INSTITUTIONAL ANIMAL CARE & USE COMMITTEE
UNIVERSITY OF MICHIGAN

University of Michigan Policy On Pain and Distress Categorization for Animals Exposed to Noxious Stimuli

Policy

Via this document, the University of Michigan's Institutional Animal Care & Use Committee (IACUC) agrees to adopt a consistent stance on the categorization of animals exposed to noxious stimuli, including established tests of analgesic potency in which animals can escape the noxious stimulus.

Procedures where the animal can escape from the noxious stimulus will be placed in Category 2, based on the temporal aspects of the definition of "painful procedure." In these studies the pain, if perceived at all, will be momentary or slight due to the animal's innate ability to move its appendage away from the noxious stimulus. Examples include rodent tail-flick assays and nonhuman primate tail-dip assays.

In order to satisfy this categorization, however, the investigator must:

(1) Detail the time limits set for exposure to the noxious stimulus in the event that complete analgesia renders the stimulus imperceptible. This time limit should be of such duration that tissue damage should **not** occur as a result of complete analgesia.

(2) Describe the consequences to the animal's skin and tissues if there were to be accidental prolonged exposure to the noxious stimulus.

(3) Address the number of repetitions of this study that an individual animal will experience in a given time period.

(4) Assure that the animal will in no way be prevented from escaping or moving its appendage by manual restraint, by additional pharmacological means beyond analgesia (e.g., muscle relaxants), or by physiological inability (e.g., genetically altered mice with neurological or muscular defects).

Satisfactory responses to these four questions would enable classification of these procedures as Category 2, rather than as Category 8.

If the **responses** to these additional questions are **not acceptable**, then those animals that receive therapeutic doses of known analgesic compounds will be placed in Category 6, but the animals that receive subtherapeutic analgesic doses, doses with unknown compounds, or no analgesics (control group) will be placed in Category 8.

If animals are anesthetized while they are exposed to a noxious stimulus that would otherwise be classified as a Category 8 procedure (e.g., noise exposure above 120 dB), and are not expected to experience more than mild residual pain and distress when recovered, then those animals will be placed in Category 3 rather than Category 8.

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Background

In most cases, research projects that specifically study the induction of pain or distress in animal models are automatically placed in the current USDA category that indicates that "animals might experience pain, discomfort, or distress for which anesthetics, analgesics, or tranquilizers ... cannot be used ..." This is equivalent to Category 8 at the University of Michigan, and Column E by the USDA.

In many of these studies, the animal has the opportunity to remove itself (or the affected part of itself) from the painful or distressful stimulus. Examples include tail flick studies in mice and tail dip studies in nonhuman primates. In the tail flick studies, a focused laser is pointed at the mouse's tail; when the mouse feels the heat from the laser it moves the tail away, and the time from laser initiation to tail movement is recorded. If analgesics have been given as part of the study, the mouse typically leaves its tail in the laser's path longer before moving it (indicating that the agent has attenuated the response to the noxious stimulus). The tail dip study is of similar fashion, except that the nonhuman primate's tail is placed in a beaker of warm water, rather than exposed to a laser.

In both of these instances, the animal cannot receive any "anesthetics, analgesics, or tranquilizers" as they would interfere with the physiologic and/or pharmacologic basis of the study. However the animal does avoid the noxious stimulus once it is perceived, and thus it only experiences slight or momentary pain.

The definition of a painful procedure, as per the USDA regulations, is "any procedure that would reasonably be expected to cause more than slight or momentary pain or distress in a human being to which the procedure was applied, that is, pain in excess of that caused by injections or other minor procedures." Unfortunately, the temporal aspects of the definition of a "painful procedure" are not transposed consistently to the descriptions for classification in pain "categories" or "columns." For example, the USDA notes the temporal aspects of a painful procedure in the description for experimental procedures that warrant inclusion in Column C (U-M's Category 2), but not in the descriptions for Column D and Column E (U-M's Categories 6 and 8, respectively)[3].

There are no specific guidelines as to how to categorize animals that are a part of pain testing from which escape is possible. Those that receive a "complete" dose of analgesia, and thus never perceive the pain, could readily be classified in Column D (U-M's Category 6) because the pain is relieved by administration of analgesics. However, those that do not receive analgesics (control group) or receive a subtherapeutic dose could be in Column C or Column E (U-M's Categories 2 and 8, respectively) depending on whether the temporal aspects of the "painful procedure" definition are applied by the reviewer. By adopting this policy, and ensuring that the four conditions noted above are satisfactorily addressed by the investigator, the IACUC ensures both consistency in categorization of animal-based procedures, and humane care of animals used in research on analgesic potency.

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References

1) National Research Council. 2003. Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research. National Academies Press, Washington, DC.

2) Le Bars D, Gozariu M, and Cadden SW. 2001. Animal models of nociception. Pharmacol. Rev. 53:597-652.

3) National Research Council. 2000. Definition of Pain and Distress and Reporting Requirements for Laboratory Animals: Proceedings of the Workshop held June 22, 2000. National Academies Press, Washington, DC.

4) US Department of Agriculture. 1997. Policy #11, Painful Procedures. In Animal Care Resource Guide.