National Institutes of Health

U.S. Public Health Service
Bethesda, Maryland 20892

Office of Science Policy
National Institutes of Health
6705 Rockledge Drive
Suite 750, MSC 7985
Bethesda, MD 20892-7985
(301) 496-9838 (Phone) (301) 496-9839 (Fax) http.//osp od mh gov¼ndex html

July 15, 2016

[redacted]
Institutional Biosafety Committee
Boston University
85 East Newton Street, Suite M-810G Boston, MA 02118

Dear [redacted]:

I am writing in response to an e-mail communication sent to the NIH Office of Science Policy (OSP) on March 8, 2016 by [redacted] in the Boston University (BLT) Office of Research Compliance requesting the lowering of containment for the cloning of full-length cDNAs of Risk Group (RG) 4 single strand, negative sense RNA virus genomes in non-pathogenic strains of E. coli. The request transmitted on behalf of [redacted] involves the cloning of Marburg, Ebola, Nipah and Hendra viruses. Upon review of the initial proposal, OSP requested clarification of several points involving (i) material flow to separate work with related viruses in order to avoid crosscontamination and (ii) additional details regarding the shipment of full-length cDNA clones to collaborating laboratories. The supplementary responses submitted by [redacted] adequately describe the procedural safeguards that will enable this research to proceed safely and securely.

We understand from the information that was submitted to the NIH OSP in March and May 2016, that [redacted] will limit her research to establishment of a reverse genetics system that will facilitate the study of viral pathogenesis of the RG4 agents listed above. All experiments will be limited to cDNA cloning only and any subsequent rescue experiments in

tissue culture will be performed under BIA containment at other off-site collaborating laboratories approved for recombinant work with these viruses.

Upon review of the information you have sent to us, we are in agreement that the information provided in the BU biosafety / biosecurity plan and additional procedural measures instituted by [redacted] satisfy the recommendations described in OSP's 'Points to Consider" document for cloning full-length cDNA constructs ofRG4 viruses.

[redacted] is authorized to lower containment to BL2 for work involving the full-length cloning of the filoviruses Marburg and Ebola and the paramyxoviruses Nipah and Hendra with the following procedural stipulations as described in the Boston University proposal:

[redacted]

Work on helper plasmids will occur at a location separate from work involving the full-length cDNA cloning in E. coli of either the filo- or paramyxo- viruses. The latter will be confined to a secure BL2 laboratory (the full-length cDNA laboratory -- FLCL) separate from the regular BL2 laboratory.

- Helper plasmids will be stored in a separate location than that used for the full-length clones. Full-length cDNA clones ofthe different RG4 viruses will be stored in separate boxes maintained in the secure FLCL.
- Workflow restrictions will be instituted to prevent cross-contamination while working with individual cDNA clones. Temporal separation between experimental procedures (to include appropriate cleaning and disinfection) will be implemented.

We understand that [redacted] will be the institutional official responsible for overseeing the biosecurity and biosafety plans; written incident reporting and response plan, including an occupational health plan; and a formal training program covering both the biosafety and biosecurity requirements. [redacted] will also ensure that an annual report regarding this research is submitted to the BU Institutional Biosafety Committee and that a copy of this report is submitted to OSP upon request.

Please note that the approval to lower containment applies only to the cloning of full-length Marburg, Ebola, Hendra and Nipah virus cDNAs in E. coli 1<12 strains and is limited to [redacted] and to her work with these particular RG4 viruses, i.e. it does not extend to any other investigator, or to the fulllength cDNA of other RG4 RNA viruses.

Thank you for your conscientious and continued adherence to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules. If you have questions about these stipulations, please let me know. Sincerely,

Jessica M. Tucker, PhD.
Director, Division of Biosafety, Biosecurity, and
Emerging Biotechnology Policy

Office of Science Policy National
Institutes of Health

cc:
[redacted]