11-16-09

According to the Paperwork Reduction Act of 1995, an agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a valid OMB control number. The valid OMB control number for this information collection is 0579-0036. The time required to complete this information collection is estimated to average 2 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

OMB APPROVED
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: 87-R-0002

Customer Number: 2

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

Utah State University
(b)(6), (b)(7)c *1450 Old Main Hill*
Logan, UT 84322

Telephone: (435) 797 1180

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					
5. Cats					
6. Guinea Pigs		10		28	38
7. Hamsters		1180	77	4572	5829
8. Rabbits					
9. Non-human Primates					
10. Sheep					
11. Pigs					
12. Other Farm Animals					
13. Other Animals					
Chinchilla	5		7		7

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 use.

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).

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

DATE SIGNED 11/6/09

APHIS FORM 7023
AUG 2009

NOV 0 9 2009

Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: 87-R-0002

2. Number 28 of animals used in this study.

3. Species (common name) Guinea Pig of animals used in the study.

4. Explain the procedure producing pain and/or distress.

See Attached Document

5. Provide 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 6 below)

See Attached Document

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency_____ CFR_____

NOV 23 2009

Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: 87-R-0002

2. Number 4572 of animals used in this study.

3. Species (common name) Hamster of animals used in the study.

4. Explain the procedure producing pain and/or distress.

   See attached document

5. Provide 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 6 below)

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

   Agency_____ CFR_____

Explanation for the use of animals listed in Column E:

All work conducted at this institution involving pain or distress in animals in which animals do not receive pain relieving substances or some other form of palliative care involve experiments examining virus infections in animal models, and associated work to evaluate potential antiviral therapeutic agents. This involves three related categories of experiments, virus titration studies in animals, dose range finding studies for novel therapeutic agents or treatments, and antiviral experiments in which virus infected animals are treated with potential antiviral agents. The same logic and experimental approach is used for both hamsters and guinea pigs involved in antiviral research, and apply to all animals listed in Column E on the USDA Annual Report of Research Facilities.

The purpose of preliminary virus titration studies is to identify the minimum viral dose required to produce mortality in approximately 90% of the animals inoculated. Titration experiments are only necessary when evaluating new virus stocks or new virus strains, and as such are performed infrequently. Animals are monitored several times daily during virus infection and severely sick or moribund animals are euthanized to minimize pain and distress. Titration experiments are vital to properly establish the animal model, and the information gained from the titration studies is used to determine the dose of virus used in subsequent antiviral experiments. The viruses being studied are often emerging infectious agents, or surrogates for such agents. As such, little is known regarding treatment, means to alleviate pain and distress, and any possible interaction between the virus and potential palliative care. Attempts to alleviate pain or distress in animals involved in virus titration experiments have the potential to alter the outcome of the infection, and thereby provide inaccurate data for the planning of future experiments.

Antiviral experiments conducted at this institution often involve the use of experimental therapeutic agents. Due to the novel and experimental nature of the compounds involved little if any information is know regarding their toxicity profile. Oftentimes, there is no toxic effect associated with any dose of agent tested in dose range finding studies, and when available, previous toxicity information or previously published data regarding compound use is used to determine appropriate drug dose and method of administration. Dose range-finding experiments using small numbers of animals are conducted to identify the maximum tolerable dose and appropriate route of administration. This ensures that animals treated with experimental compounds in subsequent antiviral experiments are not treated with an overtly toxic dose. The experimental status of the agents being tested means that little or no information is available regarding possible drug-drug interactions. Co-administration of pain relieving compounds could alter their antiviral activity or could enhance drug toxicity. Therefore, the use of pain relieving substances is avoided in these experiments.

A literature search on PubMed identified several published reports where commonly used pain medications such as opioids[3; 5; 7] and non-steroidal anti-inflammatory agents[2; 6; 8] altered virus infections. Furthermore, published reports identified potential interactions between analgesics and known antiviral drugs[1; 4] searches identified instances where

commonly Due to such possible drug-virus and drug-drug interactions pain relieving substances are not routinely administered to animals in either virus titration or antiviral experiments. Power analysis and other statistical analyses are performed prior to conducting antiviral experiments to determine the correct number of animals that must be used. This minimizes the number of animals that need to be subjected to the pain and distress associated with a virus infection.

1. **Bergasa NV, Boyella VD**. 2008. Liver derived endogenous opioids may interfere with the therapeutic effect of interferon in chronic hepatitis C. *Med Hypotheses* 70:556-559.
2. **Chen N, Warner JL, Reiss CS**. 2000. NSAID treatment suppresses VSV propagation in mouse CNS. *Virology* 276:44-51.
3. **Chuang RY, Suzuki S, Chuang TK, Miyagi T, Chuang LF, Doi RH**. 2005. Opioids and the progression of simian AIDS. *Front Biosci* 10:1666-1677.
4. **Crain SM, Shen KF**. 2004. Neuraminidase inhibitor, oseltamivir blocks GM1 ganglioside-regulated excitatory opioid receptor-mediated hyperalgesia, enhances opioid analgesia and attenuates tolerance in mice. *Brain Res* 995:260-266.
5. **Davies PW, Vallejo MC, Shannon KT, Amortegui AJ, Ramanathan S**. 2005. Oral herpes simplex reactivation after intrathecal morphine: a prospective randomized trial in an obstetric population. *Anesth Analg* 100:1472-1476, table of contents.
6. **Gaylis N**. 2003. Infliximab in the treatment of an HIV positive patient with Reiter's syndrome. *J Rheumatol* 30:407-411.
7. **Mahajan SD, Aalinkeel R, Reynolds JL, Nair BB, Fernandez SF, Schwartz SA, Nair MP**. 2005. Morphine exacerbates HIV-1 viral protein gp120 induced modulation of chemokine gene expression in U373 astrocytoma cells. *Curr HIV Res* 3:277-288.
8. **Rajic Z, Butula I, Zorc B, Kraljevic Pavelic S, Hock K, Pavelic K, Naesens L, De Clercq E, Balzarini J, Przyborowska M, Ossowski T, Mintas M**. 2009. Cytostatic and antiviral activity evaluations of hydroxamic derivatives of some non-steroidal anti-inflammatory drugs. *Chem Biol Drug Des* 73:328-338.

UTAH STATE UNIVERSITY 0002
Registration Number: 876-R-002
CURRENT IACUC APPROVED EXCEPTIONS

DATE	IACUC#	EXCEPTIONS	ANIMAL NUMBERS
09/08/2009	1079	Surgery on Hamsters (b)(2)High, (b)(7)f (not a dedicated surgery area)	77

At Utah State University survival animal surgery conducted upon animals covered by the Animal Welfare Act is preformed within the surgical suite in the (b)(2)High, (b)(7)f (b)(2)High, (b)(7)f. Animals covered under USU IACUC protocol #1079 undergo survival surgery involving the surgical implantation of osmotic pumps, either alone or attached to intracranial cannulas, or involving laminectomy of the spine. These animals are usually inoculated with the viral pathogens prior to surgery, or occasionally may be inoculated with virus as part of the surgical event. Virus inoculated animals are not allowed outside the (b)(2)High, (b)(7)f sith the (b)(2)High, (b)(7)f due to biosafety concerns. Therefore, the USU IACUC granted and exception to the rule requiring surgery be performed in the surgical suite, and allowed the procedure to be done within the (b)(2)High, (b)(7)f animal room.

When surgery is conducted within the animal room, separate areas of the room are designated as surgery preparation and post-operative recovery. The surgical procedure itself is conducted within a Class II Bio-safety cabinet. The pre- and post-operative area and the bio-safety cabinet where the surgery occur are all cleaned and prepared for surgery following standard veterinary procedures. Post-surgically, animals are warmed and observed until fully awake before being returned to their home cage. The surgical procedures, pain management procedures, and pre-and post-operative care was developed by the USU IACUC Attending Veterinarian , and all surgical training of research staff involved is done under the direct supervision of the Attending Veterinarian.

It was the consensus of the USU IACUC that maintaining bio-safety was paramount. The IACUC granted an exception to the rule regarding location of surgery after it had been assured that every reasonable effort had been made to ensure the welfare of the animals undergoing surgery.