

DETAILS OF UNIVERSITY OF WASHINGTON COMPLAINT

The alleged violations described in the complaint were examined on Oct. 26, 27, and 31, 2006. Records for the individual animals identified in the complaint were studied, as well as the approved protocols for the three investigators named in the complaint. Interviews were also carried out with one principal investigator, his associate, the attending veterinarian, the veterinary surgeon and veterinary technician involved in one of the cases, the primate center senior veterinarian, and the personnel in the IACUC office. I received full cooperation from the institution during these proceedings. The results of my investigation are described in the order presented on the written complaint and are as follows:

1. Primate 04090 developed complications after the repair of a spinal cord implant. The protocol involved three separate surgeries. The spinal cord implant was the final surgery. Post-operative analgesics were given after each procedure, and pre-operative antibiotics were given when indicated. The animal was given veterinary care after the third surgery due to anorexia and was treated for 9 days. The treatment response was good. The spinal cord implant needed repair approx. 34 days after it was placed, and a fourth surgery was done for this. Four screws had pulled out of C2-C3. Three new screws and a new chamber were implanted. Analgesics, prophylactic corticosteroids, and antibiotics were administered after this surgery. The animal began exhibiting signs of paresis after this repair and was treated intensively with supportive medications, corticosteroids, and analgesics for ten days until it was euthanized.

The approved protocol was followed and the animal was removed from the activity and given appropriate veterinary care when complications occurred. It was humanely euthanized when treatment was unsuccessful.

2. Primate A03068 was not on a protocol. The records show that the animal was generally healthy with only two incidents occurring while being housed: One was a finger abrasion which was treated with antibiotics; the other was an escape from its cage along with a male monkey. The animal was observed to have a slight limp, favoring its right leg, after its capture. The animal was sedated and given a complete exam and found to be in good health. Approx. eleven weeks later, the animal was observed to have an abnormal appearance of the left leg. Analgesics were given for five days. A physical exam was done and radiographs were taken, where severe arthritic changes were noted and a decision was made to either surgically intervene or euthanize the animal. Analgesics, glucosamine + chondroitin, and other joint fluid stimulators were given for four more days, after which the decision was made to euthanize the animal. The necropsy indicated that the caput femoris, or femoral head ligament, was not apparent. In my opinion, it may be inferred that the rupture of this ligament was the primary cause of the resultant arthritic changes, and may have occurred when the animal escaped from its cage.

Contrary to the statement in the complaint that the documentation shows no evidence of treatment, this animal was given appropriate veterinary care when problems were

noted, and was humanely euthanized to prevent further pain and suffering and as an alternative to more treatment.

3. Primate J91386 was part of the breeding colony and was not on a protocol. She was a 14 year old obese female macaque that had undergone an OVH for reproductive difficulties (non-viable fetuses and multiple C-sections). Five and a half weeks later, a complete physical was done where the chief complaint was dry skin. An incidental abdominal mass was observed. An ultrasound imagery and biopsy were performed, indicating a sterile abscess. The animal was placed on antibiotics for 12 days. Since the mass was not affecting the health of the animal, the decision was made by the clinical staff to have the animal euthanized at a later date for a combined clinical and tissue-program necropsy. The animal was stable until it was euthanized 3 months later. The necropsy revealed that the sterile mass was an encapsulated surgical sponge.

According to the pathologist, "the foreign body was an incidental finding which did not adversely affect the health of this animal. The abscess was sterile and walled off." In my opinion, although precautions are taken during surgery to prevent gauze sponges and other items from being left behind, occasionally one does get left behind. This is more likely to occur in obese patients where there is more fat, thus less visibility and more likelihood of hemorrhage. I find that appropriate veterinary care and supportive treatment were given when the problem was identified.

4. Primate 02049 was an obese adult female macaque that was part of the breeding colony. The animal was found ataxic and lethargic and rapidly went into shock. A complete exam was done by the veterinary staff that day. The animal was given supportive treatment with fluids, corticosteroids, analgesics, and other emergency medications. The animal responded and was alert by the end of the day. The following day, the animal relapsed and was euthanized. The pathologist's report stated that "The ultimate cause of acute collapse in this animal was an electrolyte disturbance: marked hypokalemia..... Terminal clinical, laboratory, gross, and necropsy findings are consistent with fatal fasting syndrome (FFS) of macaques. This poorly defined syndrome often occurs suddenly in obese mid age macaques....."

The senior primate center veterinarian provided me with copies of several articles from scientific journals and primate textbooks describing FFS of macaques. One reference states, "The disease syndrome is defined as sudden death in obese macaques with no prior indication of illness or following brief periods of anorexia or weight loss..... There is no apparent single husbandry practice or disease that accounts for the occurrence of this syndrome."

The complainant states that this animal died of sepsis, or massive bacterial infection. I found nothing in the animal's record or in the pathologist's report that substantiates this. The animal received intensive veterinary treatment when problems were first noted, and was humanely euthanized when it did not respond well to treatment.

5. Primate A01136 was identified in the complaint and described thus: "The cause of death for this animal was never determined because the researcher, in whose experimentation this animal was used, had cut off the primates' head and refused to allow the veterinary staff of the UW to examine it, despite a specific request for this vitally

important organ." This animal was on an experimental protocol in which two surgeries were to be performed. The first surgery involved the placement of a scleral eye coil which was connected to a lug, or screw, implanted in the skull. The second surgery was to take place several weeks or months after the first, and involved removing a section of cranial bone and placing a recording cylinder on the dura mater and attaching it with dental acrylic and screws. The purpose of the activity is related to determining which parts of the brain are responsible for eye and head movements. In examining the record for A01136, the chronological order of surgeries done on this animal are as follows:

- a) 1/30/02 - eye coil placed in left eye (o.l.)
- b) 5/1/02 - eye coil placed in right eye (o.d.)
- c) 6/13/02 - chamber implant done
- d) 12/17/03 - second chamber implant done (this involved a second craniotomy. The animal had 2 chambers on its head at this point)
- e) 7/22/04 - eye coils removed o.l. and o.d. Re-implanted part of device o.l.
- f) 1/10/05 - removal of implant o.l. Implanted device o.d.
- g) 2/14/05 - removal of implant o.d. Implanted device o.l.
- h) 3/2/05 - major head implant slough with large defect and copious bleeding.
Repair of defect.
- i) 3/3/05 - animal found dead in a.m.

In the description of the surgery in the protocol (approved 5/31/01 through 5/30/04) it states on PRF-14 #15(a) Number of surgeries per each animal: "There are usually two minor surgeries (no body cavities are invaded). Occasionally, if the animal rejects an implant and it needs to be repaired or if the placement of the chamber needs adjustment, a subsequent similar surgery is required." And on PRF-15 #15(j) it states, "Chamber adjustments do not require additional craniotomies (there isn't enough room on the skull). Rather, we might change the angle of the chamber or move it slightly in the craniotomy or extend the original craniotomy if the bone has re-grown or the chamber placement needs to be slightly adjusted. Chamber adjustments are rare (<1/10 animals) but lug replacement or repair is common (~1/animal)." An addendum was submitted to the IACUC on 6/21/01 for approval of additional procedures to be done between 5/31/01 and 5/30/02, which included the placement of 2 recording chambers during a single surgery. It was approved by the IACUC on 7/10/01. The 3 year renewal of the protocol did not contain this amendment.

There are several discrepancies in the written approved protocol and the actual activities performed on this animal, of which the IACUC was not aware. There is no part of this written protocol at any time that describes the placement of 2 head chambers during separate surgeries. The second head chamber was placed on the animal after the addendum had expired. However, even if it had been placed during the time frame, it was an additional surgery outside of the placement of the first chamber, and thus was not done according to the approved addendum. It was discovered during this inquiry that 2 additional animals had also had 2 head chambers placed on them during separate surgeries. These were primates A03082 and A99088. Also, the multiple repetitive surgeries involving placement of the eye coils on A01136 are outside of the realm of the approved protocol.

In addition to the above, it was discovered through interviewing the research assistant that the placement of the eye coil involves drilling through the orbital process of the cranium in order to run the wire up to the implanted lug. There is no description of this invasion of the orbital bone in the written protocol. It is important that this step be included so that the IACUC can make a proper assessment based on the added risks involved before granting approval. Also, in a separate interview, the P.I. stated that he was not entirely aware of what was in the approved protocol and any amendments or significant changes to it, but that he depends on the research associate to take care of that for him. He said he believes that the animals are approved for multiple major surgeries in the oculomotor protocol. He also stated that A01136 had 3 head chambers on it before it died. This was not corroborated by the research assistant who said that no animal had ever had more than 2 head chambers simultaneously. The records showed that this animal did not have more than 2 chambers. When asked why so many surgeries were done on A01136, the P.I. stated that he thinks it is important to get the most use out of these animals in order to minimize using additional animals. Both the P.I. and research assistant stated that the cause of death for A01136 was hypothermia caused by Ketamine anesthesia.

Another cause for concern regarding this protocol and the investigator is that when it was submitted for the Request for Annual Renewal on 2/10/06, PRF-2 #4 asks the question: "Have there been any unexpected adverse events, morbidity, or animal mortality in the past year? If so, explain the causes and measures taken to prevent future occurrences." Answer: "No" (A01136 died on 3/3/05)

I interviewed the veterinary surgeon and the veterinary technician who performed the final surgery to repair the defect. They stated that the animal was placed on a heating pad during the surgery, and that the surgery took much longer than expected (1.5 hours) and the animal was given a second dose of Ketamine before it was over. Analgesics and antibiotics were administered perioperatively. They stated that the animal was recovering and was alert when they left it. The room temperature is kept at 78-80 degrees F. The animal was found dead at ~0730 the next morning.

I asked both the senior primate center veterinarian and the attending veterinarian about the effects of Ketamine. I spoke to them separately. They both stated that Ketamine does not have analgesic properties and is not generally used for prolonged surgical procedures. They stated that it actually increases blood flow, and thus would more likely counteract hypothermia rather than cause it. When asked about the defect itself, they both stated that, in hindsight, a wound that size may have done better to have been treated medically for a period of time to stabilize the animal and start the healing process before attempting surgical repair. Unfortunately, sometimes these things are learned afterward.

In regard to the P.I. removing the head before the pathologist completed the necropsy, I spoke to both the senior primate center veterinarian, who was not at the facility when the incident occurred and the P.I. separately. The pathologist who performed the postmortem is no longer employed at the U of W. The pathologists are part of the clinical veterinary staff. According to both parties, the pathologist insisted on performing an autopsy on the head before the P.I. was to examine it. The P.I. said that it is important for the researcher to examine the head and make tissue slides first in order to obtain valuable research data before the pathologist alters it. That is why he took the head. He said that he would have given it to the pathologist when he was finished with it, but he

wasn't asked for it. I asked the senior P.C. veterinarian what is usually done in such cases. He stated that the pathologist involved with this case was very difficult to work with and created problems due to lack of people skills. He said that usually the pathologist and veterinary staff work in a cooperative manner with the P.I. so that both ends can be achieved. It could not be determined whether or not, as the complainant alleges, the P.I. was hiding anything from the veterinary staff.

The research protocols were reviewed for the 3 researchers identified by the complainant. With the exception of the researcher referred to in the above paragraphs, the protocols being done by the other 2 were well-written and were being followed as written and approved by the IACUC. Any unexpected adverse events, morbidity, or animal mortality were identified on the PRF for the IACUC to consider during annual renewals.

SUMMARY COMMENTS:

Although most of the issues identified in the complaint were not found to be valid, the items identified concerning animal A01136 and the investigator were found to be valid. During the process of this investigation, many discrepancies were uncovered. These have been documented on an Inspection Report with corrective/preventative actions addressed. The IACUC has suspended the performance of any further surgeries by this investigator until the matters can be resolved.



United States Department of Agriculture
Animal and Plant Health Inspection Service

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INSPECTION REPORT

UNIVERSITY OF WASHINGTON

Customer ID: 1016

Certificate: 91-R-0001

BOX 357190
SEATTLE, WA 98195 7190

Site: 001

UNIVERSITY OF WASHINGTON

Inspection

Type: ROUTINE INSPECTION

Date: OCT-26-2006

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DIRECT

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

<<<< A proposal to conduct an activity involving animals, or to make a significant change in an ongoing activity involving animals, must contain the following:

(3) A complete description of the proposed use of the animals.>>>>

In Protocol #2342-01, three NHP had 2 craniotomies with head chambers placed on them during separate surgeries. This is not described in the written protocol or any addendums or significant changes that were approved by the IACUC. In the same protocol, one of the three NHP had multiple repetitive surgeries involving placement of the eye coils. The protocol describes only two minor surgeries: a) placement of the eye coil, and b) a craniotomy with attachment of a recording chamber. Also, it was learned that the placement of the eye coil involves drilling through the orbital process of the cranium. This is not described in the approved protocol. The NHP that had the two craniotomies and multiple eye coil surgeries died from complications from these procedures.

The principal investigator was not following the procedures described in the approved protocol for the proposed use of the animals, which lead to the death of one animal.

The registrant stated that this has been corrected by suspending any further surgeries from being done by the investigator and the research team on the protocol until these issues can be resolved. The IACUC will convene on Nov. 16, 2006, to discuss this activity. The principle investigator has been told to submit a written significant change to be reviewed by the IACUC. The clinical veterinary staff will be given a summary of the approved surgeries for research activities which can be reviewed during preoperative physical exams for animals to be used on such activities. The veterinary staff can then provide oversight to ensure that the approved procedures are being followed.

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