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To: (b) (6)
Subject: AVA info
Date: Monday, January 24, 2000 1:15:20 PM

AVA

1. What should be done.

a) Passive studies in mice - I would prefer that these studies be contracted out. We can provide the challenge spores and antiserum.

1) Mice = CBA/J females, 10 per group, about 20 g. Inject intraperitoneally on days -1, 0, 1, 2 and 3 with one of the following: rabbit anti-rPA antiserum; rabbit anti-AVA antiserum; human anti-AVA IgG; Normal rabbit serum; normal human IgG. On day 0, challenge subcutaneously with 10LD50s of V1B spores. Check mice 3X daily for deaths and note differences in survival as well as time to death differences. If protection is seen, repeat experiment with 10 LD50s of Ames spores. If no protection is seen, drop the challenge dose down to 3-5 LD50s of Vollum 1B spores. Enough animals should be ordered to repeat experiments. Total number of animals = 400

b) Passive studies in guinea pigs. We can do these studies in the guinea pig animal room in B3.

1) Guinea pigs = Hartley strain, 8 males and 8 females per group, about 350 g at the time of the experiment. Inject intraperitoneally on days -1, 0, 1, 2 and 3 with one of the following: rabbit anti-rPA antiserum; rabbit anti-AVA antiserum; human anti-AVA IgG; Normal rabbit serum; normal human IgG. On day 0, challenge intramuscularly with 50 LD50s (5000) of Ames spores. Check guinea pigs 3X daily for deaths and note differences in survival as well as time to death differences. If protection is seen, repeat experiment with 100 LD50s of Ames spores. If no protection is seen, drop the challenge dose down to 10 LD50s of Vollum 1B spores. Enough animals should be ordered to repeat experiments. Total number of animals = 500

c) Passive studies in rabbits and monkeys (aerosol challenge). (b) (6) and I would be willing to work on this with (b) (6) if it is decided not to contract this out.

d) For ELISAs and TNAs - mice and guinea pigs - establish serology kinetics with < 10 animals that receive antiserum or IgG. (Contract this out??) For rabbits and monkeys, bleed animals daily. (Contract the tests out??)

e) Surrogate marker for non-human primate: We can either do this, or contract out the immunizations (and bleeds), then do the aerosol challenges here.

c) Assays for immunological correlates - see (b) (6) for comments.

d) Characterization of protective antibodies - see (b) (6) for comments.

We can use the budget estimates that (b) (6) has so masterfully worked out.

- Bruce