Animals in Research: Tips to Keep Out of the Doghouse

Brent C. Morse, DVM, DACLAM / Jacquelyn T. Tubbs, DVM, DACLAM
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Institutional Reporting:

- Reporting is required by PHS Policy [IV.F.3.]
  - Any serious or continuing noncompliance with PHS Policy
  - Any serious deviation from the provisions of the Guide for the Care and Use of Laboratory Animals
  - Any suspension of an activity by the IACUC
REPORTING IS A COOPERATIVE PROCESS

- OLAW will provide assistance and guidance.

- Institution must demonstrate that corrective actions are being implemented.

- OLAW will evaluate appropriateness of the actions in correcting and preventing the reportable issue.

- Self-reporting is part of enforced self-regulation.
TYPES OF REPORTABLE INCIDENTS IN 2020

- Animal Study Issues: 29%
- Failure to Follow Institutional Policies: 19%
- Animal Husbandry: 11%
- Clinical Issues: 15%
- No violations Identified: 4%
- IACUC-Specific Issues: 4%
- Physical Plant: 4%
- Other Issues: 14%
- Other: 4%
TYPES OF ANIMALS INVOLVED

- Rodents: 78%
- NHPs: 7%
- Fish: 5%
- Ungulates: 3%
- All Other Species: 4%
- Not Specified by Institution: 1%
- Carnivores: 2%
- All Other Species: 4%
- Not Specified by Institution: 1%
INDIVIDUAL RESPONSIBLE FOR REPORTABLE ISSUES:

- Investigator & Research Team: 71%
- Animal Care Staff: 12%
- None: 9%
- IACUC: 3%
- Institution: 1%
- Other: 2%
- Vet Staff: 2%
INSTITUTIONAL CORRECTIVE ACTIONS:

- Retrain personnel
- Counsel, reprimand, terminate employment
- Modify institutional policies
- Repair or modify facility
- Enhance PI and study oversight, probation
- Modify, suspend, or terminate animal study protocol
IMPLICATIONS OF REPORTABLE ISSUES:

- Corrective actions and improved systems with better research outcomes
- Special terms and conditions of awards
- Enhanced reporting requirements
- Cost disallowance. Unable to publish data or use it for grant proposals
- Suspension or termination of award (possible repayment of funds)
- Damage to reputation, assessment of peers/collaborators
- Retract or withdraw scientific publication
- Corrigendum or Errata to published article
- Criminal prosecution
COMMON FINDINGS SEEN WITH NONCOMPLIANCE:

• LAB MEMBERS LACKING FAMILIARITY WITH THE PROTOCOL.
• INADEQUATE TRAINING OF INDIVIDUALS ON THE PROTOCOL.
• USE OF EXPIRED DRUGS.
• THE CONDUCT OF UNAPPROVED ACTIVITIES ON A PROTOCOL.
• RODENT CAGES WITHOUT FOOD OR WATER.
• INADEQUATE MONITORING OF ANIMALS.
HOT ISSUES IN COMPLIANCE OVERSIGHT

• **POST-PROCEDURAL ANALGESIA** – REMOVAL OF AMBIGUOUS LANGUAGE FROM PROTOCOLS AND/OR SOPS REGARDING “PROFESSIONAL JUDGMENT” OR “WHEN REQUIRED” AND ASSISTING THE RESEARCH TEAM BY ALLOWING THEM TO CREATE RECORDS OR CHARTS TO DOCUMENT ADMINISTRATION.

• **FAILED CO2 EUTHANASIA** – INSUFFICIENT EXPOSURE TIME; LACK OF APPROPRIATE POST-EXPOSURE OBSERVATION; NO SECONDARY PHYSICAL MEANS. NO FLOW METER OR PROPER INSTRUCTIONS FOR USE OF CHAMBER(S). WELFARE ISSUE IF ANIMALS ARE FOUND TO HAVE SURVIVED CO2 AND AWOKE IN FREEZER/REFRIGERATOR. SOME INSTITUTIONS ARE MORE CLOSELY MONITORING CO2 EUTHANASIA AREAS AND/OR CARCASS DISPOSAL FREEZERS (TO MITIGATE NEGATIVE IMPACT ON THE SURVIVING ANIMAL).

• **FISH** – PHYSICAL PLANT OR HUSBANDRY FAILURES OFTEN LEAD TO CATASTROPHIC LOSSES. MANY FISH SPECIES ARE EXQUISITELY SENSITIVE TO MULTIPLE ENVIRONMENTAL PARAMETERS (TEMPERATURE, SALINITY, PH, NITRATES, CHLORINE, OXYGEN, WATER FLOW, OZONE).
MORE HOT ISSUES IN COMPLIANCE OVERSIGHT

• **LACK OF FOOD AND/OR WATER**—COMBINATION OF ISSUES RESULT IN DRINKING WATER NOT BEING AVAILABLE TO RODENTS. (WRONG CAGES WITHOUT LIXITS, RECOIL HOSE NOT CONNECTED TO RACK, CAGES NOT PROPERLY DOCKED, BOTTLES NOT PLACED PROPERLY, MICE TOO SMALL TO REACH NIPPLE, RESPONSIBILITY FOR FEEDING NOT CLEAR, NEW CAGES NOT SUPPLIED WITH FEED OR WATER, ETC.).

• **ATMOSPHERIC/TESTING CHAMBER FAILURE**—LACK OF CHAMBER (HYPOXIA, SMOKE INHALATION, UV EXPOSURE, BEHAVIORAL ACTIVITY) MONITORING AND/OR LACK OF ALARM SYSTEMS HAVE CONTRIBUTED TO ANIMAL DEATH FROM MECHANICAL FAILURE.
QUESTIONS???
Real-Life Scenarios

Photo - courtesy of Dr. Cathy Schuppli, DVM, MSc, PhD, University of British Columbia
CASE SCENARIO 1


- IS THE ADMINISTRATION OF 1 OF 2 APPROVED ANALGESICS CONSIDERED A NONCOMPLIANCE?
  - YES
  - NO
  - UNSURE
HOW CAN CASE SCENARIO 1 BE AVOIDED?

• ENSURE ALL LAB MEMBERS ARE FAMILIAR WITH THE PROTOCOL (ESPECIALLY IF AMENDMENTS WERE RECENTLY APPROVED AND ADDED TO THE PROTOCOL).

• ASSIGN ROLES AND DESIGNATE WHICH INDIVIDUALS WILL PERFORM POST-OP CARE AND ADMINISTER DRUGS. WILL IT BE THE SURGEON, LAB MANAGER, OR PERSON PERFORMING EVENING CHECKS?

• UTILIZE A POST-SURGERY FORM OR CHECKLIST TO ENSURE ITEMS HAVE BEEN COMPLETED.
CASE SCENARIO 2

- DURING MORNING HUSBANDRY CHECKS, A CAGE OF MICE WAS DISCOVERED LACKING AN APPROPRIATE AMOUNT OF SPECIAL DIET. THE MICE WERE FOUND IN POOR CONDITION BUT RECOVERED WITH SUPPORTIVE CARE. DISCUSSIONS WITH THE RODGERS LAB REVEALED THE LAB WAS RESPONSIBLE FOR PROVIDING THE SPECIAL DIET AND THE MICE HAD NOT BEEN MONITORED AS FREQUENTLY AS DESCRIBED IN THE PROTOCOL.

- WOULD YOU CONSIDER THE DECREASED FREQUENCY OF MONITORING TO BE A NONCOMPLIANCE?
  - YES
  - NO
  - UNSURE
HOW CAN CASE SCENARIO 2 BE AVOIDED?

- CREATE WEEKDAY AND WEEKEND FEEDING SCHEDULE AMONG LAB MEMBERS.
- DOCUMENT WHEN FEEDINGS OCCUR (RECOMMEND KEEPING THE FORM IN THE HUSBANDRY ROOM IF POSSIBLE).
- COMMUNICATE WITH THE HUSBANDRY TEAM THAT SERVICES THE ANIMAL ROOM. PROVIDE CONTACT NUMBERS SO LAB MEMBERS CAN BE REACHED READILY.
- REVIEW THE PROTOCOL WITH ALL LAB MEMBERS, EMPHASIZING THE IMPORTANCE OF ADHERING TO THE MONITORING PLAN AND LAB’S RESPONSIBILITIES.
CASE SCENARIO 3

• A LAB MEMBER PERFORMED CO2 EUTHANASIA INVOLVING A CAGE OF MICE. THE INDIVIDUAL DID NOT PERFORM A SECONDARY METHOD OF EUTHANASIA (AS REQUIRED BY THE EUTHANASIA SOP REFERENCED IN THE PROTOCOL). MICE THAT RECOVERED FROM THE INCOMPLETE EUTHANASIA WERE FOUND ALIVE IN THE CARCASS REFRIGERATOR LATER THAT DAY.

• WOULD YOU CONSIDER THE LACK OF CONDUCTING A SECONDARY METHOD OF EUTHANASIA TO BE A NONCOMPLIANCE?
  • YES
  • NO
  • UNSURE
HOW CAN CASE SCENARIO 3 BE AVOIDED?

• DETERMINE IF TRAINING IS APPROPRIATE (REVIEW LAB SOP, PROTOCOL TRAINING).

• DETERMINE IF POLICIES ARE CLEAR AND WELL DISSEMINATED (NOTICES VIA EMAIL, POSTING OF APPROPRIATE SIGNAGE).

• REGARDING EUTHANASIA EQUIPMENT, ONE MUST ASK: IS THE EQUIPMENT CONSIDERED EASY TO USE? IS AN AUTOMATED EUTHANASIA STATION AVAILABLE FOR USE?

• REGARDING LOCATION, IS EUTHANASIA ONLY OCCURRING IN A CENTRAL LOCATION AND/OR BY “ANIMAL RESOURCES” PERSONNEL?

• USE OF A SECURITY CAMERA/CARD READER AT EUTHANASIA STATIONS MAY BE BENEFICIAL.
CASE SCENARIO 4 (OH, NO LITTLE BUDDY!)

• DOCTOR GILLIGAN IS AN NSF-FUNDED RESEARCHER AT UNCHARTED DESERT ISLE UNIVERSITY. SHE USES SEA BASS IN RESEARCH AND SOME TANKS AT THE UNIVERSITY AQUATIC CENTER CONTAIN HER NSF-FUNDED FISH AND SOME CONTAIN BASS ON HER PROJECTS FUNDED BY THE STATE DEPARTMENT OF AGRICULTURE. RECENTLY, SEVERAL TANKS OF STATE-FUNDED FISH DIED WHEN THE BIOFILTERS FAILED DUE TO LACK OF MAINTENANCE. 600 FISH WERE LOST OVER A 4-MONTH PERIOD. NONE OF DOCTOR GILLIGAN’S NSF-FUNDED FISH WERE AFFECTED.

• IS THE LOSS OF THE 600 FISH REPORTABLE?
  • YES
  • NO
  • UNSURE