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The Pain & Distress Report
is available online at

humanesociety.org/pain_distress_report.



THE HUMANE SOCIETY
OF THE UNITED STATES

humanesociety.org

Pain & Distress Report

From the Pain & Distress Campaign of The Humane Society of the United States

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Policies+Perspectives

Pain in Laboratory Animals

The Institute for Laboratory Animal Research (ILAR) convened the first meeting of its Committee on Recognition and Alleviation of Pain in Laboratory Animals in September. The committee is tasked with creating a report on recognizing and alleviating pain in laboratory animals, which is, in part, an update of its 1992 report, *Recognition and Alleviation of Pain and Distress in Laboratory Animals*. According to ILAR, the new report will draw from current scientific literature and include information on the physiology of pain in species commonly used for research, as well as humane endpoints, pharmacologic and nonpharmacologic methods,

principles for minimizing the pain associated with specific procedures, and protocol development by Institutional Animal Care and Use Committee (IACUC) members, investigators, and animal care staff. Most of the first day of the meeting was an open session, with presentations on emotional versus nociceptive components of pain, nociception, and consciousness; objective assessment of pain; and comparative assessment of analgesic drugs. The second day of the meeting was closed to noncommittee members. ILAR has convened a similar committee to focus on distress; its report will also be available soon.

Animal Reuse

Animal research guidelines and regulations contain few recommendations on the reuse of animals in preclinical research. To address this lack of guidance, Kovalcsik et al. (2006, *Lab Animal*, 35(9), 49–53) conducted an online survey of 150 animal facilities involved in preclinical studies to learn more about how the facilities address animal reuse and the factors influencing whether or not animals can be reused. Survey questions addressed animal reuse practices, species of animals used and reused, study types involving animal reuse, and criteria for determining when animals should

no longer be used. Of the 55 responses received, 73% said they reuse animals, with dogs and nonhuman primates the most frequently reused species. Reuse was most common in pharmacokinetic, safety pharmacology, drug metabolism, and dose escalation or range-finding studies. Behavior/psychological well-being was one of the most common parameters for excluding animals from reuse. In most cases, respondents stated that the number of studies in which an animal has already been involved and the number of compounds or doses administered are not bases for excluding animals from reuse.

Three Rs Survey

The National Centre for the Replacement, Refinement, and Reduction of Animals in Research (NC3Rs), based in the United Kingdom, has launched a national survey to find out what

researchers know about the Three Rs and how relevant these principles are to their work. An NC3Rs representative noted that the recent rise in animal use

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2007 Russell and Burch Award

The HSUS recently presented its Russell and Burch Award to Rodger Curren, Ph.D., president and cofounder of the Institute for *In Vitro* Sciences, based in Gaithersburg, Md. The award honors those who have made outstanding contributions toward advancing the Three Rs—namely, the replacement, reduction, and refinement of animal research. The award, which carries a \$5,000 prize, was given at the Sixth World Congress on Alternatives and Animal Use in the

Life Sciences held in Tokyo. Dr. Curren has had a major influence on the development of nonanimal methods for toxicity testing, including the development of customized, alternatives-based testing for industries; the formulation of the prevalidation concept; educational outreach to regulatory and animal protection communities; and advocacy at key policy-setting meetings, as well as participation in the development and validation of new test methods.

Eureka Prize for Replacement

The 2007 Voiceless Eureka Prize for a breakthrough research method that reduces animal use was awarded to Maria Kavallaris, Ph.D., and Sela Pouha, Ph.D., of the Children's Cancer Institute Australia for Medical Research and Nicole Verrills, Ph.D., of the University

of Newcastle for developing a nonanimal method to identify mechanisms of drug resistance in cancer cells. This approach, which uses advanced molecular biology and cell culture techniques, will allow for a reduction of animals used in oncology research.

From the Technical Literature

Housing Refinements and Animal Preferences

Sherwin (September 2007, "Validating refinements to laboratory housing: Asking the animals," NRC3Rs e-newsletter No. 12) reports on the use of animal behavior studies to assess the necessity and validity of refinements in laboratory housing. Analyses of activities performed by animals (ethograms) and length of time spent performing activities (time budgets) can provide information on the need for housing refinements to improve welfare.

Observations of behaviors in a natural environment can also provide information on which behaviors are not exhibited in laboratory housing and should be cultivated. Other assessment methods include allowing animals to choose between two environments (choice tests), having animals choose between two or more environments that differ in only one feature (preference tests), and placing "costs" on access to refinements (consumer demand

IACUC Administrator Certification

Public Responsibility in Medicine and Research (PRIM&R) offers a Certified Professional IACUC Administrator (CPIA) program. PRIM&R has collaborated with the Professional Testing Corporation to develop standards based on a body of knowledge about the ethics and administration of animal care and use programs. For more information, go to www.primr.org/certification.aspx?id=230.

New OLAW Director of Assurances

Eileen Morgan has been promoted from senior assurance officer to director of the Division of Assurances of the National Institutes of Health Office of Laboratory Animal Welfare. The division handles assurances with facilities conducting research sponsored by the Public Health Service (PHS) and implements procedures to ensure that these facilities adhere to PHS policy.

Effects of Outdoor Housing on Primates

Fontenot et al. (2006, *Journal of the American Association for Laboratory Animal Science*, 45(5), 35–43) examined the effects of outdoor housing on self-injurious and stereotypic behavior in 13 male macaques with a history of self-wounding who were previously single-housed indoors. Five animals were single-housed outdoors as the control group; the others were placed into social groups in outdoor corncribs for six weeks. All were observed daily

for wounds and behavior. At the end of the six weeks, single-housed animals were moved indoors because of cold weather, but group-housed animals were observed outside for an additional six weeks to evaluate long-term effects of social housing.

The macaques living in social groups exhibited increased locomotion and scanning and decreased pacing compared to single-housed animals. Rates of self-biting, duration and

studies). The author provides examples of these methods, including motivation for additional space; cage color preference; extended locomotion; type of flooring, substrate, and nesting material; shelters; social contact; lighting; and novelty. The author notes that simultaneous physiological indicators would provide additional validation of the effects of housing refinements.

occurrence of self-directed stereotypies, yawning, and scratching decreased significantly when both group- and single-housed animals were kept outdoors, suggesting that outdoor housing significantly reduces self-biting and self-directed stereotypic behavior in rhesus macaques with a history of self-injurious behavior regardless of whether the animals live singly or in groups.

U.S. Animal Use Statistics for 2006

In its 2006 *Animal Welfare Enforcement Report*, the U.S. Department of Agriculture (USDA) summarizes the numbers and types of animals used in research and the corresponding pain and distress categories; the number of registered research facilities and inspections performed at these facilities; and the numbers of registered animal dealers, exhibitors, handlers, and carriers. The total number of USDA-regulated animals (warm-blooded animals other than purpose-bred mice, rats, and birds) used in research decreased by 14%, from 1,177,566 in 2005 to 1,012,713 in 2006.

Rabbits, guinea pigs, and hamsters were the regulated species most often used in research, followed by “other covered animals,” including farm animals, dogs, nonhuman primates, and cats. The use of all species decreased, except for the use of nonhuman primates, which increased by 8%. Similar to 2005, animals used in research that caused unrelieved pain or distress (Column E experiments) accounted for 7% of all animals; research that caused pain or distress but involved the use of anesthetics, analgesics, or tranquilizing drugs (Column D experiments) accounted for 37%; and research that was classified as not causing pain or distress (Column C experiments) accounted for 56% of all animals used. To view the 2005 and 2006 reports, visit www.aphis.usda.gov/animal_welfare/publications_and_reports.shtml.

The large drop in the number of animals used in 2006 may reflect a trend toward increased use of transgenic mice (who are not counted in the statistics) and is not necessarily a sign that biomedical research is using fewer animals

(regulated or not). In addition, The Humane Society of the United States (HSUS) has uncovered examples of apparent under-reporting of animals used in Column E experiments; consequently, the 7% of animals reported in Column E studies for 2006 is questionable. We believe that this underreporting is an indication that at least some laboratories are not properly assessing and addressing animal pain and distress.

British Animal Use Statistics for 2006

The British Home Office recently released *Statistics of Scientific Procedures on Living Animals: Great Britain 2006*. The total number of animals used during 2006 was 2,946,624, a 5% increase since 2005.

Similar to 2005, approximately 62% of procedures were performed with no anesthesia, 19% with general anesthesia with recovery, 10% with local anesthesia, 7% with general anesthesia at the end of the procedure without recovery, and 2% with general anesthesia throughout without recovery.

Mice, rats, and “other rodents” were used in approximately 82% of procedures, followed by fish (9%), birds (4%), and guinea pigs (1%), as well as a variety of other mammals, amphibians, and reptiles. The number of procedures using nonhuman primates decreased 10% since 2005. Breeding procedures accounted for approximately 37% of animals used, followed by fundamental biological research (32%), applied research (26%), “protection of man, animals, and the environment” (4%), and direct diagnosis (0.7%). Similar to 2005, genetically modified animals were used in 34% of procedures. The full text of the report is at www.homeoffice.gov.uk/rds/pdfs07/spanimals06.pdf.

Three Rs Survey

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“highlights the importance of refining animal use to reduce pain and suffering”

and that “if the case for animal use is still strong ... then extra focus should be placed on how the animals are used ... and how suffering can be minimized.” The survey will help determine whether

UPCOMING CONFERENCES

Alternatives & 3Rs Workshop

Hosted by the University of California at Los Angeles and the Johns Hopkins Center for Alternatives to Animal Testing

Jan. 24–25, 2008

Los Angeles, Calif.

arc@opr.ucla.edu

ATOP V: Assessment and Treatment of Animal Pain and Distress—Humane Endpoints Where Science and Welfare Meet

Hosted by The AWEN Group

Feb. 8, 2008

Waltham, Mass.

www.theawengroup.com

2008 Annual Institutional Animal Care and Use Committee (IACUC) Conference

Hosted by Public Responsibility in Medicine and Research (PRIM&R)

March 25–28, 2008

Atlanta, Ga.

www.primr.org

IACUC 101

Hosted by Public Responsibility in Medicine and Research (PRIM&R)

March 26, 2008

Atlanta, Ga.

www.primr.org/Conferences.aspx?id=2919

IACUC 101

Hosted by the University of Texas Medical Branch at Galveston

April 15, 2008

Galveston, Texas

<http://grants.nih.gov/grants/olaw/iacuc101s.htm>

more work in developing alternatives is needed in particular research areas. The survey report will be published in spring 2008. For more information, go to www.nc3rs.org.uk/news.asp?id=693.

Pain & Distress Report

Wayne Pacelle, The HSUS President & CEO • Andrew N. Rowan, Ph.D., Executive Vice President of Operations • Martin L. Stephens, Ph.D., Vice President, Animal Research Issues • Kathleen Conlee, Director, Program Management, ARI • Leah Gomez, Project Manager, ARI • Loree Talley, Alternatives Website Coordinator, ARI • Jennifer Ball, Research Assistant, ARI • Michelle Jacmenovic, Outreach Coordinator, ARI • Dawn McPherson, Research Assistant, ARI • Paula Jaworski, Creative Director • Michael Blankenship, Managing Editor • Julie Falconer, Editor • Jennifer Boyer, Angela Moxley, Associate Editors • Elizabeth McNulty, Associate Art Director.

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Special Feature

Sixth World Congress on Alternatives and Animal Use in the Life Sciences

The Sixth World Congress on Alternatives and Animal Use in the Life Sciences, held Aug. 21–25 in Tokyo, addressed recent progress and future prospects for the Three Rs of animal use in laboratories. Participants from around the world shared information through plenaries, workshops, point-counterpoint sessions, posters, and exhibits. Many of the 900 attendees were from Asia, with satellite meetings held in both Seoul and Beijing to promote the concept of alternatives in South Korea and China.

The meeting showcased recent progress in replacing animals in safety testing and risk assessment, including

activities of the newly established Japanese Center for the Validation of Alternative Methods; a major consumer product company's plans to establish a nonanimal testing approach to risk assessment; and the exciting prospects for alternatives in light of the recently published report by the National Research Council calling for a paradigm shift away from animal-based toxicity testing.

For more information on the Sixth World Congress, visit www.wc6.jp. Published proceedings will be available in 2008. The Seventh World Congress will be held in Rome, Italy, in 2009.

Helpful Websites

The HSUS and the Procter & Gamble Company recently launched *AltTox.org* to support the advancement of nonanimal methods in toxicity testing through an online exchange of technical and policy information on *in vitro* and *in silico* methods. The website features three components: "Forums" that allow user discussion and commentary and are overseen by expert moderators, a "Toxicity Testing Resource Center" with concise summaries on topics linked to relevant forums, and the "Way Forward" with expert commentaries on advancing nonanimal methods in critical areas of *in vitro* and *in silico* toxicology.

The European Centre for the Validation of Alternative Methods database on alternatives to animal experimentation (DB-ALM) provides information on advanced and alternative techniques for toxicology assessments, including method-summary descriptions and protocols, evaluation studies, details on formal validation studies, and individual test results. To access the database, go to <http://ecvam-dbalm.jrc.cec.eu.int>.

Recent Publications

Clarence, W. M., Scott, J. P., Dorris, M. C., and Paré, M. (2006). Use of enclosures with functional vertical space by captive rhesus monkeys (*Macaca mulatta*) involved in biomedical research. *Journal of the American Association for Laboratory Animal Science*, 45(5): 31–34.

Wright-Williams, S. L., Courade, J. P., Richardson, C. A., Roughan, J. V., and Flecknell, P. A. (2007). Effects of vasectomy surgery and meloxicam treatment on faecal corticosterone levels and behaviour in two strains of laboratory mouse. *Pain*, 130(1–2): 108–118.

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@humanesociety.org for a free subscription to the electronic version of the newsletter; copies are also available online at humanesociety.org/pain_distress_report.

Please share this report with your colleagues and IACUC members.



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2100 L Street, NW Washington, DC 20037
humanesociety.org

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