# The HSUS's Pain and Distress Initiative: Overview and Update

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**Summary** — The Humane Society of the United States (HSUS) publicly launched its Pain and Distress Initiative in 2000, to encourage greater attention to the prevention and alleviation of pain and distress in research animals. The initiative's ultimate goal is the phasing out of all significant pain and distress in animal research by 2020. There have been several developments to date. A survey conducted for The HSUS revealed that Americans strongly oppose the use of animals in experiments that cause them to suffer. The HSUS has begun producing a newsletter, *The Pain & Distress Report*, distributed periodically to over 2000 Institutional Animal Care and Use Committees, scientists and regulators. In 2000, the US Department of Agriculture issued a proposal to upgrade the regulation and reporting of pain and distress. We have challenged the leading research institutions over their under-reporting of unrelieved pain and distress in animals. We have written a comprehensive critique of $CO_2$ euthanasia, arguing that it causes avoidable pain and distress in animals. The National Institutes of Health has issued new guidance on $CO_2$ euthanasia. These developments lay the groundwork for a sustained effort to eliminate animal suffering in research.

**Key words**: *analgesia, animal care and use committees, animal welfare, carbon dioxide, euthanasia, institutional animal use alternatives, pain, psychological, stress.*

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## Introduction

In 2000, The Humane Society of the United States (HSUS) publicly launched its Pain and Distress Initiative. The initiative's short-term goal is to focus greater scientific attention on the recognition, assessment and alleviation of pain and distress in research animals. The long-term goal is phase out research animal pain and distress by the year 2020, with the help of the scientific, regulatory and research funding communities. While ending research animal suffering within 20 years is an ambitious goal, it is arguably within the ingenuity and skills of those who use and care for laboratory animals and the scope and responsibility of the scientific community. More importantly, while not widely recognised outside the research community, most scientists and laboratory personnel support efforts to minimise pain and distress in laboratory animals.

Pro-active efforts to eliminate research animal suffering are also consistent with the public's concerns regarding animal research. For example, a poll commissioned by the *New Scientist* (1) found that the British public's support for research on mice or monkeys declines 16% to 35% (depending on the species and field of research) when the animals are subjected to pain, illness or surgery.

In Europe, the USA and elsewhere, this public concern has led to the passage of laws and regulations that specifically call for efforts to minimise laboratory animal pain and distress and, in many countries, to report statistics on such pain and distress to national authorities.

In the USA, animal research is governed by the *Animal Welfare Act* (AWA), which is enforced by the US Department of Agriculture (USDA) and by the Public Health Service *Policy on the Humane Care and Use of Laboratory Animals*, which is enforced by the National Institutes of Health (NIH). Both the AWA and the *Policy* mandate the establishment of Institutional Animal Care and Use Committees (IACUCs), which are specifically charged with reducing the likely pain and distress that animals may experience when used in research. The USDA also mandates the research facilities submit an annual report that lists the numbers of animals of all regulated species used, according to official pain and distress categories (see below). The NIH periodically issues policies concerning specific animal-based procedures, such as monoclonal antibody production (2).

At the 3rd World Congress on Animal Use and Alternatives in the Life Sciences, held in Bologna in 1999 (3), The HSUS provided a brief introduction to the Pain and Distress Initiative and our plans for the future. In the present paper, we provide an update on our progress since 1999. We begin, however, by reviewing the components of the initiative.

## Components of the Pain and Distress Initiative

The Pain and Distress Initiative has four main components (3). First, The HSUS is seeking to work with the research community to make the reduction and ultimate elimination of animal pain and distress a higher priority. We recognise that scientists themselves will be the ones who will ultimately develop the techniques that will make the 2020 goal possible. Much of our outreach effort has been directed at IACUCs, which have major oversight responsibilities for ensuring that investigators are minimising pain and distress in their protocols.

The second component of the initiative is to encourage the US agencies that oversee animal research to implement new or revised policies and guidelines that foster the 2020 goal. For example, the USDA's pain and distress classification system has been widely criticised for failing to adequately characterise levels of pain and distress. Moreover, the classification system is subject to varying interpretations, leading to inconsistencies and inaccuracies in the reporting of pain and distress statistics.

Third, The HSUS is encouraging private and government sources to fund carefully designed research on pain and distress. Many gaps exist in our ability to recognise, measure, alleviate or avoid pain and distress in research animals. While The HSUS would not encourage research that harms animals for the sake of studying pain and distress, we would like to see questions about pain and distress "piggy backed" onto already planned and approved experiments.

Fourth, The HSUS is planning to coordinate a group of experts to produce a technical report on what is currently known about pain and distress in laboratory animals. The report will address the definitions of pain and distress; the recognition, assessment and alleviation of pain and distress; current techniques that cause significant pain and distress and how these can be replaced by more humane methods; the capacity for experiencing pain and distress in the various species used in the laboratory; and other topics.

## Update on the Pain and Distress Initiative

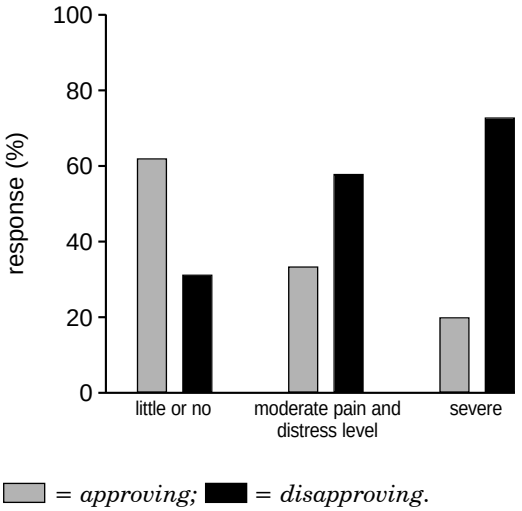
### Public opinion

Many opinion surveys have shed light on the influence of animal suffering on the public's view of animal research. However, no survey has tackled this issue directly for the American public. Consequently, The HSUS commissioned such a survey in 2001. The results indicate a dramatic impact of the level of animal suffering on the public's approval of animal research (Figure 1). Approval of animal research drops from 62% to 21% when pain and distress increases from little or none to severe. Of course, public opinion on animal research is influenced by a host of variables, including the species of animal used and the likely medical benefit of the research, but the present results provide powerful support for scientific and public policy changes aimed at alleviating research animal suffering.

### Outreach to the scientific community

As an outside organisation seeking to influence the scientific community, one of The HSUS's first tasks was to publicise the Pain and Distress Initiative to that community. Accordingly, HSUS staff have given several presentations on the initiative at scientific conferences, including those organised by the Institute for Laboratory Animal Research (1998), Department of Defense (1999), Center for Alternatives to Animal Testing (1999), Scientists Center for Animal Welfare (2000), Canadian Centre for Alternatives to Animal Research (2000), the International Council for Laboratory Animal Science and the Canadian Council on Animal Care (2001), and Public Responsibility in Medicine and Research (2002). The public launch of the Pain and Distress Initiative was in April of 2000, at a press conference at the National Press Club, Washington, DC, USA.

**Figure 1: Responses of the American public to the question: *"How strongly do you approve or disapprove of the use of animals like mammals and birds in research and testing when the animals experience severe, moderate, or little or no pain or distress?"***



Similarly, The HSUS has publicised our views on pain and distress and the initiative to the scientific community in scientific publications, including the *Massachusetts Society for Medical Research Newsletter* (1999), *Lab Animal* (2000 and 2002), *Contemporary Topics* (2000), *Chronicle of Higher Education* (2000), *Psychologists for the Ethical Treatment of Animals Newsletter* (2002) and *Nature* (2002), as well as in the proceedings of many of the conferences mentioned above.

In the fall of 2000, The HSUS began publishing the *Pain & Distress Report*, a four-page newsletter issued approximately four times per year. It provides up-to-date information on relevant new policies, resources, literature, national statistics, public opinion and websites. The HSUS sends hard copies to all the IACUCs in the United States, and electronic copies are available upon request. The *Reports* are also available online at www.hsus.org/ace/11401.

## Regulatory reform

One of The HSUS's themes in its outreach to the scientific community is that distress receives far less attention than does pain. Not all distress is pain-induced (consider, for example, fear), so ignoring distress can result in unalleviated suffering. This is especially problematic because, with the increased attention to pain and pain-relieving drugs, distress arguably now accounts for more research animal suffering than does pain. In the USA, this situation is complicated by the lack of a USDA regulatory definition of "distress". Consequently, the USDA would be hard pressed to take regulatory action against a facility for insufficient attention to distress.

In July, 2000, shortly after the HSUS launched the Pain and Distress Initiative, the USDA proposed to adopt a regulatory definition of distress. The agency called for comments on this proposed action and recommendations for a suitable definition of "distress". The HSUS and many other organisations submitted comments and, two years later, we continue to await the USDA's next steps. To keep the issue alive publicly, The HSUS analysed all the submitted comments to the USDA, picked out the most regressive, and issued a tongue-in-cheek list of the "Top Ten" comments (see www.hsus.org/ace/14797).

In its same July 2000, proposal, the USDA also announced that it was considering revising its pain and distress classification system. The system is widely considered to be out-of-date and inadequate (4, 5). It consists of three categories that correspond to columns in the USDA's annual *Animal Welfare Enforcement Report*. Briefly, "column C" corresponds to no pain or distress (i.e. a benign experiment), "column D", to pain or distress relieved by drugs, and "column E", to pain or distress unrelieved by drugs. Unfortunately, these categories do not adequately address the *levels* of pain and distress experienced; they boil down to a yes/no dichotomy of whether pain and/or distress were experienced.

A straightforward but informative system would assess the levels of pain and distress as minor, moderate or severe, such as the systems in Canada, The Netherlands and Switzerland, and the more fine-grained system in New Zealand. The HSUS supports a proposal to adopt a similar system in the USA. The proposal was developed in the mid-1990s by a working group consisting of representatives of academia and animal protection, including The HSUS. It was originally presented to the USDA several years ago and has since been advocated by The HSUS as part of the Pain and Distress Initiative. It is currently under review as the USDA considers modifications to its current scheme.

## Accuracy in reporting under the current USDA Pain and Distress Classification System

The HSUS believes that, as long as the current pain and distress categories are in place, research facilities should make good-faith efforts to accurately and completely report their annual statistics on animal usage, notwithstanding the shortcomings of the current system (see above). The HSUS has conducted painstaking analyses of facility reports submitted to the USDA, available under the US *Freedom of Information Act*. We focused primarily on column E, or unrelieved pain and distress, given the uncertainties as to whether animals reported in column D (pain- and distress-relieving drugs given) experienced any residual pain and distress. Given resource constraints, we focused further on the "Top 50" US research institutions, based on the amount of funding received from the NIH during 1998 (the most recent year for which funding data were available when our analysis began in 1999).

The Top 50 institutions report less than 1% of regulated animals in column E during 1996–1998 (150,000 or so animals; N.B. regulated animals exclude lab-bred mice and rats, as well as all non-mammals). There are several lines of evidence that collectively suggest that the Top Ten facilities chronically under-report animals in column E. First, the comparable figures for all regulated facilities nationwide ranged from 8% to 12% over these years. Second, while the reporting systems in other countries differ from that in the USA, their statistics suggest that the figures reported by the Top 50 US institutions are not credible. Canada, Switzerland and New Zealand reported that 12 to 38% of research animals experienced moderate to severe distress for the years 1996–1998, far greater

than the 1% or less reported in column E by the Top 50 US facilities. Finally, the UK categorised 57% of their project licences in the moderate and substantial severity bands in terms of pain and distress for the year 2000 (the first year for which severity bands were reported), which further casts doubt on the low figures reported by the Top 50 US institutions.

The apparent under-reporting of animals used in column E research procedures suggests a failure on the part of research facilities to fulfil their regulatory responsibilities, despite public concern about animal suffering in research and the AWA mandate to minimise animal pain and distress. It may further suggest a lack of attention to recognising, measuring, and minimising pain and distress in research animals. In January 2002, The HSUS sent a letter to each of the Top 50 institutions, bringing this situation to their attention and calling for greater accuracy in reporting animal pain and distress.

The HSUS has given special attention to one of the Top 50 institutions, the University of Wisconsin at Madison (UW-M). During the years in question (1996–1998), UW-M reported using nearly 7000 monkeys and over 350,000 other regulated animals in experiments, and yet none was reported to have experienced any unrelieved pain and/or distress. However, we uncovered several apparent examples of column E projects underway at UW-M during this period. We wrote repeatedly to the UW-M between July 2000 and February 2001; in May 2001 (ten months after The HSUS's first letter), the University sent an uninformative response. As a result, we sent another letter, providing a final opportunity to respond to our concerns before bringing the issue to a public forum. Receiving no response, we took out two advertisements in the campus newspaper, one in August 2001, and the other in October 2002, bringing UW-M's misreporting to the attention of the wider University community.

## Analyses of $CO_2$ euthanasia

One approach envisioned under the Pain and Distress Initiative is to conduct analyses of common animal-based procedures, particularly where there was evidence of unnecessary pain and distress. Such case studies might result in replacing, refining or reducing such practices. We began this approach in 2001, when we conducted an extensive review of the literature concerning the use of $CO_2$ as a euthanasia agent (see www.hsus.org/ace/11427), a widespread practice for small laboratory animals. Our analysis, summarised elsewhere (6), raised several concerns about the routine use of $CO_2$ as a euthanasia agent for small mammals. For example, adverse reactions, such as seizure, nose haemorrhage, rearing, defecation and excessive salivation have been noted in rodents and other species at $CO_2$ concentrations of greater than 50%.

Humans experience pain when the $CO_2$ concentration is 50% and higher (7). US Government Principle #4 and USDA Policy #11 both state that procedures causing pain and distress in humans should be assumed to cause pain and distress in animals, in the absence of "evidence to the contrary" (8). In the case of $CO_2$, the animal data are equivocal but the human data are clear. Therefore, The HSUS argues that the continued use of $CO_2$ as a euthanasia agent runs counter to Government Principle #4 and USDA Policy 11.

The evidence of potential pain and distress associated with the use of $CO_2$ as a sole agent for euthanasia indicates that its routine use for this purpose should, at the very least, be questioned. Consequently, refinements to the use of $CO_2$ as a sole agent for euthanasia, such as the use of an inhalation anaesthetic prior to exposing animals to $CO_2$, should be considered.

Since The HSUS publicised its concerns about $CO_2$ use, there has been an increase in attention to the issue. Most notably, the NIH's Office of Laboratory Animal Welfare (OLAW) issued an official clarification pertaining to the use of $CO_2$ as a euthanasia agent for small laboratory animals (see: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-062.html). The notice indicates that high concentrations of $CO_2$ could be distressful to animals; therefore, "pre-filling the chamber is recommended only under circumstances in which such use has not been shown to cause distress" (9). The document emphasises five additional points:

1. institutions should keep abreast of current peer-reviewed literature concerning $CO_2$ use and appropriately evaluate their $CO_2$ policies;

2. death must be verified following euthanasia of animals;

3. institutions must ensure that personnel conducting $CO_2$ euthanasia are properly trained and qualified;

4. chambers must not be overcrowded; and

5. compressed $CO_2$ in cylinders is the only source of $CO_2$ for euthanasia recommended by the American Veterinary Medical Association (AVMA).

## Funding for pain and distress research

In May 2002, The HSUS submitted appropriations testimony to Congress, specifically requesting $2.5 million for the National Center for Research

Resources to sponsor research and development on identifying and alleviating pain and distress in laboratory animals. The HSUS further requested that Congress require the NIH to "piggy-back" these investigations onto on-going, approved research that already causes pain and distress. Given the volume of existing research that involves pain and/or distress, no additional pain and distress should be inflicted solely for the purpose of this research.

The NIH has seen an explosive increase in funding over the past 25 years. For fiscal year 2002, NIH ranked second only to the Department of Defense in research and development (R&D) funding ($22.3 billion vs. $49.1 billion), and was appropriated ten times more money for R&D than was USDA ($2 billion). The NIH's budget has been projected to increase by approximately $5 billion for fiscal year 2003. Approximately half of the NIH's current budget is estimated to be devoted to some aspect of animal research. In this light, The HSUS believes that ear-marking at least some funds for the minimisation of pain and distress is warranted.

### Development of a technical report

The HSUS is still in the planning stages of developing a technical report on pain and distress issues.

## Conclusion

Targeting the suffering of research animals, rather than their use *per se*, is more consistent with public opinion and national policy governing animal research. The US regulatory community has shown some level of responsiveness to the issues raised by the Pain and Distress Initiative, with the USDA proposing to define "distress" and revamp its pain and distress categories and the NIH issuing guidance on $CO_2$ euthanasia. To date, however, the research community itself has not openly embraced the initiative, but there has nonetheless been increased attention to pain and distress issues. The initiative has taken its first steps toward its goal of eliminating all significant animal suffering in research.

## Acknowledgements

We thank Gina Alvino for her help in preparing this manuscript.

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