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A report from the Pain & Distress Campaign of The Humane Society of the United States

Policies & Perspectives

CONSENSUS ON PAIN AND DISTRESS CATEGORIZATION

In July 2000, the U.S. Department of Agriculture (USDA) sought public comments on its consideration to revise the pain and distress categorization system and to define distress in the Animal Welfare Act regulations (*Federal Register*, Docket #00-005-1). After reviewing the comments received, the USDA decided not to follow through on its initiative, citing lack of consensus among the scientific community on these issues. To explore this rationale, The Humane Society of the United States (HSUS) examined all of the comments submitted by the research community (approximately 2,151). Nearly nine of every 10 comments submitted (88.7%) expressed support for a revised categorization system. Most recommendations were for the categorization system to: (i) reflect actual rather than potential pain regardless of whether or not anesthesia or analgesia is administered, (ii) include nonpharmacological efforts to relieve pain and distress, (iii) adopt completely new categories of pain and distress, or (iv) adopt the systems developed by The HSUS or the Canadian Council for Animal Care (CCAC), which were referenced in the *Federal Register* notice (these systems largely focus on levels of pain and distress actually experienced by the animals). In addition to the near-consensus on the need for changes in the current pain and distress classification system, the comments showed a near-

consensus among the research community regarding a definition of distress (see the April 2004 *Pain & Distress Report*, 4(1)).

Full consensus on most aspects of animal welfare oversight will never be reached within the scientific community, let alone among all stakeholders. The lack of full consensus should not be used as an excuse to maintain a flawed status quo. The HSUS urges the USDA to formally propose a new or revised scale of pain and distress that reflects levels of severity. This would be a small but important step forward in improving the current reporting system and ultimately providing more meaningful oversight of animal pain and distress in research.

AALAS HIGHLIGHTS PAIN AND DISTRESS

The American Association for Laboratory Animal Science (AALAS) recognizes that “obtaining greater knowledge on eustress, stress, pain, and distress is critical to the enhancement of the welfare of laboratory animals” (www.aalas.org). The AALAS website emphasizes that scientific data on pain and distress—such as how much pain and distress is caused by certain techniques—are lacking, encourages scientists to generate information on these issues, and points out that such data are required to draw conclusions about animal pain and distress. The AALAS specifically addresses the need to define terms in order to accurately report research results; the

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Policies & Perspectives

challenges of recognizing and measuring pain, stress, and distress; and regulatory requirements. For more information, go to www.aalas.org.

The HSUS strongly agrees that scientific data on pain and distress (particularly non-pain-induced distress) are seriously lacking. We have submitted congressional testimony to request increased funding for research—to be conducted without causing pain or distress to additional animals—focused on recognition, assessment, and alleviation of pain and distress. We invite the AALAS and other members of the animal research community to make similar funding requests for fiscal year 2007. For more information, go to www.hsus.org/animals_in_research/pain_distress/funding_for_pain_and_distress_research.html.

UK PROGRESS ON ALTERNATIVES

The Nuffield Council on Bioethics established a Working Party (WP) to “encourage a rigorous ethical debate” on animal research. The WP—made up of scientists, philosophers, animal protection representatives, and a lawyer—recently published findings that conclude, in part, that researchers should take various steps to further implement the Three Rs (particularly replacement) and alleviate pain and distress. The WP agreed that a “thorough analysis” of the scientific barriers to developing replacements should be conducted so that research can be achieved without causing pain, suffering, distress, lasting harm, or death to animals. The report suggests that by advancing replacements, providing animal welfare details in publications, being more open about studies and how animals are treated, and avoiding unnecessary duplication of experiments, researchers can reduce the prevailing divisiveness on this issue. Findings are available at www.nuffieldbioethics.org/fileLibrary/pdf/RIA_Report_FINAL-opt.pdf (chapter 4 addresses animal pain, distress, and suffering).

The HSUS's comments can be found at www.nuffieldbioethics.org/go/ourwork/animalresearch/page_251.html.

Noteworthy

TECHNOLOGY MAY REDUCE ANIMAL USE

New technologies may decrease animal use in drug efficacy testing. Potential drugs can be tagged with radioactive particles, injected into animals, and then tracked using a positron emission tomography (PET) scanner. Similarly, biophotonic scanning can be used to track agents tagged with a fluorescent protein form, using a “charge coupled device” camera. Both methods allow researchers to determine whether a drug candidate reached its intended target without killing the animals. Drugs that fail to reach the intended target are eliminated from subsequent testing. Similarly, a virtual diabetic mouse allows researchers to gauge some potential drug effects on diabetic humans. Virtual animals may be created for any species for which there is sufficient data that can be applied to a computer model. All of these new technologies could result in the use of fewer animals and cost savings for pharmaceutical companies through the use of smaller amounts of experimental drugs and fewer trials. Some current obstacles, however, include the expense of the scanners as well as U.S. Food and Drug Administration drug testing requirements. For more information, visit www.technologyreview.com/articles/05/06/wo/wo_061305gartner.1.asp and www.wired.com/news/medtech/0,1286,67541,00.html.

Resources & Services

FREE REPRINTS: CARBON DIOXIDE EUTHANASIA

Free reprints of a recent and extensive review of the available literature regarding the use of carbon dioxide (CO₂) euthanasia (Conlee, Stephens, Rowan, & King, 2005, *Laboratory Animals*, 39: 137–161) are available from The HSUS. Authored by HSUS staff members, the article emphasizes pain and distress concerns regarding the use of CO₂

Upcoming Conferences

Institutional Challenges in a Changing World: How Will IACUCs and Scientists Meet the Challenge?

- ▶ Hosted by the Scientists Center for Animal Welfare (SCAW)
- ▶ December 5–6, 2005
- ▶ San Antonio, Texas
- ▶ For more information, go to www.scaaw.com/winter%20conference.htm

IACUC 101 and PRIM&R/ARENA Annual IACUC Meeting

- ▶ Coordinated by the Office for Laboratory Animal Welfare (OLAW), Public Responsibility in Medicine and Research (PRIM&R), and the Applied Research Ethics National Association (ARENA)
- ▶ March 26–28, 2006
- ▶ Boston, Massachusetts
- ▶ For more information, go to <http://grants.nih.gov/grants/olaw/workshop.htm>

IACUC 101 and 201 Seminars

- ▶ Coordinated by the Office for Laboratory Animal Welfare (OLAW) and Virginia Commonwealth University
- ▶ April 19–20, 2006
- ▶ Richmond, Virginia
- ▶ For more information, go to <http://grants.nih.gov/grants/olaw/workshop.htm>

euthanasia in rodents. Several animal-welfare-related aspects of CO₂ euthanasia are addressed, including flow rate and final concentration, presence of oxygen, and prefilled chambers versus gradual induction. Recommendations for alternatives to the use of CO₂ for euthanasia are also included.

A recent editorial by Raj, Leach, and Morton (2004, *Comparative Medicine*, 54: 470–471) discusses pain and distress concerns related to CO₂ euthanasia, emphasizing its aversiveness compared to other inhalational agents. The adverse effect of CO₂ on humans is also addressed. The authors recommend inducing unconsciousness with a less aversive agent, such as halothane or isoflurane, before using 100% CO₂.

For a copy of *The HSUS's review*, e-mail ari@hsus.org. *The HSUS hopes that this literature review will increase attention to pain and distress associated with CO₂ use for euthanizing laboratory animals and will encourage researchers to consider and implement recommended alternatives.*

HOUSING AND CARE OF AFRICAN CLAWED FROG

The Royal Society for the Prevention of Cruelty to Animals has produced a new report on the housing and care of the African clawed frog, *Xenopus laevis*. The report is based on information from legislation, scientific literature, commercial organizations, ethics committees, research facilities, and research community members. To request a copy of the report or to submit comments, e-mail breed@rspca.org.uk.

From the Technical Literature

ANIMAL STRESS: DEFINITION, MEASUREMENT, AND INTERPRETATION

Pekow (2005, *Contemporary Topics in Laboratory Animal Science*, 44, 41–45) explores means of defining, measuring, and interpreting stress of animals in research, including stress that

is beneficial or neither beneficial nor harmful. She indicates that a definition of terms is “critical to measuring and assessing stress.” The author frames distress as stress that induces a harmful adaptive response, and further states that distress occurs “only when the biological cost of stress negatively affects biological functions critical to the animal’s well-being.” Pekow uses a table to demonstrate the lack of a definition of distress in the Animal Welfare Act (AWA), AWA regulations, the U.S. Government Principles, and Public Health Service Policy, and to show the array of existing definitions of distress, most of which refer to the inability to adapt to stressors.

Factors that can serve as stressors—including housing, noise, handling, temperature, research procedures, and social interactions—are discussed, as well as types of stressors (such as acute, chronic, episodic, chronically intermittent, and anticipated) and subsequent biological responses. Stress effects can be determined by evaluating changes in behavior and physiology. Measurements of distress include animal activity and behavior; physiologic measures, such as body weight, heart rate, and body temperature; retrospective pathology; and immune function. Pekow emphasizes the difficulty of interpreting stress measures and the need for well-trained personnel to determine if an animal is actually experiencing distress. She emphasizes the need for additional data and research

on causes of stress and subsequent improvements to procedures.

The HSUS agrees with many aspects of the Pekow article, particularly the critical need to define terms in order to measure and assess stress. Consequently, it is our hope that the research community will press the USDA to move forward in adopting a uniform and sensible definition of distress.

ISCHEMIC STROKE MODELS: WELFARE CONSIDERATIONS

Graham et al. (2004, *Comparative Medicine*, 54, 486–496) considers balancing experimental aims and animal care when using animals for stroke studies. Initial factors to consider when designing stroke studies include species, type of ischemic insult, and purpose and duration of the study, as well as how to minimize the number of animals used and maximize information gathered from each animal (e.g., banking tissues for future use). Housing and handling factors, such as sociality of species and the effects of environmental enrichment, are also important considerations. Intensive care is required for “stroked” animals following surgery due to factors such as injury, visual deficits, facial paralysis, general depression, or other complications that can affect respiratory, cardiac, and nervous systems. Stroke scales typically used to evaluate the function of human

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Recent Publications

Murrell, J. C., & Hellebrekers, L. J. (2005). Medetomidine and dexmedetomidine: A review of cardiovascular effects and antinociceptive properties in the dog. *Veterinary Anaesthesia and Analgesia*, 32: 117–127.

Swallow, J., et al. (2005). Guidance on the transport of laboratory animals. Report of the Transport Working Group established by the Laboratory Animal Science Association (LASA). *Laboratory Animals*, 39(1): 1–39.

**Pain
&
Distress
Report**

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From the Technical Literature

stroke patients and general scoring systems (one has been created for the focal rodent stroke model) can be adapted and used to assess pain and distress and to determine humane endpoints. The importance of proper training and communication among all parties involved with the research is underscored.

Attitudes & Public Opinion

ANIMAL RESEARCH POLL

A poll of 1,002 American adults, conducted in April 2005 by Peter Hart Associates on behalf of the Foundation for Biomedical Research, found that 40% of respondents believe that animal research has contributed a great deal to human health care over the last few decades and 36% felt it contributed a fair amount. The poll also found that 56% of Americans think that sufficiently stringent federal regulations are currently in place governing proper and ethical treatment of animals. In addition, the public supports the research community's pursuit of alternative methods with the knowledge that current technological limitations require animal testing. To view the poll, go to

www.fbresearch.org/journalist/press-releases/Polls/HartPoll_4_15_05.htm.

While this poll shows Americans are supportive of animal research in general, multiple studies have shown that public support decreases substantially as the amount of unrelieved pain, distress, or suffering increases. For example, see www.hsus.org/animals_in_research/pain_distress/opinion_poll_on_pain_and_distress_in_research.html.

Statistics on Animal Use & Pain & Distress

CANADA RELEASES SURVEY OF ANIMAL USE FOR 2002

The Canadian Council on Animal Care recently released animal use statistics for 2002. The number of animals used in scientific procedures for research, testing, and teaching totaled 2,103,135—a 1.5% decrease from 2001. However, the number of nonhuman primates used increased by 12%. Mice, fish, rats, farm animals, and domestic birds accounted for 93% of the total number of animals. According to Canada's pain and distress classification

Helpful Websites

Altweb focuses on replacement, reduction, and refinement alternatives and assists scientists with alternatives searches, promotes information sharing, and provides news, information, and resources on alternatives. A project team of regulatory agencies, animal protection organizations, universities, and industry organizations provide vision and direction for the site. For more information, go to <http://altweb.jhsph.edu>.

system, 30% of the animals used experienced moderate to severe distress or discomfort (a 5% increase from 2001), and 5% experienced severe pain (similar to 2001). Similar to previous years, 70% of the animals who experienced severe pain were used for regulatory testing of products. To view the results, visit www.ccac.ca/en/Publications/Facts_Figures/aus2002.htm.

Pain & Distress Report

The *Pain & Distress Report* provides laboratory animal veterinarians, technicians, oversight committees, and others with up-to-date information on issues regarding pain and distress in laboratory animals.

E-mail ari@hsus.org for a free subscription to the electronic version of the newsletter; copies are also available online at www.hsus.org/pain_distress_report. Please share this report with your colleagues and IACUC members.

THE HUMANE SOCIETY OF THE UNITED STATES

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