



## Inspection Report

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

UCSF BOX 0547

Type: ROUTINE INSPECTION

SAN FRANCISCO, CA 94143

Date: Jan-24-2012

### 2.31 (d) (1) REPEAT

#### INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

2.31(d) IACUC review of activities involving animals. (1) In order to approve proposed activities... 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;

The IACUC-approved protocol "Incubation Periods of Prions and other Neurodegenerative Diseases" states that voles are to be monitored for neurologic signs following intra-cerebral inoculation with prion infected tissue "Twice weekly until the first sign, then daily Monday through Friday". According to the protocol the animals should be euthanized either "...at the earliest point possible in the clinical progression of the disease, to ensure that no animal ever suffers or is in distress" or "...following the presence of two neurological signs..." According to this protocol, an animal developing one neurologic sign on a Friday could develop additional neurologic signs over the weekend and experience unnecessary discomfort, distress, and pain prior to dying of prion disease or being humanely euthanized on Monday. Incubation period data for eight animals placed on this study showed that three animals were found dead from prion disease on a Monday, with no recorded observed neurological signs.

The IACUC should ensure that animal activities include provisions that avoid / minimize pain and distress by providing for adequate monitoring of animals as necessary to prevent discomfort, distress, and pain.

This is a REPEAT citation. There was a previous citation under this regulation on Jan 5, 2011, and it was to be corrected by April 3, 2011.

### 2.31 (e) (2)

#### INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

2.31(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;

#### Prepared By:

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Date:

Title: VETERINARY MEDICAL OFFICER Inspector 6036

Feb-01-2012

#### Received By:

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

Date:

Title:

Feb-16-2012



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\*\*\*In the IACUC-approved Amblyopia and Strabismus study protocol, the rationale for the numbers of animals to be used in the study states " In my field, the number of animals needed for research is not guided by statistical criteria or tests... Because the success rate of experiments is unpredictable, given the innate nature of scientific investigation, and the yield of data from any given animal is variable in quantity and quality, it is hard to predict the number of animals required for our research projects. The number of 15 monkeys is the most accurate projection that I can provide of expected animal use over the next 3 years. This figure is also based on our experience with the requirements for manuscripts reporting scientific results in per-reviewed publications in my field. We utilize the minimum number of animals required to meet my scientific field's publication standard. "

Stating that the number of animals to be used cannot be determined using statistical criteria or tests, because of the nature of your field or research, is not an appropriate explanation of how the numbers requested were determined unless an acceptable alternative explanation is provided. Citing requirements for publication of manuscripts is also not an adequate explanation for the need to use a specific number of animals for experimentation. The investigator is responsible for providing the IACUC committee with a rationale for animal use that includes an explanation for the number of animals that is based on specific goals, statistical thresholds, or some other more concrete criteria which reflect the purpose of the investigation, beyond manuscript publication.

\*\*\* In the IACUC-approved Incubation Periods of Prions and other Neurodegenerative Diseases protocol, the description of the criteria for the number of animals needed states "We perform on average 44 samples per year in hamsters... and 25 samples in voles." But a chart above this description showing the number of animals acquired for this protocol lists 1056 hamsters and 750 voles. There is no explanation for these numbers, and it remains unclear how many animals the investigator proposes to use for this research under this protocol.

\*\*\* In the IACUC-approved Rabbit Model of Bacterial Endocarditis protocol under Category D there is contradictory and inadequate information about the number of rabbits to be used. Under the description of statistical tests/rationales used to determine the number of animals needed, it describes the use of 100 rabbits per year for three years for a total 300 rabbits, and then later states that under category D the total is 400 rabbits , with no clear explanation as to how the extra 100 rabbits came into the equation. There is also no explanation as to how either the 100 rabbits per year nor the 300/400 rabbits total will be used to meet their stated statistical goals.

\*\*\* In the Cellular Mechanisms of Vascular Injury protocol, the rationale for the number of animals calls for two different injury models, and under each injury model there are three treatment modalities. For some unexplained reason the protocol states that each treatment modality will have its own "control - no treatment " rabbit. It is not explained why each treatment modality requires a control animal rather than having a control under each injury model, alongside the three treatment modalities for each injury model. Having a control for each treatment modality adds an additional 100 rabbits to the protocol over having one control per injury model.

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An appropriate rationale for the number of animals the investigator proposes to use is necessary to ensure that the minimum number of animals is used in an activity involving animals. Errors or lack of information in a proposed activity could result in animal use that was not approved with a clear or accurate understanding of the need for this animal use, which could jeopardize animal welfare.

The IACUC should ensure that each activity using animals contains an appropriate rationale for the numbers of animals to be used in that activity.

To be corrected by May 1, 2012.

**2.31 (e) (3) REPEAT  
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).**

2.31 (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:...

(3) A complete description of the proposed use of the animals;

\*\*\*The protocol Incubation Periods of Prions and other Neurodegenerative Diseases was approved with an incomplete description of when animals were to be monitored for neurological signs. According to the stated monitoring parameters in the protocol, following prion inoculation the animals are to be monitored " twice weekly until the first sign..." However, the protocol does not specify when the monitoring should take place during the twice a week monitoring period. As written, monitoring could take place on consecutive days leaving five days when the animals would not be assessed for neurological signs. The protocol should be more specific as to when the animals are monitored for neurological signs in order to ensure that they do not wait past study end points for euthanasia. The protocol also contains conflicting statements as to when the animals are to be euthanized. One section of the protocol states that "Each animal is humanely euthanized at the earliest point possible in the clinical progression of the disease, to ensure that no animal ever suffers or is in distress." Elsewhere in the protocol stated endpoints are "...5 days past onset of clinical signs in hamsters" and that voles "...are euthanized following the presence of two neurological signs..." The protocol also states that the animals are still able to eat, drink, and move around the cage, yet some of the neurological signs that animals are monitored for include "Can't get up", "Paralysis", and "Convulsion". The protocol does not differentiate between the animals with severe neurological signs and those with mild signs with regards to euthanasia of infected animals. Presumably, if a vole was only having convulsions it would not be euthanized because it was only showing one neurological sign.

It is the responsibility of the IACUC to ensure that the investigator provides a complete description of proposed activities that involve the use of animals in order that those activities may be adequately reviewed and determined to be in accordance with the Animal Welfare Act.

This is a REPEAT citation. There was a previous citation under this regulation on Jan 5, 2011, and it was corrected by the time of the exit interview for that inspection.

An exit interview was conducted with facility representatives.

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