THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

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January 19, 2016

Ryan T. Bayha
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RE: Loss of Containment Involving a Mouse Infected with Mouse Adapted

As required by Appendix G-II-C-2-q of *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, on August 27, 2015, the University of North Carolina at Chapel Hill ("UNC") submitted an initial report of a loss of containment involving a mouse 24 days post infection with mouse adapted derived from a recombinant infectious clone. The incident was immediately reported to Ryan Bayha, Senior Analyst for Biosecurity and Biosafety Policy at the National Institutes of Health. At the request of NIH OBA, a conference call was held on August 31, 2015 to discuss the incident. NIH OBA granted UNC additional time to address the root cause and submit a follow up report. This letter constitutes UNC's follow up report describing the incident and the steps taken to mitigate the risk of recurrence.

This incident occurred as a researcher was removing a collaborative cross mouse that was 24 days post-infection with a mouse adapted from one of the Buxco (plethysmograph) chambers inside a biological safety cabinet in an ABSL-3 facility. When attempting to remove the mouse the researcher thought she had a successful grip on the mouse's tail and fully removed the lid from the plethysmograph chamber. As this was happening the mouse twisted in the researcher's hand and got free. The mouse immediately turned towards the researcher's arm, ran out of the biosafety cabinet, onto the researchers tyvek apron and onto the floor. The mouse was promptly caught within the laboratory and returned to the cage. Both of the researchers who were in the laboratory at the time decontaminated their PPE and the floor with 70% ethanol. The researchers were wearing tyvek suits, tyvek aprons, tyvek booties, PAPR and double gloves. Neither of the researchers involved experienced a breach in PPE or respiratory protection.

The PI, Biological Safety Officer, Responsible Official and the Director of the University Employee Occupational Health Clinic were immediately notified. The incident was deemed as a potential exposure and personnel were placed on medical surveillance, reporting baseline temperatures as well as morning and evening temperatures and any signs or symptoms of infection over the following ten days. The medical surveillance period passed without incident.

The actual risk posed to the laboratorians in the August 27, 2015 incident was likely low as mice infected with mouse adapted have cleared the virus by day 10 post infection. As the mouse was at day 24 post infection, it had most likely cleared the infection and was kept primarily to study the ensuing adaptive immune responses.

UNC's approach to preventing further breaches in containment is multi-faceted.

A. Mouse users undergo extensive training prior to performing experiments with CC mice. After undergoing the standard training required of all UNC animal users, prospective CC mouse users work with personnel from the Systems Genetics Core Facility which developed the CC mice in order to understand the range of behaviors and activity levels that can occur across different mouse strains. This training includes assessments of behavior as well as safe handling and containment techniques. Following the training, individual users practice their handling and containment on uninfected animals to attain proficiency. When users are comfortable in their skillset, they then

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undergo a variety of assessments of their handling and containment to be approved for work on diverse mouse strains in ABSL-2 and ABSL-3 conditions.

B. A working group comprised of representatives from EHS, Division of Laboratory Animal Medicine (DLAM) and the research laboratories utilizing CC mice in infectious disease models have focused on reviewing previous incidents as well as the development of safety practices and engineering controls for infectious disease research involving CC mice. Successfully implemented engineering controls include screw top containers for weighing mice, individual housing for mice exhibiting jumpy or aggressive behavior and use of PVC pipes with a single opening in the biological safety cabinet. As escaping mice typically run along the vertical surfaces within the biological safety cabinet while looking for shelter, the PVC pipes take advantage of instinctive animal behavior by providing apparent shelter, which can be easily capped to facilitate recapture within the biological safety cabinet. Unfortunately, the 8/27/15 incident involved a mouse that ran directly towards the opening of the biological safety cabinet rather than the vertical surfaces.

The working group is currently evaluating the use of netting at the opening of the biological safety cabinet as a new engineering control designed to prevent further breaches of containment. The netting is attached to either the sash or the exterior of the hood and weighted down to provide contact with the work surface. Researchers are able to access the work surface by sliding their arms under the netting. We are currently working with NuAire to develop a removable frame to secure the netting to the biosafety cabinet along with an elastic opening to allow users greater ease of access and range of motion. Our ultimate goal is the creation of a professionally crafted engineering control to successfully mitigate the risk of future breaches of containment while avoiding any adverse effect on containment or impeding scientific research.

Please contact me at (919) 962-5722 or eisenman@ehs.unc.edu if you have any questions.

Sincerely,

Daniel Eisenman, PhD, CBSP
Biological Safety Officer
Environment, Health and Safety

Cc: Doug Cyr, IBC Chair
Mary Beth Koza, Director of EHS
Mitch Picker, IACUC Chair
Craig Fletcher, Director of DLAM

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January 21, 2016

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Dear Dr. Eisenman:

Thank you for your January 19, 2016, update to the National Institutes of Health (NIH) Office of Science Policy (OSP) regarding the University of North Carolina's (UNC) response to a series of incidents involving the escape of mice from primary containment during procedures performed at biological safety level 3.

The last reported incident occurred on August 27, 2015, and involved a mouse that had been infected 24 days prior with mouse adapted . From your report, we understand that the incident occurred as a researcher was attempting to remove a mouse from a container placed inside a biological safety cabinet (BSC). The mouse twisted in the researchers hand and got free. The mouse then ran out of the BSC and landed on the floor. The mouse was promptly recaptured and returned to its cage. At the time of the incident, the two researchers in the facility were wearing personal protective equipment including powered air purifying respirators. The biological safety officer and director of the University occupational health clinic were immediately notified. Both researchers were placed on medical surveillance, reporting temperatures twice daily as well as any signs of infection for ten days. You state in your report that the risk posed to the researchers was likely low, as mice infected with mouse adapted usually clear the virus 10 days post infection.

NIH subsequently requested a conference call with UNC, which was held on August 31, 2015, to discuss how UNC was responding to a series of similar incidents in order to prevent further occurrences of mice involved in infectious disease research escaping while been handled in the BSC.

From your report, we understand that in addition to the animal handling training and the use of engineering controls described in previous reports, UNC is currently evaluating the use of netting at the opening of the BSC as a new engineering control to prevent mouse escape. The netting is attached to either the sash or exterior of the BSC, and weighed down to provide contact with the work surface. Researchers are able to access the BSC by sliding their hands under the netting. UNC is currently working with the BSC manufacturer to develop a removable frame to secure the netting to the BSC along with an elastic opening to allow users greater ease of access and range of motion. The ultimate goal is the creation of a professionally crafted engineering control to mitigate the risk of future mouse escapes while avoiding any impact on the function of the BSC.

No further information is required at this time, but please provide an update when the engineering control being developed is complete and its use is implemented at UNC. Please contact NIH staff by email at oba-osp@od.nih.gov or by telephone at (301) 496-9838 if you have any questions.

Sincerely,

Ryan Bayha
Senior Analyst for Biosecurity and Biosafety Policy
Office of Science Policy

cc: Doug Cyr, Institutional Biosafety Committee Chair, UNC
Mary Beth Koza, Director, Environmental Health and Safety, UNC
Mitch Picker, Institutional Animal Care and Use Committee Chair, UNC
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Carrie Wolinetz, Ph.D., Associate Director for Science Policy, NIH
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