Title: Reporting Unexpected Adverse Events, IACUC Administrative Policy P-0019-01
Approval Date: April 21, 2016
Authorized by: Vice President for Research and the Institutional Animal Care and Use Committee (IACUC)
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I. Purpose

The Institutional Animal Care and Use Committee's primary concern is the welfare of animals used in research, teaching or outreach programs conducted at Central Michigan University. Unanticipated outcomes or adverse events may occur which affect those animals. Animal users, as well as animal care staff, have a responsibility to report unexpected adverse events (UAE's). The IACUC, as part of post-approval monitoring, is required to perform continued review of approved protocols per PHS Policy (IV.C.5) and USDA Animal Welfare Regulations [9 CFR 2.31(d)(5)]. The UAE reports permit the evaluation into the cause of the UAE's and consider whether updates are required for protocol or standard operating procedures. Failure to report an adverse event by animal users or care staff is viewed as non-compliance and will be assessed for further actions on an individual basis by the IACUC.

An unexpected adverse event is an occurrence of an unforeseen event that negatively affects the welfare of research animal(s); that is, an event that involves pain, distress, and/or death of the animal. By definition, these are events that *are not* identified as a possible risk or outcome in the IACUC approved protocol.

II. Procedures

A. Examples of occurrences that must be reported:

1. Unexpected clinical signs, either related or unrelated to a protocol procedure
2. Surgical complications, which may include recurring unexpected anesthetic deaths
3. Animal morbidity or mortality in excess of that described in the approved animal use application, including endpoints prompting euthanasia that were cited in the protocol and found to be inadequately predictive resulting in unexpected animal deaths
4. Unexpected circumstances that lead to animals being subjected to obvious harm or distress that *is not* justified and approved by the IACUC – e.g. facility or weather-associated events – HVAC or power failure, flooding, fire, housing malfunctions

B. Examples of occurrences that *are not* required to be reported:

1. Death or morbidity of animals that has been described and approved in the animal use protocol (e.g. increased mortality rates due to described phenotypic characteristics of transgenic lines, post-operative complications).
2. Since the chance of mortality increases as a function of age in all animals, the death of aged animals due to natural causes is not considered an adverse event.
3. Injury or illness unrelated to approved research procedures – for example, dermatitis or species specific behavior (among rodents could include fight wounds, barbering, and neonate cannibilization).
   Note: If these situations are noted to be increasing or in high numbers, it may be an indication of an issue and should be addressed with the veterinary staff.

C. Reporting process and expectations of PI staff:

1. All potential UAE's requiring immediate care for an animal and/or if the incident relates to husbandry or clinical care of animals must be promptly reported to the Attending Veterinarian or their designee.
2. For UAE's that are larger-scaled and encompass multiple areas and/or protocols due to facility events, the Facility Manager or Attending Veterinarian will report the event to the IACUC. All other events will be reported by the PI (or designee).
3. An Adverse Event form must be completed and submitted to the IACUC within twenty-four (24) hours of the event being observed or identified.
    a. The form is accessed and submitted within the IRBManager electronic management system.
    b. Within the appropriate protocol, the user will select "Start an xForm" in the Action tab.
    Note: For facility UAE's, the protocol will be listed under the Attending Veterinarian, titled "Unexpected Adverse Events for Animal Facilities".
    c. Select the "IACUC Adverse Event Reporting Form"
4. Information to include within the reports:
    a. IACUC protocol number, if applicable
    b. Location
    c. Number of animals involved
    d. The nature and severity of the event (describe what occurred)
    e. Any identified or potential contributing factors or additional details that may be pertinent to assessing the UAE
    f. Any treatment(s) that were initiated
    g. Suggestions or steps taken to address and prevent future occurrence
5. Concerns may be reported to the Office of Research Compliance directly or anonymously online:
    a. From any CMU web page, search for the "Office of Research Compliance" and select the "Report a Research Concern" link.
    b. The Office of Research Compliance will review information presented via this format.

D. UAE evaluation process:

1. Any individuals involved in the evaluation process should be discreet and circumspect regarding communication of the reported situation.
2. The submitted UAE form will be received within IRBManager by the IACUC Coordinator (or designee).
3. The Attending Veterinarian and the IACUC Chair (or designee) will be notified of the submitted UAE form by the IACUC Coordinator (or designee).
4. Initial questions raised during assessment review of the submission will be directed primarily to the PI.
5. Additional inquiries or assessment may be requested of the Office of Research Compliance by the IACUC Chair or Attending Veterinarian.

E. UAE determination and remediation process:

1. Based upon determination during the assessment period, the report may be:
    a. Deemed as not an UAE, no further action.
    b. Accepted with no further action necessary. The IACUC will be notified of the report submission.
    c. Referred to IACUC to review for further assessment and determination. The IACUC will discuss submission, assessment findings, determine if further investigation is required, and potential

modifications or corrective action necessary. The PI may be requested to participate in the meeting. Examples of corrective action may include:

i. Training or adjustments to training
ii. Veterinary consultation
iii. Changes to vivarium staff support or research staff procedures

Note: The IACUC will determine what submissions must be reported to regulatory agencies.

2. The protocol will be updated to reflect the final determination and appropriate documentation within the IRBManager electronic management system.