

UNITED STATES DEPARTMENT OF AGRICULTURE ANIMAL AND PLANT HEALTH INSPECTION SERVICE  <b>ANNUAL REPORT OF RESEARCH FACILITY</b> (TYPE OR PRINT)	1. REGISTRATION NO. 42-R-0009	CUSTOMER NO. 1578	FORM APPROVED OMB NO. 0579-0036
2. HEADQUARTERS RESEARCH FACILITY (Name and Address, as registered with USDA, include Zip Code)  FORT DODGE LABORATORIES 800 5TH ST N W FORT DODGE IA 50501 (B)(6) (B)(7)(c)			

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 these 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	128	937	24	286	1247
5. Cats		1254	53	181	1488
6. Guinea Pigs		5384	209	0	5593
7. Hamsters		18823	174	6912	25909
8. Rabbits		202	1348	0	1550
9. Non-Human Primates		0	0	0	0
10. Sheep		0	0	0	0
11. Pigs		60	0	0	60
12. Other Farm Animals	Cattle	27	0	0	27
	Horses	12	0	0	12
13. Other Animals	Goats	5	0	0	5
	Gerbils	5	235	0	240

**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 the 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.

<b>CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL</b> (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 C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL (Type or Print)	DATE SIGNED
(B)(6) (B)(7)(c)	(B)(6) (B)(7)(c)	21 Nov, 06

(AUG 91)

3 (Oct 88), which is obsolete

Development

PART 1 - HEADQUARTERS

NOV 22 2006

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 17
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized and inoculated (b)(4) with a virulent strain of (b)(4). The dogs were allowed to develop the clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
This animal study was conducted to develop a challenge model. A challenge model is the method used to administer the pathogen to animals so they will exhibit the clinical signs of infectious disease. This information would be used to establish vaccine efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the pathogen. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 6
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized (b)(4) virus was administered  
(b)(4) The dogs were allowed to develop (b)(4)  
clinical signs of the infection. The clinical signs were observed and recorded.
4. **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)**  
This animal study was conducted to develop a challenge model. A challenge model is the method used to administer the pathogen to animals so they will exhibit the clinical signs of infectious disease. This information would be used to establish vaccine efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
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APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 30
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized and (b)(4) with a virulent strain of (b)(4) known to cause (b)(4) in dogs. The dogs were allowed (b)(4) clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
Animals were challenged with the pathogen to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to qualify this reference vaccine. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.90 III.A. 9 CFR 101.5 definitions, "A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity." A master or working reference is necessary for *in vitro* potency testing for product release of (b)(4) containing products. Research and development at Fort Dodge Animal Health has defined the parameters for immunogenicity (b)(4) containing vaccines.  
  
APHIS VS Memorandum 800.202 3.6.1 – General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3 General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 5
3. **Explanation of the procedure producing pain and/or distress:**  
Dogs were anesthetized and inoculated with a virulent strain of (b)(4)  
(b)(4) known to cause (b)(4) in dogs. The dogs were allowed to develop the clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
This animal study was conducted to develop a challenge model. A challenge model is the method used to administer the pathogen to animals so they will exhibit the clinical signs of infectious disease. This challenge model would be used in the qualification process of a new reference vaccine. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the pathogen. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.90 III.A. 9 CFR 101.5 definitions, "A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity." A master or working reference is necessary for *in vitro* potency testing for product release (b)(4) containing products. Research and development at Fort Dodge Animal Health has defined the parameters for immunogenicity (b)(4) containing vaccines.  
  
VS Memorandum 800.202 3.6.1 – General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
VS Memorandum 800.202 1.3 General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."

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**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 10
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized and inoculated with a virulent strain of (b)(4) known to cause (b)(4) in dogs. The dogs were allowed to develop clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
Animals were challenged with the pathogen to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to qualify this reference vaccine. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**

APHIS VS Memorandum 800.90 III.A. 9 CFR 101.5 definitions, "A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity." A master or working reference is necessary for *in vitro* potency testing for product release (b)(4) containing products. Research and development at Fort Dodge Animal Health has defined the parameters for immunogenicity (b)(4) containing vaccines.

VS Memorandum 800.202 3.6.1 – General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."

VS Memorandum 800.202 1.3 General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."

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**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 5
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized and inoculated (b)(4) with a virulent strain of (b)(4) known to cause (b)(4) in dogs. The dogs were allowed to develop the clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
This animal study was conducted to develop a challenge model. A challenge model is the method used to administer the pathogen to animals so they will exhibit the clinical signs of infectious disease. This challenge model would be used in the qualification process of a new reference vaccine. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the pathogen. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
  
APHIS VS Memorandum 800.90 III.A. 9 CFR 101.5 definitions, "A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity." A master or working reference is necessary for *in vitro* potency testing for product release (b)(4) containing products. Research and development at Fort Dodge Animal Health has defined the parameters for immunogenicity (b)(4) containing vaccines.  
  
APHIS VS Memorandum 800.202 3.6.1 – General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3 General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 15
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were inoculated (b)(4) with a virulent strain of (b)(4). The dogs were allowed to develop the clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
This animal study was conducted to develop a challenge model. A challenge model is the method used to administer the pathogen to animals so they will exhibit the clinical signs of infectious disease. This information would be used to establish vaccine efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the pathogen. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 8
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized and inoculated with a virulent strain (b)(4) (b)(4) known to cause (b)(4) in dogs. The dogs were allowed to develop clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
Animals were challenged with the pathogen to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to qualify this reference vaccine. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.90 III.A. 9 CFR 101.5 definitions, "A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity." A master or working reference is necessary for *in vitro* potency testing for product release (b)(4) containing products. Research and development at Fort Dodge Animal Health has defined the parameters for immunogenicity of (b)(4) containing vaccines.  
  
APHIS VS Memorandum 800.202 3.6.1 – General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3 General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 19
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized and inoculated (b)(4) with a virulent strain of (b)(4). The dogs were allowed to develop the clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
Animals were challenged with the pathogen to see if the vaccine would protect them from exhibiting clinical signs of infectious disease to establish duration of immunity and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the pathogen. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.  
  
APHIS VS Memorandum 800.202 4.8-Duration of immunity: "Support with acceptable data specific claims for duration of immunity for any product fraction."

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 8
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized and inoculated (b)(4) with a virulent strain of (b)(4). The dogs were allowed to develop the clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
This animal study was conducted to develop a challenge model. A challenge model is the method used to administer the pathogen to animals so they will exhibit the clinical signs of infectious disease. This information would be used to establish vaccine efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the pathogen. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids and antibiotics would alter the expression of the disease.
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APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
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**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 13
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized (b)(4) virus was administered (b)(4)  
(b)(4) The dogs were allowed to develop the (b)(4) clinical signs of the infection. The clinical signs were observed and recorded.
4. **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)**  
This animal study was conducted to determine if susceptible animals could be infected with this virus and subsequently exhibit specific clinical signs of the disease and transmit the disease horizontally. This information would be used to develop a challenge model to establish vaccine efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
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APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.

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**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 7
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were inoculated with (b)(4) The dogs were allowed to develop the (b)(4) clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
Animals were challenged with the pathogen to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to establish efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
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APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 30
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized and (b)(4) virus was administered (b)(4)  
(b)(4) The dogs were allowed to develop the (b)(4) clinical signs of the infection. The clinical signs were observed and recorded.
4. **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)**  
This animal study was conducted to determine a vaccine dose. Animals were challenged with virus to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to establish efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 11
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized and (b)(4) virus was administered (b)(4)  
(b)(4) The dogs were allowed to develop the (b)(4) clinical signs of the infection. The clinical signs were observed and recorded.
4. **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)**  
Animals were challenged with virus to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to establish efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 13
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized (b)(4) virus was administered (b)(4)  
(b)(4) The dogs were allowed to develop 1 (b)(4) clinical signs of the infection. The clinical signs were observed and recorded.
4. **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)**  
Animals were challenged with virus to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to establish efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 23
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized and inoculated (b)(4) with a virulent strain of (b)(4). The dogs were allowed to develop the clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
Animals were challenged with the pathogen to see if the vaccine would protect them from exhibiting clinical signs of infectious disease to establish duration of immunity and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the pathogen. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.  
  
APHIS VS Memorandum 800.202 4.8-Duration of immunity: "Support with acceptable data specific claims for duration of immunity for any product fraction."

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 36
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized and inoculated (b)(4) with a virulent strain of (b)(4). The dogs were allowed to develop the clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
Animals were challenged with the pathogen to see if the vaccine would protect them from exhibiting clinical signs of infectious disease to establish duration of immunity and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the pathogen. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.  
  
APHIS VS Memorandum 800.202 4.8-Duration of immunity: "Support with acceptable data specific claims for duration of immunity for any product fraction."

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Canine
2. **Number of animals achieving Cat. E in this study:** 30
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Dogs were anesthetized and inoculated with a virulent strain (b)(4)  
(b)(4) known to cause (b)(4) in dogs. The dogs were allowed to develop clinical signs of the infection so that observations and sampling could be made and recorded.
4. **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)**  
Animals were challenged with the pathogen to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to qualify this reference vaccine. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.90 III.A. 9 CFR 101.5 definitions, "A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity." A master or working reference is necessary for *in vitro* potency testing for product release (b)(4) containing products. Research and development at Fort Dodge Animal Health has defined the parameters for immunogenicity (b)(4) containing vaccines.  
  
APHIS VS Memorandum 800.202 3.6.1 – General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3 General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Feline
2. **Number of animals achieving Cat. E in this study:** 30
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Cats were anesthetized and inoculated (b)(4) with a virulent strain of (b)(4) virus. The cats were allowed to develop the clinical signs of the infection. The clinical signs were observed and recorded.
4. **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)**  
Animals were challenged with virus to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to establish efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
EU Pharmacopoeia 01/2005:50207 Evaluation of Efficacy of Veterinary Vaccines

(b)(4)

7Blm2a under Directive 81/852/EEC General Requirements for the Production and Control of Inactivated Mammalian Bacterial and Viral Vaccines for Veterinary Use

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Feline
2. **Number of animals achieving Cat. E in this study:** 31
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Cats were anesthetized and inoculated (b)(4) with various strains of (b)(4) Virus. The cats were allowed to develop the clinical signs of the infection. The clinical signs were observed and recorded.
4. **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)**  
This animal study was conducted to determine the clinical signs of infection caused by different (b)(3) Viruses. This information would be used to select a possible vaccine candidate and develop a challenge model to establish vaccine efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.

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**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Feline
2. **Number of animals achieving Cat. E in this study:** 35
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Cats were anesthetized and inoculated (b)(4) with a virulent strain of (b)(4) (b)(4) virus. The cats were allowed to develop the clinical signs of the infection. The clinical signs were observed and recorded.
4. **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)**  
This animal study was conducted to determine a vaccine dose. Animals were challenged with virus to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to establish efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Feline
2. **Number of animals achieving Cat. E in this study:** 7
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Cats were anesthetized and inoculated (b)(4) with a virulent strain (b)(4) (b)(4) virus. The cats were allowed to develop the clinical signs of the infection. The clinical signs were observed and recorded.
4. **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)**  
This animal study was conducted to determine a vaccine dose. Animals were challenged with virus to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to establish efficacy and support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Feline
2. **Number of animals achieving Cat. E in this study:** 20
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Cat were anesthetized and inoculated with a virulent strain of Feline (b)(4)  
(b)(4) known to cause (b)(4) disease. The cats were allowed to develop clinical signs of the infection so that observations could be made and recorded.
4. **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)**  
Animals were challenged with the pathogen to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to qualify this reference vaccine. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.90 III.A. 9 CFR 101.5 definitions, "A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity." A master or working reference is necessary for *in vitro* potency testing for product release (b)(4) containing products. Research and development at Fort Dodge Animal Health has defined the parameters for immunogenicity (b)(4) containing vaccines.  
  
APHIS VS Memorandum 800.202 3.6.1 – General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3 General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Feline
2. **Number of animals achieving Cat. E in this study:** 28
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Cat were anesthetized and inoculated with a virulent strain of Feline (b)(4)  
(b)(4) known to cause (b)(4) disease. The cats were allowed to develop clinical signs of the infection so that observations could be made and recorded.
4. **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)**  
Animals were challenged with the pathogen to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to qualify this reference vaccine. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.90 III.A. 9 CFR 101.5 definitions, "A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity." A master or working reference is necessary for *in vitro* potency testing for product release (b)(4) containing products. Research and development at Fort Dodge Animal Health has defined the parameters for immunogenicity (b)(4) containing vaccines.  
  
APHIS VS Memorandum 800.202 3.6.1 – General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3 General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Feline
2. **Number of animals achieving Cat. E in this study:** 30
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Cat were anesthetized and inoculated with a virulent strain (b)(4) Virus (b)(4) known to cause b4 The cats were allowed to develop clinical signs of the infection so that observations could be made and recorded.
4. **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)**  
Animals were challenged with the pathogen to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to qualify this reference vaccine. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate, mask or modify the duration and severity of the clinical signs that were caused by the virus. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives and antibiotics would alter the expression of the disease.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.90 III.A.9 CFR 101.5 definitions, "A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity." A master or working reference is necessary for *in vitro* potency testing for product release (b)(4) containing products. Research and development at Fort Dodge Animal Health has defined the parameters for immunogenicity (b)(4) containing vaccines.  
  
APHIS VS Memorandum 800.202 3.6.1 – General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3 General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Hamsters
2. **Number of animals achieving Cat. E in this study:** 770
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Hamsters were inoculated (b)(4) with strains of (b)(4) (b)(4) and allowed to develop clinical signs of infection in order to harvest and titrate challenge material.
4. **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)**  
Hamsters are required for the propagation of virulent (b)(4) challenge material because in-vitro culture (b)(4) reduces the virulence of the organism. This challenge material was used in canine challenge model development, to establish duration of immunity and to support label claims. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate or modify the severity of the disease process and affect the replication of the pathogen in the animal. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids and antibiotics would alter the expression of disease and replication of the pathogen.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.202 3.6.1- General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3- General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."  
  
APHIS VS Memorandum 800.202 3.1- General Licensing Considerations: Methods. "Vaccine trials should preferably aim to compare product and placebo-treated subjects by their response to challenge with the virulent pathogen."  
  
APHIS VS Memorandum 800.202 4.2- Label claims: The label claim for this new product must be determined under the guidelines of the classifications listed in the memorandum.  
  
APHIS VS Memorandum 800.202 4.8-Duration of immunity: "Support with acceptable data specific claims for duration of immunity for any product fraction."

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**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Hamsters
2. **Number of animals achieving Cat. E in this study:** 463
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Hamsters were inoculated (b)(4) with strains of (b)(4) and allowed to develop clinical signs of infection in order to harvest and titrate (b)(4) challenge material.
4. **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)**  
Hamsters are required for the propagation of virulent b4 challenge material because in-vitro culture of b4 reduces the virulence of the organism. This challenge material was used in canine challenges for the qualification of reference vaccines. The pain and/or distress from this infectious disease could not be relieved because any therapeutics used to treat the disease would eliminate or modify the severity of the disease process and affect the replication of the pathogen in the animal. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease but treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids and antibiotics would alter the expression of disease and replication of the pathogen.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**  
APHIS VS Memorandum 800.90 III.A.9 CFR 101.5 definitions, "A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity." A master or working reference is necessary for *in vitro* potency testing for product release (b)(4) containing products. Research and development at Fort Dodge Animal Health has defined the parameters for immunogenicity (b)(4) containing vaccines.  
  
APHIS VS Memorandum 800.202 3.6.1 – General Licensing Considerations: Outcome Specification. "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement."  
  
APHIS VS Memorandum 800.202 1.3 General Licensing Considerations: Efficacy. "Efficacy is the direct effect of a medical intervention on an individual subject."

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Hamsters
2. **Number of animals achieving Cat. E in this study:** 5317
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**

Ten hamsters per serial are vaccinated (b)(4) After 14-21 days (product dependent), the hamsters are challenged (b)(4) with an appropriate dilution (b)(4) preparation. Ten non-vaccinated hamsters are given the same challenge dose and used as controls. Four groups of five non-vaccinated hamsters are given a dilution of the challenge material and used as the challenge titration determination. Hamsters are observed for 14 days, deaths recorded.
4. **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)**

The test is required by regulation as a proof of (b)(4) vaccine potency to be conducted on each serial of vaccine produced. Death of hamsters in this test has been used for many years to indicate lack of protection from (b)(4) Because the vaccine is given at a fractional dose, the test amounts to a protective endpoint determination for the vaccine being tested. (b)(4) in hamsters almost always results in acute onset and rapid death. The rapid progression of the disease in the hamster gives little opportunity for intervention. Furthermore, pathology would likely be impacted by use of anti-inflammatories. For this reason, neither Fort Dodge Animal Health (FDAH) nor USDA CVB-L uses any substance to reduce pain or distress. The impact on length of disease, duration and severity, which might occur with use of pain medications, is not known. Use of any such drugs therefore, would invalidate (according to Dr. Paul J. Hauer, USDA-CVB-PEL-private communication) the scientific value of the protection endpoint determined by the test. Lack of confidence in the endpoint would render the test itself useless for judging vaccine potency.

APHIS-USDA-CVB is engaged in developing in-vitro potency test alternatives for products that require this test and FDAH has been one of the most active industry partners in this effort. Fort Dodge Animal Health has ongoing animal studies that are currently attempting to validate *in-vivo* methods for the potency tests for releasing some serials and serovars of vaccines. As soon as this methodology is validated to the satisfaction of the USDA-CVB, they will be adapted into the Outlines of Production for the appropriate products. FDAH has incorporated the guidelines of USDA-CVB notice No. 04-09 into the outlines of production as outlined in 9 CFR 117.4 (e)
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**

(b)(4)

APHIS 9 CFR 113.9 New potency test (a).

NOV 12 2007

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Hamsters
2. **Number of animals achieving Cat. E in this study:** 230
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**  
Five hamsters per serial are vaccinated : (b)(4) After 15-20 days, the hamsters are challenged : (b)(4) with an appropriate dilution of virulent (b)(4) preparation. Five non-vaccinated hamsters are given the same challenge dose and used as controls. Four groups of five non-vaccinated hamsters are given a dilution of the challenge material and used as the challenge titration determination. The hamsters are observed for at least 14 days after the death of four control hamsters and deaths are recorded
4. **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)**  
The test is required by regulation as a proof (b)(4) vaccine potency to be conducted on each serial of vaccine produced. Death of hamsters in this test has been used for many years to indicate lack of protection from (b)(4) Because the vaccine is given at a fractional dose, the test amounts to a protective endpoint determination for the vaccine being tested. (b)(4) in hamsters almost always results in acute onset and rapid death. The rapid progression of the disease in the hamster gives little opportunity for intervention. Furthermore, pathology would likely be impacted by use of anti-inflammatories. For this reason, neither Fort Dodge Animal Health (FDAH) nor USDA CVB-L uses any substance to reduce pain or distress. The impact on length of disease, duration and severity, which might occur with use of pain medications, is not known. Use of any such drugs therefore, would invalidate (according to Dr. Paul J. Hauer, USDA-CVB-PEL-private communication) the scientific value of the protection endpoint determined by the test. Lack of confidence in the endpoint would render the test itself useless for judging vaccine potency.
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**

**Explanation for Column E  
Fort Dodge Animal Health  
Registration # 42-R-0009**

1. **Species:** Hamsters
2. **Number of animals achieving Cat. E in this study:** 132
3. **Explanation of the procedure producing pain and/or distress (Must be written as to be understood by lay person as well as scientists)**

Ten hamsters are vaccinated b4 f test vaccine. Thirty hamsters are held for use as controls during the challenge. After 21 days, all vaccinated hamsters are challenged b4 of a proper dilution b4 virus challenge material. Ten non-vaccinated hamsters are challenged b4 of the same dilution and used as challenge controls. Four groups of five non-vaccinated hamsters are given 0.1mL of diluted challenge (to be used as a challenge titration determination). All hamsters are observed for 7 days and deaths are recorded.
4. **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)**

This test is required to establish potency on each serial of vaccine produced. Death as an endpoint is the current standard and a necessary part of a valid test as determined by USDA approved Outline of Production b4 Because the challenge is given at a fractional dose, the test amounts to a protective endpoint determination for the vaccine being tested. Furthermore, pathology and the clinical expression of the infection would likely be impacted by use of anti-inflammatories. The impact on length of disease, duration and severity, which might occur with use of pain medications, is not known. Use of any such drugs therefore, would invalidate (according to Dr. Paul J. Hauer, USDA-CVB-PEL telephone communication) the scientific value of the protection endpoint determined by the test. Lack of confidence in the endpoint would render the test itself useless for judging vaccine potency without a validated protective dose and challenge dose being determined. Until such time as a validated USDA-CVB approved alternative is available, the test is obligatory. No alternatives exist at this time, and no CVB-approved means of relieving pain and distress for this use of hamsters are yet available. When the alternatives are available to a commercially applicable scale, FDAH will apply them. FDAH has incorporated the guidelines of USDA-CVB notice No. 04-09 into the outlines of production as outlined in 9 CFR 117.4 (e)
5. **Cite the agency, code of Federal Regulations (CFR) title number and the specific section number and/or VS Memoranda that require this procedure and study.**

APHIS 9 CFR 113.9 New potency test (a).