

MEMORANDUM

TO: Dr. Eric Pani, Institutional Official (IO) for PHS Assurance #A3646-01

FROM: Sharon A. Meyer, Ph.D.
Chair, Institutional Animal Care and Use Committee (IACUC)

SUBJECT: Compliance issues:
1.) Report of minor deficiency,
2.) charge of noncompliance with ULM policy in resolving animal welfare report

DATE: December 17, 2012

The ULM IACUC met December 10, 2012 to: 1) investigate a report of concern for welfare of research animals in a study covered by IACUC-approved protocol 11JLY-HMM-01 and 2) determine whether the ULM animal use program acted according to policy in response to this welfare report. All six voting members of the IACUC were in attendance.

Policy for animal use by the ULM program is prescribed by the Assurance between ULM and Office of Laboratory Animal Welfare (OLAW) of the Public Health Service (PHS) which commits the institute to operate in accordance with the *Guide for the Care and Use of Laboratory Animals (Guide)*. In addition, ULM Office of Sponsored Programs and Research (OSPR) document "Obtaining IACUC Review and Approval" requires research conduct comply with valid IACUC approval.

The animal welfare concern report was filed November 8, 2012 by an observer of study endpoints presented in a seminar that day by the graduate student conducting research assured by 11JLY-HMM-01. That student's graduate advisor is Program Director of 11JLY-HMM-01, Dr. Harihara M. Mehendale, Professor of Toxicology. Dr. Mehendale's assurance to the Institute of his adherence to IACUC-approved protocol is indicated by his signature, July 14, 2011, on the ULM Animal Welfare Assurance form. The charge that the ULM animal use program acted in noncompliance with policy was made by Dr. Mehendale. Dr. Mehendale was allowed time in the December 10 IACUC meeting by the Chair to justify the need to impose pain and distress on his study animals relative to the value of his research goals. His statement began with the charge that the procedure used by individuals of the ULM animal use program to resolve the animal welfare issue, which resulted in euthanasia of a moribund mouse on study, was not in compliance with policy.

IACUC concluded by majority vote that a minor deficiency of the Institute's program attributed to an animal user acting outside of approved protocol had occurred. The IACUC concluded that non-adherence with protocol 11JLY-HMM-01 resulted because endpoints of the study in question, "hours of sickness", differed from endpoints of the protocol. These were that mice would be "killed" and blood taken for plasma enzymes and were interpreted by IACUC as procedures to provide study metrics indicative of liver pathology that preceded morbidity. These were considered humane endpoints and adhered to protocol statement of imposing "the least amount of distress and pain to the animals". The reporter of concern for animal welfare observed data indicating imposition of ~4 days of sickness. IACUC does not consider this endpoint humane because of imposition of pain and distress associated with extended sickness and the risk that sickness will progress to morbidity. Evidence that morbidity did result from the hours of sickness endpoint was observed the

following day, November 8, 2012, upon examination of a study mouse that exhibited clinical criteria explicitly stated in the protocol that defined morbidity. Prescribed activities of the ULM-OLAW Assurance were then activated as follows. The Program Director was notified of the moribund mouse and advised by the Chair to authorize euthanasia. The Program Director refused to do this; **IACUC considers this a second non-adherence to his protocol.** The IACUC chair then proceeded to call for an on-site visit by the attending veterinarian, who then diagnosed the mouse as moribund and administered euthanasia. IACUC concluded that the program had incurred a "minor" deficiency. This deficiency was not considered "significant" because animal welfare and health was not compromised as a result of Institutional intervention. Significant, but not minor, deficiencies are reportable to OLAW by the IO.

IACUC with that vote also approved not suspending protocol 11JLY-HMM-01. The reasoning was that the moribund animal produced by the study was euthanized according to criteria explicitly specified by the protocol. Hence, because of institutional intervention, animal welfare and safety were not compromised. Protocol suspension is reportable to OLAW by the IO.

ULM-OLAW assurance requires IACUC to designate corrective action for deficiencies of the animal use program. Since IACUC concluded the protocol should continue in place, corrective action is for all parties to ensure adherence to its provisions including a requirement for euthanasia of moribund mice as evidenced by endpoints listed in the protocol. To achieve Program Director adherence with protocol, euthanasia of moribund mice must be done by animal users of his research program. If not, the same procedure will be implemented as before, i.e. post-approval monitoring by Vivarium staff, reporting of non-adherence to the IACUC chair and consultation with and, if warranted, euthanasia by the attending veterinarian. If the same offence by the Program Director occurs, the ULM-OLAW assurance requires a second IACUC review with classification as a significant deficiency of the program resulting from animal user non-adherence to an IACUC-approved protocol and protocol suspension. Both are reportable events.

The IACUC unanimously concluded that the ULM animal use personnel acted in compliance with established ULM policy and in accordance with procedures of the ULM-OLAW assurance. As such, it is believed that the IACUC and ULM animal use personnel have acted appropriately and responsibly to protect the support of other ULM animal users funded by PHS agencies, such as NIH and LaBRIN.

cc: Dr. Benny L. Blaylock, Director, CoP Vivarium and Dean, College of Pharmacy
Dr. William McCown, Director, Office of Sponsored Programs and Research