NP 1/8/18

Explanation for Column E

1. **Registration # 43-R-0014**

2. **Number of animals achieving Category E in this study:** 8

3. **Species:** Canine

4. **Explanation of Procedure producing pain and/or distress:**
This vaccine efficacy study was designed to evaluate novel vaccine formulations in the target species. According to APHIS VS Memorandum 800.202, the preferred design for animal vaccine efficacy studies is the vaccination-challenge trial. Vaccinates and placebo controls were challenged with a virulent strain of the (b) (4) pathogen and monitored for clinical signs of infection. The agent is known to cause clinical signs including fever, serous and purulent ocular discharge, conjunctivitis, (b) (4) depression, dehydration, vomiting, (b) (4)

5. **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. (For federally mandated testing, see Item 5 below)**
Since the interpretation of this study depended on observing clinical signs of disease, treatments that might interfere with those signs or alter the progression of the disease such as antibiotics, corticosteroids, analgesics and NSAIDs were withheld. This institution implements 9 CFR 117.4 which allows for the humane euthanasia of moribund animals exhibiting clinical signs consistent with the expected disease pathogenesis that are unable to rise or move under their own power.

6. **Cite the agency, Code of Federal Regulations (CFR) title number and specific section number and/or VS Memorandum that require this procedure and study.**
APHIS VS Memorandum 800.202 General Licensing Considerations: Efficacy Studies. 1.3 Design.

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Explanation for Column E

1. **Registration # 43-R-0014**

2. **Number of animals achieving Category E in this study:** 40

3. **Species:** Canine

4. **Explanation of Procedure producing pain and/or distress:**
Dogs were challenged with various doses of a (b) (4) pathogen isolate (b) (4) (b) (4) The agent is known to cause clinical signs including depression/lethargy, sneezing, (b) (4) (b) (4) ocular discharge, nasal discharge, conjunctivitis and pyrexia.

5. **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. (For federally mandated testing, see Item 5 below)**
Since the interpretation of this study depended on observing clinical signs of disease, treatments that might interfere with those signs or alter the progression of the disease such as antibiotics, corticosteroids, analgesics and NSAIDs were withheld. This institution implements 9 CFR 117.4 which allows for the humane euthanasia of moribund animals exhibiting clinical signs consistent with the expected disease pathogenesis that are unable to rise or move under their own power.

6. **Cite the agency, Code of Federal Regulations (CFR) title number and specific section number and/or VS Memorandum that require this procedure and study.**
(b) (4)

Explanation for Column E

1. **Registration # 43-R-0014**

2. **Number of animals achieving Category E in this study:** 21

3. **Species:** Canine

4. **Explanation of Procedure producing pain and/or distress:**
This challenge model validation study was designed to evaluate the challenge model in the target species. According to APHIS VS Memorandum 800.202, the preferred design for animal vaccine efficacy studies is the vaccination-challenge trial. Vaccinates and placebo controls were challenged with a virulent strain of the (b) (4) pathogen and monitored for clinical signs of infection. A new challenge strain was being validated in vaccinated and unvaccinated animals. The agent is known to cause clinical signs including (b) (4)
(b) (4)

5. **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. (For federally mandated testing, see Item 5 below)**
Since the interpretation of this study depended on observing clinical signs of disease, treatments that might interfere with those signs or alter the progression of the disease such as antibiotics, corticosteroids, analgesics and NSAIDs were withheld. This institution implements 9 CFR 117.4 which allows for the humane euthanasia of moribund animals exhibiting clinical signs consistent with the expected disease pathogenesis that are unable to rise or move under their own power.

6. **Cite the agency, Code of Federal Regulations (CFR) title number and specific section number and/or VS Memorandum that require this procedure and study.**
APHIS VS Memorandum 800.202 General Licensing Considerations: Efficacy Studies. 1.3 Design.

Explanation for Column E

1. **Registration # 43-R-0014**

2. **Number of animals achieving Category E in this study:** 16

3. **Species:** Canine

4. **Explanation of Procedure producing pain and/or distress:**
This vaccine efficacy study was designed to evaluate vaccine candidates in the target species. According to APHIS VS Memorandum 800.202, the preferred design for animal vaccine efficacy studies is the vaccination-challenge trial. Vaccinates and placebo controls were challenged with a virulent strain of the (b) (4) pathogen and monitored for clinical signs of infection. The agent is known to cause clinical signs including diarrhea, (b) (4) depression/lethargy, weight loss, inappetence, (b) (4) and dehydration.

5. **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. (For federally mandated testing, see Item 5 below)**
The primary treatments for dogs with this infectious disease include subcutaneous or intravenous fluids for dehydration and metoclopramide for persistent vomiting. Since the interpretation of the results of this study depends on clinical signs of the disease, the above treatment must be withheld. Appropriate general nursing care was provided to all animals throughout the entire study period and once an animal met CFR 117.4(e) requirements for removal from a study as judged by a veterinarian the animal was euthanized.

6. **Cite the agency, Code of Federal Regulations (CFR) title number and specific section number and/or VS Memorandum that require this procedure and study.**
(b) (4)
APHIS VS Memorandum 800.202 General Licensing Considerations: Efficacy Studies. 1.3 Design.

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Explanation for Column E

1. **Registration # 43-R-0014**

2. **Number of animals achieving Category E in this study:** (b) (4)

3. **Species:** Guinea Pig

4. **Explanation of Procedure producing pain and/or distress:**
This procedure evaluates the titer of in-process materials to be used in vaccine production. No approved in vitro test exists for this material. Guinea pigs were inoculated (b) (4)
(b) (4)

5. **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. (For federally mandated testing, see Item 5 below)**
(b) (4)
(b) (4) The use of NSAIDs or corticosteroids would mask the lesions and interfere with the validity of the test.

6. **Cite the agency, Code of Federal Regulations (CFR) title number and specific section number and/or VS Memorandum that require this procedure and study.**
USDA approved Outlines of Production 7160.00, 7410.00, 7410.01, 7410.02, 7423.00, 7425.01

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Explanation for Column E

1. **Registration # 43-R-0014**

7. **Number of animals achieving Category E in this study:** 16

8. **Species:** Guinea Pig

9. **Explanation of Procedure producing pain and/or distress:**
This procedure evaluates the safety of a live (b) (4) product prior to release. No approved in vitro test exists for safety evaluation. Guinea pigs were inoculated intramuscularly according to the specific country requirements for release of the product. (b) (4)
(b) (4)

10. **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. (For federally mandated testing, see Item 5 below)**
NSAIDs or corticosteroids would not alter the (b) (4) and could mask other signs related to product safety which would invalidate the test.

11. **Cite the agency, Code of Federal Regulations (CFR) title number and specific section number and/or VS Memorandum that require this procedure and study.**
9 CFR 113.38, USDA approved Outline of Production 1891.20

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Summary of IACUC Approved Exceptions to the AWR and Standards

Registration # 43-R-0014

1. Deviation of Sanitation Procedures. (9CFR 3.11b)

Dogs were used for an infectious pathogen challenge trial that constituted a significant zoonotic exposure risk for the staff. For the safety of the staff, regular 14 day sanitation of the primary enclosures was suspended from the first day of infectious disease challenge through the end of the study. If clinical signs progressed to the defined endpoint, animals were euthanized prior to the expiration of the 14 day sanitization requirement. Seventy two (72) dogs were affected by this exemption.

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Explanation for Column E

1. **Registration # 43-R-0014**

2. **Number of animals achieving Category E in this study:** (b) (4)

3. **Species:** Hamster

4. **Explanation of Procedure producing pain and/or distress:**
This vaccine efficacy study was used to assess potency of experimental vaccines as well as products for product release. Animals were vaccinated with an experimental vaccine or vaccine serial, or left unvaccinated as a control. Animals were later challenged with a virulent culture of the (b) (4) agent. The agent is known to cause clinical signs including rough hair coat, lethargy, irritability, hematuria, labored breathing, (b) (4) (b) (4) drooping ears, moribund appearance or death.

5. **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. (For federally mandated testing, see Item 5 below)**
The test is required to assess the potency of experimental vaccines and replaces the use of more sentient species. In addition, the test is required by regulation to be conducted on each serial of vaccine produced. Death of hamsters in this test is used to indicate lack of protection. This disease in hamsters almost always produces acute onset of clinical signs and rapid death, offering little opportunity for intervention. Furthermore, pathology and signs, length and severity of clinical disease would be impacted by use of non-steroidal anti-inflammatory drugs, antibiotics, corticosteroids and/or analgesics. Use of any such drugs therefore would compromise the scientific value of the protection endpoint determined by the test. Sudden deaths are expected and required by 9 CFR. No treatment can be given but moribund animals are euthanized as allowed according to 9 CFR 117.4. This institution implements 9 CFR 117.4 which allows for the humane euthanasia of moribund animals exhibiting clinical signs consistent with the expected disease pathogenesis that are unable to rise or move under their own power.

6. **Cite the agency, Code of Federal Regulations (CFR) title number and specific section number and/or VS Memorandum that require this procedure and study.**
(b) (4)
APHIS VS Memorandum 800.202

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Explanation for Column E

1. **Registration # 43-R-0014**

2. **Number of animals achieving Category E in this study:** (b) (4)

3. **Species:** Hamster

4. **Explanation of Procedure producing pain and/or distress:**
Hamsters were inoculated with a virulent (b) (4) pathogen and allowed to develop the clinical signs of infection in order to harvest and titrate challenge material for use in potency and efficacy testing. The agent is known to cause clinical signs including labored breathing, (b) (4) rough hair coat, drooping ears, lethargy, irritability and moribund appearance.

5. **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. (For federally mandated testing, see Item 5 below)**
This study was conducted for the propagation of virulent bacterial cultures to be used as challenge material in potency and efficacy testing of specific bacterins. No antibiotics, corticosteroids or non-steroidal anti-inflammatory drugs could be administered as they would suppress the bacterial infection or alter the normal immune response of the animals to the infectious agent. This institution implements 9 CFR 117.4 which allows for the humane euthanasia of moribund animals exhibiting clinical signs consistent with the expected disease pathogenesis that are unable to rise or move under their own power.

6. **Cite the agency, Code of Federal Regulations (CFR) title number and specific section number and/or VS Memorandum that require this procedure and study.**
(b) (4)
APHIS VS Memorandum 800.202

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