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Pain & Distress Report is available online at www.hsus.org/pain_distress_report.



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

Policies & Perspectives

AUDIT OF ANIMAL WELFARE ACT ENFORCEMENT RAISES SERIOUS CONCERNS

An internal audit of the U.S. Department of Agriculture's Animal and Plant Health Inspection Service's (USDA APHIS) enforcement of the Animal Welfare Act (AWA) has revealed a number of serious concerns related to oversight of research facilities and has prompted the USDA to recommend several corrective actions. For example, APHIS has been lax in enforcing sanctions of AWA violators. Fines, if assessed, were automatically discounted up to 75% if the facilities agreed to settle out of court. The Animal Care regional offices have been inconsistent in penalizing AWA violators—the Eastern Region failed to take action against 30% of violators. The report also expresses concern that Institutional Animal Care and Use Committees are not effectively monitoring mandated activities such as reviewing painful and distressful procedures and searching for alternatives. Some APHIS inspectors did not verify the number of animals used in research, yet 13 out of 16 facilities misreported the number of animals used in research, with most facilities underreporting the number.

Based on the audit, the USDA has made recommendations to clarify enforcement policy, review cases of "declined" enforcement, eliminate the

automatic 75% fine "discount," and increase fines, along with calculating fines according to numbers of animals affected. The USDA also plans to revise the *Research Facility Inspection Guide* to require veterinary medical officers to verify that reported numbers of animals used are accurate.

Noteworthy

CHIMPANZEE BREEDING MORATORIUM EXTENDED

The National Center for Research Resources (NCRR) has extended the chimpanzee breeding moratorium (officially in effect since 1995) until December 2007. NCRR houses the National Institutes of Health Chimpanzee Management Program, which "supports long-term, cost-effective housing and maintenance at NCRR-supported facilities for chimpanzees." The decision to extend the moratorium was based on recommendations by the Chimpanzee Management Plan Working Group. For more information, go to www.ncrr.nih.gov/compmed/cm_chimp.asp.

DUTCH SCIENTIST WINS RUSSELL AND BURCH AWARD

The HSUS recently bestowed its Russell and Burch Award on Bert van Zutphen, Ph.D., professor emeritus of Utrecht University in the Netherlands,

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Noteworthy

for his outstanding contributions toward advancing Russell and Burch's concept of the Three Rs—namely, the replacement, reduction, and refinement of animal use in research. The award, which carries a prize of \$5,000, was given in Berlin at the Fifth World Congress on Alternatives and Animal Use in the Life Sciences. Dr. van Zutphen cofounded the World Congress on Alternatives and Animal Use in the Life Sciences in 1993 and also cofounded the Netherlands Centre for Alternatives. In the mid-1980s, he established laboratory animal science courses that emphasized the Three Rs for students, young scientists, and veterinarians. These courses were later mandated by law and serve as a model for the education of scientists.

DECLARATION SIGNED TO SUPPORT ANIMAL RESEARCH

Following the closing of a guinea pig farm in the United Kingdom as a result of extensive activist activities, more than 700 scientists signed a declaration drafted by the Research Defense Society in support of the use of animals in biomedical research. A similar declaration was signed 15 years ago, but the recent version goes further to incorporate concepts such as the adoption of alternatives (including replacement, reduction, and refinement), improved animal housing, increased researcher openness and dialogue with the public, and justification of animal use during the ethical review process. The inclusion of these research community obligations may have been prompted by increasing public concern about the use of animals in research, but some people question whether the newly adopted concepts are being implemented to the extent espoused.

The HSUS does not engage in or support the use of violence or intimidation in the name of protecting animals. To see our full statement on nonviolence, go to www.hsus.org/about_us/about_hsus_programs_and_services/hsus_statement_on_nonviolence.html.

Resources & Services

REFINEMENT AWARDS AVAILABLE

The Animal Welfare Institute is accepting proposals for up to eight \$6,000 grant awards to North American residents whose studies are aimed at refinement of housing and handling conditions of animals used in research or education. Studies that inflict avoidable stress or involve the killing of animals during or after the data collection process will not be considered. Applicants should explain in letter form of not more than three pages how the study is likely to enhance animal welfare and “outline in detail the methodology that will be applied to achieve this objective.” Proposals should be sent to Viktor Reinhardt at viktor@snowcrest.net. For more information, go to www.awionline.org/lab_animals/proposal.htm.

NTP “ROADMAP” EMPHASIZES ALTERNATIVES

According to a new “Roadmap for the Future,” the U.S. National Toxicology Program (NTP)—an interagency program led by the National Institute of Environmental Health Sciences—is calling for full incorporation of the Three Rs (replacement, reduction, and refinement) in experimental design, including minimization and elimination of pain and distress, as well as training in humane science for researchers who work with animals. A Humane Society of the United States (HSUS) representative participated in an NTP retreat that helped shape the Roadmap. The long-term goal of the Roadmap is to evaluate toxicological effects based on mechanistic tests as opposed to the current one-animal-test-per-endpoint. To read the full report, go to <http://ntp.niehs.nih.gov/index.cfm?objectid=B4DA3C38-F1F6-975E-7168BAC6475F1E5B> and click on “Roadmap to Achieve the NTP Vision.”

Upcoming Conferences

3rd Annual Assessment and Treatment of Pain (ATOP) and Distress in Animals Conference

- ▶ Coordinated by The AWEN Group
- ▶ February 9, 2006
- ▶ Fort Lauderdale, Florida
- ▶ For more information, go to www.theawengroup.com/ATOPIII.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>

IACUC 101 Workshop

- ▶ Coordinated by the Office of Laboratory Animal Welfare (OLAW) and the University of Texas at Austin
- ▶ May 8, 2006
- ▶ Austin, Texas
- ▶ For more information, go to <http://grants.nih.gov/grants/olaw/workshop.htm>

From the Technical Literature

BEHAVIORAL STUDIES OF CHRONIC PAIN IN ANIMALS

Mogil and Cramer (2004, *Pain*, 112: 12–15) discuss the need for improved dependent measures in animal pain models and point out that although pain models are advancing, measures have remained relatively unchanged. Researchers have heavily relied upon hypersensitivity, changes in response to evoked mechanical/tactile stimuli (such as von Frey fibers), or evoked thermal stimuli (such as the paw-withdrawal test) as pain measures. A number of drugs have failed in human clinical trials despite repeatedly showing efficacy against hypersensitivity states

in nonhumans. Measurement of spontaneous behavior in animals has been largely missing, perhaps stemming from lack of agreement on what behaviors should be measured. The authors single out behaviors that are most frequently exhibited, reflect sensitive to subtle changes, and are prevalent in the widest number of pain models. Pain behaviors must also be distinguished from those resulting from sickness, non-pain-induced distress, and fear. Some measures proposed by the authors include analgesic self-administration, attention deficits, food intake, gait disturbance, grooming, paw lifting, and vocalization.

Although this paper focused specifically on the use of animals for pain research, the information generated from pain research on animals can also be applied to improve the welfare of animals used in painful research as well as the quality of science produced from such research.

completing surgery. Body weights were also measured daily. Analysis allowed selection of 17 behaviors that consistently defined main group differences; these included fall, stagger, partial back-arch, writhe, twitch, belly press, teeth grind, hop, high rear, lick wound, flinch, stretch, and paw shake (frequency parameters), and crouch-curl, attentive, crouch-hunch, and eyes closed (duration parameters). Since no single behavior could be used, a composite score was used to compare the groups. Results suggest that pain lasted 270 to 390 minutes following surgery and was alleviated throughout its duration by subcutaneously administered carprofen or buprenorphine as well as orally administered buprenorphine. Major signs of pain were prominent only during the first 270 minutes in the saline group. Effects of all analgesics persisted beyond 390 minutes. Although the behavior of rats given saline differed significantly from those given analgesics, they did not show significantly greater weight loss than analgesic groups, perhaps because they were juveniles and growth may have masked postoperative effects. Overall, these assessments can be completed rapidly and can be useful when examining pain on a case-by-case basis, since various factors can influence pain, such as the success of surgery.

Recent Publications

Drobac, E., Durand, E., Laudenbach, V., Mantz, J., & Gallego, J. (2004). A simple method for short-term controlled analgesia in newborn mice. *Physiology & Behavior*, 82: 279–283.

Richebé, P., Rivat, C., Laulin, J., Maurette, P., & Simonnet, G. (2005). Ketamine improves the management of exaggerated postoperative pain observed in perioperative fentanyl-treated rats. *Anesthesiology*, 102: 421–428.

Whitehead, A., & Stallard, N. (2004). Opportunities for reduction in acute toxicity testing via improved design. *Alternatives to Laboratory Animals*, 32: 73–80.

BEHAVIOR-BASED PAIN ASSESSMENT IN RATS FOLLOWING LAPAROTOMY

Roughan and Flecknell (2004, *Behavioural Pharmacology*, 15: 461–472) examined a behavior-based pain scoring system in order to assess the presence and duration of pain following laparotomy. Thirty Fischer 344 rats were given either saline (0.2 ml/100 g subcutaneously), carprofen (5 mg/kg subcutaneously), or buprenorphine (0.05 mg/kg subcutaneously or 0.4 mg/kg by gavage) one hour prior to laparotomy. The surgery, performed by the same surgeon on each rat, was part of a cancer research project that involved injection of tumor cell suspension into the bladder wall. The rats were housed singly for behavioral observation by camera for 390 minutes in 10-minute periods beginning 30 minutes after

Statistics on Animal Use Pain & Distress

2004 U.S. ANIMAL USE STATISTICS

The U.S. Department of Agriculture (USDA) 2004 Animal Welfare Report summarizes the numbers and types of animals used in research and the corresponding pain and distress categories, as well as the numbers

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**Pain
&
Distress
Report**

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Statistics on Animal Use Pain & Distress

of registered research facilities and animal dealers and the number of inspections performed at these regulated facilities. The total number of USDA-regulated animals (warm-blooded animals other than purpose-bred mice, rats, and birds) used in research decreased slightly from 1,188,469 in 2003 to 1,101,958 in 2004. Rabbits, guinea pigs, and hamsters were the species most often used in research, followed by dogs, pigs, primates, cats, sheep, and others. Animals used in research involving unrelieved pain or distress ("Column E" experiments) accounted for 8% of all animals, similar to 2003. Research that caused pain or distress but involved the use of anesthetics, analgesics, or tranquilizing drugs ("Column D" experiments) accounted for 36% of all animals. Research that was not classified as painful or distressful ("Column C" experiments) accounted for 56% of all animals used. To view the 2003 and 2004 Animal Welfare Reports, go to www.aphis.usda.gov/ac/pubs/publications.html.

The HSUS has found that pain and distress in U.S. research are often

underreported. We also believe that the current pain and distress reporting system is misleading and should be changed to reflect levels of pain and distress actually experienced by the animals, similar to the categorization systems used by Switzerland, Canada, New Zealand, and other countries. Furthermore, although the number of USDA-regulated species has declined, it is likely that the total number of animals used has increased due to the increasing use of mice and rats.

MORE THAN 10 MILLION ANIMALS USED IN EUROPE IN 2002

Recently released animal research use statistics reveal that a total of 10,731,020 animals were used in the European Union in 2002, a 9% increase from 1999 (when the last statistics were released). Mice, rats, and fish were the most commonly used species. Use of reptiles; horses, donkeys, and crossbreds combined; prosimians; amphibians; and fish each increased by 50% or more since 1999. Fundamental biology studies accounted for 35% of animal use, followed by research and development

of human medicine and dentistry products and veterinary products (28%), production and quality control of human medicine and dentistry products (14%), toxicology (10%), other research (6%), education and training (3%), production and quality control of veterinary products (2%), and diagnosis of disease procedures (2%). Greece, Finland, Austria, Germany, and Luxembourg had the greatest increases in numbers of animals used. Similar to 1999, France used the greatest number of animals in 2002 (2.2 million), followed by Germany and the United Kingdom.

Helpful Websites

NORINA (Norwegian Inventory of Audiovisuals) has updated its website—<http://oslovet.veths.no>—which contains a database of more than 3,500 alternatives with links to suppliers, a database of laboratory animal science textbooks with links to bookstores, and information on legislation, education, and ethics.

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.

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