Questions for the Committee

Based on the information regarding the natural history of inhalational anthrax (disease due to *Bacillus anthracis*) in different species, rabbits and monkeys, the pharmacokinetics, mechanism of action, efficacy and safety of raxibacumab in the animal studies, and the safety of raxibacumab in normal volunteers:

VOTE: Does the evidence from the pivotal animal studies support the conclusion that raxibacumab at 40 mg/kg is reasonably likely to have efficacy in humans?

If not, what additional studies should be conducted?

VOTE: Does the evidence from the pivotal animal studies and human safety studies support the conclusion that the benefits of raxibacumab therapy outweigh its risks for the treatment of inhalational anthrax?

If not, what additional studies should be conducted?

In animal models (both rabbit and monkey) of inhalational anthrax disease, a single dose of raxibacumab 40 mg/kg IV given in combination with antimicrobial therapy (levofloxacin in rabbits, ciprofloxacin in monkeys) resulted in similar observed efficacy as antimicrobial alone.

VOTE: Does the evidence provided support the conclusion that raxibacumab will not diminish the anticipated efficacy of antibiromicrobials in inhalational anthrax?

If not, what additional studies should be conducted?

VOTE: Given the high efficacy of the antimicrobial arms in the rabbit (95%) and monkey (100%) studies, the added benefit of raxibacumab to antimicrobial could not be determined. Should evidence be requested that raxibacumab makes a contribution to the efficacy over the antimicrobial alone (in rabbit and monkey animal models)?

If yes, what types of additional studies should be requested and conducted?

DISCUSSION

The safety of raxibacumab 40 mg/kg infused IV was assessed in healthy normal volunteers, who also received diphenhydramine.

Are there additional comments or further recommendations for safety evaluation in humans?

If yes, what are these recommendations?
Based on the information provided from the animal models of disease and human volunteers, what information would be useful to include in product labeling, if the product is approved:

- Efficacy of raxibacumab including raxibacumab use alone or in combination with antimicrobials?

- Other information, including safety information, specific information for patients?

For products approved under the Animal Rule, applicants need to agree to conduct field studies in the event there are patients with inhalational anthrax and the product is used. FDA can also ask that applicants commit to conducting additional studies that are needed.

- What additional studies should be requested?