This report is required by law (7 USC 21 43) Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150

See reverse side for additional information

Interagency Report Control No. 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. REGISTRATION NO. 31-R-0021
CUSTOMER NUMBER: 228

FORM APPROVED
OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY (Name and Address, as registered with USDA Include Zip Code)

Battelle Memorial Institute
505 King Avenue
Columbus, OH 43201
Telephone: (614) 424-7444

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS (Sites)

See Attached Listing

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (Attach additional sheets if necessary or use APHIS FORM 7023A)

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used	E. Number of animals upon which teaching experiments, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in those animals and the reasons such drugs were not used must be attached to this report)*	F. TOTAL NO OF ANIMALS (Cols. C + D + E)
4. Dogs	20	656	70		726
5. Cats					
6. Guinea Pigs		2,620	1	1,313	3,934
7. Hamsters		141		61	202
8. Rabbits	88	1,226	121	382	1,729
9. Non-human Primates	44	313	261	138	712
10. Sheep					
11., Pigs	6	43	77		120
12. Other Farm Animals					
13 Other Animals					
Ferrets	36	248		108	356

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). A summary of all such exceptions is attached to this annual report. In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL

(Chief Executive Officer or Legally Responsible Institutional Official)

I certify that the above is true, correct, and complete (7 U.S.C. Section 2143).

SIGNATURE OF CEO OR INSTITUTIONAL OFFICIAL

(b)(6), (b)(7)(c)

DATE SIGNED
2-18-09

APHIS FORM 7023 (AUG 91)

(Replaces VS FORM 18-23 (OCT 88) which is obsolete

NOV 2 5 2008

Summary of Exceptions to the Regulations or Standards

Note: Exceptions were IACUC reviewed and approved.

A. Dog Exercise

1. An exception was granted to the dog exercise plan.

   a. The dogs had been instrumented with telemetry transmitters for cardiovascular data collection. Data could only be collected while animals resided in their home cages. Exercise activity would have interfered with data collection and would have confounded data analysis. This baseline and study monitoring occurred while the animals had unrestricted activity within their home cages. This exemption was of short duration (1 day).

   b. Species: Dog

   c. Number of animals used: 6

B. Sanitization of Primary Enclosures

1. A one to seven day delay was granted to the cage change requirement.

   a. This delay was granted to avoid interference with cardiovascular data collection. The cages were cleaned twice daily as per standard procedure.

   b. Species: Dog

   c. 1 day – 16 animals;
   1 week – 16 animals

2. A one day delay was granted to the cage change requirement. The cages were cleaned twice daily as per standard procedure.

   a. This delay was granted to minimize handling of animals being transferred offsite.

   b. Species: Primate

   c. Number of animals used: 19

3. A one day delay to cage change required. The cages were cleaned twice daily as per standard procedure.

   a. This variance was granted due to end of study considerations.

   b. Species: Pig

   c. Number of animals used: 2

C. Cage Size

1. An exception was made to the cage size requirement.

   a. Due to telemetry data collection requirements, the animals were housed in single cages for ~12 hours prior to dosing and for ~24 hours post dosing for 4 consecutive times with ~72 hours of rest between each dose.

b. Species: Dog

c. Number of animals used: 2

2. An exception was made to the cage size requirement.

a. This exemption was made to allow the collection of cardiovascular data. Cages were cleaned at least every other day and the animals could turn around, express normal postural adjustments, had ready access to food, water and clean bedding.

b. Species: Guinea pigs

c. Number of animals used: 6 animals, 5 days maximum

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 35

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

4. Explain the procedure producing pain and/or distress: Subcutaneous injection or intranasal instillation. The dosing procedure involved an injection with a proprietary vaccine which did not cause more than momentary pain or distress. The administration of infectious material via intranasal instillation was carried out under anesthesia, and did not cause any distress, however the resultant viral infection may have caused pain and/or distress.

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 and sedatives may potentiate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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 determine the efficacy of a proprietary vaccine and provide proof of concept for the development of an anti-viral prophylactic [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: 53

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

4. Explain the procedure producing pain and/or distress: Intramuscular injection. The dosing procedure involved an injection with a proprietary vaccine which did not cause more than momentary pain or distress. The administration of infectious material via intranasal instillation was carried out under anesthesia, and did not cause any distress, however the resultant viral infection may have caused pain and/or distress.

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 and sedatives may potentiate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of

symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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 determine the efficacy of a proprietary vaccine and provide proof of concept for the development of an anti-viral prophylactic [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: 20

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

4. Explain the procedure producing pain and/or distress: The administration of infectious material via intranasal instillation was carried out under anesthesia, and did not cause any distress, however the resultant viral infection may have caused pain and/or distress.

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 and sedatives may potentiate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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].

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 478

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

4. Explain the procedure producing pain and/or distress: Intradermal injection. The dosing procedure involved an injection with bacterial spores which did not cause more than momentary pain or distress. The resultant bacterial infection may have caused pain and/or distress.

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 and sedatives may potentiate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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].

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 68

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

4. Explain the procedure producing pain and/or distress: The guinea pigs were subjected to an IM and SQ injection. The IM treatment injections and the SQ challenge dosing procedure did not cause more than momentary pain or distress. Seizure activity, if present, may have caused pain and/or distress.

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.

   To estimate the physiological effects in man, guinea pigs were exposed to compounds. It is necessary to use a species of animal known to respond to compounds in a manner similar to that of man. There are no known characterized, surrogate markers to predict mortality. Animals exhibiting mild clinical signs often recovered without signs of pain and those with severe signs died rapidly.

   Anesthetics, analgesics and tranquilizers would have interfered with the physiological effects of this compound. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. These data are critical to human safety in the event of exposure.

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].

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 313

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

4. Explain the procedure producing pain and/or distress: The guinea pigs were subjected to an IM and SQ injection. The IM treatment injections and the SQ challenge dosing procedure did not cause more than momentary pain or distress. Seizure activity, if present, may have caused pain and/or distress.

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.

   To estimate the physiological effects in man, guinea pigs were exposed to compounds. It is necessary to use a species of animal known to respond to compounds in a manner similar to that of man. There are no known characterized, surrogate markers to predict mortality. Animals exhibiting mild clinical signs often recovered without signs of pain and those with severe signs died rapidly.

   Anesthetics, analgesics and tranquilizers would have interfered with the physiological effects of this compound. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. These data are critical to human safety in the event of exposure.

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, 21CFR.314.610, approval based on evidence of effectiveness from studies in animals (under subpart I--approval of new drugs when human efficacy studies are not ethical or feasible), and 21CFR601.91, approval based on evidence of effectiveness from studies in animals (under 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: 36

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

4. Explain the procedure producing pain and/or distress: Neurotoxin administration. The dosing procedure involved an oral gavage which did not cause more than momentary pain or distress. The resultant intoxication may have caused pain and/or distress.

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 and sedatives may have masked and/or potentiated the effects of botulinum intoxication and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that

death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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:

   N/A

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 119

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

4. Explain the procedure producing pain and/or distress: Intradermal injection. The dosing procedure involved an intradermal injection with bacterial spores which did not cause more than momentary pain or distress. The resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of monoclonal antibodies, antibiotic treatment and/or vaccination (proprietary).

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 and sedatives may potentiate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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:

   N/A

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 236

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

4. Explain the procedure producing pain and/or distress: Neurotoxin administration. The dosing procedure involved an intramuscular injection which did not cause more than momentary pain or distress. The resultant intoxication may have caused pain and/or distress. This work was conducted to evaluate the efficacy of therapeutic and post exposure prophylaxis.

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 and sedatives may have masked and/or potentiated the effects of botulinum intoxication and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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, 21CFR.314.610, approval based on evidence of effectiveness from studies in animals (under subpart I--approval of new drugs when human efficacy studies are not ethical or feasible), and 21CFR601.91, approval based on evidence of effectiveness from studies in animals (under 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: 16

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

4. Explain the procedure producing pain and/or distress: Neurotoxin administration. The dosing procedure involved an intramuscular injection which did not cause more than momentary pain or distress. The resultant intoxication may have caused pain and/or distress. This work was conducted to evaluate the efficacy of therapeutic and post-exposure prophylaxis.

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 and sedatives may have masked and/or potentiated the effects of botulinum intoxication and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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].

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 6

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

4. Explain the procedure producing pain and/or distress: Intramuscular challenge of toxins. The dosing procedure involved an injection of a bacterial toxin solution which did not cause more than momentary pain or distress. The resultant toxicity may cause pain and/or distress. This study evaluated the efficacy of immune globulin given 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 and sedatives may potentate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs are not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs that met the criteria for euthanasia established in the protocol or those which were moribund were euthanized to alleviate pain and distress. This data is critical to human safety in the event of human exposure.

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:

   CFR: As appropriate, study conducted under Title 21, Food and Drugs, specifically, 21CFR.314.610, approval based on evidence of effectiveness from studies in animals (under subpart I--approval of new drugs when human efficacy studies are not ethical or feasible), and 21CFR601.91, approval based on evidence of effectiveness from studies in animals (under 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: Guinea Pig

4. Explain the procedure producing pain and/or distress: Intradermal injection. The dosing procedure involved an injection with bacterial spores which did not cause more than momentary pain or distress. The resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of vaccination (proprietary).

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 and sedatives may potentiate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those

which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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].

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 233

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

4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed using a muzzle-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of monoclonal antibodies, antibiotic treatment and/or vaccination (proprietary).

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, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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].

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 130

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

4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed using a muzzle-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress. This work was

conducted to evaluate the effectiveness of monoclonal antibodies, antibiotic treatment and/or vaccination (proprietary).

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, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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, 21CFR.314.610, approval based on evidence of effectiveness from studies in animals (under subpart I--approval of new drugs when human efficacy studies are not ethical or feasible), and 21CFR601.91, approval based on evidence of effectiveness from studies in animals (under 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: 3

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

4. Explain the procedure producing pain and/or distress: Intraperitoneal dosing with human plasma. Due to the large dosing volume, the challenge procedure itself may have been painful and rabbits had a hemolytic reaction to the test material and were euthanized. This work was conducted to determine the tolerance and pharmacokinetics of human plasma to be used for passive immunization.

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.

   Pain was not anticipated on this pharmacokinetic study. When toxicity was observed the animals were evaluated by a veterinarian and were euthanized. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues.

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:

   N/A

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 16

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

4. Explain the procedure producing pain and/or distress: The rabbits were subjected to IM injections. Although the IM injections did not cause more than momentary pain or distress, the test article produced abnormal clinical signs in some dose groups.

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.

   To estimate the effects in man, rabbits were dosed with a new therapeutic. There are no known characterized, surrogate markers to predict mortality. Anesthetics, analgesics and sedatives may potentiate the effects of the test article and could confound results, or could mask the clinical appearance, affecting the experimental data. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Animals exhibiting mild clinical signs recovered without treatment; some of those severely affected succumbed rapidly, without time for intervention. Animals exhibiting clinical signs meeting euthanasia criteria per standard operating procedure or those which were moribund were immediately euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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:

   N/A

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 13

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

4. Explain the procedure producing pain and/or distress: Aerosol challenge with infectious bacteria. The challenge was performed under Telazol® anesthesia using a head-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of a therapeutic treatment (proprietary).

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, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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].

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 99

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

4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed under Telazol® anesthesia using a head-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of a therapeutic treatment and/or vaccination (proprietary).

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, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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, 21CFR.314.610, approval based on evidence of effectiveness from studies in animals (under subpart I--approval of new drugs when human efficacy studies are not ethical or feasible), and 21CFR601.91, approval based on evidence of effectiveness from studies in animals (under 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: 12

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

4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed under Telazol® anesthesia using a head-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress.

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, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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].

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used: 14

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

4. Explain the procedure producing pain and/or distress: Aerosol challenge with infectious bacteria. The challenge was performed under Telazol® anesthesia using a head-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress.

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, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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].

Column E Explanation Form

1. Registration Number: 31-R-0021 837

2. Number of animals used: 61

3. Species (common name) of animals used in this study: Syrian Golden hamsters

4. Explain the procedure producing pain and/or distress: Subcutaneous injection of virus. The injection did not cause more than momentary pain or distress, however the resultant viral infection may have caused pain and/or distress. This work was conducted to evaluate the proper dose and strain of virus for future studies to evaluate the effectiveness of monoclonal antibodies for therapy.

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, and sedatives could not be provided because they had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs meeting euthanasia criteria per protocol or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

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].