



Inspection Report

UNIVERSITY OF KANSAS MEDICAL CENTER

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3901 RAINBOW BLVD

1040 WESCOE PAVILION - MS 2014

UNIVERSITY OF KSMENTAL RETARDATION RESEARCH

Type: ROUTINE INSPECTION

Date: Apr-14-2009

KANSAS CITY, KS 66160

2.31 (d) (1) (ii) **REPEAT**

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

(d) IACUC review of activities involving animals. (1) In order to approve proposed activities or proposed significant changes in ongoing activities, the IACUC shall conduct a review of those components of the activities related to the care and use of animals and determine that the proposed activities are in accordance with this subchapter unless acceptable justification for a departure is presented in writing; Provided, however, That field studies as defined in part 1 of this subchapter are exempt from this requirement. Further, the IACUC shall determine that the proposed activities or significant changes in ongoing activities meet the following requirements: (ii) The principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animals, and has provided a written narrative description of the methods and sources, e. g., the Animal Welfare Information Center, used to determine that alternatives were not available;

Three protocols were identified in which the investigators failed to conduct an appropriate search for alternatives to procedures that may cause more than momentary or slight pain or distress:

- 1) Protocol 2008-1735 is a macaque protocol. Nonhuman primates on this protocol undergo surgical procedures including craniotomies for placement of head chambers and placement of electrodes into muscles of the fore and hind limbs. The search for alternatives did not include terms that relate to the procedures that may cause more than momentary or slight pain or distress. Search words included: motor cortex, stimulation, ICMS, EMG.
- 2) Protocol 2007-1703 is a guinea pig protocol. Animals on this protocol have their ovaries surgically removed. The search for alternatives did not include terms that relate to the procedures that may cause more than momentary or slight pain or distress to the animals. Search words included: pregnancy, guinea pig, vascular smooth muscle, endothelium, G-protein.
- 3) Protocol 2007-1680 is a macaque protocol. The nonhuman primates on this protocol are infected with SIV and treated with morphine and/or antiviral drugs; some of the animals develop clinical signs associated with AIDS including encephalitis. The search for alternatives did not include search terms that relate to all of the procedures that may cause more than momentary or slight pain or distress. Search words included: SIV, HIV, morphine, brain.

Principle investigators must consider alternatives to procedures that may cause more than momentary or slight pain or distress in order to protect the health and well-being of the animals. The principle investigator must provide a written narrative describing the methods and sources used to determine that alternatives were not available. The

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written narrative should include adequate information for the IACUC to assess that a reasonable and good faith effort was made to determine the availability of alternatives or alternative methods. If a database search or other source identifies a bona fide alternative method (one that could be used to accomplish the goals of the animal use proposal), the written narrative should justify why this alternative was not used.

The IACUC must ensure that the principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animals.

This is a repeat non-compliant item. It was also not in compliance on March 10, 2009.

2.31 (d) (1) (viii)

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

(d) IACUC review of activities involving animals: (1) In order to approve proposed activities or proposed significant changes in ongoing activities, the IACUC shall conduct a review of those components of the activities related to the care and use of animals and determine that the proposed activities are in accordance with this subchapter unless acceptable justification for a departure is presented in writing; Provided, however, That field studies as defined in part 1 of this subchapter are exempt from this requirement. Further, the IACUC shall determine that the proposed activities or significant changes in ongoing activities meet the following requirements: (viii) Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures;

Protocol 2007-1703 involves survival surgeries and blood draws on guinea pigs. Guinea pig #004 died unexpectedly on 3/20/2009, the day after being anesthetized for a blood draw by a research associate. The protocol states that the principle investigator's responsibilities are "surgical procedures." This principle investigator's training records were examined. He has not completed the following training modules identified as mandatory for all individuals completing survival guinea pig surgeries: "Aseptic Surgery Rodents", "SOP Prog 13 Medical Records", "SOP Vet 3 Anesthesia and Analgesia", and "SOP Vet 4 Survival Surgery Rodents". Training records for the research associate included on this protocol were also examined. The principle investigator stated that this research associate had completed surgeries and blood draws on an anesthetized guinea pig (#004). The protocol lists this individual's only responsibilities as "euthanasia". Training records indicate that this research associate had not completed the training module "Guinea pig & rabbit video", which is mandatory for all guinea pig handlers.

Personnel conducting procedures on regulated species must be appropriately qualified and trained in those procedures in order to protect the health and well-being of the animals.

The IACUC must ensure that all personnel conducting procedures on regulated species are appropriately qualified and trained in those procedures.

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**2.31 (d) (5) REPEAT DIRECT NCI
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).**

(d) IACUC review of activities involving animals. (5) The IACUC shall conduct continuing reviews of activities covered by this subchapter at appropriate intervals as determined by the IACUC, but not less than annually;

Three protocols were identified in which investigators are not conducting animal activities as delineated in the IACUC approved protocol:

1) Protocol 2007-1703, a surgical guinea pig protocol.

a) The principle investigator stated that guinea pig #004 was not given any buprenorphine after its ovariectomy (surgical removal of the ovaries) on 3/9/2009 because he "didn't feel it was necessary", despite the fact that the approved protocol states that buprenorphine will be given post-operatively for pain.

b) The principle investigator stated that guinea pigs are given 80 mg/kg ketamine and 1-3 mg/kg xylazine when anesthetized for surgical procedures. The approved protocol states that guinea pigs will be given 80 mg/kg "ketamin" and 1 mg/kg xylazine in a dosing chart.

c) The approved protocol indicates that the research fellow's only responsibilities are "euthanasia"; however the principle investigator stated that this research fellow had conducted surgical procedures and blood draws under anesthesia on guinea pig #004.

2) Protocol 2008-1735, a macaque protocol.

a) The description of the MRI anesthetic procedures states that nonhuman primates will be tranquilized with ketamine. A chart in the protocol states that ketamine will be given at a dose of 10 mg/kg i.m. 1 time per month. The laboratory's actual written procedure for MRIs utilized by laboratory staff states that the animals are given a full dose of ketamine followed by "Dormitor" for transport, which is then followed by a 1/2 dose of ketamine every 30 minutes thereafter.

b) The description of care of the cortical chamber states that "the chamber is opened and cleaned each day before recording and at least once a week if we are not recording." An entry in the medical records for a male macaque (ID# 99R1027) on 12/7/2008 states that the "chamber had not been cleaned in 3 weeks."

3) Protocol 2007-1680, a macaques protocol.

a) The protocol states that morphine will be given subcutaneously, 4 times daily, at a dose of 3.5 mg/kg for up to 12 months. Principle investigator records for the nonhuman primates indicate that the morphine is given at doses other than at the approved level and that the morphine is administered intramuscularly rather than subcutaneously. Records indicate that animals A2-5A9, A5-3A5, B2-4A4, B5-AL11, and A1-3A0 received morphine at 1 mg/kg 4 times a day intramuscularly for one week, at 2 mg/kg 4 times a day intramuscularly for two weeks, and then began receiving morphine at 3 mg/kg 4 times a day intramuscularly from that point forward.

b) The protocol states that plasma will be examined every 2 weeks after virus inoculation. Principle investigator records indicate animals B5-AL11, B4-2A0, B2-4A4, A5-3A5, A2-5A9, and C1-57Z had two blood draws prior to virus inoculation, one blood draw at virus inoculation, one blood draw weekly for the first 4 weeks after inoculation, and then one blood draw every 4 weeks (unless the nonhuman primate died or was euthanized).

c) The protocol states that cerebral spinal fluid (CSF) is collected every 2 weeks after virus inoculation. Principle investigator records indicate that animals B5-AL11, B4-2A0, B2-4A4, A5-3A5, A2-5A9, C1-57Z, and C2-5A3 had CSF collected weekly for the first 4 weeks after inoculation and then every 4 weeks (unless the nonhuman primate died or

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was euthanized or they were unable to obtain a sample).

d) The protocol defines criteria that will prompt removal of animals from the study or euthanasia of an animal. The protocol states that "any animals developing AIDS (chronic weight loss of more than 20% body weight, anorexia for more than two days, uncontrolled diarrhea or respiratory distress and onset of neurological signs) will be euthanized." The protocol does not specify at what interval the animals will be weighed. Records indicate the animals were not weighed until 8 weeks after virus inoculation and then were generally weighed every 4 weeks. This time interval does not appear to be adequate as attested to by the following: Animals B4-2A0 and B5-AL11 died five weeks after virus inoculation. Their weights were not checked at any point after virus inoculation prior to their death. Animal B4-2A0 was not weighed at necropsy, but the necropsy weight of B5-AL11 indicated that the nonhuman primate had lost 26.8% of its weight. Its weight had dropped from 4.1 kg at virus inoculation to 3 kg 5 weeks later.

Continuing review of animal activities is necessary to ensure that they are conducted as stated in the approved protocol is required in order to ensure that all activities are conducted in compliance with the Animal Welfare Act regulations in order to protect the health and well-being of the animals.

The IACUC must conduct continuing review of activities in order to ensure that all animal activities are conducted as stated in the approved protocols and in compliance with these regulations.

This is a repeat non-compliant item. It was also not in compliance on March 10, 2009.

2.31 (e) (2)

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

(e) A proposal to conduct an activity involving animals, or to make a significant change in an ongoing activity involving animals, must contain the following: (2) A rationale for involving animals, and for the appropriateness of the species and numbers of animals to be used;

In protocol 2007-1680, a macaque protocol, the justification for the animal numbers states: "The grant application that has been favorably reviewed proposes to use 44 macaques. However, the reviewers thought there were too few macaques. A supplemental application may have to be submitted to increase these numbers. Thus, we are already proposing to use too few animals for this potentially important study." The rationale for the appropriateness of numbers of animals to be used must be scientifically justified for reasons such as, but not limited to, statistical significance, results of pilot studies, or other scientific reasons in order to ensure that an appropriate, but not excessive, number of animals are utilized. The IACUC must ensure that all protocols include an appropriate rationale for the number of animals to be used.

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2.31 (e) (3)

REPEAT

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

(e) A proposal to conduct an activity involving animals, or to make a significant change in an ongoing activity involving

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animals, must contain the following: (3) A complete description of the proposed use of the animals;

Three protocols were identified that did not contain a complete description of the proposed use of the animals:

1) Protocol 2007-1703 is a guinea pig protocol. The principle investigator told inspectors that guinea pig #004 was anesthetized on 3/19/09 for a blood draw. The approved protocol does not state that any blood draws will be conducted.

2) Protocol 2007-1680, a macaque protocol.

a) The investigator states that he plans to gradually withdraw morphine by decreasing the dose over a two week period. The protocol does not specify at what rate the dose will be decreased.

b) The protocol states that AS-DNA will be given intravenously weekly to some nonhuman primates. Instead of specifying the dose that will be given, the chart in the protocol states "will be determined." No information concerning how the dose will be determined or possible ranges of doses is included.

3) Protocol 2008-1735, a macaque protocol.

a) The protocol states that the space inside the macaque's cortical chamber will be filled with antibiotic ointment, but the protocol does not state what kind of product(s) will be contained in this ointment.

b) The protocol states that the animals will receive prophylactic antibiotics after surgery, but it does not state which antibiotic(s) will be given or how long they will be given.

c) The protocol states that prior to euthanasia the nonhuman primates will be anesthetized with pentobarbital, but the dose and route of administration are not specified.

A complete description of the proposed use of the animals is required in order to facilitate evaluation of the protocols by the IACUC to ensure that they are in compliance with the Animal Welfare Act regulations in order to protect the health and well-being of the animals.

The IACUC must ensure that all proposals to conduct animal activities contain a complete description of the proposed use of the animals.

This is a repeat non-compliant item. It was also not in compliance on March 10, 2009.

2.31 (e) (4) REPEAT

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

(e) A proposal to conduct an activity involving animals, or to make a significant change in an ongoing activity involving animals, must contain the following: (4) A description of procedures designed to assure that discomfort and pain to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research, including provision for the use of analgesic, anesthetic, and tranquilizing drugs where indicated and appropriate to minimize discomfort and pain to animals;

Protocol 2007-1703, a guinea pig protocol, includes conflicting information concerning the dose and/or route of administration of anesthetic and analgesic drugs:

1) The protocol states that buprenorphine will be administered after animals undergo an ovariectomy, which the principle investigator referred to a "castration" throughout the protocol. In one location it states that "Buprenorphine

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(0.5 mg/kg s.c.) is given for the first postoperative day." In the same paragraph it says "Buprenorphine (0.5 mg/kg s.c.) will be administered postoperative 3 days after castration for pain control." A chart immediately following this section states that buprenorphine will be given "s.c." (subcutaneously) at a dose of 0.5 mg/kg for the first postoperative day. None of the description for the use of buprenorphine indicate how many times a day the analgesia will be given.

2) The protocol dosing chart for anesthetic drugs indicates that xylazine will be given i.p. (intraperitoneally) at a dose of 1 mg/kg. In another section of the protocol, it states that xylazine will be given i.m. (intramuscularly) at a dose of 2 mg/kg.

All proposals to conduct an activity involving animals must include a sufficiently detailed description of the procedures designed to assure that discomfort and pain to animals will be limited to that which is unavoidable. This is necessary to facilitate IACUC evaluation of the proposals in order to ensure that the activity is in compliance with Animal Welfare Act regulations and in order to protect the health and well-being of the animals.

The IACUC must ensure that all proposals to conduct an activity involving animals contain an appropriate description of the procedures designed to assure that discomfort and pain to animals are limited to that which is unavoidable for the conduct of scientifically valuable research, including provision for the use of analgesic, anesthetic, and tranquilizing drugs where indicated and appropriate to minimize discomfort and pain to animals.

This is a repeat non-compliant item. It was also not in compliance on March 10, 2009.

2.31 (e) (5)

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

(e) A proposal to conduct an activity involving animals, or to make a significant change in an ongoing activity involving animals, must contain the following: (5) A description of any euthanasia method to be used.

Conflicting information concerning the method of euthanasia that will be utilized was identified in protocol 2008-1735, a macaque protocol. In two locations the protocol states that when animals are euthanized they will first be tranquilized with a large dose of ketamine and then given an overdose of barbiturate intravenously. In another location it states that animals will be given ketamine and "metatomandine" followed by "Beuthanasia" and exsanguination.

A description of any euthanasia method to be used must be included in all proposals to conduct an activity involving animals. This is necessary to facilitate IACUC evaluation to ensure that the protocol is in compliance with Animal Welfare Act regulations and in order to protect the health and well-being of the animals.

The IACUC must ensure that all proposals to conduct an activity involving animals contain an appropriate description of the method of euthanasia to be used.

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2.32 (a)

PERSONNEL QUALIFICATIONS.

(a) It shall be the responsibility of the research facility to ensure that all scientists, research technicians, animal technicians, and other personnel involved in animal care, treatment, and use are qualified to perform their duties. This responsibility shall be fulfilled in part through the provision of training and instruction to those personnel.

The facility requires personnel to complete the "Animal Research Protection Program Refresher" and pass with a minimum score of 90% each year by March 31. This training includes topics such as IACUC submissions, occupational health and safety, pain relief and medical records, euthanasia, animal management, post approval monitoring, and reporting suspected non-compliance. Training records for a nonhuman primate principle investigator were examined and indicated that he had failed to pass this training with the required score for two successive years; on 3/18/08 and 3/18/09 he received a score of 80%.

All individuals involved in animal care, treatment and use must be qualified to perform their duties and appropriately trained in order to protect the health and well-being of the animals.

The research facility must ensure that all scientists, research technicians, animal technicians, and other personnel involved in animal care, treatment, and use are qualified to perform their duties.

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2.33 (b) (2) REPEAT DIRECT NCI
ATTENDING VETERINARIAN AND ADEQUATE VETERINARY CARE.

(b) Each research facility shall establish and maintain programs of adequate veterinary care that include: (2) The use of appropriate methods to prevent, control, diagnose, and treat diseases and injuries, and the availability of emergency, weekend, and holiday care;

Two squirrel monkeys (ID#668 and ID#702) were observed wearing beaded metal collars that were rusty. The rusty surface may become rough and injure or irritate the skin of the animals. Squirrel monkey #A50 was wearing a jacket for its protocol. The jacket was frayed around the shoulders to the point that several long fabric strings were present. These strands could be ingested by the nonhuman primate or become tangled around the fingers, toes or other appendages of the animal. The registrant must ensure that all husbandry related items utilized for the nonhuman primates are kept in good repair to protect the health of the animals and to prevent injury.

On 10/14/2008, the veterinarian examined a male macaque (ID#99R1027) due to a problem with his cortical chamber. The veterinarian prescribed liquid "children's Tylenol" (acetaminophen). The principle investigator stated that he gave the macaque liquid "children's ibuprofen" instead. Medications must be given as prescribed by the veterinarian in order to protect the health of the animals. Substitution of medications without consultation with the veterinarian could result in unanticipated side effects, ineffective treatment outcomes, or other complications.

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The description of procedures to maintain the cortical chamber for macaques on protocol 2008-1735 states that "the chamber is opened and cleaned each day before recording and at least once a week if we are not recording." This is done in order to prevent infection of the chamber that is located inside an opening in the animal's skull; the chamber provides access to the animal's brain. On 12/7/2008 medical records for a male macaque (ID# 99R1027) state that the "chamber had not been cleaned in 3 weeks." At that time the veterinarian removed two milliliters of serous fluid from the chamber. Animals must receive adequate preventative maintenance when implanted with chambers as directed in the protocol and as part of a program of veterinary preventive medicine in order to prevent infection, pain, discomfort and other medical complications.

Protocol 2007-1680, a macaque protocol involving morphine and SIV, describes circumstances that will prompt euthanasia of study animals. One section states that the investigators "will euthanize animals as soon as any signs of neurological distress become evident." Another section of the protocol states that "any animals developing AIDS (chronic weight loss of more than 20% body weight, anorexia for more than two days, uncontrolled diarrhea or respiratory distress and onset of neurological signs) will be euthanized." In the grant application to NIH, the agency that funds the research, the investigators stated that "SIV causes a persistent, progressive infection and many animals will be expected to progress into AIDS characterized by more than 20% loss of body weight, gastroenteritis, pneumonia, or neurological disease. Appearance of any of these clinical signs will provide the signal to euthanize the animals."

Medical records were examined for macaque ID#0A0. On 10/7/08 notes from a research assistant indicate that "he has loose stool and is not eating his biscuits well." On 10/15/08 notes from the research assistant indicates that the nonhuman primate was not recovering well from the anesthesia used to obtain a protocol blood sample. She states that "he is VERY skinny and not eating well. He still has very loose stool." Investigator records indicate that on 10/15/08 the animal weighed 3 kg, which was 22% lower than its weight on 7/21/08 when it was inoculated with SIV. In an email to the principle investigator on 10/16/08 at 10:37 am the research assistant indicates that the animal "left quite a few of his biscuits from yesterday and he has diarrhea. He was sitting curled up on his perch while I was hosing his cage and would make a screeching sound. I gave him a cereal bar, but he was having difficulty picking it up. I gave him grapes and he was eating those. He is very feeble, he can't stand on his legs, he scoots. His hand eye coordination is very bad, he has a pronounced tremble in his hands and has to try several times to grab things. He is doing a lot of grimacing and makes a horrible screeching/chirping noise...I know he is scheduled for tomorrow, but I'm not sure he will make it that long." Notes in the medical record by the research assistant on 10/16/08 re-iterate the presence of the same clinical signs. The record indicates that the nonhuman primate was euthanized at 12:30 on 10/16/08. Despite the fact that the animal appears to have met criteria for euthanasia on 10/15/08 (>20% weight loss, gastroenteritis, anorexia, and neurological abnormalities) the research assistant's email on 10/16/08 indicates that the animal was not scheduled for euthanasia until 10/17/08. The medical records for the nonhuman primate do not document that any veterinarian performed any evaluations, physical examinations, diagnoses, or developed any treatment plans during this time period.

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Medical records were examined for macaque ID#3A0. On 10/7/08 the research assistant indicates in the medical record that she had contacted the principle investigator with concerns and that the nonhuman primate "has been pulling hair, has loose stool and isn't acting normally." An email on 10/9/08 at 3:32 pm from the research assistant to a principle investigator indicates that the nonhuman primate has been vomiting, appears to be eating and drinking, has soft feces with a "sick" smell, and that he "acts very peculiar." She states that "he hunches in the corner, lowers his head and grimaces, almost like he is in pain. This monkey appears to be skinny and he just isn't doing well. I am concerned with the weekend coming up as his issues seem to be getting worse as the week goes on...I, like Dr ----- recommend euthanasia." The principle investigator responded to the email at 7:43 pm stating "this will be discussed at the lab meeting on Friday morning." On 10/10/08 the research assistant indicated that the "monkey appears to have improved overnight. He drank half of Gatorade and ate well. He still has loose stool with bad smell, but he is more active. He does have a small tremble to extremities." The medical record does not contain any further notations, but records from the principle investigator dated 10/20/08 stated "shaking, trembling increased during last few weeks, weight decreased, rough hair, frequent diarrhea. Emergency necropsy." Despite the fact that the animal appears to have met criteria for euthanasia on 10/7/08 (loose stool, abnormal behavior), 10/9/08 (abnormal feces, abnormal behavior that appears to indicate pain), 10/10/08 (loose stool, trembling), and the recommendation of euthanasia from a veterinarian and a research assistant on 10/9/2008, the animal was not euthanized until 10/20/08 when symptoms had progressed even further. The medical records for the nonhuman primate do not document that any veterinarian performed any evaluations, physical examinations, diagnoses, or developed any treatment plans during this time period.

Protocol 2007-1703, a surgical guinea pig protocol, states that the operative and post-operative records will be maintained in the LAR medical records database. Guinea pig #004 underwent ovariectomy on 3/9/09, but no records were created in the database. Records from the principle investigator only indicate "3/9 - operation" but there is no description of anesthetic doses or any monitoring procedures before, during, or after the surgical procedure. The principle investigator stated that the animal was anesthetized on 3/19/09 for a blood draw; no records of this procedure or any anesthetic doses or any monitoring procedures were included on the investigator's record. On 3/20/09 guinea pig #004 was found dead in its cage. The protocol's description of criteria for removal of animals from study or euthanasia includes "a marked failure to gain weight in proportion to others." The principle investigator's records for this animal do not contain any weights.

In protocol 2008-1735, macaques are given ketamine and "dormitor" for transport and additional ketamine during an MRI. The principle investigator does not maintain any records concerning drug doses given to the animals or a description of any monitoring that occurs before, during, or after the MRI procedure.

In protocol 2008-1735, macaques are food restricted in order to facilitate behavioral training. The protocol states that "monkeys are weighed on a regular basis to check for normal weight gain." The only weight recorded in any of the medical records for a male macaque (ID#99R1027) assigned to this protocol was obtained on 4/1/2004 during the

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animal's first quarantine exam, seven days after the animal was acquired by the facility. Another macaque (ID#RQ3787) assigned to this protocol was weighed on 4/2/2009, but the most recent weight recorded prior to this time on 11/10/2003. Food restricted animals must be regularly weighed in order to protect their health and ensure that significant changes in weight are detected in a timely manner.

Medical records for several other nonhuman primates were examined. The following animals did not have any recent entries in their records: 674 (no medical record entries since 2005; no weights recorded since 2004); 622 (no medical record entries since 2004); 702 (no medical record entries since 2004); 668 (no medical records entries since 2004); 695 (no medical record entries since 2004).

Every facility must have a system of health records sufficiently comprehensive to demonstrate the delivery of adequate health care. The health records system should be consistent with professional standards, must be current, legible, and include, at a minimum, the following information: identity of the animal; descriptions of any illness, injury, distress, and/or behavioral abnormalities and the resolution of any noted problem; dates, details, and results (if appropriate) of all medically-related observations, examinations, tests, and other such procedures; dates and other details of all treatments, including the name, dose, route, frequency, and duration of treatment with drugs or other medications; treatment plans should include a diagnosis and prognosis, when appropriate; detail concerning the type, frequency, and duration of any treatment and the criteria and/or schedule for re-evaluation(s) by the attending veterinarian. Health records may be held by the registrant (including, but not limited to, the investigators at research facilities) or the attending veterinarian or divided between both (if appropriately cross-referenced), however all components of the records must be readily available and the record as a whole must meet or exceed the current veterinary professional standards.

The research facility must establish and maintain a program of adequate veterinary care that includes the use of appropriate methods to prevent, control, diagnose, and treat diseases and injuries, and the availability of emergency, weekend, and holiday care in order to protect the health and well-being of the animals.

This is a repeat non-compliant item. It was also not in compliance on August 27, 2008.

2.33 (b) (3) REPEAT ATTENDING VETERINARIAN AND ADEQUATE VETERINARY CARE.

(b) Each research facility shall establish and maintain programs of adequate veterinary care that include: (3) Daily observation of all animals to assess their health and well-being; Provided, however, That daily observation of animals may be accomplished by someone other than the attending veterinarian; and Provided, further, That a mechanism of direct and frequent communication is required so that timely and accurate information on problems of animal health, behavior, and well-being is conveyed to the attending veterinarian;

Checklists are used by the nonhuman primate animal caretaker staff to document completion of husbandry tasks and daily health observations. Checklists reviewed during this USDA inspection showed that completion of the daily health check was not documented on four occasions; all of these dates fell on the weekend: Room 5009 (Saturday, April 11 and Sunday, April 12 no daily health check documented); Room 3026 (Saturday, April 4 and Sunday, April 5

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no daily health check documented).

Daily observation of all animals to assess their health and well-being is required in order to ensure that timely and accurate information on problems of animal health, behavior, and well-being is conveyed to the attending veterinarian.

The registrant must develop and follow an effective program to ensure that daily of observation of the animals to assess their health and well-being occurs at all times.

This is a repeat non-compliant item. It was also not in compliance on March 10, 2009.

2.38 (f) (2) (ii)

MISCELLANEOUS.

(f) Handling.(2)(ii) Deprivation of food or water shall not be used to train, work, or otherwise handle animals; Provided, however: That the short-term withholding of food or water from animals, when specified in an IACUC-approved activity that includes a description of monitoring procedures, is allowed by these regulations.

Protocol 2008-1735, a macaque protocol, includes food restriction in order to facilitate behavioral training. The protocol states that "During initial training, monkey chow is modestly restricted (for example, 8 biscuits per day) to increase appetite and motivation to learn the tasks. In some cases, mild restriction of monkey chow is necessary during periods of recording to maximize performance." The protocol states that the periods of food restriction "generally last about 4-8 weeks." The protocol also says that "monkeys are weighed on a regular basis to check for normal weight gain." The protocol does not clearly define to what degree the feed is restricted nor does it specify at what interval the animal's weight will be monitored.

Inspectors asked the principle investigator how often the nonhuman primates are weighed. He stated that the veterinary staff was responsible for this. When inspectors asked the veterinary staff how often they weighed the nonhuman primates on this protocol, they stated it was the responsibility of the investigator's staff. Inspectors examined the medical records for two animals assigned to this protocol: The only weight recorded in any of the medical records for a male macaque (ID#99R1027) assigned to this protocol was obtained on 4/1/2004 during the animal's first quarantine exam, seven days after the animal was acquired by the facility. Another macaque (ID#RQ3787) assigned to this protocol was weighed on 4/2/2009, but the next most recent weight recorded prior to this time was approximately 5.5 years previously on 11/10/2003.

When the short-term withholding of food from animals is specified in a protocol, a description of appropriate monitoring procedures must be included in order to protect the health and well-being of the animals.

The IACUC must ensure that all approved protocols involving the short-term withholding of food or water from animals include a description of monitoring procedures in order to protect the health and well-being of the animals of the animals.

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TO BE CORRECTED BY: May 12, 2009

3.75 (c) (1) (i) **REPEAT**

HOUSING FACILITIES, GENERAL.

(c) Surfaces (1) General requirements. The surfaces of housing facilities -- including perches, shelves, swings, boxes, houses, dens, and other furniture-type fixtures or objects within the facility -- must be constructed in a manner and made of materials that allow them to be readily cleaned and sanitized, or removed or replaced when worn or soiled. Furniture-type fixtures or objects must be sturdily constructed and must be strong enough to provide for the safe activity and welfare of nonhuman primates. Floors may be made of dirt, absorbent bedding, sand, gravel, grass, or other similar material that can be readily cleaned, or can be removed or replaced whenever cleaning does not eliminate odors, diseases, pests, insects, or vermin. Any surfaces that come in contact with nonhuman primates must: (i) Be free of excessive rust that prevents the required cleaning and sanitization, or that affects the structural strength of the surface;

The metal hook on one of the black rubber straps used to secure the perches in a squirrel monkey enclosure had rusted to the point that it no longer can be effectively cleaned and sanitized. All surfaces that come in contact with nonhuman primates must be free of rust to facilitate the required cleaning and sanitization in order to protect the health of the animals.

The registrant must develop and follow a program of monitoring and maintenance to ensure that all surfaces are free of excessive rust that prevents the required cleaning and sanitization or affects the structural strength of the surface.

This is a repeat non-compliant item. It was also not in compliance on March 10, 2009.

3.75 (c) (1) **REPEAT**

HOUSING FACILITIES, GENERAL.

(c) Surfaces (1) General requirements. The surfaces of housing facilities -- including perches, shelves, swings, boxes, houses, dens, and other furniture-type fixtures or objects within the facility -- must be constructed in a manner and made of materials that allow them to be readily cleaned and sanitized, or removed or replaced when worn or soiled. Furniture-type fixtures or objects must be sturdily constructed and must be strong enough to provide for the safe activity and welfare of nonhuman primates. Floors may be made of dirt, absorbent bedding, sand, gravel, grass, or other similar material that can be readily cleaned, or can be removed or replaced whenever cleaning does not eliminate odors, diseases, pests, insects, or vermin.

In room 5019, housing 15 squirrel monkeys, there were areas of chipping and peeling paint on the wall in at least two areas exposing the bare cinder blocks, which can not be effectively cleaned and sanitized. One area was approximately 3 by 3 inches; the other was approximately 3 by 1 inch.

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All surfaces within housing facilities must be constructed in a manner that allows them to be readily cleaned and sanitized in order to protect the health of the animals. The registrant must develop a program of monitoring and maintenance to ensure that all surfaces of housing facilities are constructed in a manner that allows them to be readily cleaned and sanitized at all times.

This is a repeat non-compliant item. It was also not in compliance on August 27, 2008 and March 10, 2009.

3.75 (e) REPEAT

HOUSING FACILITIES, GENERAL.

e) Storage. Supplies of food and bedding must be stored in a manner that protects the supplies from spoilage, contamination, and vermin infestation. The supplies must be stored off the floor and away from the walls, to allow cleaning underneath and around the supplies. Food requiring refrigeration must be stored accordingly, and all food must be stored in a manner that prevents contamination and deterioration of its nutritive value. Only the food and bedding currently being used may be kept in animal areas, and when not in actual use, open food and bedding supplies must be kept in leakproof containers with tightly fitting lids to prevent spoilage and contamination. Substances that are toxic to the nonhuman primates but that are required for normal husbandry practices must not be stored in food storage and preparation areas, but may be stored in cabinets in the animal areas.

"SOP HUSB 1 Food, Water and Bedding Management" states that "bedding must be stored with sufficient clearance from walls to allow adequate sanitation (sweeping). This should be at least 6 inches." A pallet of bedding in the second floor storage room, used to store primate feed and other animal supplies, was stored against the wall, preventing the required cleaning and husbandry practices. Supplies of food and bedding must be stored off the floor and away from the walls to allow for cleaning underneath and around the supplies to prevent contamination of the supplies.

The registrant must develop and follow a program of monitoring and maintenance to ensure that supplies of food and bedding are stored in a manner that protects the supplies from spoilage, contamination, and vermin infestation and facilitates the required cleaning practices.

This is a repeat non-compliant item. It was also not in compliance on March 10, 2009.

3.76 (c)

INDOOR HOUSING FACILITIES.

(c) Lighting. Indoor housing facilities must be lighted well enough to permit routine inspection and cleaning of the facility, and observation of the nonhuman primates. Animal areas must be provided a regular diurnal lighting cycle of either natural or artificial light. Lighting must be uniformly diffused throughout animal facilities and provide sufficient illumination to aid in maintaining good housekeeping practices, adequate cleaning, adequate inspection of animals, and for the well-being of the animals. Primary enclosures must be placed in the housing facility so as to protect the nonhuman primates from excessive light.

At least 13 enclosures housing squirrel monkeys and 3 enclosures housing macaques had insufficient lighting that

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made it difficult to perform routine inspection and observation of the animals. The lighting was not uniformly diffuse, causing the back half of the enclosure to be darkened and shadowed. Lighting must be uniformly diffuse and provide sufficient lighting to permit routine inspection and cleaning of the facility, and facilitate observation of the nonhuman primates.

The registrant must ensure that all non-human primates have adequate lighting that is uniformly diffuse and that all non-human primates are provided with a regular diurnal lighting cycle of either natural or artificial light.

TO BE CORRECTED BY: July 5, 2009

3.80 (c)

PRIMARY ENCLOSURES.

(c) Innovative primary enclosures not precisely meeting the floor area and height requirements provided in paragraphs (b)(1) and (b)(2) of this section, but that do provide nonhuman primates with a sufficient volume of space and the opportunity to express species-typical behavior, may be used at research facilities when approved by the Committee, and by dealers and exhibitors when approved by the Administrator.

The IACUC approved temporary use of a human infant incubator for post-operative recovery of squirrel monkeys after craniotomies until a new incubator is received. The current human infant incubator does not meet the minimum requirements established in 3.80 (b) (2) (i), as it is only 18 inches high; the minimum enclosure height for nonhuman primates in this group is 30 inches. The insufficient height may prevent the squirrel monkeys from standing in a normal position, and the monkeys could injure the surgical site on their heads if they attempt to stand. The IACUC may approve the use of innovative primary enclosures not precisely meeting the floor area and height requirements only if they provide nonhuman primates with a sufficient volume of space and the opportunity to express species-typical behavior in order to protect the health and well-being of the animals and to prevent injury. The IACUC must ensure that all approved innovative enclosures for nonhuman primates provide the nonhuman primates with a sufficient volume of space, the opportunity to express species-typical behavior, and protect the animals from injury.

TO BE CORRECTED IMMEDIATELY

3.81 (b) REPEAT

ENVIRONMENT ENHANCEMENT TO PROMOTE PSYCHOLOGICAL WELL-BEING.

(b) Environmental enrichment. The physical environment in the primary enclosures must be enriched by providing means of expressing noninjurious species-typical activities. Species differences should be considered when determining the type or methods of enrichment. Examples of environmental enrichments include providing perches, swings, mirrors, and other increased cage complexities; providing objects to manipulate; varied food items; using foraging or task-oriented feeding methods; and providing interaction with the care giver or other familiar and knowledgeable person consistent with personnel safety precautions.

"SOP Prog 8 Environmental Enrichment and Psychological Well-being of Non-human Primates" states that "all mirrors that are scratched and are no longer reflective will be removed." At least 4 metal circular discs, which are

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supposed to be reflective and act as mirrors to provide enrichment for the nonhuman primates, were scratched to the point that the surface was no longer reflective. At least 3 "chew toys" for nonhuman primates were observed that had been chewed to the point that the surface was extremely grooved and pitted. These toys had been cleaned and disinfected by the facility but brown to tan grimy material was visible in the roughened surfaces on two of these items; the third item had an accumulation of hair present on it. This accumulation of dirt and grime could result in transmission of diseases between the animals since the roughened surface of these worn toys prevents effective cleaning and sanitization; the hair could be ingested by the nonhuman primates, which could result in gastrointestinal problems. All enrichment items must be kept in good repair to ensure that they effectively provide enrichment to the animals and can be effectively cleaned and sanitized in order to protect the health and well-being of the animals.

The registrant must develop and follow a program of monitoring and maintenance to ensure that all enrichment items for nonhuman primates are kept in good repair and can be effectively cleaned and sanitized.

This is a repeat non-compliant item. It was also not in compliance on March 10, 2009.

3.81 (c) (2) REPEAT DIRECT NCI ENVIRONMENT ENHANCEMENT TO PROMOTE PSYCHOLOGICAL WELL-BEING.

(c) Special considerations. Certain nonhuman primates must be provided special attention regarding enhancement of their environment, based on the needs of the individual species and in accordance with the instructions of the attending veterinarian. Nonhuman primates requiring special attention are the following: (2) Those that show signs of being in psychological distress through behavior or appearance;

The section of "SOP Prog 8 Environmental Enrichment and Psychological Well-being of Non-human Primates" concerned with behavioral signs of psychological distress states that "if it is determined that the clinical sign may be associated with psychological distress, then an individualized treatment plan will be established." It also states that "an individual record will be maintained for the animal showing possible psychological distress." The veterinarian stated that at the time of this USDA inspection he only considered one nonhuman primate, macaque ID#DE52 who stereotypically hops, to be showing possible signs of psychological distress. At the time of this USDA inspection, an individualized treatment plan had not been developed and an individual record was not being maintained.

The following nonhuman primates exhibited a variable amount of hair loss and/or abnormal stereotypic behaviors which may be associated with psychological distress. The facility had not identified any of these animals as possibly being in psychological distress at the time of this USDA inspection. The animals had variable degrees of hair loss ranging from partial to full loss of hair on the tail to patchy hair loss on the body. Some nonhuman primates were observed actively plucking or stripping hair from their bodies or tails or exhibiting stereotypic behaviors such as flipping, pacing, circling, swaying, excessively scratching, or overgrooming. Animals observed by inspectors to be showing signs of possibly being in psychological distress through their behavior and/or appearance included:

MACAQUES: 99R1463 (sitting in a crouched position, self-clasping), CL8R (hair loss on his forearms, legs, and tail), 3A5/A5 (patchy hair loss on tail), 5A9/A2 (hair loss on tail), 1A1/A4 (clasping leg in a hunched over posture), 57Z/C1 (self clasping, stroking tail, lip smacking), 5A3/C2 (hair loss on top of thighs and tail), I92 (patch of hair loss on its

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back on the right side of the spine; patchy hair loss on the arms, right shoulder, legs; circling), ER65 (hair loss on tail), RCL10 (flipping; hair loss on tail), AV82 (thin hair coat on bottom half of legs; hair loss on tail), A597 (hair loss on bottom 2/3 tail; patchy hair loss on legs), AZ20 (hair loss on bottom 1/2 tail)

SQUIRREL MONKEYS: A65 (circling), 94B (flipping; hair loss on its tail), 674 (circling, scratching), 622 (observed stripping hair from its tail), 796D (hair loss on its tail), B6C (hair loss on the top 1/3 of tail; thin appearance), 398 (scratching), A51 (observed excessively scratching and stripping hair from its tail), A50 (hair loss on its left knee and tail; observed stripping hair from its tail), A56 (hair loss on the tip of its tail; thinning hair on tail; self-clasping), A49 (hair loss on knees; skin on right knee had a reddened appearance; hair loss on tail), 698 (observed scratching excessively; hair loss on sides, back, head and base of tail; observed over-grooming side and knee; circling; thin), 668 (self-clasping; not moving from the bottom of the cage), 695 (thinning hair on bottom 1/3 of tail; hair loss on left thigh and behind left shoulder; observed scratching excessively), 697 (hair loss at base and tip of tail; scratching excessively; pacing), 10B (hair loss on bottom 1/3 of tail; pacing), A64 (circling in cage), A21 (thin; pacing on perch, grabbing ceiling and grabbing back support in a stereotypic manner), 877 (pacing; walking over backwards on ceiling), 1926 (pacing; wall bouncing; bottom 2/3 of tail bare; hair loss on thighs and legs), 1921 (bottom half of tail bare), 1910 (observed stripping hair from tail; tail completely bare; hair loss on legs, sides of abdomen by legs), 3769 (scratching excessively; standing on legs grabbing ceiling, twirling, and pacing on perch), 922 (scratching excessively), 88B (scratching excessively; patchy hair loss; tail bare on bottom one third), 1928 (patchy hair loss on tail with bottom 1/3 bare; excessively scratching), 1931 (whole tail nearly bare), 88E (patchy hair loss on bottom half of tail; pacing along three walls of the cage in a U shaped pattern), 1917 (patchy hair loss whole tail; tip of tail bare), 1927 (patchy hair loss whole tail), 88D (flipping; patchy hair loss whole tail), 1929/1930/88C (all housed in same enclosure; one had patchy hair loss on body and tail; one had hair loss on the bottom one third of the tail and the tail tip; the third had thin hair on the bottom 1/3 of its tail), A22/060 (housed together; one had patchy hair loss on entire tail and sides; observed excessively scratching at sides), E19/947 (housed together; one had a bare tail and was observed scratching excessively; the other had patchy thinning of the hair on the tail), 830/11F (housed together; one had tail that was nearly entirely bare; the other had patchy hair loss on the top 2/3 of the tail), FOE/B37 (housed together; one had thinning hair coat on the back, shoulders, entire tail; the other had hair loss on the entire tail); C58/36B (housed together; one had whole body patchy hair loss; the other had hair loss on its sides, patchy hair loss on its back, and the bottom 2/3 of its tail was bare), A42/335 (housed together; one had hair loss on its whole tail and thighs; the other had hair loss on the bottom 1/3 of its tail), 555/01C (housed together; one had patchy hair loss on its sides and thighs and the entire tail was bare; the other had hair loss on the bottom 1/3 of its tail), 270/165 (housed together; one had hair loss on the back half of its abdomen and thinning hair on its entire tail)

The registrant must develop and follow a plan to ensure that those nonhuman primates that show signs of being in psychological distress through behavior or appearance receive special considerations with regard to enhancement of their environment, in order to protect the health and welfare of the animals.

This is a repeat non-compliant item. It was also not in compliance on March 10, 2009.

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3.125 (c) **REPEAT**

FACILITIES, GENERAL.

(c) Storage. Supplies of food and bedding shall be stored in facilities which adequately protect such supplies against deterioration, molding, or contamination by vermin. Refrigeration shall be provided for supplies of perishable food.

"SOP HUSB 1 Food, Water and Bedding Management" states that "bedding must be stored with sufficient clearance from walls to allow adequate sanitation (sweeping). This should be at least 6 inches." The ground floor storage room, used to store gerbil bedding, was nearly filled with pallets of bedding leaving only a small area open at the entrance of the room, preventing the required cleaning and husbandry practices. The pallets were pushed up against three of the walls. A pallet of bedding in the second floor storage room, used to store gerbil feed and other animal supplies, was stored against the wall, preventing the required cleaning and husbandry practices. Supplies of food and bedding must be stored in a manner that protects the supplies from deterioration, molding, or contamination in order to protect the health of the animals.

The registrant must develop and follow a program that ensures that all supplies of food and bedding are stored in facilities which adequately protect such supplies against deterioration, molding, or contamination by vermin.

This is a repeat non-compliant item. It was also not in compliance on March 10, 2009.

This routine inspection was conducted April 14-17, 2009 by Katheryn Ziegerer, VMO, Ruth Bakker, VMO, and facility representatives.

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