



## IACUC Policy: USDA Pain and Distress Categories- Guidelines for Assignment

**Policy Intent:** 1) To assist IACUC members in proper assessment and assignment of research, teaching or demonstration animals into USDA pain and distress categories during protocol review. 2) To guide Principal Investigators in protocol preparation in formulation of humane endpoints and recognition of pain and/or distress.

### Table of Contents

1. USDA Policy #11
2. Introduction
3. References
4. Appendices
  - a. Appendix 1: Definition and Examples of USDA Pain and Distress Categories
  - b. Appendix 2: Clinical Signs of Pain or Distress

### 1. USDA-APHIS Painful and Distressful Procedures Policy #11

AWA Section 2143

9 CFR, Part 2, Sections 2.31(d)(1)(i,ii,iv), 2.31(e)(4), 2.33(b)(4), 2.36(b)(5,6,7)

#### **Policy:**

A painful procedure is defined as “any procedure that would reasonably be expected to cause more than slight or momentary pain or distress in a human being to which that procedure is applied, that is, pain in excess of that caused by injections or other minor procedures”. The Institutional Animal Care and Use Committee (IACUC) is responsible for ensuring that investigators have avoided or minimized discomfort, distress and pain to the animals; appropriately considered alternatives to any procedures that may cause more than slight or momentary pain or distress; and consulted with the attending veterinarian in the planning of the procedures.

Examples of procedures that may cause more than momentary or slight pain include, but are not limited to, the following:

- **Surgery (survival or terminal):** considered a painful procedure in which pain is alleviated by anesthesia. Survival surgery may also require the use of peri-operative analgesia.
- **Freund’s Complete Adjuvant:** may cause a severe inflammatory reaction depending on the species and route of administration.
- **Ocular or Dermal Toxicity Testing:** the dosing procedure itself is generally not painful but the reaction caused by the product being tested may cause pain.

Examples of procedures that may cause more than momentary or slight distress include, but are not limited to, the following:



## Institutional Animal Care and Use Committee™

- **Food and/or water deprivation or restriction** beyond that necessary for normal presurgical preparation.
- **Noxious electrical shock or thermal stress** that is not immediately escapable.
- **Paralysis or immobility** in a conscious animal.
- **Forced exercise** (e.g., swimming or treadmill protocols).
- **Infectious and inflammatory disease models.**

Some procedures, including any of those in the lists above, may cause both pain and distress. Examples of procedures that may cause more than momentary or slight pain as well as distress would include studies involving extensive irradiation, inhalation toxicity studies or those involving tumor growth.

Animals exhibiting signs of pain, discomfort, or distress such as weight loss, decreased appetite, abnormal activity level, adverse reactions to touching inoculated areas, open sores/necrotic skin lesions, abscesses, lameness, conjunctivitis, corneal edema, and photophobia are expected to receive appropriate relief unless written scientific justification is provided in the animal activity proposal and approved by the IACUC.

- 2. Introduction:** Vertebrate animals used in teaching, research and demonstration will be approved through the IACUC review process and protocol will be assigned to USDA pain and distress categories. The definition of pain or distress is simply a procedure or situation that is known to cause pain or distress in humans.

From the Guide, page 120

"In general, unless the contrary is known or established it should be assumed that procedures that cause pain in humans also cause pain in animals (IRAC 1985)."

From the *U.S. Government Principles For The Utilization And Care Of Vertebrate Animals Used In Testing, Research, And Training*:

"IV. ...Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.

<http://grants.nih.gov/grants/olaw/references/phspol.htm#principle>

Protocols will be categorized based on the most painful/distressful procedure if multiple procedures will be performed. Multiple categories will not be assigned to one protocol. The USDA category of pain will be determined for each submitted protocol on a case by case basis.

### 3. References

- Guidelines for the care and use of mammals in neuroscience and behavioral research. 2003. Institute for Laboratory Animal Research. Washington DC: The National Academies Press.
- Guide for the Care and Use of Laboratory Animals 8<sup>th</sup> edition. 2011. Institute for Laboratory Animal Research. Washington DC: The National Academies Press.
- Laboratory Animal Medicine, 2<sup>nd</sup> edition. 2002. Fox, J.G., L.C. Anderson, F.M. Loew, F. W. Quimby. Academic Press.
- The Laboratory Xenopus. 2010. Green, S.L. CRC Press.
- [http://oacu.od.nih.gov/ARAC/documents/USDA\\_Reports.pdf](http://oacu.od.nih.gov/ARAC/documents/USDA_Reports.pdf)



## Institutional Animal Care and Use Committee™

- <http://www.iacuc.cornell.edu/documents/IACUC009.01.pdf>
- [http://www.aphis.usda.gov/animal\\_welfare/downloads/policy/policy11.pdf](http://www.aphis.usda.gov/animal_welfare/downloads/policy/policy11.pdf)

### 4. Appendix 1: Definitions of USDA Categories of Pain and Distress and Examples

| Category B   | Category C  | Category D   | Category E  |
|--|---|--|---|
| Animals being held, bred, or conditioned for use in teaching, experiments, research or surgery, but not yet used for such purposes.  | Animals that are subject to procedures that cause no pain or distress, or only momentary or slight pain or distress and do not require the use of pain-relieving drugs.   | Animals subjected to potentially painful or stressful procedures for which they receive appropriate anesthetics, analgesics and/or tranquilizer drugs.   | Animals subjected to potentially painful or stressful procedures that are not relieved with anesthetics, analgesics and/or tranquilizer drugs. Withholding anesthesia/analgesia must be scientifically justified in writing and approved by the IACUC.  |
| Examples   | Examples  | Examples   | Examples  |
| <ol style="list-style-type: none"> <li>1. Holding protocol</li> <li>2. Animal breeding, pregnancy, parturition or lactation</li> <li>3. Observation of animal behavior in the wild without manipulating the animal or its environment</li> </ol> | <ol style="list-style-type: none"> <li>1. Physical or chemical restraint and husbandry procedures, such as applying identification tags, ear notching, tattoos, ect.</li> <li>2. Routine agricultural husbandry procedures approved by the IACUC in a protocol or SOP (as listed in the Ag Guide)</li> <li>3. Holding or weighing animals in teaching, demonstration or research activities</li> <li>4. Observation of animal behavior in the lab</li> <li>5. Ear punching of rodents</li> <li>6. Tail snips in mice <math>\leq 21</math> days old</li> <li>7. Peripheral injections, blood collection or catheter implantation</li> <li>8. Gastric gavage</li> <li>9. Feed studies, which do not result in clinical health problems</li> <li>10. Live trapping</li> <li>11. Electrofishing</li> <li>12. Positive reward training or research</li> <li>13. Euthanasia alone using AVMA approved methods (2013)</li> <li>14. Euthanasia followed by tissue or organ harvest</li> <li>15. Euthanasia of breeding animals or unused offspring</li> <li>16. Exsanguination with anesthesia</li> <li>17. Exposure to alteration in environmental conditions (not extreme) with appropriate conditioning and microenvironment</li> <li>18. Food restriction that reduces</li> </ol> | <ol style="list-style-type: none"> <li>1. Diagnostic procedures such as laparoscopy or needle biopsies.</li> <li>2. Non-survival surgical procedures.</li> <li>3. Survival surgical procedures.</li> <li>4. Post-operative pain or distress w/ analgesics.</li> <li>5. Retro-orbital blood collection.</li> <li>6. Surgical catheter implantation</li> <li>7. Induced infections or antibody production</li> <li>8. Tail snips in mice <math>&gt; 21</math> days old</li> <li>9. Genetically engineered phenotype that causes pain or distress that will be alleviated.</li> <li>10. Tumor induction or implantation if alleviation of pain/distress</li> <li>11. Terminal cardiac blood collection</li> <li>12. Anesthetize and Release (i.e. for blood sampling) of wildlife</li> <li>13. Studies that involve special housing requests which are exceptions to The Guide such as: housing rodents on wire bottom cages; cages that do not conform to space and height recommendations; requests to house animals outside recommended temperatures.</li> </ol> | <ol style="list-style-type: none"> <li>1. Toxicological or microbiological or infectious disease research that requires continuation after clinical symptoms are evident without medical relief or require death as an endpoint.</li> <li>2. LD50 studies</li> <li>3. Ocular or skin irritancy testing</li> <li>4. Food or water deprivation beyond that necessary for ordinary pre-surgical preparation.</li> <li>5. Application of noxious stimuli that the animal cannot avoid/escape.</li> <li>6. Any procedure for which needed analgesics, tranquilizers, sedatives, or anesthetics must be withheld for justifiable study purposes.</li> <li>7. Exposure to extreme environmental conditions.</li> <li>8. Paralysis or immobilization of a conscious animal</li> <li>9. Genetically engineered phenotype that causes pain or distress that will not be alleviated.</li> <li>10. Euthanasia by procedures not approved by the AVMA (2013)</li> <li>11. Use of adjuvants which cause death of tissue resulting in tissue sloughing.</li> <li>12. Induction of radiation sickness.</li> <li>13. Long-term restraint (days to weeks)</li> <li>14. Forced exercise</li> <li>15. Infliction of burns or trauma.</li> <li>16. Disease and cancer models that involve chronic clinical signs of disease and impairment of motor function.</li> </ol> |



|  |   |  |  |
|--|---|--|--|
|  | the animals weight by no more than 20% of normal age matched controls |  |  |
|--|---|--|--|

## Appendix 2: Clinical Signs of Pain/Distress by Species

| Species          | Behavior  | Appearance   |
|------------------|---|--|
| <b>Rodents</b>   | Decreased activity; excessive licking/scratching; self-mutilation; avoidance or aggression; abnormal locomotion (stumbling); writhing; no nest building   | Piloerection; rough or stained haircoat; abnormal stance or hunched back; porphyrin staining (rats); rapid, shallow respirations                               |
| <b>Rabbits</b>   | Head pressing; bruxism; aggressive or avoidance; increased vocalizations; reluctant to ambulate; self-mutilation  | Hypersalivation; hunched posture; rapid, shallow respirations  |
| <b>Dog</b>       | Excessive licking; increased aggression or avoidance; increased vocalizations (whimpering, howling and growling); self-mutilation; reluctance to ambulate | Stiff body movements; rough haircoat-lack of grooming; trembling; guarding; rapid, shallow respirations; hypersalivation                                       |
| <b>Cat</b>       | Hiding; increased vocalizations (growling, hissing); increased aggression   | Stiff body movements; rough haircoat-lack of grooming; trembling; guarding; rapid, shallow respirations; hunched posture; tail twitching; flattened ears       |
| <b>Swine</b>     | Increased vocalization and aggression; reluctance to move; altered gait; decreased activity   | Immobile; pilo-erection; rapid, shallow respirations; increased muscle tension around the eyes   |
| <b>Ruminants</b> | Increased vocalization; isolation; bruxism; decreased activity or reluctance to move; restlessness  | Stiff body movements; rapid, shallow respirations; tucked abdomen  |
| <b>Horses</b>    | Aggression or avoidance to handling; restlessness; kicking at abdomen; rigid stance   | Anxious appearance; profuse sweating; increased respiratory rate   |
| <b>Fish</b>      | Improper buoyancy; lethargy; surface breathing  | Opercular flaring; sloughed mucus; clamped fins; petechiation or hemorrhage; change in body color; scale loss; whirling  |
| <b>Xenopus</b>   | Buoyancy problems- reluctance to dive; slow to respond; swim upside down or circle  | Excess skin shedding; petechial and ecchymosis of integument; cloudy eyes; sunken, hour-glass shape of the coelomic cavity or large, distended coelomic cavity |
| <b>Reptiles</b>  | Weakness or lethargy  | Incomplete shedding, included retained spectacles; discoloration   |
| <b>Birds</b>     | Inappetance; Altered gait or posture  | Wasting (decreased pectoral muscles); ruffled feathers; rapid open mouth breathing (panting); dull eyes  |