



18 March 2008

Michael Budkie AHT
Executive Director
Stop Animal Exploitation Now
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Dear Mr Budkie,

Official Reporting of Pain and Distress Experienced by Laboratory Animals

As you are aware, I am a practicing veterinarian and hold licenses to practice within both the US and the UK. I hold a post-graduate Certificate in Animal Welfare Science and have a special interest in laboratory animal use. Since 2005 I have published within peer-reviewed biomedical journals a series of studies analyzing laboratory animal use, three of which received awards at international scientific conferences in 2005-2006.

You have asked me to comment on the accuracy of official reporting of pain and distress experienced by laboratory animals, and the consequent scientific implications.

The federal Animal Welfare Act (AWA) prohibits subjecting animals to experiments likely to cause more than "*momentary or slight pain or distress*," unless written evidence has been provided demonstrating that a detailed search for non-animal alternatives was unsuccessful. In such cases, "*appropriate sedatives, analgesics or anesthetics*" must be used, unless "*withholding such agents is necessary for scientific reasons*," in which case the experiment must not continue for longer than necessary.

Where it is considered scientifically necessary to conduct procedures likely to result in significant pain or distress, without the use of sedatives, analgesics or anesthetics, such animal use must be correctly categorized as causing "*unrelieved pain or distress*" within the *Annual Report of Research Facility*, filed by the Facility with the United States Department of Agriculture (USDA), together with an explanation as to why the procedure and protocol were necessary. As you are aware, responsibility for oversight and enforcement of the AWA rests with the USDA Animal & Plant Health Inspection Service (APHIS).

Unfortunately, it appears that these requirements are met with variable compliance by US animal research laboratories. Although you have provided only a small number of protocols for comment, even within these few it appears that violations of these requirements are common. Examples include:

1. Prolonged water or food deprivation of primates, for training purposes. Such deprivation results in situations in which the animals are unable to meet basic biological needs, within the limitations of their cage environments. The fundamental urge to meet those needs combined with the inability to do so inevitably results in stress. It was disturbing to read that some experimental protocols may deny water for up to 22 hours daily, for days to weeks on end.
2. The close confinement of primates within restraint chairs, sometimes with surgical implants, for periods of several hours, repeated most days, for periods lasting several weeks or longer. The denial of the ability to engage in normal behavior, and, indeed, simply to move freely, also frustrates the basic natural urges of species which are characterized by their relatively high intelligence, inquisitiveness, and environmental interactivity.
3. The use of animal models of human toxicity frequently results in distress and suffering when toxic effects are severe or chronic. Long-term studies such as the common two-year rodent carcinogenicity assay frequently monitor the progression of toxic effects over the duration of the subject's lifespan.¹ In lethal dose (LD) studies, these effects are sufficiently severe as to cause death. Many other pathological studies result in the induction of diseases that may reasonably be expected to cause distress or suffering, but unfortunately, chemical relief does not appear to be routinely provided.

Such violations of good laboratory practice also occur elsewhere. Around 60% of procedures are conducted without anaesthetics within the UK.² While the use of anaesthetics or analgesics undoubtedly alters normal physiology, claims that such alterations are sufficiently important to hypotheses under investigation, to warrant their exclusion, require careful scrutiny.

That the failure to relieve pain or distress is an international, rather than distinctly US problem, is neither an excuse nor a defense for failing to correctly categorize unrelieved pain or distress, as required by the AWA. Such failures markedly undermine the credibility of official reporting of laboratory animal use. It is reasonable to assume that the intent of such misrepresentation is to minimize legitimate scientific, regulatory and social concern about, and possible restriction of, laboratory animal use.

For example, unrelieved pain or distress raises substantial scientific concerns. Recent comprehensive reviews published in laboratory animal science journals have revealed that even routine laboratory procedures such as handling, blood collection, and gavaging³ (insertion of a throat tube for the forced administration of a test compound) and standardised laboratory housing⁴ may cause significant stress, to which laboratory animals may not habituate. The results include the distortion of normal physiology, disruption of hormonal regulation, impedance of neuroanatomical development and cognitive ability, behavioral stereotypies, immunosuppression, and increased susceptibility to adverse drug reactions or other pathologies.

From a scientific perspective, such treatment of these animals damages them as experimental models. The scientific outcomes that result are likely to be even further removed from human outcomes than would be achieved by the use of healthy, non-stressed animals, as intended by the

¹ Knight A, Bailey J, Balcombe J. Animal carcinogenicity studies: 1. poor human predictivity. *Altern Lab Anim.* 2006; 34(1):19-27.

² Hudson M & Bhogal N. An analysis of the Home Office Statistics of Scientific Procedures on Living Animals, Great Britain 2004. *Altern Lab Anim.* 2006;34(1):85-103.

³ Balcombe J, Barnard N, Sandusky C. Laboratory routines cause animal stress. *Contemporary Topics in Laboratory Animal Science* 2004;43(6):42-51.

⁴ Balcombe J. Laboratory environments and rodents' behavioural needs: a review. *Laboratory Animals* 2006;40(3):217-35.

AWA. Such scientific distortion further compounds the marked biological and mathematical obstacles that impede the accurate extrapolation of animal test results to predicted human outcomes.⁵

The accurate reporting and disclosure to the scientific and regulatory communities, and the general public, of the level of unrelieved pain and distress experienced by laboratory animals, along with the reasons for the denial of chemical relief in such cases, are fundamental to good laboratory practice, to maximizing the utility of laboratory animal models, and the scientific robustness of animal data, and to minimizing scientific and social controversy surrounding laboratory animal use. It is clear, therefore, that greater enforcement of accuracy within official reporting of laboratory animal use is required.

Yours sincerely,

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⁵ Knight A, Bailey J, Balcombe J. Animal carcinogenicity studies: 2. obstacles to extrapolation of data to humans. *Altern Lab Anim* 2006;34(1):29-38.