From: Ivins, Bruce E Dr USAMRIID
To: (b) (6) [redacted]
Subject: FW: VERY HOT ITEM FROM MG PARKER: FW: Topics of possible assistance
Date: Wednesday, February 09, 2000 2:37:59 PM
Importance: High
Sensitivity: Private

Hi, (b) (6) I told you that General Parker wants us to solve Bio-Port's problems with AVA. Below is the list. UGH!! We are having a meeting today starting at 4 pm in the Commander's office. Oh, well, maybe they'll order pizza if the meeting goes on for awhile. :)

- Bruce

Subject: Topics of possible assistance

MG Parker,

When you visited BioPort recently, you asked that I outline areas where your Command could assist in the furtherance of the AVA Biologics License Application (BLA) approval process and the resolution of issues with doses in inventory made previous to the renovation.
We received a complete Response Letter from FDA on December 29, 1999, have completely reviewed the letter and developed a work plan to address issues raised in the letter. From these activities I have generated the following list of possible participation and facilitation.

1. Evaluation of the final product:
a. Develop and qualify assay to identify the presence of bio-active LF, if any;
b. Serve as a site for inter-laboratory comparison of the present guinea pig potency test;
c. Develop methods for quantitative elution of antigens from aluminum hydroxide adjuvant and characterization of the eluted antigens;
d. More fully develop and validate a surrogate animal model of efficacy and evaluate new lots and lots in inventory with that model.
2. Validate and transfer to BioPort the Elisa assays for PA, LF and EF antigens.
3. Serve as subject matter experts, providing technical, consultative advice on:
a. Process stream (intermediate fractions) characterization;
b. Final product characterization;
c. Method development and validation of characterization methods;
d. Specifically, utilization and interpretation of SDS-PAGE and Western Blot evaluations of process streams.
4. Prepare, characterize and qualify reagents to be utilized in evaluation of the AVA manufacturing process and final AVA product.
5. Develop and qualify an AVA reference vaccine.
6. Develop and validate a n alternative potency test that is more

reproducible and correlative of results found with the rabbit and primate vaccination /challenge studies.

Parts of items 1-4 can have a positive impact on the BLA approval process. Items 5 and 6 are probably future activities. There are also areas of infrastructure support that could be considered such as assistance in corporate safety programming, regulatory affairs and improved coordination of adverse event investigation, documentation and compliance.
Perhaps our respective staffs could meet soon to determine areas where assistance would be provided and to develop joint objectives and work plans in the selected areas.