



Inspection Report

WAKE FOREST UNIVERSITY

Customer ID: 825

Certificate: 55-R-0001

Site: 001

ANIMAL RESOURCES PROGRAM DOWNTOWN CAMPUS

MEDICAL CENTER BOULEVARD

Type: ROUTINE INSPECTION

WINSTON SALEM, NC 27109

Date: Jun-15-2010

**2.31 (c) (7) DIRECT NCI
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).**

IACUC functions. With respect to activities involving animals, the IACUC, as an agent of the research facility, shall:
(7) Review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the care and use of animals in ongoing activities;

***Three rabbits on protocol A09-605 involving implantation of artificial ear cartilage had large aural hematomas on one affected ear. These rabbits had not received a pressure bandage sutured to the ear post-surgery as described in the approved protocol. Instead, the surgeon had applied some gauze which was only taped to the ear and apparently was removed or fell off shortly after the procedure. (The surgeon was out of town during this inspection and unavailable for comment. The Principle Investigator was not present during the surgery and did not know why the pressure bandage was not applied.) Failure of the Investigator's team to follow the protocol as approved resulted in the formation of the large hematomas and could have been prevented. All researchers and team members need to be familiar with and follow approved protocols to prevent pain and distress to animals. Facility has planned meeting with surgeon and PI to address these issues as soon as surgeon returns. In the interim, hematomas are being drained and analgesics administered.

***On protocol A09-603 involving drug-induced diabetes in rabbits, researcher had difficulty establishing a stable diabetic state in the rabbits due to multiple factors. As a result, he injected 46 rabbits with alloxan instead of the initially approved number of 10. The protocol had been approved for 10 controls and 10 alloxan-injected rabbits initially to establish this model since this researcher had never used this model before. The use of the extra 36 rabbits to establish a stable model was not approved in the protocol. (Note: An additional 92 rabbits were approved for the second part of the protocol, which involved the actual research project, but this part has not been started due to the difficulties in establishing a stable model.) Of the 46 rabbits injected with alloxan, 21 died at various stages post-injection, (46% mortality rate). The approved protocol only expected a 20-30% mortality rate. There should have been some mechanism in place to alert the IACUC to the unexpected deaths and action should have been taken at that point.

***On protocol A09-603, glucose monitoring was not done according to approved protocol amendments. After first rabbit died, the protocol was amended to include daily monitoring of glucose. This was approved on 2/1/2010. A review of the medical records indicates this was not done for every rabbit. Some

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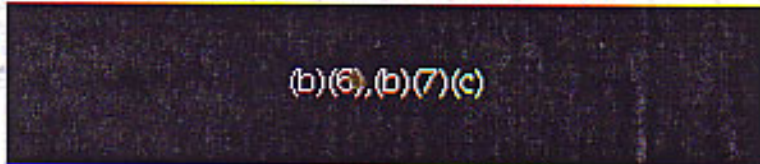
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rabbits did receive daily or even more frequent monitoring, but many did not. Several rabbits were found dead and there were many problems regulating the blood glucose levels in these rabbits. Glucose levels swung wildly up and down, some rabbits were hyperglycemic and had to be given insulin and some were hypoglycemic and had to be given dextrose or other supplements. Some rabbits died in spite of treatment. Given the nature of the study, frequent glucose monitoring is crucial to the survival of these rabbits. While interviewing the research team, one of them stated that daily glucose testing was only instituted "a couple of months ago" about April, but the protocol was actually amended 2/1/2010. It is clear that the research team had major issues in understanding the importance of glucose monitoring and communication was lacking to ensure that all team members were following the approved protocol.

***Protocol A09-603 - Insulin dose and route was not being given as approved in the protocol. Protocol states that 1 IU fast-acting insulin will be given SQ for every 100 units the glucose level is above 200. A review of the medical records shows that the insulin was often given IM and the dose varies widely. The protocol was not always followed which contributed to the problems regulating glucose levels. If the protocol needs to be changed, then an amendment should be approved by the IACUC.

The IACUC must approve all changes to a protocol and the researchers must follow the approved protocol unless an amendment is approved. Correct by June 21, 2010.

2.31 (d) (1) (i)

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC).

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;

***According to the facility's computer records, Protocol A09-603 was initially approved to only require glucose monitoring once/month after alloxan injection. Given the nature of this study and the well-known difficulties in stabilizing glucose levels, this level of monitoring is not sufficient to avoid or minimize discomfort, distress, or possible death due to hypo/hyperglycemia. While the protocol was amended shortly after approval to include daily monitoring of glucose, this was apparently not enough to prevent deaths. On May 27, 2010, the IACUC partially suspended this protocol so that no more rabbits could be injected with alloxan until a new protocol was approved. Any new protocol should include more frequent monitoring of glucose levels post injection, especially in the first few days, to ensure that distress is minimized. Correct for all future protocols.

2.32 (a)

PERSONNEL QUALIFICATIONS.

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.

***One researcher exhibited a clear lack of experience and knowledge in regard to animal treatment. On

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one occasion, he euthanized a rabbit in distress by air emboli because he did not know how to access euthanasia solution after hours. On at least one other occasion, he gave the wrong dose of insulin because he was unfamiliar with measuring insulin units and the use of insulin syringes. As a result, the rabbit received 10 times the dose. Other researchers in this group did not appear to have adequate experience and knowledge managing diabetic rabbits as evidenced by their lack of adequate glucose level monitoring. Institution needs to assess all persons involved in animal work to ensure they have the knowledge and experience to perform their work properly. Correct by July 15, 2010.

2.35 (a) (1)

RECORDKEEPING REQUIREMENTS.

The research facility shall maintain the following IACUC records:

(1) Minutes of IACUC meetings, including records of attendance, activities of the Committee, and Committee deliberations;

***Minutes of IACUC meetings were kept, however, they did not contain Committee deliberations in some cases. The minutes were so brief that it could not be determined just what the Committee discussed and how issues were resolved. Other records indicate that indeed deliberations took place, but there are insufficient details present. Minutes should include enough detail for the inspector to determine that all important points are discussed and resolved. Correct for all future minutes.

Exit interview conducted with facility representatives.

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