

Drexel University Animal Care and Use Committee Policy for Assigning Pain and Distress Categories on IACUC Protocols

OBJECTIVE: Drexel University (DU) Institutional Animal Care and Use Committee (IACUC) has established this policy to assist Principal Investigators in protocol preparation by providing guidelines for assigning research and teaching animals into appropriate pain and distress categories.

RESPONSIBILITY: Principal investigators (PI) recommend the pain and distress category for animal assignment on an IACUC protocol. If an adverse or other event occurs that changes the approved pain and distress category, the PI is responsible for reporting changes to the IACUC in the form of an amendment so that the event may be accurately reported. The IACUC confirms, accepts or modifies the recommended pain and distress category during the review of the protocol application or amendment for animal use. This policy should be used as a baseline for assigning pain categories to animal use procedures. The IACUC will use performance standards to determine the most appropriate pain category upon full review of specific procedures.

Note: For Field Studies, based on the study complexity, the PI should use his/her knowledge and experience when determining the appropriate pain category.

CONSIDERATION OF ALTERNATIVES TO PROCEDURES WHICH MAY CAUSE PAIN AND DISTRESS:

If an IACUC protocol indicates that an animal will experience pain or distress, whether or not it is fully alleviated (Pain Category D or E), the PI must conduct a literature search for alternatives to the painful and distressful procedures and complete Question 19 of the protocol form.

PROCEDURES:

1. Assign each animal listed on a protocol to one of the pain and distress categories (C, D or E) in Question 18 of the protocol form.
2. List each animal under the most painful pain and distress category that will apply to the animal at any time while the animal is on the protocol, even if it is for a short duration of time.
3. Do not include non-research related veterinary care in determining pain and distress categories.
4. Not alleviating pain and distress (Pain Category E) caused by a procedure must be justified for scientific reasons in writing by the PI and approved by the IACUC. Justification for these procedures must be included in Question 18c of the protocol form.

Note: If there are any questions about how to categorize a procedure that may not be included below, please contact the IACUC office for assistance at IACUC@drexel.edu. The Attending

Veterinarian may also be contacted with any questions at Richard.Huneke@DrexelMed.edu.

ASSIGNING PROCEDURES TO PAIN CATEGORIES:

Pain Category C: Procedures which do not involve pain and/or distress or involve only very slight or momentary pain (e.g. needle stick), and for which the use of anesthetics, analgesics or tranquilizers are not indicated or required.

PROCEDURE TYPE	EXAMPLES
Animal Identification	Ear-tagging; ear-punching; microchipping; tattooing; toe-clipping mice ≤ 7 days of age
Breeding and Genotyping	Maintaining a breeding colony of rodents, weaning pups, collection of small tissue sample from pups up to 28 days of age to determine genotype.
Animal Models with Abnormal Phenotypes	Models that do not elicit pain or distress, thus do not require any treatment and for which the need for humane euthanasia is not anticipated
Behavioral Study	Non-invasive and ‘low impact’ studies: <ul style="list-style-type: none"> • Activity observation • Open –field, mazes and other tests that allow animals to explore and move to preferred locations, conditioned place preference • Positive reward conditioning • Mild allodynia and hyperalgesia tests (e.g. von Frey, Hargreaves, tail flick) • Gait analysis • Strength and climbing tests • Rotorod and balance beams • Object recognition, marble burying, set shifting • Running wheel, treadmill, bicycle exercise with appropriate monitoring • Food/fluid preference • Elevated plus maze • Pre-pulse inhibition • Light/dark box
Blood/Fluid Collection	Blood collection from peripheral vessels, collection of other fluids with mild/brief restraint. Submandibular blood collection.
AVMA approved method of Euthanasia with or without post-mortem procedures	By definition, euthanasia is ‘ending the life of an individual animal in a way that minimizes or eliminates pain and distress’ (AVMA)
Food /Water Restriction	Caloric or fluid restriction for which appropriate monitoring methods to ensure animal health are conducted and weight reduction is not more than 20% of normal

	age matched controls
Injection/Dosing	Injection or oral gavage of agents or other dosing when there is no expectation of pain/distress or deleterious effects.
Restraint or Anesthesia for non-painful procedures	Brief handheld restraint, brief anesthesia or restraint in a device to which animals are acclimated - duration of restraint is less than 60 minutes with proper monitoring
Special Diets/Liquids	In most cases, provision of special food or medicated water should not induce pain or distress
Special Housing and Husbandry	Variations of standard housing modalities that should not lead to stress/distress.

Pain Category D – Procedures that are expected to cause more than slight or momentary pain or distress that is alleviated by anesthetics, analgesics, tranquilizers, removal from study, euthanasia, or other approved methods. This category implies that the ‘pain/distress’ is in excess of that caused by injections or other minor procedures. If AVMA approved euthanasia is utilized to relieve pain and distress, humane endpoints and appropriate monitoring methods must be described in the protocol form.

PROCEDURE TYPE/EXAMPLES	ALLEVIATION OF PAIN/DISTRESS
Animal Models with Abnormal Phenotypes	Appropriate treatment or euthanasia.
Invasive Blood/Fluid Collection <ul style="list-style-type: none"> Any collection procedure in rodents requiring anesthesia (e.g. cardiac, CSF sampling, cut-down) 	Local anesthetic or general anesthesia as applicable
Genotyping (tail biopsy on rodents > 28d old)	General anesthesia (isoflurane)
Non-Surgical Procedures with Potential for Pain or Distress	Anesthesia, analgesia, other appropriate treatment or euthanasia
Survival Surgery	Appropriate anesthesia and analgesia is provided peri-operatively. Surgical procedure does not cause lasting pain/distress
Non-survival Surgery	Appropriate anesthesia for duration of procedure followed by humane euthanasia before animal regains consciousness, including perfusion / exsanguination under anesthesia
Tumor Production with experimental endpoints that result in no more than minimal or momentary pain or distress or for which pain and distress is alleviated.	Appropriate monitoring and treatment when specific clinical signs are observed or euthanasia

Pain Category E – Procedures that are expected to cause more than slight or momentary pain or

distress NOT alleviated by anesthetics, analgesics, tranquilizers or other approved methods for scientific reasons.

PROCEDURE TYPE/EXAMPLES	JUSTIFICATION
<p>Experimentally induced Animal Models with Abnormal Phenotypes or Conditions, Non-Surgical Procedures with Potential for Pain or Distress</p> <ul style="list-style-type: none"> • ALS, MS, EAE, Parkinson’s disease • Administration of Influenza, pneumonia virus, HIV, corona virus, infectious agents • Injections leading to inflammatory pain • Administration of tumor cells • Genetic models 	<p>Experimental endpoints of the model require a painful, distressful, or moribund condition for a scientifically justified period of time.</p> <p>Appropriate nursing care, assistance to access food and water, and other refinements should be described.</p>
<p>Behavioral Study</p> <ul style="list-style-type: none"> • Forced Aggression (resident intruder) • Depression tests (forced swim, tail suspension). Application of noxious stimuli such as electric shock that the animal cannot avoid/escape • Predator odor stress 	<p>Experimental tests that require inducing pain or distress and are scientifically justified.</p>
<p>Survival Surgery</p> <ul style="list-style-type: none"> • Spared nerve injury • Incision induced pain • Chronic Constriction injury • Arthritis model (ACL transection) 	<p>Experimental models of injury induced by a surgical manipulation under appropriate anesthesia but resulting in a chronically painful condition that is scientifically justified</p> <p>Procedures that require withholding post-op anesthesia due to interference with model development and are scientifically justified (Note: surgical plane of anesthesia always required during surgery)</p>
<p>Tumor Production for which an exception to IACUC policy is justified and approved. Experimental endpoints may result in some pain or distress to animals that cannot be alleviated for scientific reasons.</p>	<p>Animals are closely monitored and humanely euthanized as soon as approved endpoints are reached.</p>
<p>Toxicological testing</p>	<p>Testing is scientifically justified and requiring symptoms to develop without relief</p>
<p>Any other procedures for which needed analgesics, tranquilizers, sedatives, or anesthetics must be withheld for justifiable study purposes</p>	

Note: IACUC approval of a procedure’s categorization as Pain Category E does not imply or infer that those animals may be maintained indefinitely or with a condition that is not specifically described and justified in the protocol describing procedures. Animals may only be maintained

under Category E conditions while being appropriately monitored for specific humane endpoints described within the protocol and for no longer than the precise time approved in the protocol. Consideration of non-pharmaceutical pain relief should be considered (soft bedding, extra nesting materials, modification of diets such as floor feeding or soft food, etc). If an animal reaches the endpoint criteria prior to a specified experimental endpoint, they must be removed from study, appropriately treated, or euthanized. Extending any endpoints, experimental or humane, or adding clinical signs to a condition requires submission of a protocol amendment including scientific justification, description of increased monitoring, and IACUC approval.

DEFINITIONS:

Pain: A complex experience that typically results from stimuli that damage or have the potential to damage tissue; such stimuli prompt withdrawal and evasive action.

Distress: An aversive state in which an animal fails to cope or adjust to various stressors with which it is presented.

Experimental Endpoint: The point when the scientific aims and objectives have been reached.

Humane Endpoint: The point at which pain or distress in an experimental animal is prevented, terminated, or relieved.

Painful and/or distressful procedure: A 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.

Pain Category C: Procedures which do not involve more than momentary pain and/or distress, and for which the use of anesthetics, analgesics or tranquilizers is not indicated.

Pain Category D: Procedures that are expected to cause more than slight or momentary pain or distress, and the pain or distress is alleviated by anesthetics, analgesics, tranquilizers or other approved methods – i.e. pain in excess of that caused by injections or other minor procedures.

Pain Category E: Procedures that are expected to cause more than slight or momentary pain or distress, and the pain or distress is NOT alleviated by anesthetics, analgesics, tranquilizers or other approved methods for scientific reasons.

References:

USDA Policy #11: Painful and Distressful Procedures. Issue Date: March 25, 2011 References: AWA Section 2143, 9 CFR, Part 2, Sections 2.31(d)(1)(i,ii,iv), 2.31(e)(4), 2.36(b)(5,6,7)

Guide for the Care and Use of Laboratory Animals 8th edition. 2011. Institute for Laboratory Animal Research. Washington DC: The National Academies Press.

USDA Annual Report. http://oacu.od.nih.gov/ARAC/documents/USDA_Reports.pdf

Approval Date: 2/26/2016