ADVERSE EVENTS AND OTHER ANIMAL WELFARE CONCERNS

PERFORMANCE STANDARD: Personnel having concerns regarding animal care and/or animal welfare shall report those concerns via one of several avenues, to allow animal program or institutional authorities to address issues regarding animal well-being. Investigation of adverse events, allegations, or complaints against the animal care & use program, including researchers, care providers, or program managers are conducted in a legal, impartial, and professional manner; focusing on protecting animal welfare / well-being, institutional integrity, and personnel corrective action trainings.

BACKGROUND/PURPOSE: Experimental manipulation of animals in research, testing, or teaching may occasionally result in serious, unanticipated, or adverse clinical consequences. The Duke IACUC believes that effective communication between researchers, veterinarians, and animal care staff is crucial for clear and timely management of animal disease, injury, or adverse outcomes. In addition to the obligation to report adverse events to the clinical veterinary staff, the IACUC must also be aware of adverse events that involve animals owned or housed by Duke University or listed on Duke IACUC approved protocols. The Duke IACUC must be informed of conditions outlined in this policy as partial fulfillment of the institution’s obligations of effective regulatory and/or oversight agencies. The Duke IACUC shall determine which events / outcomes must be reported to regulatory and/or oversight agencies, whether protocol modifications are required (e.g., changes in procedures, monitoring, humane endpoints, etc.), whether SOP changes are necessary, or whether specific corrective actions, beyond those which may be PI-generated, are required to ensure animal well-being.

APPLICABILITY: The requirements specified in this policy for informing the IACUC of adverse events or other animal welfare concerns apply to all vertebrate animal species and cephalopods used in Duke University facilities, protocols, SOPs, or projects, including those not covered by the Animal Welfare Act. In select cases, proactive project status reporting, including accountability for mortality may be required by the IACUC as a condition for project approval or annual renewal (Annual Progress Reports). Any such conditions mandated as part of the approval process will supersede requirements specified in this policy.

DEFINITIONS:
1. Animal: Any vertebrate or any member of the cephalopod class (invertebrate) used for research, testing, teaching, training, or exhibition under a Duke IACUC protocol or SOP.
2. Adverse event: An instance of unfavorable or unanticipated (not in the approved protocol) signs or outcomes. Adverse events include suboptimal well-being (i.e. poor welfare), animal death, disease, distress, or trauma that was not the anticipated result of approved protocol or SOP activity.
3. Animal welfare concern: Any concern regarding actual or perceived suboptimal well-being in a Duke-owned animal, regardless of whether the suboptimal state is related to work carried out under an IACUC-approved protocol or some other reason. Such a concern may be brought by protocol-associated personnel or by other individuals.
4. ‘First aid’: The immediate measures provided to an animal in response to a newly observed disease or injury to limit pain/distress or removes the animal from immediate danger.
5. Advisement: The initial alert to the IACUC, via phone, email or other means, of an adverse event involving Duke-owned animals, work on a Duke approved protocol or SOP, or Duke personnel working with animals. An advisement does not equal a notification or a report.
6. **Notification:** Written documentation of an adverse event via email submission of the Potential Adverse Event / Unanticipated Event Notification form (available on the animal program website). A notification may be submitted initially, or in lieu of an advisement. Submission of the notification form to iacuc@duke.edu concludes the individual’s responsibility for timely descriptions of adverse events or unanticipated outcomes of animal care or use. A notification to the IACUC does not necessarily mean that a report (see below) will be made to regulatory and/or oversight agencies.

7. **Report:** An IACUC-determined outcome wherein the Committee determines that the details of the advisement, notification, and subsequent investigation exceed the minimum thresholds for obligatory institutional reporting to the regulatory and/or oversight agencies. The name of the person who made the original notification shall not be included in any such report. Only those notifications that are determined by the IACUC to exceed minimum thresholds shall result in a report.

**ROLES:**

1. The Director (or designee), Office of Animal Welfare Assurance (OAWA) shall provide operational oversight and management of the investigation process and assure the IACUC receives notifications and updates on items of concern.

2. The IACUC Chair (or designee) and/or Attending Veterinarian (AV, or designee) will be consulted for guidance on issues or concerns.

3. The IACUC will determine when a formal investigation is required.

**POLICY:**

1. **IDENTIFICATION OF AN ANIMAL WELFARE CONCERN:** Concerns regarding any actual or perceived suboptimal well-being of any Duke-owned animal may be brought to IACUC attention via phone or electronic versions of the Animal Welfare Hotline or by direct communication with animal program leadership. The person who receives the concerns will immediately notify the the Director of DLAR to arrange for veterinary care if needed, the Director of OAWA, and the IACUC Chair (or their designees) unless the concerns are directly related to any of these individuals. In most situations, the OAWA will carry out the initial investigation of the concerns, to gather sufficient information for the IACUC to determine what additional information or action may be required. The Director of DLAR and the IACUC Chair will serve in a predominately advisory role for these investigations. In time-sensitive situations where immediate action is required to assure animal welfare, DLAR and the IACUC will coordinate any actions taken with OAWA to ensure a unified response of the animal program. All legitimate animal welfare concerns submitted via the Animal Welfare Hotline will be presented to the IACUC, either verbally at an IACUC meeting or in the meeting agenda file.

2. **IDENTIFICATION OF AN ADVERSE EVENT:** When an adverse event or unanticipated outcome occurs involving animal(s) under a Duke approved protocol or SOP; the personnel working with, providing care for, or assuring treatment of animals shall assure:
   a) **The animal receives care:** Provide immediate ‘first-aid,’ then notify the veterinary staff.

   **NOTE:** Any member(s) of the Duke animal care and use program may provide ‘first-aid’ to an animal in pain or distress. Your provision of ‘first-aid’ must be limited to:
   
   (1) The level of your skills,
   (2) Species for which you have received EOHW clearance; and
   (3) Only as an immediate measure to terminate animal pain / suffering or protect the animal from continued pain / suffering until the veterinary staff may be contacted.
NOTE: Do not place yourself in danger. Caution should be exercised as animals in pain / distress are more likely to bite or scratch. Certain species, such as non-human primates, cats, swine, or dogs, can cause serious injuries.

b) The veterinary staff is notified: Notify the DLAR or DLC veterinarian of the injured, diseased, or distressed animal so that the animal may receive definitive care. Veterinarians shall prescribe and/or provide appropriate veterinary care, based on their assessment of the patient's condition. Therefore, regardless of severity, all issues relating to sub-optimal health, disease, injury, or well-being of animals on Duke campus must be conveyed to the supporting veterinary staff through established information mechanisms:

(1) For animals maintained at the Lemur Center (DLC): DLC veterinarians may be reached by calling (919) 407-7244 or (919) 401-7221 or the emergency numbers posted in the facility.

(2) For animals maintained / used elsewhere on campus (DLAR): DLAR veterinarians may be reached by paging (919) 970-9410.

(3) For animals participating in off-site research, testing, or teaching (local supporting veterinarian): Off-site veterinary support shall be identified in the protocol (or SOP).

c) The IACUC is advised: In addition to informing the DLAR/DLC or local veterinary support, the Principal Investigator or other individual having knowledge of the adverse event must also inform the IACUC in a timely manner. There are two methods for informing the IACUC:

i) ADVISEMENT: Advisements are a thumbnail sketch of what occurred and may be verbal or via email. Advisements do not need to include complete details. An advisement does not equal notification. An advisement should generally occur immediately or within 24 hours of recognition of the adverse event / unanticipated outcome, but does not need to be complete in terms of details (see below). Thus, while an advisement is helpful to alert the IACUC to expect a more detailed notification, an advisement is not mandatory. Even when filing an advisement, submission of a notification remains a required action. An advisement may be accomplished by calling (919-668-6720) or emailing (IACUC@duke.edu). You can also contact any member of the Office of Animal Welfare Assurance (only one is necessary).

NOTE: DLAR and the DLC may submit a weekly summary of active cases in lieu of routine advisements regarding animals within their charge. Upon review of the weekly summary, the IACUC Chair, Attending Veterinarian, Director of OAWA, or their designees may further require submission of a Potential Adverse Event / Unanticipated Event Notification for specified weekly case summary(s). DLAR and DLC weekly summaries will include adverse events / unanticipated outcomes that rise to or above the level of requiring surgery, more than one dose of systemic analgesics/ sedatives, institution of a treatment lasting more than 5 days, or any of the conditions described in Section 4 below.

ii) NOTIFICATION: The Potential Adverse Event / Unanticipated Event Notification may be submitted initially (in lieu of an advisement), or may follow the advisement by 1-2 days. Notification should be as complete as possible, but in certain cases, all of the requested information may not be available at the time of submission. Submission of the notification concludes the responsibility to inform the IACUC of adverse or unanticipated outcomes of animal care or use. Notifications should be submitted to IACUC@duke.edu. You can also contact any member of the Office of Animal Welfare Assurance.
3. **WHEN TO SUBMIT AN ADVISEMENT / NOTIFICATION:** As noted in the 8th Edition of The Guide, all program participants are obligated to assure animal well-being, and that includes immediate ‘first-aid,’ engaging definitive veterinary care, and informing the IACUC promptly of adverse events and unanticipated outcomes due to experimental manipulations. The IACUC also has determined that the Committee must be notified of adverse events or unanticipated outcomes that are non-protocol-related. The general guidelines for primary responsibility for informing the IACUC are:

   a) **If Protocol-Related:** The Principal Investigator (PI) is responsible for notifying the IACUC of protocol-related conditions/events. The PI may delegate the task to a certified Research Animal Coordinator (RAC) or other member of their laboratory, but retains the obligation for prompt and accurate reporting.

   b) **If Non-Protocol-Related:** The individual with responsibility for the care of the animal has primary responsibility for informing the IACUC of adverse event / unanticipated outcomes. Any individual with knowledge of the adverse event / unanticipated outcome is also obligated to confirm the IACUC has been informed or should submit an advisement / notification.

4. **WHAT EVENTS REQUIRE ADVISEMENT / NOTIFICATION:** The IACUC must be advised / notified of any adverse condition or unanticipated outcome that affects animals at Duke, regardless of whether the condition or event is protocol-, or non-protocol-related. The list below is not intended to be all inclusive, but provides examples of events / outcomes which may be considered as guidance for determining when the IACUC should / should not be informed. When in doubt of whether the incident requires notification, the IACUC encourages that it be informed of the event (more communication, information sharing, and transparency is a good thing).

   a) Levels of mortality greater than those anticipated in the approved protocol. This includes both spontaneous animal deaths and animals euthanized at other than study-specified endpoints. In many studies, initial mortality may be higher than that experienced later in the project – a “learning/experience curve” effect. Although advisements / notifications are not definitively required until there are animal losses exceeding levels approved in the protocol, it is considered advantageous to notify the IACUC of unexpectedly high levels of early, relative mortality (i.e. mortality to date divided by animals used to date).

   b) Mortality due to complications unanticipated in the approved protocol.

   c) Animals that sustain an injury that impacts the animal’s well-being, such as death, loss of limb function (e.g. the limb is bandaged in a manner which restricts/interferes with mobility or use), or loss of a substantial quantity of blood or tissue regardless of protocol relationship.

   d) Animals that require the use of bandages which were not part of the approved protocol and for which interfere with or prohibit normal function of an organ system (e.g. E-collars which may interfere with nutrition or bodily functions).

   e) Animals that develop disease conditions or have been treated for a condition and have not responded appropriately to that treatment, or have a decline in condition which requires subsequent treatment or euthanasia.

   f) Cases where bandaging, amputation, or surgical repair of an injury was necessary for conditions which were treated conservatively when the injury was first identified.

5. **WHAT THE IACUC DOES NOT EXPECT TO BE INFORMED OF:** Animals that are injured and respond well to the initial treatment do not necessarily require notification of the IACUC, but the project and staff may find such reporting beneficial to enhance communication with the Committee. The IACUC does not expect notification for every skin abrasion or minor cut which when treated, heals without complications. Adverse events or unanticipated outcomes
specifically exempted from the requirement for advisement / notification (e.g., things the IACUC does not wish to know) include:

a) Dermatitis affecting a few animals,
b) Wounds that when treated conservatively or with minor surgery resolve completely in less than 10 days.
c) Barbering between cage mates which is uncomplicated, (i.e., having no skin damage, but may have alopecia),
d) Alopecia without underlying skin involvement,
e) Dystocia or rectal prolapse in rodents (unless there are large numbers involved).

6. **PROCESS FOR REVIEW OF ADVISEMENTS / NOTIFICATIONS:** The Office of Animal Welfare Assurance will review the initial advisement / notification and gather all available information for submission to the IACUC for its review. This action will be performed behalf of the IACUC and/or as directed by the IACUC Chair, Attending Veterinarian, Director of OAWA, or their designees. Actions performed (generally by the OAWA Compliance Liaison) will include:

   a) Initial review of the incident advisement / notification within 24 hours of receipt;
   b) Entry of the incident in the adverse event compliance tracking database;
   c) Review/investigation of the incident details and preparation of a synopsis for the IACUC, if needed;
   d) Providing an alert to the IACUC Chair, Attending Veterinarian, and the OAWA Director as necessary (via email routinely; phone call in an emergency);
   e) Tracking/trending of incidents to serve as a potential basis for training initiatives or policy development.

**NOTE:** If other persons become aware of an adverse event that requires PI notification of the IACUC, they are obligated to inform the PI. The IACUC should be copied on this communication, so the IACUC may ensure appropriate follow up. Remember: knowledge of an adverse event / unanticipated outcome means you have an ethical obligation in the matter! Failure to inform the IACUC in a timely manner may be considered by the IACUC in defining any necessary corrective measures.

7. **INFORMING THE FULL IACUC:** At each regularly scheduled IACUC meeting, the OAWA shall inform the IACUC of any new item of concern that exceeds the minimum thresholds established by OLAW and other items determined as significant by the Duke IACUC according to the most current IACUC policy on compliance monitoring. The IACUC, after hearing the information presented, shall determine if:

   a) If a formal IACUC investigation is necessary.
   b) If the information is sufficient and the incident shall be closed.
   c) If the information is not sufficient and the IACUC requires additional information to allow an informed decision to proceed or to terminate the process.

8. **CONDUCTING INVESTIGATIONS:** If the IACUC determines a formal investigation is necessary:

   a) The IACUC Chair, or designee, shall:
      i) Appoint an Investigation Subcommittee with membership determined by the Chair, or designee, to be appropriate and reflective of the necessary skills to fully assess the allegation / complaint. While willingness to serve is essential for appointment, it may not be possible or advisable to appoint all willing volunteers to any specific Subcommittee.
      ii) Notify the Institutional Official of the initiation of the investigation, if appropriate.
      iii) Appoint the Subcommittee Chair.
b) The Subcommittee Chair shall:
   i) Call the Subcommittee meetings;
   ii) Manage the Subcommittee review process;
   iii) Instruct administrative support staff (generally OAWA) to collect additional information / data as determined necessary by the Subcommittee for Subcommittee deliberations.
iv) Notify the subject of the complaint (e.g., Principal Investigator, animal facility administrator, or other responsible individual) of the IACUC's intention to carry out the investigation through the Subcommittee process. This notification may be delayed if there is an expectation that immediate notification would interfere with the investigation process. The subcommittee may perform unannounced investigations, if the Subcommittee believes such an investigation is necessary. Notification, when it occurs, should include:
   (1) Citation of the section of the federal regulations which allow for investigations of concerns related to animal care and use (optional)
   (2) A description of the complaint;
   (3) A request for information concerning the incident;
   Notification may also include an invitation for one or more subjects to meet with the Subcommittee to discuss the allegation / complaint.
iv) Provide a written or verbal report to the full IACUC with the Subcommittee’s conclusion(s). The Subcommittee report may be at a regularly scheduled or a called meeting of the IACUC (determined by the Chair, or designee).

c) The IACUC Subcommittee shall:
   i) Use any legal method it deems necessary to obtain information to assist in the investigation.
   ii) Investigative tools may include, but are not limited to the following:
       (1) Unannounced visits to the laboratory or animal facility in question;
       (2) Review of procedures, lab and/or facility documents, whether written or electronic;
       (3) Interview (and/or obtain written statements from) personnel (e.g., complainant, co-workers, employees, etc.);
       (4) Review records for the affected animals, projects, or procedures. Such documentation could include: research records relating to animal experimentation, surgical records, animal health records, purchase orders, standard operating procedures, diagnostic laboratory reports, quality assurance reports, or others document which will provide information for the Subcommittee.
       (5) Request an interview, written statement, or other documentation from the individual(s) who is/are allegedly at fault;
       (6) Review of Animal Care and Use Protocols, IACUC inspection reports, Reports of Programmatic Reviews, USDA or AAALAC inspection reports, or any other pertinent animal care & use program record;
       (7) Solicit letters or documentation from individuals who are not directly affected by the allegation but who could provide insight into the issues under review;
       (8) Review evaluation reports related to the complaint and performed by external reviewers chosen by the committee; or
       (9) Interview any other person who the Subcommittee believes can provide information concerning the investigation.
d) Upon receipt of the Subcommittee’s report, the IACUC shall:
  i) Review the Subcommittee’s report, including the Subcommittee’s findings, conclusions, and recommendations.
  ii) Determine which items, if any, require a written statement from the affected party(s), and a deadline for receipt of the written statement.
  iii) Deliberate the written statement (above) and the Subcommittee’s final report, including the Subcommittee’s findings, conclusions, and recommendations.
  iv) Determine, by majority vote, the outcomes of the investigation; including any reportable issues, findings, conclusions, and necessary corrective actions.

**NOTE:** The IACUC may invite individuals involved in the complaint to directly address the Full Committee, if in the opinion of the IACUC, such exchange would be warranted.

**NOTE:** Individuals may request audience with the Committee, but it is the decision of the IACUC whether the individual is invited to present verbally to the IACUC. Individuals may submit written statements, if they believe such will be useful to the IACUC’s deliberations.

**NOTE:** If an invitation is extended, it will also include the specific items of discussion, the party (or parties) invited, and a date, time, and time limit for the meeting.

**NOTE:** Individuals having conflicts of interest with the concern or issue being discussed shall not participate in the IACUC investigation, discussion, or deliberation. The same rules of conflict of interest (IACUC Expectations Policy) shall apply to engagement of investigations, Full Committee discussions, or deliberative actions.

  v) At the conclusion of the IACUC’s deliberation, the IACUC will vote upon the recommendation of the Subcommittee.

  1. The IACUC can choose to accept the Subcommittee report in full, in which case, the Subcommittee report will become the IACUC report. The IACUC Chair will have final responsibility for editing the Subcommittee report to indicate that it is now an IACUC report.
  2. The IACUC can accept the Subcommittee report with defined revisions, in which case, the Subcommittee report will become the IACUC report. The IACUC Chair will have final responsibility for editing the Subcommittee report to include the specified revisions and to indicate that it is now an IACUC report.
  3. The IACUC can reject the Subcommittee report, in which case, the Subcommittee shall continue the investigation. In this situation, the IACUC should decide whether a change in Subcommittee composition may be necessary.

  e) Following IACUC determination of an outcome:

  i) The IACUC Chair, or designee, shall:

   1. Notify the Institutional Official of the Committee’s decision and corrective actions, if appropriate;
   2. Notify the affected individual(s) of the Committee’s decision and corrective actions;
   3. Communicate the findings of the IACUC to the complainant, if possible. In most circumstances, the details of the investigation or details of the findings will not be conveyed to the complainant.

  ii) The Director, OAWA, or designee, shall:
(1) Prepare the regulatory notification documents and submit the required notifications to the affected individuals(s)
(2) Prepare the regulatory notification documents to the federal, state, or other oversight bodies.
(3) File all investigative materials and documents in the Committee archival folder.