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Subject: External Review of the Centers for Disease Control and Prevention Animal Biosafety Level 3 Vivarium Facility

Dear Dr. Meechan,

During the week of September 17 to 21, 2012, the Animal Biosafety Level 3 (ABSL3) Vivarium Facility located in the Emerging Infectious Diseases Laboratory was inspected by a team of four Canadian biosafety experts from the Public Health Agency of Canada and two United States (U.S.) biosafety experts recommended by the American Biological Safety Association.

The team is satisfied that the CDC facility inspected is compliant with applicable requirements set out in the Fifth Edition of the *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) and the current U.S. Select Agent Regulations and the *NIH Guidelines for Research Involving Recombinant DNA Molecules*. There were no observed findings of regulatory non-compliance or missing elements that, in the opinion of the team, pose a risk to CDC employees, the surrounding laboratory/building space, the public or the environment.

Included in this report, is a summary of the compliance verification process and results. The process included an extensive review of all physical systems, including two site inspections of the facility (one overview and one detailed) and the interstitial mechanical space. It also included a review of four program biosafety protocols and interviews with key personnel, including program, security and medical surveillance. A review of best practices was also conducted by the team, resulting in some recommendations for this facility and its operations.

Compliance to Requirements

To verify compliance with existing U.S. biosafety requirements, the team was requested to review all functions pertaining to the physical systems of the facility, including: physical layout, finishes, HVAC system, air flow (rate and direction), hardware, and life safety features (including egress function).

The facility meets requirements set out in the BMBL, and international best practices, for physical layout, finishes, HVAC, airflow (rate & direction) and hardware. Inspection results also confirm that the life safety features have been constructed in accordance with applicable life safety and building codes.

Airflow

To assess the relationship of the air flow in the facility to adjacent spaces (e.g. clean corridors, Q-fever laboratory, incinerator, cage wash facility), the compliance verification process included checking the air flow monitoring devices (visual tell-tails and Baulin tubes), as well as performing smoke tests on the outside and inside of the suites. These tests were performed under normal operating conditions.

Inward directional air was also verified at the door from the clean corridor into procedure room SSB 922 during the opening and closing of the door between procedure room SSB 922 and the animal holding room SSB 922A. Three tests were conducted and directional airflow was maintained at all times.

In the vivarium, the airflow directions are:

- from the clean corridor into the procedure rooms;
- from the clean corridor into the anterooms;
- from the anterooms into the procedure rooms;
- from the procedure rooms into the animal holding rooms,
- from the grey corridor into the animal holding rooms; and
- from the grey corridor into the dirty corridor (SSB 800B)

Airflow in the entire ABSL 3 vivarium is consistent with the facility design and operational needs.

HVAC Systems

The vivarium has an independent HVAC system separate from the systems serving the adjacent Q-fever and cagewash areas. The system is compliant with BMBL requirements and international best practices.

Safety Procedures

The compliance verification process included a review of facility processes that impact safety, including: gowning; traffic flow within the facility; decontamination and disposal practices; and circulation of the animal care staff between suites.

A review of the maintenance processes confirmed that existing practices meet current BMBL requirements, and some exceed international best practices, ensuring the safe and efficient operation of the building systems serving the vivarium. Further, the standard biosafety operating procedures described in the biosafety manuals are also compliant with current BMBL requirements and international best practices.

Security Practices

Security practices were also reviewed, including inventory tracking, the determination of who has access, the strength of access control, and response to intrusion notification. The standard security practices described in the manuals, and verbally communicated and demonstrated by the Security Operation Center, meet the requirements set out in the current BMBL, current U.S. Select Agent Regulations and international best practices.

Canada/US Collaboration

The compliance verification process reinforced the need for Canada and the U.S. to advance work on the assessment and verification of existing biocontainment requirements and engineering practices. A key element of this work is engagement with the standards setting bodies. For example, the team observed that both Canada and the U.S. include the requirement for 100 percent single pass air at BSL3. This is not the standard for WHO or Australia.

Review of Best Practices

The multipurpose vivarium facility inspected reflects the most common design type and new construction witnessed by the inspection team. In our opinion, the design offers the greatest flexibility for existing programs, program expansions, and for responding to new emerging public health threats.

The challenge that comes with any shared space is the number of different program-specific needs and requirements. The reality of a multipurpose suite is that while program work is frequently conducted in isolation within inner suites, there is still a sharing of common areas (entry, exit, and waste handling) that pose a biosafety risk.

To enhance biosafety in your existing programs, we recommend some best practices drawn from the following standards: BMBL; Canadian *Laboratory Biosafety Guidelines*; WHO *Laboratory Biosafety Manual*, 3rd Edition, and guidelines from the United Kingdom and Australia.

Program Risk Assessments

At your institution, the Institutional Biosafety Committee (IBC) is responsible for the review of risk assessments related to research involving recombinant nucleic acids and/or recombinant organisms. We recommend that all Vivarium program risk assessments be reviewed by the IBC, including all research protocols for work involving infectious agents, animal use, recombinant DNA and genetically modified materials. This best practice promotes standardized biosafety practices, and is consistent with the WHO and Canadian biosafety guidelines. It is also consistent with the BMBL that recommends risk assessments be reviewed with a biosafety professional, subject matter expert, and the IBC.

Inward Directional Airflow

There is a common understanding of how to maintain inward directional airflow among the international community, and respective biosafety standards. Inward directional airflow can be achieved through a combination of engineering controls and operational procedures to limit the simultaneous opening of multiple doors within containment. One engineering control is an interlocking door system. In the absence of this engineering feature, operational procedures are critical to maintain inward airflow. Based on program-level discussions, it is evident that operational procedures are in place for the vivarium facility and applied in day-to-day practice. However, these procedures are not documented in the program biosafety manuals. It is therefore recommended that the operational procedures for maintaining inward directional airflow be documented in all facility biosafety manuals, and communicated via signage posted at relevant doors.

Contributions to International Biosafety Community

The inspection team is also recommending that areas of advanced biosafety observed in the CDC facility be shared with other countries to strengthen biosafety practices. For example, this facility has a unique working group with representation from all areas including program, animal care, security and maintenance. The High Containment Laboratory Operations Group (HOG) should be recognised as a best practice. In a multi-purpose facility, the HOG provides a common platform to raise and discuss vivarium-specific issues, and to solve problems as a collective. This

concept will be taken back to our Canadian program to see how we can best incorporate into the forthcoming *Canadian Biosafety Standards and Guidelines*, and new regulations being developed under the *Human Pathogens and Toxins Act*.

The team thanks the CDC for the opportunity to conduct an external review of the multi-purpose vivarium facility. The high level of expertise and staff dedication to biosafety is clearly evident from both the scientific programs and the facility operational groups. To this end, the inspection team is satisfied that the Animal Biosafety Level 3 (ABSL3) Vivarium Facility located in the Emerging Infectious Diseases Laboratory, Building 18, is compliant with all U.S. regulatory requirements and guidelines, and poses no risk to the health and safety of the public.

Sincerely,

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