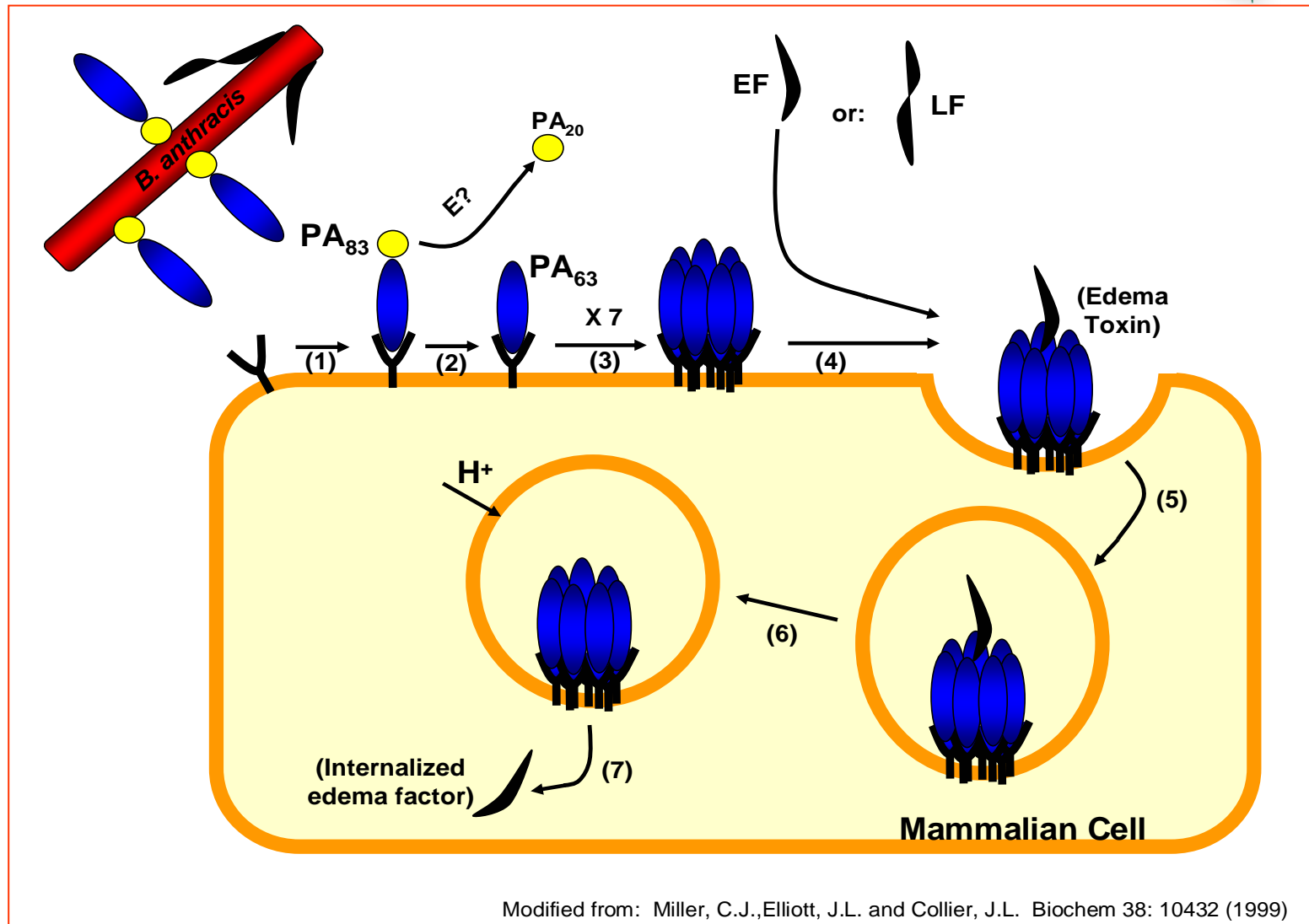
D. RYNKIEWICZ<sup>1</sup>, M. RATHKOPF<sup>2</sup>, J. RANSOM<sup>3</sup>, I. SIM<sup>4</sup>, L. GIRI<sup>5</sup>, J. QUINN<sup>2</sup>, T.  
WAYTES<sup>5</sup>, M. AL-ADHAMI<sup>4</sup>, W. JOHNSON<sup>6</sup>, C. NIELSEN<sup>7</sup>

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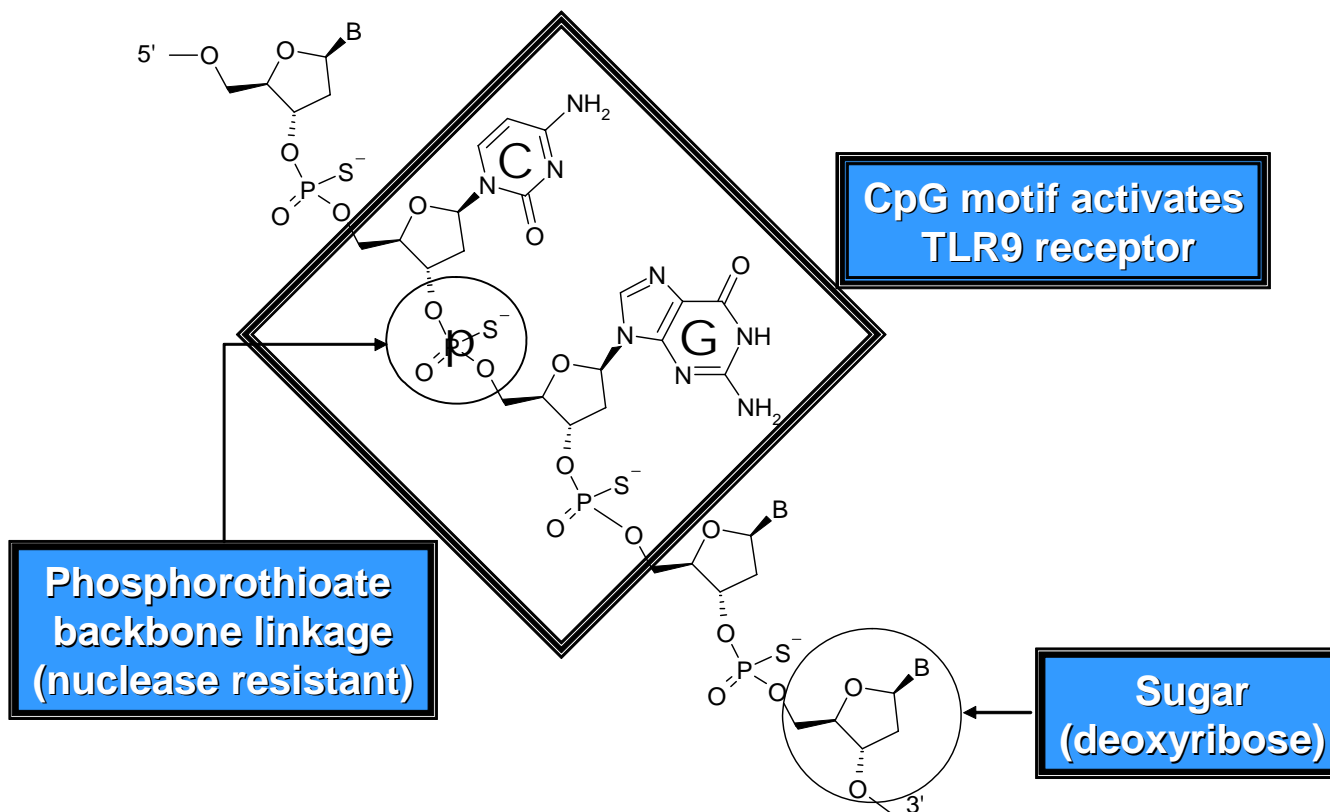
# ROLE OF PA IN ANTHRAX PATHOGENESIS



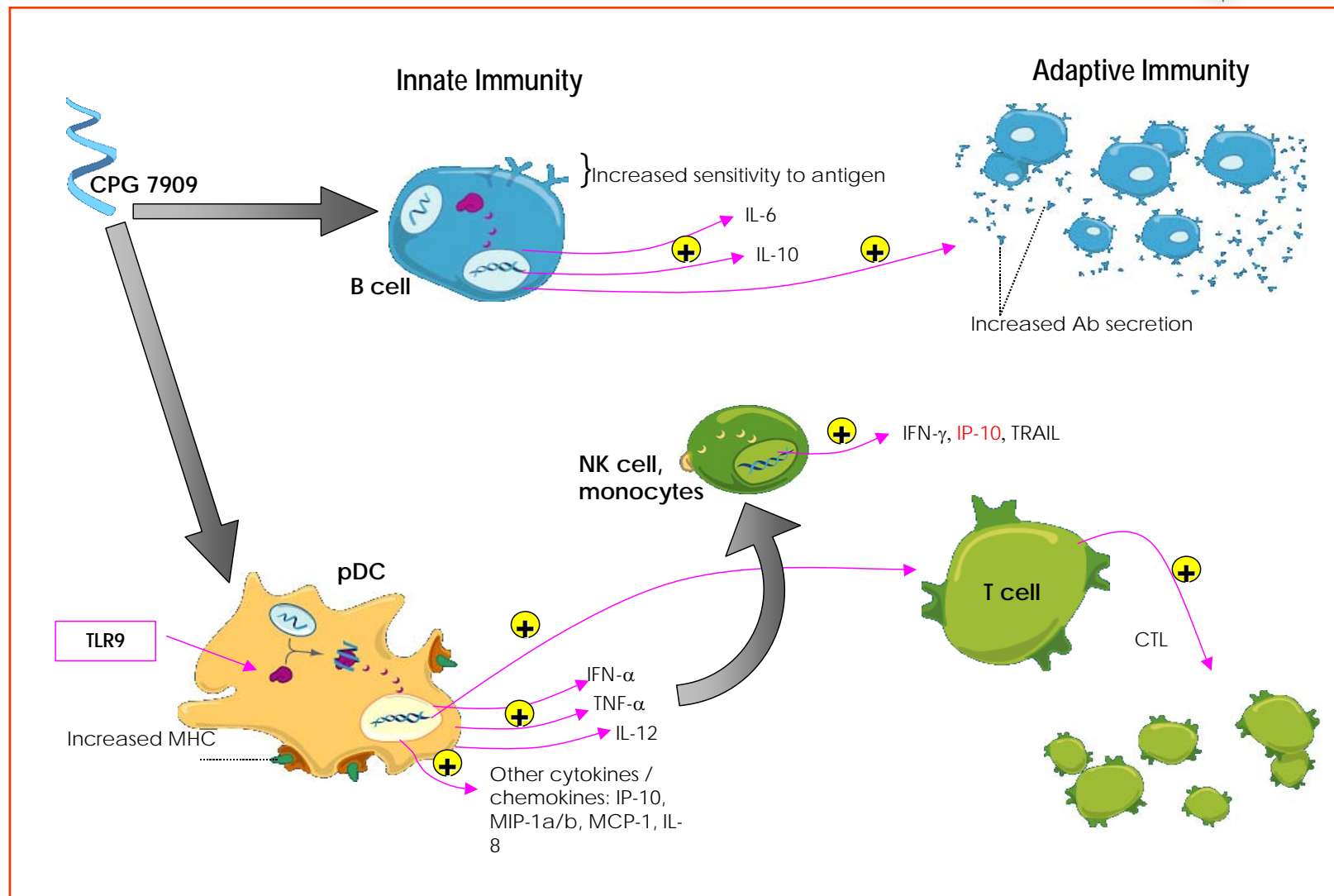
# CPG 7909 (VAXIMMUNE)



5' – TCGTCGTTTTGTCGTTTTGTCGTT – 3'



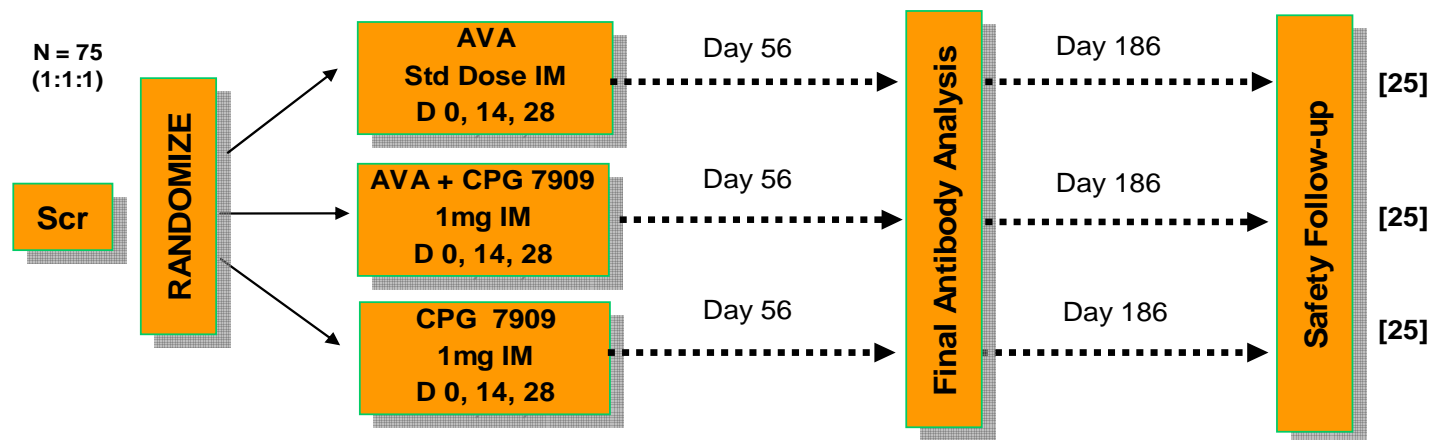
# MECHANISM OF ACTION OF CPG 7909





## ANTHRAX VACCINE ADSORBED PLUS CPG 7909 CLINICAL STUDY DESIGN

Phase I/II proof-of-concept, double blind, randomized, controlled trial in healthy volunteers



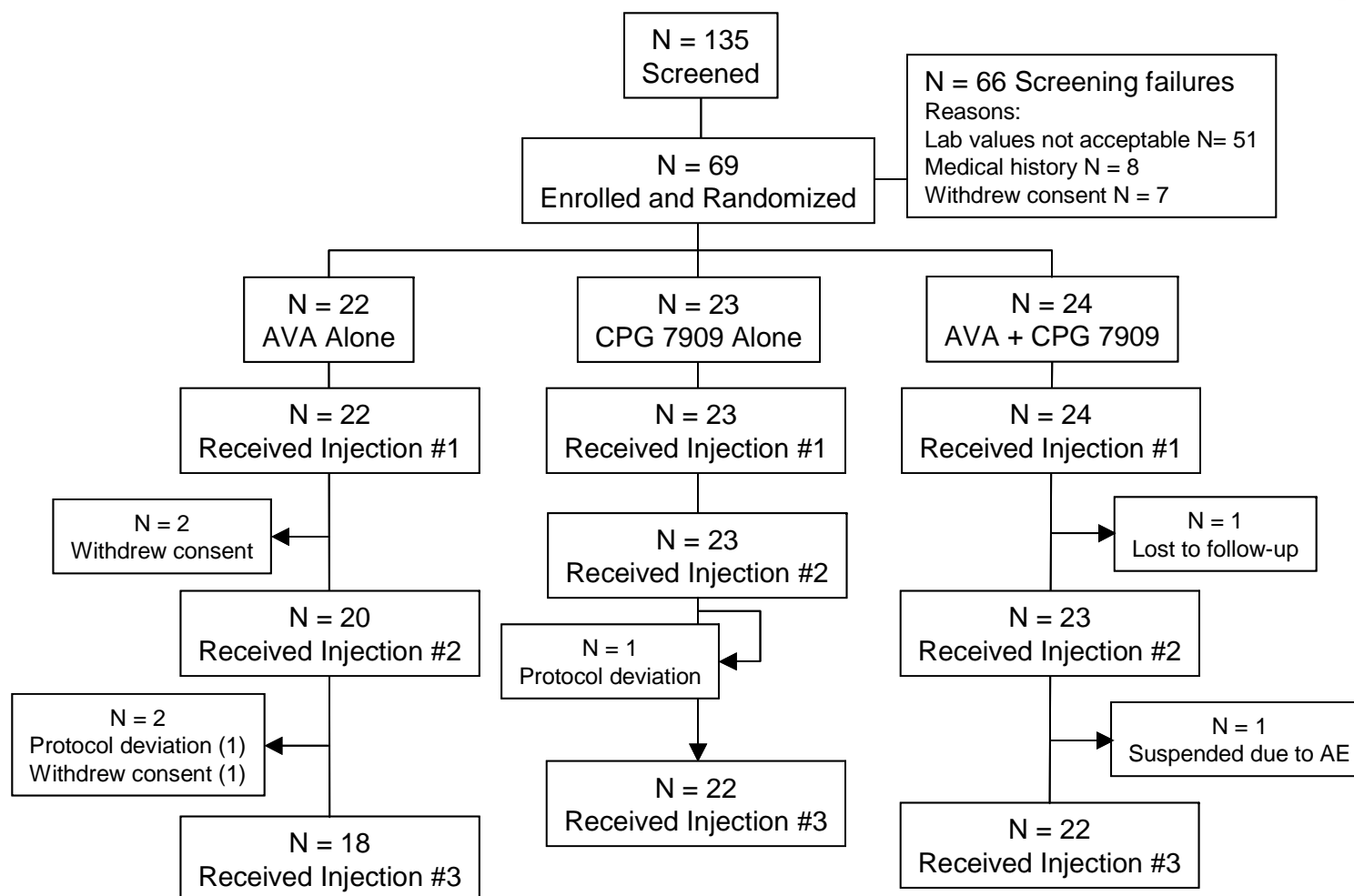
- Healthy volunteers, age 18-45 years, male and female, at 2 study sites
- Subjects received study treatment on days 0, 14 and 28
- Subjects assessed for anti-PA and anti-TNA antibody response on days 7, 10, 14, 16, 21, 24, 28, 30, 35, 42, 49, 56.
- Safety assessed before immunization and at least weekly in clinic through day 56 and at month 6, reviewed subject-maintained diaries

## Demographic Characteristics of All Randomized Subjects

Characteristic	AVA alone	CPG 7909 alone	AVA + CPG 7909	All 3 Groups
Gender – n	22	23	24	69
Male, n (%)	11 (50.0)	12 (52.2)	12 (50.0)	34 (49.3)
Age (at consent) – n	22	23	24	69
Mean (SD)	25.8 (5.8)	27.5 (4.7)	29.0 (6.7)	27.5 (5.9)
Median	24.0	26.0	27.5	26.0
Race – n (%)	22	23	24	69
White	18 (81.8)	18 (78.3)	18 (75.0)	54 (78.3)
Black/African	0 (0)	0 (0)	1 (4.2)	1 (1.5)
Amer.	1 (4.6)	1 (4.4)	4 (16.7)	6 (8.7)
Asian	0 (0)	1 (4.4)	0 (0)	1 (1.5)
Not specified	3 (13.6)	3 (13.0)	1 (4.1)	7 (10.1)
Others <sup>a</sup>				
Ethnicity – n (%)	22	23	24	69
Non-Hispanic	17 (77.3)	15 (65.2)	21 (87.5)	53 (76.8)
Hispanic or Latino	5 (22.7)	8 (34.8)	3 (34.8)	16 (23.2)

<sup>a</sup>Others include those who reported a race that was not listed on the demographics case report form or who reported multiple races. Races not represented were excluded from the table listing.

# DISPOSITION OF TRIAL SUBJECTS



# SUMMARY OF EFFICACY



**Mean peak antibody concentration was 6.3-fold (anti-PA) and 8.8-fold (TNA) greater in the AVA plus CPG 7909 group, both  $p < 0.001$**

**The maximum anti-PA concentration (220 $\mu$ g/mL) achieved in the AVA group (median time 42.5 days) was achieved 21 days earlier in the AVA plus CPG 7909 group ( $p < 0.001$ )**

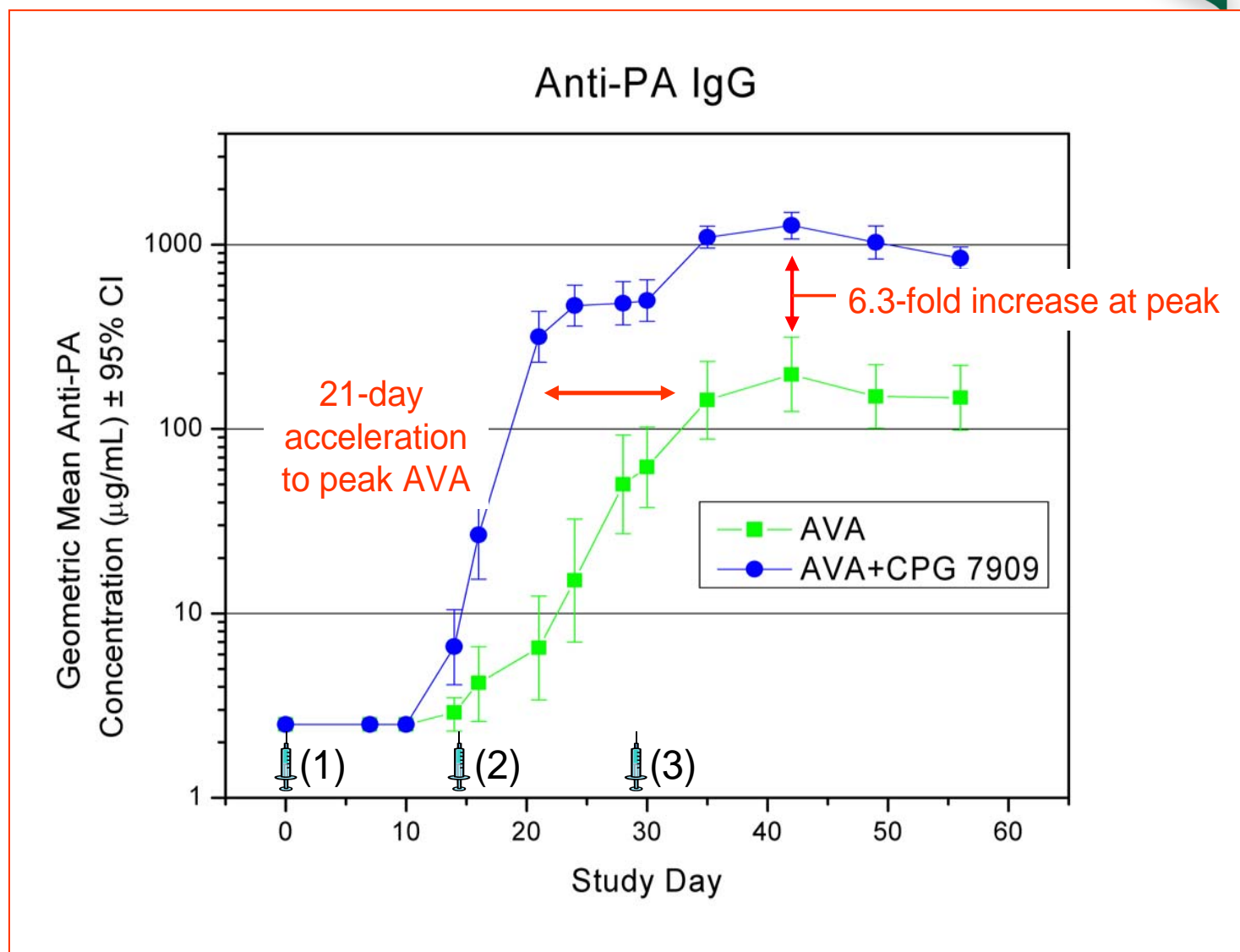
**The maximum TNA concentration (159 $\mu$ g/mL) achieved in the AVA group (median time 46 days) was achieved 24 days earlier in the AVA plus CPG 7909 group ( $p < 0.001$ )**

**12 of 22 (55%) of subjects in the AVA plus CPG 7909 group were seropositive for anti-PA after a single immunization (day 14) compared to 2 of 18 (11%) of subjects in the AVA alone group**

**Significant difference in the geometric mean anti-PA antibody concentrations between the AVA and AVA plus CPG 7909 arms first detected at Day 14 ( $p < 0.001$ )**

**At peak response, 22/22 (100%) subjects in the AVA plus CPG 7909 group achieve an anti-PA concentration of  $\geq 220\mu$ g/mL compared to only 11/18 (61%) of subjects in the AVA alone group**

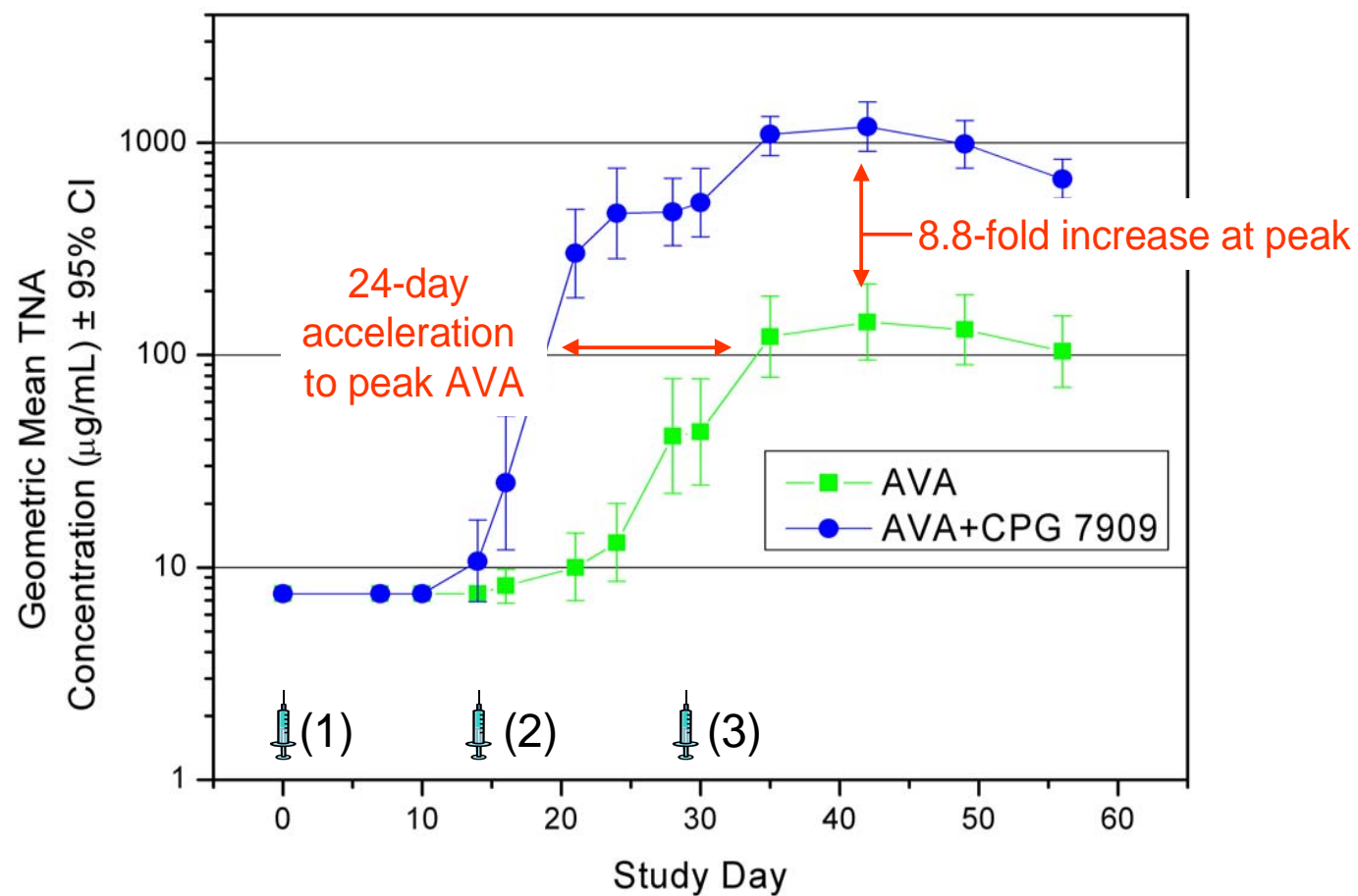
# RESPONSE TO ANTRAX PA (ELISA)



# TNA RESPONSE



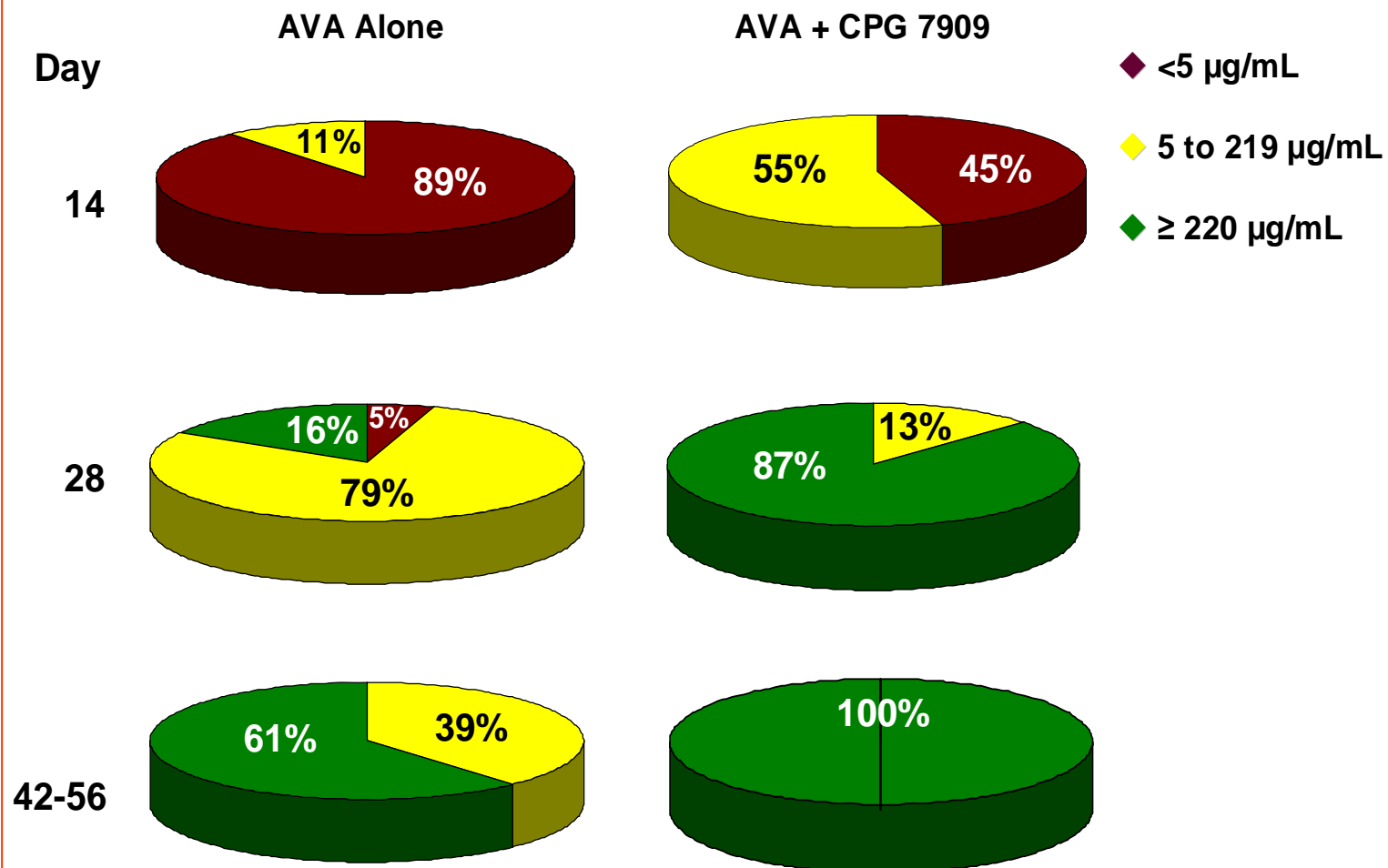
## Toxin Neutralizing Antibody (TNA)



# RATE OF SEROCONVERSION



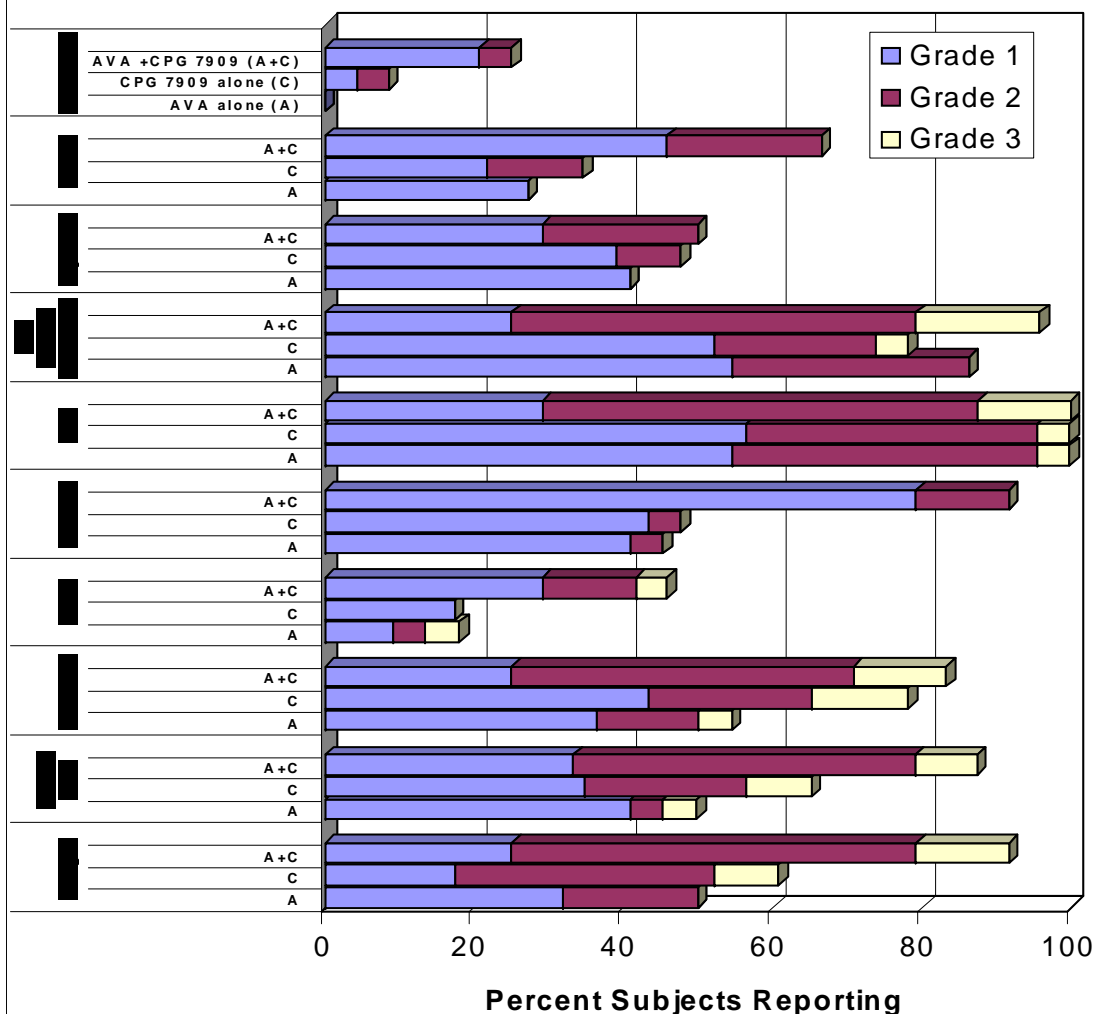
## Proportion of Subjects with Anti-PA IgG Response



# SAFETY



## Local and Systemic Adverse Events\*



\* Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers  
Enrolled in Preventive Vaccine Clinical Trials – FDA, April 2005

## LABORATORY FINDINGS

- No clinically significant changes in laboratory analyte levels were observed.
- Grade one leukopenia was seen in all study arms.
- Hypokalemia was reported in 50%, 43.5%, and 62.5 % of participants in the AVA, CPG 7909, and AVA + CPG 7909 groups, respectively, suggesting that potassium levels may have been affected by the combination treatment.



# CONCLUSIONS



## Safety

**AVA plus CPG 7909 was reasonably well tolerated**

**The local injection site reactions and systemic symptoms were expected and were the most common adverse events**

**There was a trend to greater frequency and severity of adverse events in the AVA plus CPG 7909 group compared to the AVA alone and CPG 7909 alone groups but this was not statistically significant**

## Immunogenicity

**AVA plus CPG 7909 elicited a heightened (6 to 8-fold increase) and accelerated (21 to 24 days) antibody response ( $p < 0.001$ ) compared to AVA alone**

**AVA plus CPG 7909 elicited a positive anti-PA antibody response in >50% of subjects within 14 days of a single immunization**