



INSPECTION REPORT

UNIVERSITY OF CALIFORNIA,
SAN FRANCISCO

Customer ID: 9199
Certificate: 93-R-0440

████████ CALIFORNIA STREET, ██████████
BOX ██████████
SAN FRANCISCO, CA 94143 ██████████

Site: 001
THE UNIVERSITY OF CALIFORNIA
SAN FRANCISCO
Inspection
Type: ROUTINE INSPECTION
Date: MAY-29-2008

2.31 (d)(1)(i)

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

Sec. 2.31 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. Further, the IACUC shall determine that the proposed activities or significant changes in ongoing activities meet the following requirements:
(i) Procedures involving animals will avoid or minimize discomfort, distress, and pain to the animals.

Animal Number V000335 was euthanized following the previous inspection. Thus the animal was taken off study and this noncompliant item has been corrected in part. Animal Number MMU 35184, however, remains on study. According to staff members at the facility, the IACUC had not as yet conducted a review of the health concerns of this specific animal.

Previous correction date: May 30, 2008

Note: The purpose of this inspection was to evaluate activities involving animals cited in the previous inspection report of April 15, 2008.

Prepared By: _____
MARCY ROSENDALE, V.M.O. , USDA, APHIS, Animal Care

Title: VETERINARY MEDICAL OFFICER , Inspector ID: 5039

Date:
JUN-02-2008

Received By: _____
SENT BY E-MAIL

Title:

Date:
JUN-10-2008



UNIVERSITY OF CALIFORNIA,
SAN FRANCISCO

Customer ID: 9199
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Site: 001

THE UNIVERSITY OF CALIFORNIA
SAN FRANCISCO

██████████ STREET, ██████████
BOX ██████████
SAN FRANCISCO, CA 94143 ██████████

Inspection
Type: ROUTINE INSPECTION
Date: APR-15-2008

2.31 (d) (1) (i) DIRECT
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; (i) Procedures involving animals will avoid or minimize discomfort, distress, and pain to the animals;

Two of the animal records and protocols that were reviewed during this inspection indicated that the animals were in avoidable distress and discomfort.

Animal Number V000335 was assigned to a food restriction protocol. Records for this animal showed aggressive implant/skin margin cleaning, differing antibiotics, and supplemental nutrition. The weight of the animal near the start of the study was 9.65 kgs (March 2007) and the weight of the animal at the time of this inspection was 7.12 kgs. (25% weight loss). The veterinarian removed this animal from the food restriction portion of the protocol at 10-15% of weight loss but allowed the primary investigator of the research study to continue to manage the diet of the animal. This animal was also being treated for a chronic infection of the soft tissue of the skull caused by a surgical procedure. The description in the record of this animal indicated a malodor coming from the area of the cranial implants. It was also noted in the records a problem with the temporomandibular joint. It was later determined by the investigator that there was a possible fibrosis of the muscles surrounding the mandible. This animal continued working for food supplements in the restraint chair for the purpose of collecting protocol related data. Animal Number MMU 35184 is another animal identified during this inspection described atopic and severely pruritic.

The records of both animals indicate a distress and discomfort while continued use for the collection of data for research. Animals that have chronic infections directly related to the surgical procedures associated with the study and a severe weight loss of undetermined cause, or as in the case of the other animal, atopic and severely pruritic indicates animals that may be distressed and discomforted. It is the IACUC's responsibility to assure that distress and discomfort are addressed in research animals. The IACUC should have in concert with the veterinarian determined if these two animals were distressed and/or discomforted and made efforts to correct their conditions prior to allowing the continuance of their use as research subjects. There were records indicating notification to the IACUC that one animal would be removed from food restriction for weight loss but no action taken, even with the investigators continued use by feeding the animal in the restraint chair. There were no records of IACUC involvement/intervention or review of these animals for distress and discomfort and it is their responsibility to ensure the avoidance of pain, distress and discomfort as per this section of the regulations.

Correct by May 30, 2008

Prepared By: _____
MICHAEL SMITH, V.M.O. , USDA, APHIS, Animal Care
Title: VETERINARY MEDICAL OFFICER , Inspector ID: 5019
Received By: _____

Date:
APR-15-2008

Title:

Date:
APR-15-2008



INSPECTION REPORT

3.75 (a)

HOUSING FACILITIES, GENERAL.

(a) Structure: construction. Housing facilities for nonhuman primates must be designed and constructed so that they are structurally sound for the species of nonhuman primates housed in them. They must be kept in good repair, and they must protect the animals from injury, contain the animals securely, and restrict other animals from entering.

Animal MMU 35184 has a history of getting extremities caught in different areas of the primary enclosure. There were 4 instances of this animal having extremities trapped in the last 3 years. The most recent occurrence was in February 2008 when the left arm of the animal was trapped in a small area on the front corner of the primary enclosure. There has been no adjustment or alteration to the animal enclosure at the time of this inspection to prevent recurrence.
Correct by May 15, 2008.

Prepared By: _____
MICHAEL SMITH, V.M.O. , USDA, APHIS, Animal Care
Title: VETERINARY MEDICAL OFFICER , Inspector ID: 5019
Received By: _____
Title: _____

Date:
APR-15-2008

Date:
APR-15-2008



A. Eugene Washington, M.D.
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and Provost
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September 13, 2007

Robert Gibbens, DVM
Regional Director -- Animal Care
Western Regional Office
USDA Animal and Plant Health Inspection Service
2150 Centre Avenue, Bldg B, Mailstop 3W11
Fort Collins, Co 80526-8117

Dear Dr. Gibbens,

RE: Registration Number 93-R-0440

IACUC Protocol # [REDACTED]

Species: [REDACTED]

This letter serves as full explanation and follow-up reporting of an IACUC suspended activity and details of the corrective action taken.

On June 5th, 2007, the Committee voted to suspend protocol [REDACTED]. A protocol audit uncovered several non-compliances. Specifically, anesthesia records indicated that several animals showed reflexes during the surgical portion of the procedure, there were documentation errors in several animal medical records, and lab personnel were not properly trained. After discussion, the Committee required that the PI:

1. Explain the circumstances of the issues listed above and why they occurred.
2. Explain what systems have been instituted to ensure that similar incidents will not recur, including how personnel will be properly trained.
3. Meet with LARC veterinarians to discuss the anesthesia regimen outlined in the protocol and possible alternatives.
4. Notify NIH of this suspension and provide the IACUC with documentation.
5. Meet with Eugene Washington, Executive Vice Chancellor and Provost, who will emphasize the seriousness of these violations and explain how these violations may put the entire UCSF animal research program in jeopardy.
6. Attend an IACUC meeting to address these issues with the Committee.

The PI responded as follows, in italics:

1. Explain the circumstances of the issues listed and why they occurred.

- a) Anesthesia records indicate that several animals showed reflexes during the surgical portion of the procedure.

The surgical procedures (tracheotomy, scalp incision to expose the skull, and trephination of the skull) were performed under areflexia. The monitoring records only reflect those moments when a supplement was necessary. The procedures were interrupted when reflexes were present until areflexia was reached again.

- b) There were documentation errors in many records. Vital signs were not recorded for the first 2-3 hours of the procedure and bupivacaine was not documented as being administered on several animals.

The missing vital signs were all during the initial sedation period, when the animal was still light, prior to reaching surgical levels of anesthesia. Previous reviews of the monitoring records by LARC and Compliance personnel had not identified this as a problem, however, we will now monitor vital signs during the early, pre-surgical periods, i.e., before the EKG is connected. The missing entries of bupivacaine were a regrettable oversight (likely because it is administered as integral part of the surgical procedure). We will note its use in all future monitoring appropriately.

- c) Lab personnel were not properly trained.

The training of personnel is continuous. The two new investigators on the protocol have observed several procedures before they actively took part in them and have shown under my supervision their ability to conduct the surgery. They have received feedback about the monitoring from myself and from LARC personnel. They also have received extensive instruction and feedback about reflex assessment and adjustment of anesthetics. Unforeseen situations, e.g., management of uncharacteristic high heart rates or the consequences of absorption and release of anesthetic in obese animals were addressed through feedback at the time.

2. Explain what system you have instituted to ensure that similar incidents will not recur, including how personnel will become properly trained.

Regarding the ongoing training of the new personnel: The next three to four experiments will be under the leadership of highly experienced lab personnel (more than 5 years), (including Dr. X, MD., Dr. X, Veterinarian). The new personnel will assist during the surgery and the monitoring of drug administration and vital signs will be reiterated. The following experiments will have the participation of at least one experienced person on the protocol until we have confidence that the new personnel has sufficient experience (~10 cases). Also, experienced personnel will discuss each experiment with the new individuals and go over the monitoring records after the experiments and sign off the records.

We have added an additional column on our monitoring sheets to record the time of individual procedural steps. Also, we will use a more detailed system to indicate the strength of the reflexes (e.g., 0: no reflex; 1: trace; 2:

muscle tension present; 3: slight withdrawal; 4: moderate withdrawal; 5: strong withdrawal).

3. Meet with LARC veterinarians to discuss the anesthesia regimen outlined in the protocol and possible alternatives.

I met with Dr. Washington from LARC on 6-15-2007 and discussed the anesthetic regimen as well as potential interactions with LARC to reduce the variability in survival time of the experimental animals.

4. Attend an IACUC meeting to address these issues with the Committee.

5. Meet with the Institutional Official.

An appointment with Dr. Washington is pending, depending on his schedule this week. We also responded to the vital sign monitoring issue in a minor modification of our protocol and follow the guidelines of monitoring frequency as indicated on the LARC website. (The modification will be RIO-submitted by the end of this week).

The PI attended an IACUC meeting on 6/19/2007. After discussion, the Committee required that the PI address the following prior to reinstatement:

1. Provide a written response detailing training for current personnel as well as future personnel. This training program should address what skills will be taught, how training will be documented and how proficiency will be determined.
2. Consider the use of isoflurane instead of pentobarbital.
3. Meet with Eugene Washington, Executive Vice Chancellor and Provost.

The PI responded as follows:

1. New personnel will undergo the following sequence in the training of the required surgical skills and monitoring of anesthesia for non-survival surgery. A) Observation of at least two full sequences of the surgical anesthesia and surgery procedure conducted by highly experienced lab personnel (minimum of 2+ years and at least 12 cases of experience). Special emphasis on induction and maintenance of anesthesia, assessment of depth of anesthesia, record keeping regarding anesthesia and vital signs; clean surgical techniques and record keeping for surgical procedure, including drug administration. B) Perform at least three cases of anesthesia and surgery-related procedures under presence and instruction of highly experienced lab personnel (minimum of 2+ years and at least 15 cases of experience). If surgical and anesthesia monitoring skills are not judged to be proficient by the PI, perform further cases under instruction as needed. C) Perform anesthesia monitoring and surgery in at least 9 cases under supervision of highly experienced lab personnel. Supervisor signs off on procedure performance and anesthesia monitoring documentation. D) We will keep a training log documenting the training cases and the supervisor's assessment of the surgical and anesthesia skills of the trainee. The current personnel under training will observe induction, maintenance and assessment of anesthesia as well as surgical procedures in 2 more cases

(they already have observed two and participated in 5 surgeries). Each of the trainees will then perform at least 2 cases under direct supervision to assess their proficiency in surgery, anesthesia and monitoring. If judged proficient by the PI, a minimum of 9 following cases will have a supervisor assigned to the trainee to insure quality of anesthesia, surgery and adherence to protocol.

2. We will arrange to perform two cases of isoflurane anesthesia for our surgical procedure (either with help from LARC or other personnel experienced in this procedure) within 90 days following reinstatement of the protocol. Dr. Washington assured me that we can proceed with our original regiment after reinstatement, before assessing a potential switch to isoflurane for the surgical portion of our experiments. We require this, since two of our experienced lab personnel (Drs. X and X, each has more than 6 years of experience in our lab) urgently have to finish two long-standing series of experiments that require the use of the current regimen...

3. After approval of this letter by the IACUC I will meet with Executive Vice-Chancellor Washington and discuss the issues.

4. Attached is our modified monitoring sheet that will be used during the initial surgery as well as during the following experiment. The experienced supervisor assigned to each case will monitor and signoff on the monitoring sheets at the end of the experiment to assure compliance...

On July 17, 2007 the IACUC reviewed the PI's response and discussed the following requirements prior to reinstatement:

1. Increased frequency of monitoring is required. Revise the protocol accordingly in RIO.
 - a) No less than every 15 minutes to be documented during the surgical portion of the procedure and
 - b) No less than every 30 – 60 minutes for the recording portion of the procedure.
2. The comments section of the monitoring form must reflect clearly when the surgical portion of the procedure begins and ends in addition to other "individual procedural steps" that you have indicated you will document. Please upload the revised monitoring form into the "Documents" section in RIO.
3. LARC veterinary staff must be present for the surgical portion of the next procedure to observe implementation of new documentation standards and to observe the training of new staff.
4. Notify the IACUC when your current new staff has completed their training. LARC veterinary staff must then be present during the surgical portion of the first procedure that these staff members perform.
5. For the next 6 months, all documentation of procedures completed under this protocol must be submitted to the IACUC within 30 days of completion of the procedure.
6. In your response letter dated 6-18-07, you noted that you will use a reflex scale of 0 – 5. While this scale is acceptable, we remind you that your approved protocol states that, "The anesthesia will be maintained at surgical (areflexic) level". Therefore, no procedures may be performed unless the animal is at a reflex level of 0.
7. Meet with our Institutional Official, Dr. Washington, who will emphasize the seriousness of these violations and explain how these violations

- may put the entire UCSF animal research program in jeopardy.
8. Identify to the IACUC which funding sources cover the suspended activities of this protocol.
 9. Notify your NIH Grant Program Official of the suspension and copy the IACUC on correspondence.

On August 17th 2007 the PI responded:

1. We changed the protocol accordingly.
2. We did so.
3. We will inform LARC about the timing of the next procedure and coordinate.
4. We will inform the IACUC and LARC when new staff will perform their first independent procedure.
5. We will do so.
6. We agree.
7. An appointment with Dr. Washington is pending, depending on IACUC notification of his office.
8. The research is supported by NIH grant DC002260 as well as Departmental funds.

9. Below is the e-mail interaction with the NIH:

Date: Fri, 3 Aug 2007 07:57:06 -0400
Thread-Topic: animal protocol
From: [REDACTED] Ph.D.
To: Dr. X

Hi Dr. X,
Have forwarded this on to the appropriate people and will let you know if they need anything further. For now, this is sufficient for us being notified and thank you for doing. Will let you know if anything further is needed.

Best,

[REDACTED]

[REDACTED], Ph.D.

Program Director
National Institutes of Health
National Institute on Deafness and Other Communication Disorders

[REDACTED]

[REDACTED]
[REDACTED] mail.NIH.gov

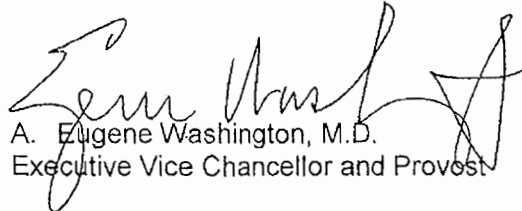
Tel: (301) [REDACTED]
Fax: (301) [REDACTED]

This PI met with me as the Institutional Official on August 29th, 2007 at 11:30 am. During I reiterated the importance of compliance with Animal Welfare Act Regulations, PHS Policy, and UCSF policies and guidelines. Following this meeting, the IACUC issued the PI a Full Reinstatement letter.

I believe that the corrective actions taken by the IACUC will help to assure future compliance by this investigator.

Should you have any additional questions, please do not hesitate to contact me.

Sincerely,



A. Eugene Washington, M.D.
Executive Vice Chancellor and Provost

cc: Interim AVC and Attending Veterinarian, Clifford Roberts
IACUC Chair John Taylor
IACUC Director [REDACTED] # 27819
Interim LARC Director [REDACTED] # P13



A. Eugene Washington, M.D.
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December 19, 2007

Robert Gibbens, DVM
Regional Director – Animal Care
Western Regional Office
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2150 Centre Avenue, Bldg B, Mailstop 3W11
Fort Collins, Co 80526-8117

Dear Dr. Gibbens:

RE: Registration Number 93-R-0440

IACUC Protocol # [REDACTED]

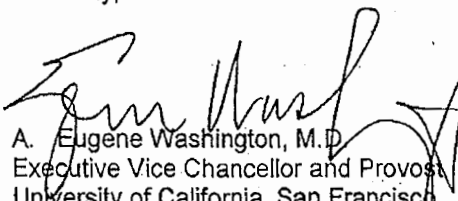
This letter serves as full explanation and follow-up reporting of an IACUC suspended activity and details of the corrective action taken.

A post approval monitoring review of animal medical records revealed that rabbits had not been monitored according to the approved protocol after receiving an inoculation of bacteria, or after undergoing a catheterization procedure. The animals had been monitored daily; however, the protocol stated that the animals would be monitored twice per day. The protocol was suspended on August 21, 2007 by the IACUC until the PI could put a plan in place to assure that laboratory personnel fully understood the obligations listed in the protocol. The PI has consulted with a LARC veterinarian and the laboratory staff has undergone extensive training. The Training and Compliance staff has performed follow up visits to conduct training on medical records documentation and protocol compliance. The protocol was reinstated at the IACUC meeting on December 18, 2007.

In addition, I will meet with this PI on January 4, 2008 to reiterate the importance of compliance with all regulatory requirements and believe that the corrective actions taken by the IACUC and our institution will help to ensure future compliance by this investigator.

Should you have any additional questions, please do not hesitate to contact me.

Sincerely,



A. Eugene Washington, M.D.
Executive Vice Chancellor and Provost
University of California, San Francisco

cc: Interim AVC and Attending Veterinarian Clifford Roberts
IACUC Chair John Taylor
IACUC Director [REDACTED] # 27819
Interim LARC Director [REDACTED] # 193