SH

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0579-0036

This report is required by law (7 U.S.C. 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.

Interagency Report Control No. 0180-DOA-AN

Fiscal Year: 2009

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

REGISTRATION NUMBER: 23-R-0016

Customer Number: 269

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, include ZIP Code)*

University Of Pittsburgh
3500 Terrace Street
(b)(2)High, (b)(7)f
Pittsburgh, PA 15261

Telephone: (412) 648 8950

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 on these animals and the reasons such drugs were not used must be attached to this report.)*	F. TOTAL NUMBER OF ANIMALS (Cols. C + D + E)
4. Dogs			87		87
5. Cats	1		93	7	100
6. Guinea Pigs		108			108
7. Hamsters					
8. Rabbits	68	289	898		1187
9. Non-human Primates	27	26	578	7	611
10. Sheep			38		38
11. Pigs			258		258
12. Other Farm Animals					
Goats			21		21
13. Other Animals					
Ferrets	24		210	13	223
Cows			8		8
Musk Shrews	179				0

ASSURANCE STATEMENTS

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

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

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

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

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

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

SIGNATURE OF C.E.O. OR I.O.

NAME AND TITLE OF C.E.O. OR I.O. *(Type or Print)*

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

DATE SIGNED
11/20/09

APHIS FORM 7023
AUG 2009

EC
12-3-09
NOV 23 2009

Certificate Number: 23-R-0016; 289
University of Pittsburgh
USDA Annual Report for the Reporting Period 10/1/2008 through 9/30/2009

Summary of exceptions to the regulations and standards, specified and explained by the principal investigators and approved by the IACUC

IACUC review and justification for exception to AWA Regulation: CFR Title 9 1.A to section 3.2 (a) for indoor housing facilities. Three protocols from two investigators were approved for the removal of mandated resting boards for cats.

Protocols: 0705681, 0712856, and 0801862

Species affected: Cats

Dispensation from the use of resting board in feline caging systems

Explanation: The resting surface required for cats under the AWA was removed after vestibular system lesions. Animals become posturally unstable following these lesions, such they may injure themselves when trying to jump onto the raised platform. In addition, this metal structure is approximately at the level of the animal's head, and damage to head implants could occur if the animal stumbles into the platform as a result of its postural stability.

A mat is placed on the bottom of the cage to provide a comfortable resting surface after the raised metal platform is removed.

1) Registration Number: 23-R-0016

2) Species (common name) used in study: Cynomolgus macaque

3) Number of animals used in this study: 2

4) Explanation of procedures producing pain and/or distress and scientific justification why pain and/or distress could not be relieved:

Protocol # 0802011
The NHPs on this protocol were infected with *M. tuberculosis*. Most animals were either treated with antibiotics or were euthanized before developing disease sufficient to cause pain or distress. However, two animals did develop sufficient disease. These animals were in the "No drug" control group and therefore could not be treated with antibiotics without interfering with the outcome of the study. Instead, these animals were euthanized as soon as practical once disease sufficient to cause pain or distress was recognized.

Justification for Category E designation from Protocol/ PI: (type or copy here):

Appropriate anesthesia and analgesia are used for all procedures outlined in this protocol. However, occasionally during the course of M. tuberculosis infection, an animal will rapidly progress to disease, and may potentially be in distress. If this animal is in the control group, it would not be treated with antibiotics. However, we closely monitor the animals, and would euthanize an animal that became acutely ill during the experiment. Rapid progression occurs in ~5% of infected monkeys, but most of these would be treated with antibiotics to alleviate any associated pain or distress. In addition, performing bronchoscopy on monkeys with substantial lung disease could also lead to distress, perhaps even necessitating a necropsy, so this is covered under the E category as well.

1) Registration Number: 23-R-0016

2) Species (common name) used in study: Cynomolgus macaque

3) Number of animals used in this study: 2

4) Explanation of procedures producing pain and/or distress and scientific justification why pain and/or distress could not be relieved:

Protocol # 0808244
The NHPs on this protocol were infected with *M. tuberculosis*. Most animals are euthanized before developing disease sufficient to cause pain or distress. However, two animals did develop sufficient disease and were euthanized as soon as practical once that fact was recognized.

Justification for Category E designation from Protocol/ PI: (type or copy here):

Appropriate anesthesia and analgesia are used for all procedures outlined in this protocol. The distress that we are considering will come directly from the course of tuberculosis. For most of these studies, drugs will be used to treat the monkeys as they develop tuberculosis, so these animals are not in Category E. For the control animals that will not be treated with antibiotics (since that would prevent them from being controls), they will be monitored closely for signs of disease. At the time of active TB (or reactivation TB), these monkeys will be euthanatized and necropsied. We have substantial experience with this model now, and our close monitoring allows us to determine which monkeys have active disease. TB is a chronic disease and can develop slowly. It does not lead to acute pain in the human situation. However, we acknowledge the possibility that a monkey could progress more rapidly to fulminant TB or present with an unusual manifestation such as meningitis or skeletal TB, and may experience discomfort. As soon as this is recognized, the monkey would be treated with pain medications, as indicated by the veterinarian in charge. However, in the event that the monkey may experience pain from this infection, we are estimating ~5% of monkeys may be placed in the Category E. This is likely an overestimate, but will cover the possibility of rapidly progressing M. tuberculosis infection, which we see in <5% of cases, as well as rapid reactivation of latent infection upon treatment with the immunosuppressive regimen.

1) Registration Number: 23-R-0016

2) Species (common name) used in study: Cynomolgus macaque

3) Number of animals used in this study: 1

4) Explanation of procedures producing pain and/or distress and scientific justification why pain and/or distress could not be relieved:

Protocol # 0902242
The NHP on this protocol were infected with *M. tuberculosis*. Most animals were euthanized before developing disease sufficient to cause pain or distress. However, one animal did develop sufficient disease. This animal was euthanized as soon as practical once disease sufficient to cause pain or distress was recognized.

Justification for Category E designation from Protocol/ PI: (type or copy here):

Appropriate anesthesia and analgesia are used for all procedures outlined in this protocol. The distress that we are considering will come directly from the potential disease course of tuberculosis. For most of these studies, macaques are euthanized before or shortly after they develop any signs of tuberculosis, so these animals are not in Category E. All animals will be monitored closely for signs of disease. At the time of active TB (or reactivation of TB), these monkeys will be euthanized and necropsied. We have substantial experience with this model now, and our close monitoring allows us to determine which monkeys have active disease. TB is a chronic disease and generally develops slowly, and does not lead to acute pain in the human situation. However, we acknowledge the possibility that a monkey could progress more rapidly to fulminant TB, and may experience discomfort. For that reason, we are estimating ~5% of monkeys may be placed in the Category E. This is likely an overestimate, but will cover the possibility of rapidly progressing M. tuberculosis infection, which we see in <5% of cases, as well as rapid reactivation of latent infection upon treatment with the immunosuppressive regimen.

1) Registration Number: 23-R-0016

2) Species (common name) used in study: Cats

3) Number of animals used in this study: 7

4) Explanation of procedures producing pain and/or distress and scientific justification why pain and/or distress could not be relieved: These studies explored the physiological role of the vestibular system in the control of blood distribution in the body during movement and changes in posture. As part of the protocol, the blood flow through the femoral vein, common iliac vein and inferior vena cava is reduced following a bilateral vestibular neurectomy (surgical removal of vestibular inputs). This surgical procedure leaves the animal with a permanent balance impairment that was deemed to be potentially distressful.

Protocol # 0801862

Justification for Category E designation from Protocol/ PI: (type or copy here):
Anesthetics were employed during every surgery, and analgesia was delivered after every surgery. Nonetheless, deep sedation would be required to assure than animals are not distressed by the postural instability and balance deficits that they experience immediately following removal of vestibular inputs. Such a level of analgesia would not be prudent because it would impact on the data collected after the surgery and would also interfere with the animal's compensation for the effects of the lesion. It is well established in the human literature that compensation after vestibular lesions occurs more readily if movement is attempted than if the patient remains sedentary. Vestibular rehabilitation is based on the notion that improvement can only occur following vestibular lesions if subjects make frequent head and body movements. Thus, even if we were to sedate animals for several days following surgery, they would likely experience distress after the sedation is discontinued (as they did not compensate for the lesion after surgery). We thus deem it most beneficial both scientifically and for the long-term condition of the animal to refrain from providing sedation following removal of vestibular inputs. However, Ketoprofen was provided after the surgery to ensure that the animals do not experience post-surgical pain.

1) Registration Number: 23-R-0016
2) Species (common name) used in study: Ferrets
3) Number of animals used in this study: 13
4) Explanation of procedures producing pain and/or distress and scientific justification why pain and/or distress could not be relieved: Protocol # 0901871 Justification for Category E designation from Protocol/ PI: (type or copy here): Unvaccinated animals that are infected will lose weight and display clinical signs. We will not use analgesics, etc. due to: Non-steroidal, anti-inflammatory drugs that act by inhibiting the release of prostaglandins by inflammatory cells…ie such as aspirin, ibuprofen… or other analgesic act to reduce immune reactions. The point of the study is to determine the effectiveness of our vaccine and compare to non-vaccinated animals. The animals in category E will be non-vaccinated or vaccinated animals, where the vaccine was ineffective. Therefore, these are the controls for the experiment. We cannot observe the reduced/dampened inflammatory response in vaccinated mice followed by viral challenge and compare to non-vaccinated animals with a "wild-type" inflammatory response to infection, if we artificially reduce the inflammatory response to infection using analgesics Opioids can produce several well known adverse events, and, as has recently been recognized, can interfere with the immune response. The immunomodulatory activities of morphine have been characterized in animal and human studies. Morphine can decrease the effectiveness of several functions of both natural and adaptive immunity, and significantly reduces cellular immunity (Palliative Medicine, Vol. 20, No. 8 suppl, 9-15 (2006).

1) Registration Number: 23-R-0016
2) Species (common name) used in study: Rhesus Monkey
3) Number of animals used in this study: 2
4) Explanation of procedures producing pain and/or distress and scientific justification why pain and/or distress could not be relieved: Protocol # 0810243 Justification for Category E designation from Protocol/ PI: (type or copy here): Anesthetics will be employed during every surgery, and analgesia will be delivered after every surgery. Nonetheless, deep sedation would be required to assure that animals are not distressed by the postural instability and spatial disorientation that they experience immediately following removal of vestibular inputs. Such level of analgesia would be impractical because it would impact the behavioral responses we seek to characterize the time course of rehabilitation following a vestibular lesion. In fact, human literature indicated that recovery is delayed in patients that remain sedentary following a vestibular lesion surgery. Thus, it is possible that continued analgesic treatment would prolong the period of distress because it will extend the duration of recovery from vestibular deficits.