Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 21

3. Species (common name) of animals used in this study: Rhesus macaque

4. Explain the procedure producing pain and/or distress:

   The dosing procedure involved intramuscular administration of nerve agent and treatments which did not cause more than momentary pain or distress; however the resultant intoxication with nerve agent may have caused pain and/or distress including respiratory distress and fasciculations. This work was conducted to determine the efficacy of scopolamine in the nonhuman primate following nerve agent exposure.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

   Analgesics, analgesics or tranquilizers would be expected to mask the clinical appearance or potentiate the effects and thus confound results or invalidate the study. Experienced staff veterinarians and animal technicians were on site to monitor the animal status and health during study conduct, and any potential animal welfare issues. The development of scientifically robust data was critical to the development of human safety data for eventual FDA licensure of scopolamine.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

   This work was conducted to validate or qualify a model and/or develop data necessary for definitive studies [that are required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 41

3. Species (common name) of animals used in this study: Rhesus macaque

4. Explain the procedure producing pain and/or distress:

   The dosing procedure involved intramuscular administration of nerve agent and treatments which did not cause more than momentary pain or distress; however the resultant intoxication with nerve agent may have caused pain and/or distress including respiratory distress and fasciculations. This work was conducted to determine the pharmacokinetics and efficacy of HI-6 in the nonhuman primate following nerve agent exposure.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

   Analgesics, analgesics or tranquilizers would be expected to mask the clinical appearance or potentiate the effects and thus confound results or invalidate the study. Experienced staff veterinarians and animal technicians were on site to monitor the animal status and health during study conduct, and any potential animal welfare issues. The development of scientifically robust data was critical to the development of human safety data.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

   Agency: FDA

   CFR: As appropriate, study conducted under Title 21, Food and Drugs, specifically, 21CFR314.610, approval based on evidence of effectiveness from studies in animals (under subpart I -approval of new drugs when

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Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 24

3. Species (common name) of animals used in this study: Swine

4. Explain the procedure producing pain and/or distress:

   The swine were subjected to an inhalation exposure to chlorine gas. The chlorine exposure did cause more than momentary distress in animals. Animals exhibited clinical signs such as labored breathing, and often returned to normal prior to euthanasia. This work was conducted to support future efforts planned to assess candidate countermeasures.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

   Analgesics, analgesics or tranquilizers would be expected to mask the clinical appearance or potentiate the effects and thus confound results or invalidate the study. Experienced staff veterinarians and animal technicians were on site to monitor the animal status and health during study conduct, and any potential animal welfare issues. The development of scientifically robust data was critical to the development of human safety data.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

   This work was conducted to validate a model and develop data necessary for definitive studies [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

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Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 30

3. Species (common name) of animals used in this study: New Zealand White rabbit

4. Explain the procedure producing pain and/or distress:

   Aerosol challenges with bacterial spores. The challenge procedure itself is not painful but resultant bacterial infection with select agent may have caused pain and/or distress including lethargy, respiratory distress in some animals and occasionally seizures. Some animals show no signs prior to being found dead. This work was conducted to evaluate the protective efficacy of a candidate treatment administered prior to challenge.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

   Anesthetics, analgesics or tranquilizers would be expected to alter the pathogenesis, signs/symptoms and/or progression of any resulting infectious process and thus confound results or invalidate the study. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the animal status and health during study conduct, and any potential animal welfare issues. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which were moribund were euthanized to alleviate individual animal specific pain and distress. The development of scientifically robust data was critical to the development of human safety data.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

   This work was conducted to validate or qualify a model and develop data necessary for definitive studies [that are required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

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