



**Duke University
Office of Animal Welfare Assurance
Policy**



COMPLIANCE MONITORING

PERFORMANCE STANDARD: The goal of compliance monitoring is to provide program assurance, that animals used in Duke activities are used according to federal regulations, IACUC approved protocol or institutional SOP.

BACKGROUND: Compliance Monitoring (CM) is process performed by the Office of Animal Welfare Assurance (OAWA) under the direction of the Duke IACUC. CM is intended to be a focused attentiveness which helps meet the requirements for on-going oversight of animal use activities. CMs work under the guidance of the Director, OAWA and according to the intentions and needs of the IACUC. Compliance Liaisons (CL) serve as the eyes and ears of the IACUC, without voting privileges, but with obligations to advocate on behalf of the IACUC when interacting with researchers and research associates. The CL confirms compliant performance by observation and document review; assuring the animal care or use activity is being performed in accordance with federal regulations, approved IACUC protocols or institutional SOPs.

ROLES:

- Investigators and laboratory staff work with the CL to schedule, coordinate, and perform procedures which will be monitored by the CL.
- The CL(s) serve as the eyes and ears of the IACUC, working with the investigator, research staff, and care staff to observe animal use activity, to prepare accurate reports of observations made, to provide recommendations for returning to/maintaining compliant activity, and provide necessary or beneficial training.
- The Director, Office of Animal Welfare Assurance (OAWA) provides operational oversight and daily management of the CL and the institution's animal compliance monitoring program. The Director assures the IACUC receives reports or updates on items of concern, provides direction to the CLs in performance of their duties, assists in development of appropriate corrective actions, and provides training support, as required, to assure compliance.

PROTECTION POSTURES REQUIRED: The CL (and other visitors) shall wear the PPE prescribed for the specific animal activity area.

POLICY EXPECTATIONS:

I. Activities subject to Review:

- a. Active procedures (as found in protocols), regardless of pain or distress category;
- b. Clinical care activities and animal procedural SOPs involving Duke owned animals;
- c. Duke managed care or use operations (PI Managed housing areas);
- d. Allegations of misuse, neglect or inappropriate protocol performance involving Duke owned or funded animal activities;
- e. Active procedures which have not been monitored during the past year and in the opinion of the Annual Progress Report reviewer require a commitment to coordinate a monitoring session prior to approval of the Annual Progress Report;
- f. Any activity that is determined by the Chairman, IACUC, Director, DLAR, or Director, OAWA to require monitoring.

II. Who may serve as a reviewer: This policy addresses the compliance monitoring process performed by members of the Office of Animal Welfare Assurance, and utilizes the job description of Compliance Liaison for the purpose of providing the IACUC with real time, clear, accurate information concerning animal care and use within the Duke animal care & use program.

III. Methodology of the assessment:

- Routine Review: The CL schedules a monitoring session with the Principal Investigator or delegated laboratory personnel based upon a pre-determined risk assessment of procedures being performed, and species being used in the Duke animal care & use program.
- Select or 'For cause' Review: The CL conducts monitoring with or without advance notice to the Principal Investigator. 'For Cause' reviews may be performed when requested by federal agencies, the IACUC, DLAR, or OAWA.
- Follow-up Review: Assessments may be performed for the purpose of confirming resolution of the concern. These reviews may be scheduled or unscheduled. In addition to CL observed activity, concerns noted during Semi-Annual Facility Inspections may also be assessed by a follow-up CL visit. The Semi-Annual Facility Inspection may also be used to confirm corrected behavior of previously identified non-compliant activity.

IV. Monitoring Process:

a. Advisement of a Routine Review:

- The CL will use Email notification to schedule announced visits. Initial correspondence with the PI should contain the information noted in the 'COMPLIANCE LIAISON VISIT' memo (APPENDIX A), although the actual Appendix A is not required.
- The CL coordinates a visit according to the PI/PI personnel calendar and scheduled animal use procedures. This is arranged by either email or phone with the personnel in the lab.

b. Performing a Review:

- The CL performs the review along the guidance provided in the 'COMPLIANCE MONITORING GUIDELINES' (APPENDIX B). This document is only a guide; other documents from the Duke Reference Resource List may also be used as

reference standards when the situation would require additional assessment not covered on the 'Guidelines.'

- The CL will compare procedures conducted in the laboratory, with those listed in the approved protocol (or SOP, or approved procedural plan).
- Issues that pose an immediate threat to animal welfare shall be referred to the Attending Veterinarian or another DLAR/DLC veterinarian for immediate resolution.

c. Exit Briefing of a Routine Review:

- At the conclusion of the review, the CL shall discuss the observations with the personnel who performed the work as well as the PI or senior laboratory representative, if these individuals are available.
- The goal of this interaction is to confirm observations are accurate and the CL and the laboratory staff agree on the observations. The laboratory may offer additional information, but the CL may not negotiate or require any specific laboratory corrective plan.

d. Post Review:

- If potential deviations / concerns exist: An email shall be provided to the PI and delegated laboratory representative (if any), describing the observed concern(s). Corrective actions performed by the PI and / or the laboratory shall also be reflected in this memo. A copy of this memo will be provided to the Director, OAWA and placed in the protocol file. See Appendix D for a template of this message.
- If no potential deviations / concerns exist: An email shall be provided to the PI and delegated laboratory representative (if any), noting the fully compliant nature of the review. See APPENDIX C for a template of this message.
- In cases where the PI desires to initiate corrective actions prior to the IACUC meeting, the CL may assist the laboratory (if requested) with completing PI initiated corrective actions. Assistance may include coordinating / providing required training and / or form preparation for amendment submission.

V. IACUC Reporting:

- a. **Prior to the IACUC meeting**, the CL shall meet with the Director, OAWA to review the observations for which they may be a potential non-compliance. This meeting is intended to assure completeness and clarity of the available information. The IACUC Chairman and/or Attending Veterinarian may be consulted for advice and counsel with observed activities. The Compliance Liaison, in consultation with the Director, OAWA and/or the Attending Veterinarian and/or the Chairman, IACUC, and according to the federal guidance, and the IACUC's predetermined policies, shall determine what will be reported to the IACUC using one of the two methodologies listed below:

- Written Trends Report: The following items will be reported to the IACUC by means of a written 'trends' report. The trends report will be included in the IACUC disk for member review:
 - A list of PIs for which no deficiencies were identified (attaboy/attagirl list);
 - Unapproved personnel who are performing procedures proficiently and who pose no recognized welfare risk to the animal;
 - Outdated cage cards, the incorrect cages cards, improperly labeled cages;
 - Location of the procedure does not match the protocol;

- Minor procedural deviations to approved procedures that although a deviation, is performed according to Duke guidelines and did not change the outcome or goal of the study, nor did the deviation have a negative impact the general welfare of the animals; and when the PI has, upon notice by the CL, returned to the approved protocol and has terminated further use of the deviated procedure until submission and approval of an amendment for the observed modification;
 - Incidents involving limited numbers of animals that are distressed, when that distress is clearly related to mechanical systems failure.
- **Verbal Report:** The following items will be reported to the IACUC for discussion by the Committee, to determine which are (or are not) reportable to the OLAW, and specific IACUC corrective actions:
 - Items listed in the OLAW Notice concerning reportable conditions (APPENDIX E);
 - Anesthetics/analgesics withheld or provided inconsistently with the approved protocol resulting in an animal welfare concern;
 - Recurrent deficiencies (even if not on the OLAW Notice list);
 - Allegations of misuse and the subsequent investigation; or
 - OAWA, DLAR, or IACUC concerns with specific animal use activity.

NOTE: All compliance audit activities will be reported to the IACUC.

NOTE: As per federal regulation, any member can request full discussion by the IACUC of any of the items, regardless of inclusion in the Written Trends Report or the Verbal Report.

- b. **At the IACUC meeting:** The CL (or designee) shall present the potential non-compliant activity to the IACUC. The CL shall provide two specific recommendations:
 - Does the item meet or exceed minimum criteria defined in the OLAW notice, or does the item merit specific consideration of other justifications for reporting to OLAW, USDA, or AAALAC?
 - Are there specific corrective actions the IACUC should consider imposing?

VI. Post IACUC Decision:

- a. The Director, OAWA will report the IACUC's decision to the PI as soon as practical after the IACUC meeting. A verbal report may be provided, but a written report is required. The written report will follow the template in APPENDIX G.
- b. The CL will re-visit with the laboratory at a CL determined point post incident resolution to confirm the effectiveness of the corrective action. This visit may or may not be announced and may be requested by the IACUC as part of the resolution of the item.
- c. On occasion, additional monitoring sessions may be part of the follow-up process.

- VII. **Process of Addressing Concerns:** Investigators who disagree with the CL review or IACUC decision concerning the review may appeal to the IACUC, either in writing or in person.

VIII. Recordkeeping:

- a. **Filing a Compliance Database Entry:** Database entries will be made for direct allegations of adverse events or when a Compliance Liaison audit results in an adverse event identification. Animal deaths, if an anticipated or probable outcome of normal animal care or use activities, are not routinely entered into the compliance database.
- b. **Records of Compliance Liaison Audits:** CL reports shall be kept in the protocol file. Items which are taken to the IACUC for consideration / decision are maintained either within the protocol file, if applicable to protocol procedures, or outside of the protocol file but within other OAWA files, if not applicable to a protocol. Items which go to the IACUC are maintained within the database or PI files of the CLs to track email communications surrounding the incident. For SOP related activity, the reports will be kept under the name of the SOP authority. All information shall be entered into the Compliance Database for use as institutional trending, educational initiative development, or CL follow-up. All PI memos are maintained on the OAWA shared server.
- c. **Regulatory Communications:** All Regulatory Communications concerning adverse event reports to regulatory agencies (OLAW, USDA, AAALAC, International) are maintained on the OAWA shared server.

APPENDIX A

COMPLIANCE LIAISON VISIT

PI:

Date:

Protocol Registry Numbers:

Dear Colleague:

The Duke Institutional Animal Care & Use Committee (IACUC) has instructed the Office of Animal Welfare Assurance (OAWA) to perform Compliance Liaison visits to Duke approved animal care or use activities. The purpose of this visit is simply to collect evidence of good performance and conclude with a commendation for your laboratory for adherence to the approved animal use protocol or SOP.

This process is intended to be collegial and supportive of animal based research on our campus. The goal of the Compliance Liaison is to serve as the 'eyes and ears' of the IACUC and OAWA. The Compliance Liaison will work diligently to facilitate your research and help your laboratory understand and stay fully compliant with the expectations of the animal care and use program at Duke. **While the Compliance Liaison may provide your laboratory expert counsel or advice and may encourage your laboratory to consider specific corrective actions, the Principal Investigator for the protocols identified above remains obligated to submit any required amendments, reports, or explanations of on-going activities.**

After completing the protocol audit, the Compliance Liaison will provide an 'Exit Briefing' to an available member of your laboratory. The purpose of this 'Exit Briefing' is to assure the accuracy of the observations. Protocol deviations or problematic conditions will be shared with the laboratory staff member(s) present during the Exit Briefing. **This IS NOT the time to argue or attempt to negotiate an outcome. The Compliance Liaison does not have the authority to approve or disapprove any process change. That role belongs solely to the IACUC.**

Within a few days of this visit, an Email will be sent to the Principal Investigator describing the outcome of this visit and identifying any items that may require corrective attention. You should initiate corrective actions (if any) in response to this Email.

While the IACUC will be notified of all Compliance Liaison visits, only certain visits will require specific IACUC discussion and decision. At any time (preferably prior to the IACUC meeting), the Principal Investigator may communicate to the IACUC in writing to clarify concerns or offer a plan for correction. After the IACUC has reviewed the concerns, and any correspondence received from the Principal Investigator, the IACUC will issue a decision. This decision will be communicated to the Principal Investigator shortly after the IACUC meeting.

The animal care & use program appreciates your partnering to assure the integrity of the biomedical research enterprises of the institution.

APPENDIX B

Duke University IACUC Post-Approval Monitoring Guidelines

The Protocol and Personnel

- Does the PI have the most recent version of the complete protocol, including amendments?
- Does the laboratory personnel have easy access to the most recent version of the complete protocol, including amendments?
- Have the investigators read the protocol?
- Are the people performing the study listed on the protocol?
- Are the people performing the study approved to perform the IACUC approved procedures?

Study Procedures

- Does the protocol number on the animal's cage card match the protocol number?
- Are the procedures performed consistent with those in the approved protocol?
- Are lab personnel appropriately trained to perform these procedures?
- Are investigators wearing PPE and/or other attire (e.g. masks & gloves) appropriate for the species and procedures performed?

Anesthesia

- Are the methods of anesthesia in compliance with the protocol?
- Are anesthetized animals monitored according to the approved method in protocol?
- Are the animals maintained at an appropriate depth of anesthesia for the procedure performed?
- If inhalant anesthetics are used, are they scavenged properly?
- Are anesthetic machines serviced and calibrated?

Surgery

- Is surgery performed in a location that has been approved by the IACUC?
- Is the location and method of animal prep appropriate and in accordance with the approved protocol?
- Is survival surgery performed using sterile instruments, sterile gloves, a surgery mask and aseptic technique?
- Is an appropriate heat source used to keep the animal warm throughout the procedure?
- Are incisions closed appropriately and in accordance with the approved protocol?
- Is there an appropriate recovery area for the animals?

Post-Surgical Care

- Is post-surgical care in compliance with the protocol?
- Are the methods of analgesia (dose, frequency, duration) consistent with the approved protocol?
- Is post surgical (post procedural) care adequately documented?

Euthanasia

- Does the method of euthanasia correspond with what is written in the protocol?
- Is death assured by performing an appropriate physical method of euthanasia when required?
- Are proper methods of carcass/tissue disposal in place?

General Record Keeping

- Is there an up to date and complete surgical log?
- Are animals identified by protocol number and individual numbers or cage cards?
- Are medical and post-procedure care progress notes complete and accurate?
- Is medication administration accurately documented?
- Are injections, blood collection, and fluid collection amounts dated documented?
- Are controlled substance records maintained and accurate?

Laboratory

- If animals are housed in the lab for greater than 12 hours, has the lab been approved by the IACUC?
- Are drugs, suture material and other items within the noted package expiration dates?
- Are controlled substances stored appropriately?
- Are there any safety issues or other concerns that pose a threat to human or animal safety, or animal welfare?

APPENDIX C

To:
CC:
Protocol Registry Number:
Protocol Title:
Procedures Observed:

Dear Dr. *

On <insert date> , a routine animal program audit of the activities approved under the protocol identified above, was conducted by <insert name of CL>, Compliance Liaison, Duke Office of Animal Welfare Assurance, on behalf of the Duke Institutional Animal Care and Use Committee (IACUC).

With respect to the procedures observed under this protocol, all procedures observed were performed as approved in the protocol. Please commend your staff for the attention to detail, the professional manner in which the animal activities were conducted, and the humane manner in which the animals were handled.

Successful audits such as this provide clear evidence of institutional regulatory compliance, as dictated by the Animal Welfare Act and the Public Health Service. Thank you and your staff for your gracious hospitality and your support of our institution's commitment to quality care and progressive research. Congratulations for a job well done!

A copy of this memo will be maintained in your protocol file.

APPENDIX D

To:
CC:
Registry Number:
Protocol Title:
Procedures Observed:

Dear Dr. <insert name>,

On <insert date>, <insert name of CA>, Compliance Liaison with the Duke Office of Animal Welfare Assurance, performed a routine animal care and use program audit of IACUC approved procedures. Thank you and the laboratory staff for the collegial manner of assisting with this program audit.

Monitoring experimental animal procedures post-approval is one method the Duke Institutional Animal Care and Use Committee (IACUC) uses to assure regulatory agencies that animal studies are conducted in accordance with approved Duke IACUC protocols, as dictated by the federal Animal Welfare Act, Public Health Service Policy, and the NIH's Guide for the Care and Use of Laboratory Animals.

With respect to the procedures observed under this project, there were a few issues that require attention:

OBSERVATION:
SUGGESTION:

OBSERVATION:
SUGGESTION:

We realize that certain observations may not be entirely accurate, and we encourage responses which provide clarifying information obtained during the Compliance Liaison visit. For the observations that are accurate, please provide a response and include a plan for correction.

We also realize that on occasion, research may drift from the original proposal - indeed the very nature of research requires original and creative thought - and may become unintentionally non-concordant with the original approval. When non-compliant activities are identified, the research laboratory must either return immediately to the original animal use approval or suspend the change and submit an amendment request to the IACUC for their consideration and approval.

Thank you for your consideration, clarification, and response of these items. Our audit is not intended to be negative, but rather a collegial review of approved activities, and an opportunity for education and information sharing of the research process and expectations for research at Duke University. The IACUC appreciates your adherence to the procedures in the approved protocol until any proposed amendments are reviewed and approved.

APPENDIX E

Guidance on Prompt Reporting to OLAW Under the PHS Policy on Humane Care and Use of Laboratory Animals

Notice Number: NOT-OD-05-034

Release Date: February, 24, 2005

Issued by: Office of Laboratory Animal Welfare (OLAW), Office of Extramural Research
(<http://grants.nih.gov/grants/olaw/olaw.htm>)

This Notice provides guidance to Public Health Service (PHS) awardee institutions and Institutional Animal Care and Use Committees (IACUCs) on the prompt reporting requirements of the PHS Policy on Humane Care and Use of Laboratory Animals (Policy) (<http://grants.nih.gov/grants/olaw/references/phspol.htm>). This guidance is intended to assist IACUCs and Institutional Officials in determining what, when, and how situations should be reported under IV.F.3 of the Policy, and to promote greater uniformity in reporting. This Notice supersedes the January 12, 1994 Dear Colleague letter from the former Division of Animal Welfare, Office for Protection from Research Risks (now the Office of Laboratory Animal Welfare, or OLAW).

Background: PHS Policy, IV.F.3, requires that: "The IACUC, through the Institutional Official, shall promptly provide OLAW with a full explanation of the circumstances and actions taken with respect to:

- a) any serious or continuing noncompliance with this Policy;
- b) any serious deviation from the provisions of the Guide [for the Care and Use of Laboratory Animals]; or
- c) any suspension of an activity by the IACUC."

IACUC suspensions of activities are cited at IV.C.6 and 7 of the Policy, and require a convened meeting of a quorum of the IACUC and the vote of a majority of the quorum present. The Institutional Official must review the reasons for suspension in consultation with the IACUC, take appropriate corrective action and report that action with full explanation to OLAW.

All institutions with Animal Welfare Assurances are required to comply with the provisions of IV.F.3. The Institutional Official signing the Assurance, in concert with the IACUC, is responsible for this reporting.

Reporting promptly to OLAW under IV.F.3 serves dual purposes. Foremost, it ensures that institutions deliberately address and correct situations that affect animal welfare, PHS-supported research, and compliance with the Policy. In addition, it enables OLAW to monitor the institution's animal care and use program oversight under the Policy, evaluate allegations of noncompliance, and assess the effectiveness of PHS policies and procedures.

The underlying foundation of the PHS Policy is one of institutional self-evaluation, self-monitoring and self-reporting. Public Law 99-158 (<http://grants.nih.gov/grants/olaw/references/hrea1985.htm>) requires that institutions be provided a reasonable opportunity to take corrective action before a grant or contract is suspended or terminated, and it is OLAW's role to assess whether the corrective actions reported by institutions under IV.F.3 are adequate. OLAW will assist the reporting institution in

developing definitive corrective plans and schedules if necessary. Compliance actions affecting an award are rare because institutions are usually able to address incidents successfully and take appropriate actions to prevent recurrence.

Guidance on prompt reporting: A comprehensive list of definitive examples of reportable situations is impractical. Therefore, the examples below do not cover all instances but demonstrate the threshold at which OLAW expects to receive a report. Institutions should use rational judgment in determining what situations meet the provisions of IV.F.3 and fall within the scope of the examples below, and consult with OLAW if in doubt. OLAW welcomes inquiries and discussion and will provide guidance with regard to specific situations. Situations that meet the provisions of IV.F.3 and are identified by external entities such as the United States Department of Agriculture or the Association for Assessment and Accreditation of Laboratory Animal Care International, or by individuals outside the IACUC or outside the institution, are not exempt from reporting under IV.F.3.

Examples of reportable situations:

- conditions that jeopardize the health or well-being of animals, including natural disasters, accidents, and mechanical failures, resulting in actual harm or death to animals;
- conduct of animal-related activities without appropriate IACUC review and approval;
- failure to adhere to IACUC-approved protocols;
- implementation of any significant change to IACUC-approved protocols without prior IACUC approval as required by IV.B.7.;
- conduct of animal-related activities beyond the expiration date established by the IACUC (note that a complete review under IV.C is required at least once every three years);
- conduct of official IACUC business requiring a quorum (full Committee review of an activity in accord with IV.C.2 or suspension in accord with IV.C.6) in the absence of a quorum;
- conduct of official IACUC business during a period of time that the Committee is improperly constituted;
- failure to correct deficiencies identified during the semiannual evaluation in a timely manner;
- chronic failure to provide space for animals in accordance with recommendations of the Guide unless the IACUC has approved a protocol-specific deviation from the Guide based on written scientific justification;
- participation in animal-related activities by individuals who have not been determined by the IACUC to be appropriately qualified and trained as required by IV.C.1.f;
- failure to monitor animals post-procedurally as necessary to ensure well-being (e.g., during recovery from anesthesia or during recuperation from invasive or debilitating procedures);
- failure to maintain appropriate animal-related records (e.g., identification, medical, husbandry);
- failure to ensure death of animals after euthanasia procedures (e.g., failed euthanasia with CO₂);
- failure of animal care and use personnel to carry out veterinary orders (e.g., treatments); or
- IACUC suspension or other institutional intervention that results in the temporary or permanent interruption of an activity due to noncompliance with the Policy, Animal Welfare Act, the Guide, or the institution's Animal Welfare Assurance.

OLAW recognizes that there may be levels of morbidity and mortality in virtually any animal-related activity, including those associated with the care and use of animals in research, testing, and teaching that are not the result of violations of either the Policy or the Guide. OLAW offers the following examples of situations which may not meet the threshold for reporting, based on consideration of the circumstances by the IACUC.

Examples of situations not normally required to be reported:

- death of animals that have reached the end of their natural life spans;
- death or failures of neonates to thrive when husbandry and veterinary medical oversight of dams and litters was appropriate;
- animal death or illness from spontaneous disease when appropriate quarantine, preventive medical, surveillance, diagnostic, and therapeutic procedures were in place and followed;
- animal death or injuries related to manipulations that fall within parameters described in the IACUC-approved protocol; or
- infrequent incidents of drowning or near-drowning of rodents in cages when it is determined that the cause was water valves jammed with bedding (frequent problems of this nature, however, must be reported promptly along with corrective plans and schedules).

Time frame for reporting: Institutions should notify OLAW of matters falling under IV.F.3 promptly, i.e., without delay. Since IV.F.3 requires a full explanation of circumstances and actions taken and the time required to fully investigate and devise corrective actions may be lengthy, OLAW recommends that an authorized institutional representative provide a preliminary report to OLAW as soon as possible and follow-up with a thorough report once action has been taken. Preliminary reports may be in the form of a fax, email, or phone call. Reports should be submitted as situations occur, and not collected and submitted in groups or with the annual report to OLAW.

Information to be reported: Include as many of the following items of information as possible in the initial contact with OLAW. A follow-up report may address anything not known at the time of the initial report and should summarize the institution's corrective action. If a long term plan is necessary, describe the plan and include a reasonable schedule. This information will allow OLAW to assess the circumstances and actions taken to correct and prevent recurrence of the situation.

Information to be included: Animal Welfare Assurance number; relevant grant or contract number(s) if the situation is related to an activity directly supported by PHS; a full description of any potential or actual affect on PHS-supported activities if the situation is not directly supported by the PHS but is in a functional, programmatic, or physical area that could affect PHS-supported activities (e.g., inadequate program of veterinary care, training of technical/husbandry staff, or occupational health; inadequate sanitation due to malfunctioning cage washer; room temperature extremes due to HVAC failures); full explanation of the situation, including what happened, when and where, the species of animal(s) involved, and the category of individuals involved (e.g., principal or co-principal investigator, technician, animal caretaker, student, veterinarian, etc.); description of actions taken by the institution to address the situation; and description of short- or long-term corrective plans and implementation schedule(s).

Preliminary and final reports made to:

Axel V. Wolff, M.S., D.V.M.

Director, Division of Compliance Oversight

Office of Laboratory Animal Welfare

National Institutes of Health

Rockledge 1, Suite 360, MSC 7982

6705 Rockledge Drive

Bethesda, MD 20892-7982

Phone: 301-594-2061

FAX: 301-402-2803

E-mail: wolffa@od.nih.gov

Addendum to Appendix E:

The NIH, PHS, and OLAW are taking a more narrowed view of funded activity which is not IACUC approved (e.g. deviation from approved protocol), even when the resultant non-compliant activity does not result in animal welfare concerns. NIH Notice Number: NOT-OD-07-044 (NIH Policy on Allowable Costs for Grant Activities Involving Animals when Terms and Conditions are not Upheld) specifies the following:

The Office of Management and Budget Cost Principles and the NIH Grants Policy Statement (NIHGPS) do not permit charges to grant awards for the conduct of animal activities during periods of time that the terms and conditions of the NIHGPS are not upheld. Specific situations under which charges are not allowable are:

- i. The conduct of animal activities in the absence of a valid Assurance on file with OLAW.
- ii. The conduct of animal activities in the absence of valid IACUC approval of the activity.

While neither items i. or ii. are a change in long term policy, the interpretation of item ii. has morphed to a more marrow interpretation and is now being applied to ALL aspects of animal utilization such as routine matters of anesthetic or analgesic use, method of euthanasia, or changes in protocol specified husbandry.

OLAW uses 'professional judgment' to determine when the potential expense associated with a non-compliant activity is minimal, which they do not forward to the funding agency, and when the non-compliant activity could have greater financial impact (which they will forward). Since professional judgment is used, there is no simple formula to determine what OLAW will or will not forward to the funding manager.

Funding agency grant managers have the discretion to pursue recouping funds associated with the non-compliant procedure. An informal survey of a number federal agencies provided the following information: if the affected funds are negligible, then the managers will not request re-imburement, but if the funds associated with the non-compliant activity are substantial, then funds will be requested for return to the grant. While both ends of the spectrum of minima to substantial would be clear to all, it not clear at what point along the spectrum that minimal become substantial.

The return of funds which could be required of researchers are funds specifically associated with a specific non-compliant activity. For example, consider a case where an unapproved anesthetic was used for anesthesia of 100 mice. If we assume that this example meets the agency's definition of substantial, then the cost of the animals, anesthetic, surgical supplies, and personnel time for the surgery using the unapproved anesthetic could be recouped by the federal funding agency. Generally, federal funding agencies do not require recoupment of funds for other aspects of the research project or on-going veterinary care not related to the specific non-compliant activity (e.g. the use of the unapproved anesthetic), standard institutional husbandry, or normal animal maintenance requirements.

The Duke IACUC is charged to:

1. Continue with the present program of compliance liaison observations, IACUC deliberations, and reporting.
2. When the IACUC determines a non-compliant activity has occurred, then:
 - a. The PI should assure the IACUC that funds used for the non-compliant activity were other than federal funds (e.g. discretionary or non-federal grant). If federal funds were used for the non-compliant activity, then the PI should transfer discretionary funds back to the grant line item for the cost of the specific non-compliant activity. If funds transfer is not an option, then;
 - b. The institution should contact the grant funds manager and explain the situation and determine a 'workable plan' for the expended non-compliant fund expenditure.

In these cases, the letter to OLAW should specify that 'no federal funds were expended for the non-compliant item,' and/or 'we have discussed the issue with the grants funds manager and they have determined no additional action is required.' When receiving a letter with either or both of these statements in it, OLAW will trust the integrity of the institution and will not forward the letter to the funding agency.

APPENDIX F

IACUC REPORT COMPLIANCE CONCERN (verbal template report)

1. Reporting Individual (CA):
2. Compliance Item Registry:

3. Species:
4. PI:
5. Protocol:
6. Protocol Title:
7. PHS Funded Activity:
8. Date of incident:
9. Date of investigation:
10. Date of IACUC review:

11. Method of initial discovery of the concern:
12. Issue / Concern / Incident:
13. Immediate action taken by the PI/Laboratory:
14. Actions required by Attending Vet or Director, OAWA
15. Number of animals involved in this incident:
16. OAWA assessment of the incident:
17. OAWA recommendation to the IACUC:
 - a. Corrective actions:
 - b. Reportable to OLAW/USDA/AALAC:

APPENDIX G

EXAMPLE of POST-IACUC REPORT TO THE PI

(Note: This is not a real case, but a creation to describe the use of this memo template)

To: *

From: Dr. Ron E. Banks, Director, Office of Animal Welfare Assurance

Date: *

Re: IACUC Review of Potential Noncompliance Involving IACUC Approved Protocol (Protocol Title <insert title>, Registry No: <insert protocol number>)

The Duke IACUC has reviewed the following descriptions of animal activities: During a recent compliance visit by a Duke Compliance Liaison, a rodent survival surgical procedure involving intrahepatic tumor injection was observed. Certain aspects of the surgical procedure were inconsistent with the general IACUC expectations and the approved protocol:

- Aseptic technique was not followed in both the patient preparation (3 alterations of Betadine/alcohol were not performed) and the surgeon preparation (sterile gloves were not worn, so all surgical instruments/drape/suture material were no longer sterile once they were handled).
- The abdominal incision was created with scissors instead of a scalpel blade
- Improper post-operative analgesia was administered. (Butorphanol was administered, while the protocol called for the use of Ketoprofen).

The PI provided a response to the concerns by noting:

- Aseptic technique will be followed as per the guidelines posted on the Duke ACUP website
- Incisions will be made with a sterile scalpel blade.
- An amendment for Butorphanol will be submitted.

After consideration of the report and the PIs response, the IACUC determined the following corrective actions are required:

- The incidents were of sufficient magnitude to exceed the minimums necessary for reporting to the NIH's Office of Laboratory Animal Welfare (OLAW). OAWA will prepare the report and submit the report to OLAW.
- Dr. Smith and Dr. Jones must meet with the Director, Office of Animal Welfare Assurance to discuss the incident, corrective actions performed, and measures employed to prevent future incidents of this nature. Please contact Suzy Johnson (suzy.johnson@duke.edu) to arrange an appointment for this meeting.
- Within 60 days from the date of this memo, the individuals listed below must complete the AALAS Learning Library web module entitled, "Working with the IACUC: Non-VA Version." Additionally, Dr. Jones must complete a second module entitled, "Aseptic Technique for Rodent Surgery." Instructions are provided on the following page.

All of the listed corrective actions must be completed within 60 days of the date of this letter. With successful completion of these actions, the IACUC will consider this matter closed.