



Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

DEC 21

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President, Council on Accreditation
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Dear Dr. Martin:

The Centers for Disease Control and Prevention (CDC) is writing to you in response to your letter of December 1, 2005, about the proposed decision of the Council on Accreditation of the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC International) with regard to CDC's AAALAC accreditation status. CDC is taking the report of the recent site visit very seriously and is holding itself accountable for correcting all deficiencies that were noted as quickly as possible. We have made substantial progress since the exit briefing by the site visitors, and we know that much remains to be done to achieve the excellence in animal care and use that we intend to accomplish. We are addressing specific issues raised by the site visitors; and, even more importantly, we are also improving our system of procedures and our quality assurance mechanisms to ensure high quality animal care. [REDACTED]

[REDACTED] is responsible for designing our corrective strategy and operational improvements. His staff will work in cooperation with the Institutional Animal Care and Use Committee (IACUC), the CDC Office of Health and Safety (OHS), the CDC Buildings and Facilities Office (BFO), and other relevant CDC components. In this letter, I will give you an overview of our progress. Although this is not a comprehensive response to every item in the report, I will reference some specific sections of the report in this response. To provide a more detailed perspective on our progress and to address some areas of the report that do not accurately reflect the true situation at CDC, we request an oral appeal before the Council and have initiated steps to travel to Mexico for the January 15 meeting.

CDC is committed to providing appropriate veterinary, animal technician, and health and safety access to the Biosafety Level (BSL)-4 area. In response to AAALAC's concerns in section I. of the report, I am pleased to report at this time that the Animal Resources Branch has two veterinarians and two animal technicians with independent access to both sides of the BSL-4 suite. The technician who reports to the principal investigator in the BSL-4 suite no longer performs animal care. Instead, an Animal Resources Branch animal technician who reports directly to the Attending Veterinarian is now responsible for animal care in the BSL-4 suite. Weekend, holiday, and emergency duties are shared between two animal technicians who report to the Attending Veterinarian and each has independent access to the BSL-4 suite. A Letter of

Veterinary Authority, addressed to CDC investigators and signed by the Director of CDC, has been sent to formalize the Animal Resource Branch's oversight of veterinary care and animal husbandry in all areas where laboratory animals are used, including the BSL-4 laboratories.

Also in response to AAALAC's concerns listed in section 1. of the report, CDC is taking action to enable easy viewing of the BSL-4 suite. CDC is arranging for video monitoring of the animal area within the BSL-4 suite. This video will not only provide a better view than the limited view available from the corridor, but it can be monitored by multiple sources. The video will feed to security (as the central camera already does) and also to the [REDACTED] so that they and the IACUC can monitor the BSL-4 suite on an ongoing basis.

Because we now have animal care staff working in the BSL-4 suite who report directly to the Attending Veterinarian, incidents such as those mentioned in section 1.a.3) are unlikely to reoccur. The BSL-4 Attending Veterinarian is responsible for independent veterinary oversight and for follow up on any issues of concern (including those identified by the IACUC). Furthermore, we are in the process of improving record keeping (including purchasing additional software), hiring staff to ensure that records are appropriately maintained, and designing training to further address this concern.

We regret that the site visitors were denied access to records of animal care in the BSL-4 suite. This is unacceptable. We assure you that we will make these records readily available to AAALAC and to the Attending Veterinarians in the future.

The Council expressed concern over IACUC oversight in the BSL-4 area in section 2. of the report. CDC assures the Council that methods will be developed to enhance IACUC oversight of the BSL-4 suite. External expert consultants [REDACTED] have agreed to conduct a comprehensive review of the deficiencies noted by AAALAC and to make appropriate recommendations and, in particular, to address IACUC oversight of the BSL-4 laboratories. We will continue to engage additional expertise that might be useful to us as we re-examine and make changes to our program.

With regard to the IACUC and AAALAC's concerns about structure and function (section 3.a.), CDC is moving the IACUC program office from the National Center for Infectious Diseases to the Office of the Director, CDC. The IACUC office will now be a function within the CDC Office of the Chief Science Officer, which is also the location of the Office of Scientific Regulatory Services and the CDC Human Research Protections Office. This move is intended to convey the great importance CDC places on the animal care and use program, increase its visibility and provide the leadership and leverage it needs to function well. We will provide any additional resources necessary for the IACUC to function optimally. At the present time, all IACUC policies and procedures are being reviewed and revised as necessary. To clarify the appropriate oversight authority of the IACUC, the CDC Animal Policy Board discussed in section 3.b. in the report will be abolished. We will establish instead an Animal Care and Use Advisory Committee similar to the model used at the National Institutes of Health. The Chairs

of our three IACUCs (Atlanta, Morgantown, and Ft. Collins) will sit on this committee. In addition, at least annually, the CDC Executive Leadership Board, chaired by the CDC Director, will review the IACUC's recommendations to ensure that all needed actions are properly addressed and resourced.

The IACUC has also taken steps to improve operational efficiency in discharging duties to provide oversight of the animal care and use program. Specifically, the committee has adopted a rigorous protocol for the correction of deficiencies identified during the semi-annual inspections. This is now a fixed item on the committee's agenda each month. The IACUC recognizes that the semiannual review of the animal care and use program needs to be significantly augmented, and the committee is working with an external consultant to achieve this. Right now the committee is revising the current animal use protocol form to allow significantly more information to be submitted for review. IACUC policy letters are currently under development, and will be reviewed by the external consultant.

Significant modifications to the investigator training program are planned within the next two months. The entire didactic portion of the program will be changed to an online training program that is readily available to investigators and researchers at any time. The online training program is being adapted from the Veterans Administration Training and Research Program to reflect CDC's specific training needs. In addition, a hands-on training protocol has been developed to supplement the technical skills of animal handling. This required training is targeted to investigators, veterinarians, and technicians at CDC.

With regard to issues raised in section 3.a.5), water lixits are checked by animal care staff twice each day. The procedure for checking the water lixits includes caretakers using clean stainless steel rods to manually deflect the lixit in each and every occupied cage in order to visually verify the proper flow of clean water from the lixit. A select number of animals (Aotus, Saimiri, and select macaques) also receive a supplemental fluid bottle containing Pedialyte, affixed to the front of the cage and filled/changed daily. Area supervisors also check rooms daily to ensure proper positioning and functioning of water lixits, among other daily checklist items.

The Council expressed concern about three animals that experienced procedure-related deaths (section 3.a.5)ii.). The incident mentioned in this section happened while using published recommended doses of injectable anesthetic and analgesic combinations. Those published doses have been reviewed in consultation with veterinary colleagues outside CDC and judged too high; thus, future doses will be decreased appropriately. This particular protocol has been discontinued, and any future similar procedures will be performed in the Animal Resources Branch Treatment/Surgery suite with adequate personnel and support, as recommended by the IACUC.

With regard to practices concerning chimpanzee management in section 3.c. of the report, recent IACUC changes now require chimpanzee protocols to be reviewed by the Interagency Animal Models Committee (IAMC). All current CDC chimpanzee protocols were reviewed and approved by the IAMC as of December 8, 2005. A chimpanzee holding protocol has been

reviewed and approved by the IACUC. We are concerned that there may have been some miscommunication between the AAALAC site visitors and CDC staff about certain issues, including chimpanzee management practices. For example, we have reviewed our records and interviewed staff, and we are confident that "limit feeding" of chimpanzees is not practiced at CDC. Also, the reference to two survival procedures in section 3.c.3) requires clarification. We believe that the report was referring to two percutaneous biopsy passes. Chimpanzees are used for hepatitis research at CDC and require periodic percutaneous hepatic biopsy. Regarding the issue mentioned in section 3.d.1)iii, the attempt to perform a percutaneous biopsy a total of 10 times should not have occurred. Based on discussion and expert advice, the IACUC established a limit on the maximum number of percutaneous biopsy passes attempted on an animal. Currently, a maximum of three percutaneous biopsy passes using an 18 gauge needle is allowed by the IACUC, and this policy will be disseminated to be sure all investigators are aware and compliant. We look forward to clarifying these issues at an appeal. CDC is committed to being in compliance with the Department of Health and Human Services (HHS) and other federal requirements for chimpanzee management.

As expressed in section 3.d. of the report, we agree that proper medical record keeping, health care tracking, and anesthetic and analgesic use recording are ethical and scientific imperatives. The agency will provide resources to acquire and maintain adequate record systems, including electronic systems, for animal management, animal care, animal experimentation and controlled drug storage and use. In the meantime, medical records have been prepared for each species regulated by the Animal Welfare Act. In addition, a new Standard Operating Procedure, consistent with that used by our occupational health clinic, has been established for the procurement, management, storage, and disposition of controlled substances at CDC. This should help avoid confusion about the disposition of certain drugs that occurred during the recent site visit (which were located in a cabinet for disposal since they had passed the expiration date).

In section 3.d.1)i, the Council expressed concern for the treatment of animal #2145. We would like to clarify that this animal was actually housed and cared for [REDACTED]. The major operative procedure performed was not a fracture repair, but amputation at the knee. The procedure was performed on June 27, 2005. The analgesic buprenorphine was prescribed and administered twice daily from June 27, 2005 to July 10, 2005, according to the treatment plan. This is documented in the file on the treatment sheet. If we have misinterpreted the issue of concern or if there has been any miscommunication, we will be happy to discuss this issue further at the appeal.

The issues raised in section 3.e. in the report certainly need to be addressed; however, just for clarification, these incidents occurred in the BSL-3 area [REDACTED] not in the BSL-4 area, with the exception of item 3.e.3). CDC has taken actions to address the issues raised. For example, in coordination with OHS and the Influenza Branch, practices and related standard operating procedures within the BSL-3 area have been modified so that no cages containing experimental animals are uncovered unless and until positioned inside the biological safety cabinet within the room. Procedures conducted and performed in the common corridor area,

including the transport of animals from animal rooms to necropsy, have been reviewed with OHS, and detailed procedures for properly decontaminating the area are in place. In the BSL-3 area, mixing of naïve and experimental rodents within the same rack has been discontinued; experimental rodents are maintained in shoebox cages within the rooms, which are under negative pressure relative to the hallway and common area. Naïve animals are maintained under positive pressure inside BioClean units. According to current BSL-4 (MCL) practices, all rodents—naïve and experimental—are maintained in covered shoebox cages housed in Thoren HEPA filtered units. Rodents of different species (i.e., mice and rats) are maintained in different Thoren units. The BSL-4 practices will be reviewed by our OHS and modified according to their recommendations.

Regarding deficiencies in husbandry and sanitation programs discussed in section 4. of the report, CDC is taking a number of steps to address AAALAC's concerns. An overall assessment is underway by the Scientific Resources Program and will continue over the next 3 to 6 months to determine the number of animals needed and the staffing requirements for caring for the animals. Work orders have been submitted to address the existing sanitation equipment problem. Alternative arrangements have been made to provide back-up cage wash capabilities when the primary cage wash is undergoing repairs. A cage wash and autoclave facility has been funded by the agency and approved by HHS [REDACTED]. A temporary cage wash/autoclave facility is slated to be on-site by February 2006. The creation of this facility will eliminate the need to access the area mentioned in section 5.d that needs repair of flooring and lighting and will thus eliminate the risk to personnel. Until this can be completed, the BFO will immediately implement work orders to repair the flooring and improve the lighting in the [REDACTED] in question. The permanent cage wash facility is scheduled to follow the placement of the temporary facility. We will bring additional documentation to the appeal about the construction of the cage wash/autoclave facility [REDACTED]. Other items mentioned in section 4. of the report have either already been resolved or are currently being resolved. We can discuss these items in more detail with you at the appeal.

With regard to section 5. of the Council's report, as part of the IACUC review process, safety professionals from the OHS review every animal protocol that is submitted. This review includes a risk assessment that takes into account not only the containment of infectious organisms, but the health and safety of both the animal care staff and the animals within the facility. Based on the results of these risk assessments, personnel entering animal areas, including scientific and support personnel, are medically cleared by the OHS. This clearance involves initial consultation, testing, and vaccinations, followed by annual reviews. The initial Animal Resources Branch Fitness for Duty exam is a comprehensive physical exam that includes a baseline serum sample, appropriate immunizations, TB skin testing, individual risk assessments, and many other tests of fitness for duty. We can provide details on the risk assessments and Fitness for Duty exam at the oral appeal.

In addition, as indicated in the Council's report (section 5.b), OHS staff will, in consultation with the IACUC and Animal Resources Branch, remove all non-HEPA filtered vacuums from animal use environments.

Council expressed concern about changing of small animal cages. In areas containing infected animals, biosafety cabinets will be used for the changing of small animal cages according to the recommendations published in the Guide and in the Biosafety in Microbiological and Biomedical Laboratories manual (BMBL, 1999). Where biosafety cabinets are not available, cage changing stations or other appropriate primary containment devices will be purchased and used for cage changing. OHS staff will work with the IACUC and veterinary support staff to identify these locations and acquire the equipment. Standard operating procedures are being modified to reflect recent recommendations for cage changing by OHS.

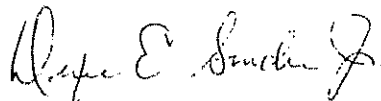
Although not mentioned in the written report, there were several issues mentioned at the exit interview on which we have taken action. For example, the Animal Disaster Plan for all CDC campuses in Atlanta has been developed and is currently being approved at the agency level. In addition, replacement of wooden cabinets with stainless steel cabinets in certain areas recommended by the site visitors were completed this week. CDC has contracted with a consultant, [REDACTED] the American Society of Primatologists, [REDACTED] to help us improve our enrichment programs.

As mentioned previously, we have a new [REDACTED]
[REDACTED]
[REDACTED] He was hired in February 2005 in an effort to bring further expertise and develop a new spirit of cooperation with AAALAC. As you know [REDACTED] brings outstanding expertise and a track record of success which will further help us in establishing a high quality animal care program.

I hope this overview of the actions we have taken to date and the challenges we are tackling is helpful, and conveys the sincerity of our commitment and the importance we place on animal care and use at CDC. In the long term, our goal is to be recognized for having an exemplary program and to operate a program based on prevention of problems rather than responding to corrective actions. We realize that in the short term we will need to work with you, external consultants, and with our own staff to bring our program up to AAALAC's expectations for accreditation.

Thank you for the opportunity to provide this response. I look forward to your reply and to an opportunity for an appeal before the Council. We will plan to address each item in more detail at that time.

Sincerely,



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