



Science Directorate

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Regulatory Analysis and Development
Program Planning and Development
Animal and Plant Health Inspection Service (APHIS)
U. S. Department of Agriculture (USDA)
Suite 3C03
4700 River Road, Unit 118,
Riverdale, MD 20737-1238

Re: Docket No. 00- 005-1

Animal Welfare; Definitions for and Reporting of Pain and Distress

The Committee on Animal Research and Ethics (CARE) of the American Psychological Association (APA) submits these comments on the proposed definitions for and reporting of pain and distress (Docket No. 00-005-1). As a standing committee of the APA, representing a membership of over 159,000 researchers, educators, clinicians, consultants, and students, committed to the humane treatment of laboratory animals for 75 years, CARE has been involved in developing and regularly updating guidelines for the humane care and treatment of nonhuman animals in research. Because research with animals is an integral component of the science of behavior, APA has strongly supported the efforts to improve laboratory animal welfare that do not include policies or regulations that would compromise scientific research.

CARE would like to take this opportunity to address issues arising from the use of the terms *pain* and *distress* in the Animal Welfare Act (AWA) regulations, as well as the classification system currently employed by the USDA to report number of animals.

CARE recommends eliminating the use of the term *distress* and suggests an alternative scheme for allowing local Institutional Animal Care and Use Committees (IACUCs) to consider the issue of pain while reviewing scientific proposals involving research with animals, other than humans.

Executive Summary

CARE recommends elimination of the term *distress* from the AWA regulations on the following grounds: The extremely subjective and vague nature of the concept makes it impossible to define and compare among humans, much less across different species.

- ◆ A global definition of *distress* in terms of animal use in research fails to take account of the objectives of animal use. Any distress experienced by laboratory animals needs to be evaluated in the context of the experimental question and goals.
- ◆ There is experimental evidence that animals can experience stress or some pain without being distressed.

As an alternative to the current pain classification system, CARE suggests that experimental procedures be classified by their degree of aversiveness, rather than by the distress they may cause.

Problems with a general definition of pain

CARE's objection to the use of the term *pain* in the USDA regulations pivots around the definition of pain from a purely human perspective. This is an entirely subjective definition that completely disregards the well being and/or needs of the animal. An important limitation of applying human subjective judgments of painful procedures is that such criteria ignore or by-pass the special or unique sensory, perceptual, and expressive systems of various species. Pain cannot be measured on an absolute scale, nor can it be scaled and compared across species. Instead, pain can be placed on a continuum from minimum threshold levels of perception to maximum levels of

tolerance. Pain may not be maladaptive or produce distress until it reaches a level of maximum tolerance where it dominates behavior. An animal can be distressed without pain and may experience some pain without distress. It is broadly recognized that animals can experience pain, as evidenced by efforts to avoid or escape noxious stimuli. It is important that the IACUC evaluate these difficult issues in a rigorous manner while reviewing protocols. Thus, we seek to establish conditions and procedures that are appropriate for our animal subjects when they are being used for justifiable research (See alternative classification system proposed below).

Problems with any definition of distress

Subjectivity -- Distress primarily means to "cause discomfort, anxiety, or suffering," and is defined purely by subjective response. This subjectivity makes it impossible to measure or apply it to laboratory animals. Distress is likely to be manifested in very different ways not only between species but also among different individuals within a species. It is important to emphasize that distress should not be confused with stress, which can be related more easily to environmental stimuli that can be arranged, at least in nominal order, from mild to severe. Further, stress can be related to measurable biological responses. Life is full of stressors, and its function in behavior is complex. Most stressors have no long-term negative effects, and many of which serve important functions in normal homeostasis or survival. In rats, for example, pup separation from a dam is stressful to the pups (and the mother), but it is a normal part of the developmental process. Moreover, studies have shown that early mild stress reduces later stress vulnerability. There are no simple physiological or behavioral criteria to mark the point where an animal that experiences stress becomes distressed.

Adaptive Value of Pain and Stress -- It should be noted that many animals, including humans, are subject to stress in their natural environments, yet they show remarkable adaptive resilience. Exposure to stressful situations is a part of normal development and is crucial for the development of a normal healthy individual. For example, all children go through a stage of being fearful of strangers (i.e., stranger

anxiety), but gradually learn to cope with it. Analogous to infant immunizations, which help the child develop resistance to various illnesses, exposure to stress enables the animal to acquire resistance and healthy coping skills. It has also been shown that stress hormones protect as well as damage the body. Therefore, the mere presence of stress should not be presumed to be an unacceptable state. In addition, fear and pain provide evolutionary benefits in terms of alerting an animal to the need to defend against environmental threats (fear) and to recuperate from tissue damage (pain). There is also evidence that fear and anxiety inhibits sensitivity to painful stimuli. Thus, interactions such as these indicate fear, anxiety, and pain cannot be treated as additive phenomena.

Distinction Between Necessary and Unnecessary Pain -- Yet another difficulty with a global definition of *distress* in terms of animal use in research is that it does not take into account the objectives of the particular study. The most important point is that the distress experienced by the laboratory animals be evaluated in the context of the experimental question. That is, one needs to assess whether any potential distress that maybe caused to the laboratory animal is necessary or whether it can be avoided without compromising the scientific or educational goals. Thus, the acceptable level of distress varies across studies, and the simple reporting of distress and/or pain out of the context in which it occurs provides spurious information. For example, a study that examined the effect of forelimb deafferentiation on food intake would be unacceptable, while a study that assessed recovery of function following deafferentiation of a forelimb using food reinforcement for use of the deafferented limb would be appropriate. Also, it is problematic to classify research where pain is not a by-product but is the focus of the study. The goal of any classification system should be to prevent procedures that are unnecessarily painful, and not to thwart research that will help better understand pain, in and of itself.

Responses to the Questions Posed by the USDA:

1. Would adding a definition for distress to the regulations help institutions using animals for research, testing, or teaching better recognize, minimize, and report animal distress?

No. The USDA should not define *distress* in the regulations, as any attempt to do so relies only on a fragile and useless anthropomorphism. The extremely subjective nature of the concept makes it impossible to define and compare across organisms and individuals.

We suggest instead that experimental procedures be classified by how aversive they are, rather than the distress they may cause. This should be defined relative to an animal's normal homeostatic state. If a procedure challenges an animal's normal homeostatic state, this can be detected by the animal's active attempts to return to its normal balance. For example, restricting water access for animals that normally live in the desert would be appropriate (perhaps even healthy) and non-aversive, while restricted water access would be aversive to animals used to a habitat with more water.

Decisions regarding how pain will be classified, monitored, dealt with, and reported for internal purposes, should be left to the discretion of the individual institutions/IACUC.

2. If a definition for distress is added to the regulations, what key elements should be included in that definition?

As mentioned above, we believe that the USDA should not add a definition of *distress* to the regulations. If however, the USDA does decide to do so, then the definition should take into consideration the educational and scientific objectives of the procedure and the natural history of the species.

3. What are the benefits and limitations of [the USDA] pain and distress classification system?

There are two major benefits of the requirement to classify anticipated levels of pain. First, it assists the IACUC in reviewing protocols more thoroughly; and second, it sensitizes the researcher to the issue, thereby encouraging a thorough search for alternative less or non-painful/aversive procedures.

Three major limitations of the current system are as follows:

- ◆ *Forced misclassification of procedures* – the somewhat vague and arbitrary nature of the categories disregards vital parameters such as intensity and duration of the pain caused by a procedure, leaves the institutions with little choice but to force-fit the protocols into one of the categories, regardless of the actual appropriateness. For example, in a conditioning paradigm, a mild foot shock maybe of such short duration as to preclude any avoidance behavior on the part of the animal. Depending on the philosophy of the IACUC such a protocol may then be classified either as Category C or Category E;
- ◆ *Inconsistent application* – the poorly defined nature of the categories leave it open to interpretation, resulting in its inconsistent application across IACUCs. This renders numerical aggregates and comparisons across institutions worthless;
- ◆ *Increased administrative burden on institutions and increased regulatory burden on the USDA, with no impact on the quality of care afforded to the laboratory animals' welfare* -- there is no evidence that the act of reporting has any impact on the welfare of the laboratory animal itself. The current reporting requirement is of no value for several reasons. First, the data obtained under the current system is spurious given the differences in reporting practices across (and possibly within) institutions. This would also be true of any other reporting system due to variations in the operating procedures and philosophy of different IACUCs (which might depend on the make-up of the IACUC, its experience with different kinds of research, etc.) that would affect how animals are classified and reported. Second, reporting of these fallacious figures annually serves no purpose other than to provide anti-animal research groups with erroneous data on which to base their argument for the complete elimination of laboratory animal research. Thus, the

requirement to classify and report potential pain (or aversiveness of proposed procedure) in research animals should be an institutional exercise, and should not be included in the annual animal facility report to the USDA.

4. Should [the USDA] animal pain and distress classification system be modified or replaced? If so, what specific modifications or alternate classification systems should [the USDA] consider?

We are proposing an alternative, comprehensive, and non-subjective classification system. It consists of four simple questions that should satisfy the concerns raised by the USDA, while improving the ability of animal care and use committees to assess, in advance, the intrusiveness of a proposed protocol. It should be noted that these questions are specifically related to the issue and assessment of potential pain in a proposed study, and the standard considerations for evaluating the other parts of a proposal are still essential to consider.

Alternate Classification System for Recognizing and Minimizing Pain and/or Aversiveness of Procedures in Laboratory Animal Research

Question 1

Is the procedure non-aversive or does it involve no, or minimal pain?

If yes, given the other important considerations (scientific merits, appropriate design, justification, sample size, etc.), then approve protocol.

If no, go on to Question 2

Question 2

If the procedures are potentially aversive or painful, will adequate measures be taken to prevent, counteract, or relieve any pain or discomfort?

If yes, given other considerations (scientific merits, appropriate design, justification, sample size, etc.), then approve protocol.

If no, go on to Question 3

Question 3

If the procedures are potentially aversive or painful and measures cannot be taken to prevent, counteract or relieve it, are the procedures thoroughly justified by the scientific merits of the study?

If yes, go to Question 4.

If no, disapprove.

Question 4

Have other alternatives been considered?

If yes, given other considerations (scientific merits, appropriate design, justification, sample size, etc.), then approve protocol.

If no, disapprove.

The use of these four questions would provide the necessary guidance to the IACUC to determine if a potentially painful or aversive procedure is appropriate.

5. Should animal pain and distress be prospectively or retrospectively reported?

Prospective reporting of pain to the IACUC is necessary, and in most cases sufficient, to ensure the welfare of the laboratory animals. Such reporting assists the IACUC in reviewing protocols more thoroughly. In addition, it serves to sensitize the research team to the issue, thereby encouraging a thorough search for alternatives. Only in instances where new techniques or procedures are being employed should retrospective reporting to the IACUC be required. This retrospective reporting would serve an educational function for the entire research team (IACUC to researcher to lab animal technician). In addition, it would truly benefit the animals themselves by ensuring that future protocols are reviewed and amended accurately.

In closing, the Committee recommends that the USDA consider the more comprehensive and objective classification system proposed by CARE. The system proposed by the Humane Society of the United States (HSUS) lacks merit since it further complicates an already dysfunctional system, rendering it more ambiguous and subjective, resulting in increased administrative burden with less meaningful data and no benefit to the laboratory animals. In addition, the HSUS' Pain and Distress Initiative, which is a component of a larger campaign, called Campaign 2020, calls for "Elimination of ALL pain and distress in research animals." The exhaustive list of examples given indicates that this means all research with laboratory animals, including research specifically on pain and stress. This contradicts congressional intent in passing the AWA, which is to acknowledge the value of animal research and the need to support such research. Thus, the emphasis should be on reducing and eliminating **unnecessary** pain in laboratory animals – unnecessary to the extent that measures taken to alleviate or eliminate it do not interfere with the research question. The alternative system proposed by CARE is vastly superior in being simpler and more objective. It will serve to ensure that while the welfare of laboratory animals is safeguarded, the invaluable research of which these animals are an integral part will continue, thus benefiting both humans and other animals.

Respectfully submitted by,

APA Committee on Animal Research and Ethics

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