This report is required by law (7 USC 2143). 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 21

See attached form for additional information.

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

1. CERTIFICATE NUMBER: 42-R-0009
CUSTOMER NUMBER: 1578

FORM APPROVED
OMB NO. 0579-0036

Fort Dodge Laboratories
Division Of Wyeth
800 5th St N W
Fort Dodge, IA 50501

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

FACILITY LOCATIONS (Sites) - See Atached 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 animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o 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 an 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 wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reas such drugs were not used must be attached to this report	F. TOTAL NUMBER OF ANIMALS (COLUMNS C + D + E)
4. Dogs	221	683	102	231	1016
5. Cats		928	48	404	1380
6. Guinea Pigs		3180	96	0	3276
7. Hamsters		13691	455	7057	21203
8. Rabbits		70	1745	0	1815
9. Non-human Primates		0	0	0	0
10. Sheep	3	0	0	0	0
11. Pigs		5	0	0	5
12. Other Farm Animals					
13. Other Animals: Cattle		78	0	0	78
13. Other Animals: ~~Horses~~		~~18~~	~~12~~	~~0~~	~~30~~
13. Other Animals: Gerbils		60	360	0	420

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese 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 ap 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 inc 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)

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DATE SIGNED 11/17/08

APHIS FORM 7023 (Replaces VS FORM 18-23 (OCT 88), which is obsolete.)
(AUG 91)

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:** 18

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 organism. 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 organism 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 organism. 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.

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:** 18

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 organism. The dogs were allowed to develop 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)**
Product-and placebo-vaccinated animals were challenged with the virulent organism 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 organism. 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, antivirals, 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.**
APVMA (Australian Pesticides and Veterinary Medicines Authority) Guideline 47
Data requirements and guidelines for registration of new veterinary immunological products.
Part 8 Efficacy and Target Animal Safety. Guidelines for trials to generate efficacy and safety data
Parameters of efficacy trials i) clinical parameters (eg mortality, morbidity, lesions, weight gain, epizootiological impact)
Controls and trial design- efficacy trail should compare a group of vaccinated animals with an equivalent group of unvaccinated or placebo-vaccinated controls. Define in the study what the purpose of the control group serves-evidence that exposure to infection took place.

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:** 62

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 organism. The dogs were allowed to develop 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)**
Product-and placebo-vaccinated animals were challenged with virulent organism 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 organism. 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, antivirals and antitussives 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 4.5 Species-Establish efficacy in each species for which the product is recommended. 4.6 Age and susceptibility-Conduct target species immunogenicity studies in fully susceptible animals of the youngest age for which the product is recommended.

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:** 27

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 organism. The dogs were allowed to develop 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)**
Product-and placebo-vaccinated animals were challenged with virulent organism to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to establish duration of immunity. 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 organism. 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, antivirals and antitussives 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 4.5 Species-Establish efficacy in each species for which the product is recommended. 4.6 Age and susceptibility-Conduct target species immunogenicity studies in fully susceptible animals of the youngest age for which the product is recommended. 4.8 Duration of immunity- Conduct duration of immunity studies to support vaccination recommendations for all new product fractions presented for licensure.

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:** 12

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 organism. The dogs 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 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 organism. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease. However treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives, antivirals 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.**

APVMA (Australian Pesticides and Veterinary Medicines Authority) Guideline 47
Data requirements and guidelines for registration of new veterinary immunological products.
Part 8 Efficacy and Target Animal Safety. Guidelines for trials to generate efficacy and safety data
Parameters of efficacy trials i) clinical parameters (eg mortality, morbidity, lesions, weight gain, epizootiological impact)
Controls and trial design- efficacy trail should compare a group of vaccinated animals with an equivalent group of unvaccinated or placebo-vaccinated controls. Define in the study what the purpose of the control group serves-evidence that exposure to infection took place.

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:** 9

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 organism. The dogs were allowed to develop 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)**
Vaccinated and non-vaccinated animals were challenged with the organism to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to determine if one antigen in the vaccine would interfere with the ability of the other antigen in the vaccine to protect against disease. 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 organism. 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, antibiotics and antitussives 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.**
APVMA (Australian Pesticides and Veterinary Medicines Authority) Guideline 47
Data requirements and guidelines for registration of new veterinary immunological products.
Part 8 Efficacy and Target Animal Safety. Guidelines for trials to generate efficacy and safety data
Parameters of efficacy trials i) clinical parameters (eg mortality, morbidity, lesions, weight gain, epizootiological impact)
Controls and trial design- efficacy trail should compare a group of vaccinated animals with an equivalent group of unvaccinated or placebo-vaccinated controls. Define in the study what the purpose of the control group serves-evidence that exposure to infection took place.

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:** 65

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 a virulent organism. The dogs 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)**
This animal study was conducted for the qualification of a new master reference vaccine. Reference vaccine and non-vaccinated animals were challenged with the virulent organism to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. 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 organism 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.**

A master or working reference is necessary for *in vitro* potency testing for product release. VS Memorandum 800.90 III.A. "A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity".
9CFR 113.8 (d)(2) requires the use of an unexpired reference for *in vitro* tests for serial release.

VS Memorandum 800.202 3.6.1 "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement".

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."

VS Memorandum 800.202 1.3 "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:** 1

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 virulent organism was administered. The dogs were observed for the first signs of infectious disease. At the first signs of infection the dogs could be euthanized with a barbiturate overdose. However this animal did not exhibit any signs of infection on one day of observation and was dead the next day of observation before it could be euthanized.

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, duration of immunity and support label claims. The pain and/or distress from this infectious disease could have been relieved with euthanasia using a barbiturate overdose if the signs of infection were observed before death

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: 4.5 Species-Establish efficacy in each species for which the product is recommended. 4.6 Age and susceptibility-Conduct target species immunogenicity studies in fully susceptible animals of the youngest age for which the product is recommended. 4.8 Duration of immunity- Conduct duration of immunity studies to support vaccination recommendations for all new product fractions presented for licensure.

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 virulent organism was administered. The dogs were observed for the first signs of infectious disease. At the first signs of infection the dogs could be euthanized with a barbiturate overdose. However these animals did not exhibit any signs of infection on one day of observation and were dead the next day of observation before they could be euthanized.

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)**
Vaccinated and non-vaccinated animals were challenged with virulent organism to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to establish duration of immunity and support label claims. The pain and/or distress from this infectious disease could have been relieved with euthanasia using a barbiturate overdose if the signs of infection were observed before death.

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: 4.5 Species-Establish efficacy in each species for which the product is recommended. 4.6 Age and susceptibility-Conduct target species immunogenicity studies in fully susceptible animals of the youngest age for which the product is recommended. 4.8 Duration of immunity- Conduct duration of immunity studies to support vaccination recommendations for all new product fractions presented for licensure.

b4

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 organism. The dogs 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 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 bacteria. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease. However 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.**

APVMA (Australian Pesticides and Veterinary Medicines Authority) Guideline 47
Data requirements and guidelines for registration of new veterinary immunological products.
Part 8 Efficacy and Target Animal Safety. Guidelines for trials to generate efficacy and safety data
Parameters of efficacy trials i) clinical parameters (eg mortality, morbidity, lesions, weight gain, epizootiological impact)
Controls and trial design- efficacy trail should compare a group of vaccinated animals with an equivalent group of unvaccinated or placebo-vaccinated controls. Define in the study what the purpose of the control group serves-evidence that exposure to infection took place.

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 virulent organism was administered. The cats were observed for the first signs of infectious disease. At the first signs of infection the cats could be euthanized with a barbiturate overdose. However these animals did not exhibit any signs of infection on one day of observation and were dead the next day of observation before they could be euthanized.

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)**
Vaccinated and non-vaccinated 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 duration of immunity and support label claims. The pain and/or distress from this infectious disease could have been relieved with euthanasia using a barbiturate overdose if the signs of infection were observed before death.

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 4.5 Species-Establish efficacy in each species for which the product is recommended. 4.6 Age and susceptibility-Conduct target species immunogenicity studies in fully susceptible animals of the youngest age for which the product is recommended. 4.8 Duration of immunity- Conduct duration of immunity studies to support vaccination recommendations for all new product fractions presented for licensure.

b4

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 organism known to cause 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)**
Cats 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 organism. 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, antivirals 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.

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:** 21

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 with a virulent organism. The cats were allowed to develop the clinical signs of 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)**
Product-and placebo-vaccinated 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 determine duration of immunity. 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, antivirals 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.**

b4

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:** 14

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 various strains of a virulent organism. 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 strains of an organism affecting cats. 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 organism. 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, antivirals 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.

NOV 2 1

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:** 53

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 with a virulent organism. The cats were allowed to develop the clinical signs of 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)**
Product-and placebo-vaccinated 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 determine the vaccine dose, onset of immunity and efficacy. 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, antivirals 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.**

b4

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:** 39

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 with a virulent organism. The cats were allowed to develop the clinical signs of 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)**
Product-and placebo-vaccinated animals were challenged with the organism to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to determine the booster efficacy and duration of immunity. 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, 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**

b4

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:** 49

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 with a virulent organism. The cats were allowed to develop the clinical signs of 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)**
Product-and placebo-vaccinated 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 determine duration of immunity. 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, antivirals 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.**

b4

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:** 50

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 with a virulent organism. 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)**
Product-and placebo-vaccinated animals were challenged with a virulent organism to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used 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 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, antivirals 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 4.5 Species-Establish efficacy in each species for which the product is recommended. 4.6 Age and susceptibility-Conduct target species immunogenicity studies in fully susceptible animals of the youngest age for which the product is recommended. 4.8 Duration of immunity- Conduct duration of immunity studies to support vaccination recommendations for all new product fractions presented for licensure.

b4

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:** 38

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 with a virulent organism. 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)**
Product-and placebo-vaccinated animals were challenged with a virulent organism to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used 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 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, antivirals 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 4.5 Species-Establish efficacy in each species for which the product is recommended. 4.6 Age and susceptibility-Conduct target species immunogenicity studies in fully susceptible animals of the youngest age for which the product is recommended. 4.8 Duration of immunity- Conduct duration of immunity studies to support vaccination recommendations for all new product fractions presented for licensure.

b4

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:** 49

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 with a virulent organism. 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)**
Product-and placebo-vaccinated animals were challenged with a virulent organism to see if the vaccine would protect them from exhibiting clinical signs of infectious disease. This information would be used to establish the vaccine dose. 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 organism. 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, antivirals 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."

b4

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:** 26

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 with a virulent organism The cats were allowed to develop the clinical signs of 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. 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 organism. The attending veterinarian was consulted for possible therapeutic treatment for the pain and distress of the disease. However treatment with antipyretics, analgesics, non-steroidal anti-inflammatories, corticosteroids, antitussives, antivirals 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."

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:** 38

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 organism known to cause 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 virulent organism 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 organism. 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, antivirals 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. 9CFR 113.8 (d)(2) requires the use of an unexpired reference for *in vitro* tests for serial release.

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 (revised)
Fort Dodge Animal Health
Registration # 42-R-0009

1. **Species:** Hamsters

2. **Number of animals achieving Cat. E in this study:** 200

3. **Explanation of the procedure producing pain and/or distress:**
Hamsters were inoculated with a virulent organism 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 challenge material because in vitro culturing reduces the virulence of the organism. This animal study was conducted for the propagation and titration of challenge material to be used in the qualification of a new reference vaccine and to establish efficacy. To produce virulent challenge material in the hamster, the animal must develop clinical signs of infection. The attending veterinarian was consulted for treatment of pain and/or distress. The pain and/or distress from this infectious disease could not be relieved because any antibiotics used to treat the disease could kill the organisms being propagated. Anesthetic, analgesic, antipyretic and non-steroidal anti-inflammatory therapy would mask or alter the progressive development of illness that is used to determine if the organism is virulent and has propagated to sufficient numbers in the animal before harvest.

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.**

A master or working reference is necessary for *in vitro* potency testing for product release b4 containing products. VS Memorandum 800.90 III.A. "A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity".

VS Memorandum 800.202 3.6.1 "The outcome may be specified in terms of a case definition, severity categorization, or natural scale of measurement".

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

VS Memorandum 800.202 3.1 General study design. Clinical efficacy studies should be prospective, placebo-controlled, randomized, and double blinded. Vaccine trials should preferably aim to compare product- and placebo-treated subjects by their response to challenge with virulent pathogen.

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:** 6251

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. After 14-21 days (product dependent), the hamsters are challenged b4 with an appropriate dilution of live b4 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 c b4 vaccine potency to be conducted on each serial of vaccine produced. Death of hamsters in this test is used to indicate lack of protection from b4 ;. Because the vaccine is given at a fractional dose. the test amounts to a protective endpoint determination for the vaccine being tested. b4 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 and signs, length and severity of clinical disease would be impacted by use of non-steroidal anti-inflammatories, antibiotics, corticosteroids, and analgesics. For this reason Fort Dodge Animal Health (FDAH) does not use any substance to reduce pain or distress. Use of any such drugs therefore, would invalidate 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. Fort Dodge Animal Health has ongoing animal studies that are currently attempting to validate *in-vitro* methods for the potency tests for releasing serials.
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.**

b4

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:** 337

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 of 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 of 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 b4 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 vaccine is given at a fractional dose, the test amounts to a protective endpoint determination for the vaccine being tested. Furthermore, pathology and signs, length and severity of clinical disease would likely be impacted by use of non-steroidal anti-inflammatories, corticosteroids and analgesics. Use of any such drugs therefore, would invalidate 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).

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:** 269

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 b4 After 15-20 days, the hamsters are challenged b4 with an appropriate dilution of virulent organisms. 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 of vaccine potency to be conducted on each serial of vaccine produced. Death of hamsters in this test is used to indicate lack of protection. Because the vaccine is given at a fractional dose, the test amounts to a protective endpoint determination for the vaccine being tested. This disease 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 and signs, length and severity of clinical disease would be impacted by use of non-steroidal anti-inflammatories, antibiotics, corticosteroids, and analgesics. For this reason Fort Dodge Animal Health (FDAH) does not use any substance to reduce pain or distress. Use of any such drugs therefore, would invalidate 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.**
b4