



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
nih.gov/index.html](http://osp.od.nih.gov/index.html)

October 6, 2016

[REDACTED]
[REDACTED]

Institutional Biosafety Committee

Boston University

85 East Newton Street, Suite M-81 OG Boston, MA
02118

Dear [REDACTED]:

I am writing in response to your e-mail communication sent to the NIH Office of Science Policy (OSP) on September 1, 2016 requesting the lowering of containment for the cloning of full-length cDNA of Lloviu cuevavirus (LLOV) in non-pathogenic strains of *E. coli*. We understand from the information provided that LLOV is a filovirus isolated from bats in Spain and that there are no reported cases of human infection associated with this virus. However, as noted in the information provided, LLOV may have the potential to cause severe disease in humans.

[REDACTED] is authorized to lower containment to BL2 for work involving the full-length cloning of LLOV under the existing procedures used for Ebola and Marburg full-length clones as described in the Boston University proposal dated 3/3/2016, with the following stipulations as stated in the OSP approval letter dated July 15, 2016:

- Work on helper plasmids will occur at a location separate from work involving the full-length cDNA cloning in *E. coli* of LLOV. The latter will be confined to a secure BL2 laboratory (the fulllength 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 of the different RG4 viruses of the [REDACTED] laboratory 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 presume that [REDACTED], will continue to 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 [REDACTED]

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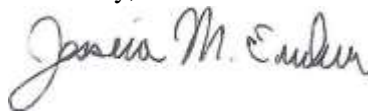
annual report regarding this research is submitted to the BU Institutional Biosafety Committee and that a copy of this report is submitted to OSP upon request.

Please note that the approval to lower containment applies only to the cloning of full-length LLOV virus cDNA (as well as to other RG4 virus cDNAs previously approved) in E. coli K 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 full-length cDNA of other RG4 RNA viruses.

We also understand that experiments involving work with live recombinant LLOV virus will occur under biosafety level 4 containment at the NIH Rocky Mountain Laboratory, pending review of the planned work by CDC-DSAT. Please let us know whether CDC-DSAT determines that work with this recombinant virus is under their purview. If it is not, then work with the with live recombinant LLOV virus falls under the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines).

Thank you for your conscientious and continued adherence to the NIH Guidelines.

Sincerely,



Jessica M. Tucker, PhD.
Director, Division of Biosafety, Biosecurity, and
Emerging Biotechnology Policy
Office of Science Policy National
Institutes of Health

Enclosures:

"Points to Consider" guidance

Approval letter dated 7/15/2016

cc:

[REDACTED] [REDACTED]