

**RESPONSE**

**Depends on context**

**Sylvia J. Singletary, DVM, DACLAM**

This scenario illustrates the difficulties faced by IACUCs that try to answer complex humane and ethical questions using established federal policies and guidelines. In my opinion, neither the question posed by the new member nor the answer of the established IACUC Chairman is controversial. This situation is a crossroads between a strict interpretation of federal standards and an expanded interpretation of a more progressive culture of humane science in animal welfare.

It is clear from both the literature and anecdotal accounts that a combination of subjective and objective observations and knowledge of the disease pathology must be applied to determine the level of pain and distress in an animal model. During my residency, in 1992, I had the opportunity to observe MPTP-treated rhesus monkeys. Their care and husbandry required a great deal of time and attention to detail. It was clear that these animals were debilitated. However, grading and ‘treating’ distress was more difficult than assessing pain and administering analgesics. This animal model demonstrates one of the issues that still must be addressed by our federal regulatory agencies: how do you meet USDA category guidelines for animals that are clearly distressed, but will not benefit from the use of analgesics?

IACUCs have the freedom to evaluate any given procedure and categorize it as C, D, or E depending on the circumstances in which the procedure is employed. The MPTP-treated animals are distressed but receive intensive postprocedural care to address their condition. Although this care is not pharmaceutical, it is beneficial. Thus, they are not a good fit for Category C. Category D would seem to be the most logical, if postprocedural care is included in the list of agents used to address pain and distress.

Listing the animals in Category E, however, seems to be the most appropriate

based on the USDA guidelines. Nevertheless, Great Eastern should be concerned about having nonhuman primates listed as Category E on an internet-accessible annual report. It is very possible that this issue will have a significant impact on the outcome of the discussion. The opinion of the USDA inspector may be beneficial since the school appears not to have had problems reporting these animals as category C in the past; change might not be required. However, more discussion between the biomedical research community and the regulatory authorities is necessary to address these complex issues.

Although the animals undergoing the gene therapy trial will be debilitated, their condition is not the result of a major surgical procedure. Thus, the protocol does not fall under the guidelines outlined in USDA Policy #14 (ref. 1). I agree with the Chair’s interpretation of this policy.

This situation (and the many others like it) indicate that the USDA needs to reevaluate its current policies. It is important that views like those expressed by the new IACUC member are given adequate time for discussion and consideration. I hope that more consideration will be given to animal care and its ability to address postprocedural issues.

1. USDA APHIS AC. Animal Care Policy #14. Major Survival Surgery (14 April 1997). <http://www.aphis.usda.gov/ac/publications/policy/policy14.pdf>.

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**RESPONSE**

**Category E (with caveats)**

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Research on humans with Parkinson’s disease has shown that chemical changes in the brain cause depression<sup>1</sup> and anxiety

in patients beyond the depression caused by the physical disabilities associated with the disease. In addition—though often overshadowed by more obvious symptoms such as tremors—pain has been reported in over half of these patients<sup>2</sup>. It can therefore be deduced that untreated Parkinson’s symptoms cause pain and distress in both humans and animals.

The first group of animals receiving MPTP will not have therapeutic intervention to relieve their symptoms. They will receive supportive daily care, but this is not sufficient to be considered Category C because the care will not relieve their pain or distress. These animals should instead be considered Category E.

The other animals fall into a gray area. If it is clear that there is sufficient anesthesia and postsurgical analgesia, then the surgery animals are in the appropriate category (D). In addition, as the induction of Parkinson’s disease in these animals does result in a major physiological change, the protocol should be categorized as having multiple major operative procedures for those animals that also undergo stereotaxic surgery.

If the treatments (AAV2 with the gene and AAV2 without the gene) are effective in relieving the symptoms caused by MPTP, then the animals can be safely put in Category D. If these agents are not effective in relieving these symptoms, then these animals too should be in Category E.

The Committee might suggest a small pilot study be done where the parameters of pain and distress are measured in both the MPTP and the treatment groups. This study would also help determine how effective the therapeutic agents are in relieving pain and distress in the animals.

1. Mayo Clinic Online. Parkinson’s Disease, Complications. <http://www.mayoclinic.com/health/parkinsons-disease/DS00295/DSECTION=7>.
2. Parkinson’s Disease Foundation. Pain in Parkinson’s Disease. [http://www.pdf.org/Publications/newsletters/winter04\\_05/Pain\\_in\\_Parkinsons\\_Disease.cfm](http://www.pdf.org/Publications/newsletters/winter04_05/Pain_in_Parkinsons_Disease.cfm).

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