



July 28, 2016

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Via e-mail: wolffa@od.nih.gov

Dear Dr. Wolff,

I am writing on behalf of People for the Ethical Treatment of Animals (PETA) and our more than 5 million members and supporters to request that your office investigate possible noncompliance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy) and the *Guide for the Care and Use of Laboratory Animals* (the *Guide*) related to the use and treatment of animals in the laboratories of MPI Research, Inc. (MPI; PHS Approved Animal Welfare Assurance # A3181-01), located at 54943 N Main Street in Mattawan, MI.

PETA was recently contacted by an anonymous whistleblower who attested to the following problems at MPI:

1. Failure to minimize discomfort, distress, and pain of animals;
2. Failure to promote the psychological well-being of nonhuman primates;
and
3. Failure to minimize the numbers of animals used.

I. Failure to minimize discomfort, distress, and pain of animals

Principle IV of the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training emphasizes the “imperative” to avoid or minimize “discomfort, distress, and pain” to animals. The *Guide* carefully itemizes the topics that should be considered in the IACUC’s review of a protocol, including “a clear and concise sequential description of the procedures involving the use of animals,” “impact of the proposed procedures on the animals’ well-being,” and “postprocedural care and observation.” Additionally, the *Guide* advises that “[v]eterinary care is an essential part of animal care and use Program,” noting that such a program should include “effective management” of “protocol-associated disease, disability, and other sequelae” and “pain and distress.”

However, the insider informed PETA that MPI maintains a colony of approximately 18 dogs who are used to study the delivery of drugs across the blood-brain barrier and are subjected to procedures where discomfort, distress and

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pain to the dogs is not minimized. According to the informant, the dogs have metal ports surgically implanted into their bodies and an attached catheter is run up to the lower part of the spinal column to facilitate multiple collections of cerebrospinal fluid (CSF). The ports are flushed every two weeks with saline solution. The informant stated that staff members in MPI's pharmacokinetics department conduct the lumbar punctures and port-flushes. Staff members carry out the punctures and flushes quickly. This and/or possibly other procedural problems make the process especially uncomfortable for the dogs, who clearly show in their behavior that they are experiencing intense pain, which can be long-lasting. In some instances, the dogs experience seizures. They shake violently and their eyes roll up in their heads. The insider informed PETA that the dogs are not anesthetized prior to the procedure and they are given analgesia only if they experience a seizure—and only after staff members receive approval from supervisors.

The insider told PETA that as with humans, dogs can experience migraines during lumbar puncture. That humans may suffer side effects including incapacitating headaches from lumbar puncture is well-documented in the human medical literature; and there are also cases of humans who have experienced seizures after an epidural injection. Principle IV of the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training advises that “investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.” However, the insider informed PETA that nothing is done to alleviate the dogs' pain and discomfort.

The insider also told PETA that the dogs are euthanized when they are 3 or 4 years old and replaced by young puppies who are approximately three to five months of age. The whistleblower reported that one of the new puppies who was subjected to a lumbar puncture was screaming and flailing through the process.

We contacted with Dr. Daniel Smeak, DVM, Professor and Chief of Small Animal Surgery at Colorado State University, who stated that he had consulted on a project similar to the one that we described but he did not witness any adverse signs during CSF collection; and that if a small amount of saline is used and administered at a slow rate, there should be no changes in behavior or heart rate and there should not be any other signs of discomfort or anxiety during the saline flush.

Additionally, the veterinary literature recommends specific elementary refinements that may reduce the pain and discomfort experienced by dogs who are subjected to lumbar injections, including proper placement of the catheter¹ and avoiding high speed injections.² These refinement techniques are apparently not being used. The human medical literature documents that accidentally injecting air into a catheter can cause headaches, dizziness, and seizures.³

¹ Swalander, David, et al. (2000). Complications associated with the use of indwelling epidural catheters in dogs: 81 cases (1996-1999). *Journal of the American Veterinary Medical Association*, 216 (3), 368-370.

² Son, WG et al. (2014, September). The effect of epidural injection speed on epidural pressure and distribution of solution in anesthetized dogs. *Veterinary Anaesthesia and Analgesia*, 41 (5), 526-533.

³ Arora, Dheeraj, Yatin Mehta, Aashish Jain, and Naresh Trehan (2012). Headache and seizures after cervical epidural injection in a patient undergoing coronary artery bypass grafting. *Annals of Cardiac Anesthesia*, 15 (3), 244-246.

The failure on the part of MPI's IACUC to ensure that the distress, discomfort, and pain experienced by dogs used in the protocol described above was minimized appears to constitute a failure on the part of the facility to comply with the *Guide*.

II. Failure to promote the psychological well-being of nonhuman primates

The *Guide* specifies that “animals should be housed under conditions that provide sufficient space as well as supplementary structures and resources required to meet physical, physiologic, and behavioral needs” and cautions that failure “to meet the animals’ needs may result in abnormal brain development, physiologic dysfunction, and behavioral disorders ... that may compromise both animal well-being and scientific validity.” The *Guide* further “endorses social housing as the default” for nonhuman primates, noting: “Like all social animals, nonhuman primates should normally have social housing.”

The insider informed PETA that several monkeys at MPI are caged alone and exhibit signs of psychological distress, pacing in their cages. The informant stated that some of the monkeys have “picked themselves raw” and one monkey who is caged alone has pulled out much of his hair. The informant did not believe that special attention was provided to this monkey.

III. Failure to minimize the numbers of animals used

The *Guide* encourages institutions “to give careful and deliberate thought to the decision to use animals, taking into consideration the contribution that such use will make to new knowledge [and] ethical concerns.”

However, the insider reported to PETA that it is common for MPI to order too many rats. When it's determined that there are more rats than needed for experiments, the supervisors will say without remorse, “Just CO2 them.”

We urge you to investigate the concerns summarized in this letter and, if the claims are substantiated, to take swift and decisive action against MPI.

If you have any questions, please contact me at 202-829-0974 or AlkaC@peta.org. Thank you for your time and consideration.

Sincerely,



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