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 2150.

See reverse side for additional information.

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. REGISTRATION NO. 43-R-0009 CUSTOMER NO. 1399

FORM APPROVED OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY (Name and Address, as registered with USDA, include Zip Code)
Midwest Research Institute
425 Volker Blvd
Kansas City, MO 64110

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					
5. Cats		59		1	60
6. Guinea Pigs					
7. Hamsters				27	27
8. Rabbits			10	30	40
9. Non-Human Primates					
10. Sheep					
11. Pigs					
12. Other Farm Animals					
13. Other Animals					
Ferret			22	48	70

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.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional official)
I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)

SIGNATURE OF 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)		11/4/09

APHIS FORM 7023 (AUG 91) (Replaces VS FORM 18-23 (Oct 88), which is obsolete

PART 1 - HEADQUARTERS

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Column E Explanation

Facility Registration Number: 43-R-0009

Number of animals used in Study: 26 (only 1 animal is Category E)

Species: Cat

Explain the procedure producing pain and/or distress:
Blood was being collected from the jugular vein for study related sample collection. The animal was appropriately restrained and a needle was inserted into its neck to withdraw the blood sample from the jugular vein. While the needle was inserted, the animal jerked suddenly and the needle was withdrawn immediately. Shortly after the needle was withdrawn, the cat became hypoxic with blue discoloration of the tongue and mucous membranes. The animal died shortly thereafter before veterinary care could be provided. Necropsy revealed a large amount of blood in the connective tissue of the neck and the subcutaneous tissue of the right thorax as well as in the thoracic cavity (thymic area). It was determined that the animal died due to excessive blood loss consistent with the tearing of one of the major blood vessels in the neck during the blood collection process.

Provide scientific justification why pain and/or distress could not be relieved:
The animal died very quickly due to a tear in the jugular vein during the blood collection process before pain or distress could be relieved.

Column E Explanation

Facility Registration Number: 43-R-0009

Number of animals used in Study: 27

Species: Hamsters

Explain the procedure producing pain and/or distress:

In the production of life saving protein therapies from pooled human plasma, individual plasma donations have the potential of being contaminated with viruses and the agent of variant CJD, which is a human form of transmissible spongiform encephalopathies (TSEs). To ensure the safety of plasma-derived therapeutic proteins, the manufacturers must evaluate the reduction capacity of relevant purification steps with respect to TSE agent. Scrapie strain 263K (type of prion protein), which is a worldwide accepted animal model of transmissible spongiform encephalopathies, was specifically selected to grow in hamsters. Hamsters are the preferred model for generating high yields of strain 263K prion proteins, and the most sensitive system for detecting the presence of 263K prion protein. Hamster bioassay is the only method accepted by regulatory agencies for conducting an evaluation of prion reduction. Clinical signs of prion disease include: generalized tremor, abnormality of gait, ataxia and head bobbing.

To test the purification process, 27 hamsters were anesthetized and dosed with different levels of purified Scrapie strain 263K by intracerebral injection. Of the 27 animals dosed, the majority of the animals developed the clinical signs noted above. Following two positive observations for clinical prion syndrome the animals were euthanized.

Provide scientific justification why pain and/or distress could not be relieved:

While the clinical signs associated with prion syndrome would not be considered painful, the generalized tremors, abnormal gait, ataxia and head bobbing may be distressful to the animal. Initial clinical signs of prion syndrome can be very subtle and not easily detectable and can be confused with normal activity of the animal. To prevent premature euthanasia of the animal and a loss of study integrity, a second positive observation was required, thus the natural progression of the disease was allowed to continue.

Column E Explanation

Facility Registration Number: 43-R-0009

Number of animals used in Study: 30

Species: Rabbit

Explain the procedure producing pain and/or distress:
Rabbits were exposed to different levels of *Francisella tularensis* by inhalation to determine the median lethal dose of the bacteria in the rabbit in preparation for a vaccine challenge study. During the course of the disease progression, animals experienced an elevation in body temperature, anorexia, decreased water intake, listlessness and in some cases animals died before they could be euthanized.

Provide scientific justification why pain and/or distress could not be relieved:
Exposing the rabbit to an aerosol preparation of *Francisella tularensis* to determine the median lethal dose is a new route of exposure (at MRI). To fully access the amount of bacteria that would cause death in the rabbit, the animal needed to become ill and the natural progression of the disease followed up to a point to which the animal would not recover. Administering pain relieving drugs could have altered the natural progression of the disease or hidden clinical signs used to determine the course of the disease. Euthanizing animals at a time point prior to the animals demonstrating clinical signs would have altered the outcome of the study, as some animals demonstrated elevated temperatures and a decreased appetite, but then ultimately recovered from the disease.

Column E Explanation

Facility Registration Number: 43-R-0009

Number of animals used in Study: 48

Species: Ferret

Explain the procedure producing pain and/or distress:
Ferrets received a dose of one of four highly pathogenic Avian Influenza strains by either the intranasal route, by placing droplets of saline containing the virus into the nares or by exposing them to an aerosol containing the virus. The disease was allowed to progress to then determine the median infectious dose of each virus by each route of administration. Animals developed neurological deficits including ataxia, motor dysfunction, depression and convulsions. They also experienced diarrhea and anorexia. Animals were euthanized once neurological signs were observed.

Provide scientific justification why pain and/or distress could not be relieved:
The purpose of the study was to determine the pathogenicity of the four strains of highly pathogenic Avian Influenza by each route. Providing the animals with pain relief may have altered the course of the disease or covered or accentuated the clinical signs used to determine the pathogenicity of the virus under study. Besides obtaining the median lethal dose for the study, the infectious dose was also determined from clinical observations. Providing pain relief could have masked the signs altering the determination of the infectious dose. Euthanizing the animals before they began to show clinical signs would not have allowed for the determination of which animals actually became infected with the virus and became ill and those that only had virus circulating in their bodies.