

**Exhibit 15**

- 15) May 7, 2013 letter from OLAW to UW IO outlining the findings of the site visit and listing specific recommendations.

FOR US POSTAL SERVICE DELIVERY:

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May 7, 2013

Name

Title

University of Wisconsin-Madison

Room # Bascom Hall - 500 Lincoln Drive  
Madison, WI 53706

Dear

Name

On behalf of the Office of Laboratory Animal Welfare (OLAW) and the site visitors, I would like to thank you and your staff for accommodating our visit to the University of Wisconsin- Madison on such short notice. We appreciated being able to immediately access the study and housing areas, to examine the cats, to review the requested records, to meet with the Principal Investigator (PI) and technicians, and to interact with the Attending/Institutional Veterinarian (AV) and the clinical veterinarians. It was extremely useful for us to examine the animals first hand and to see the areas to which the cats have access and in which they are housed. It was also informative to obtain in depth information about specific practices and procedures from the investigative, husbandry, and facilities staff. The following represents the collective observations and impressions of the site visit team as well as some recommendations for improvement:

- All of the seven cats currently on study were physically examined by myself, another senior veterinarian from a federal oversight agency, and a clinical veterinary subject matter expert. We collectively found the cats to be in excellent clinical condition. Specifically, the cats were in good body condition, had good hair coats, were very well socialized to conspecifics as well as people, and exhibited normal behavior. One cat was observed performing in one of the approved behavioral study procedures and was found to be a willing participant. None of the cats showed any lesions or signs of pain, distress, or adverse responses during handling, transport, examination, or during the experimental trial. The cats were demonstrated entering cat carriers or restraint bags cooperatively on command when shown the objects.
- The AV and clinical veterinarians were knowledgeable and caring and were familiar with the cats, their clinical conditions and history, as well as with the details of the study. The AV stressed that all veterinarians are empowered to remove animals from study if well being is in question. The animal care supervisor and caretaker were also compassionate and actively engaged with the cats. They were familiar with the sanitization procedures for the cats' primary housing, their hammocks, and related equipment and readily provided documentation of appropriate cleaning regimens.
- The PI and research technicians were very concerned about the well being of the cats and handled them carefully and gently during transport and the behavioral trials. They monitored the animals closely while the cats were performing tasks in the specialized sound chambers.


All individuals involved with handling and observing the cats were trained in the recognition of signs of pain or distress, and verified that any animal health concerns are promptly reported to the veterinary staff.

- The site visit team was apprised on the refinements made to the study since its inception which included enhanced veterinary oversight and support during surgeries, stricter oversight over fluid and anesthetic administration during surgery, and improved overall monitoring. Review of the records found that superficial infections of the skin tissue surrounding the head cap have occurred sporadically over the past six years and were treated successfully.
- As was noted in our discussions with the key individuals involved with the study, we strongly support the continued provision of environmental enrichment for the cats, including access to a play area and frequent interaction with people and other cats. We recommend that a non-laboratory area be dedicated for this activity and that it is readily sanitized to include the floors, walls, and any climbing and resting structures.
- Development of laboratory specific standard operating procedures (SOP) is recommended for the cleaning, sanitization, and sterilization of all equipment used for head cap care. These performance standards should be developed in consultation with the veterinary staff, applied to all surgical tools, sterilizing chemicals, feeding tubes, head hardware, restraints, probes, and other devices, and reviewed and approved by the Animal Care and Use Committee (ACUC).
- In addition to controlling environmental contaminants, attention should be given to reduce or eliminate any pathogen transmission between animals, especially if infection is present. Adequate infection control must be exercised including animal quarantine, use of personal protective equipment, and management of fomites. In addition to directly addressing any adverse clinical presentation, a root cause analysis of recurring events, such as infections, should be conducted by the veterinary staff and appropriate preventive action taken.
- We encourage the PI and veterinary staff to remain current with ongoing advances in the care and maintenance of head caps and related hardware and to communicate with other experts in this field to remain abreast of best practices.
- We were informed that the protocol was being rewritten and resubmitted for ACUC review. As discussed, use of the cat as the only acceptable model should be addressed, animal numbers should be clearly justified, the procedures performed on each animal should be clearly outlined, humane endpoints should be specific, and although variable ranges (drug dosage, duration of trials) can be proposed to allow flexibility, the specific procedures described should not be ambiguous or imprecise. The ACUC is to balance the potential adverse effects on an individual animal against the potential scientific value to be obtained and make this a primary consideration in the review process. The PI is strongly encouraged to advise the NIH program officer should any unexpected or unusual events occur during the course of the study.

Animal models have been instrumental in many significant scientific discoveries and have enabled researchers to identify new ways to extend human life, and to improve health and well-being. As you know, the NIH supports the judicious and ethical use of animals in research, in the smallest possible numbers to achieve scientific objectives and in accordance with all applicable laws, regulations and policies. We appreciate your cooperation in ensuring that all research participants at the University of Wisconsin- Madison receive the highest standards of humane care.

As part of the ongoing investigation of case A3368-4P, please provide a copy of the revised protocol upon approval by the ACUC, a copy of any new SOPs addressing the laboratory cleaning procedures, relocation of the enrichment play area, and information regarding any additional changes to policies and procedures, if applicable.

Sincerely,



Axel Wolff, M.S., D.V.M.  
Director  
Division of Compliance Oversight

cc: [Redacted Name], [Redacted Title]  
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