Hunter, Renee (NIH/OD) [C]

From: McKinney, Michelle (NIH/OD) [E]
Sent: Friday, February 21, 2020 10:11 AM
To: Matt Anderson; NIH guidelines
Cc: Shi-Hua Xiang; Amit Mitra; Dan Hoyt; Clayton Kelling; Tucker, Jessica (NIH/OD) [E]; Harris, Kathryn (NIH/OD) [C]
Subject: RE: Report of Non-compliance at UNL

Dear Dr. Matthew Anderson,

Thank you for your below report to the National Institutes of Health (NIH) Office of Science Policy (OSP). We have reviewed the information you provided, and the actions taken in response to this incident appear appropriate.

No further information about this incident is required at this time. Please contact Dr. Kathryn Harris, Senior Outreach and Education Specialist, by email at harriskath@od.nih.gov or by telephone at (301) 496-9838 if you have any additional questions.

Regards,

Michelle McKinney

Michelle McKinney, MS, CBSP
Health Science Policy Analyst, OSP, NIH
Phone: 301-402-7465
Mobile: Redacted by agreement
michelle.mckinney@nih.gov

From: Matt Anderson <manderson11@unl.edu>
Sent: Wednesday, February 12, 2020 2:48 PM
To: NIH guidelines <NIHguidelines@od.nih.gov>
Cc: Shi-Hua Xiang <sxiang2@unl.edu>; Amit Mitra <amitra1@unl.edu>; Dan Hoyt <dhoyt2@unl.edu>; Clayton Kelling <ckelling1@unl.edu>
Subject: Report of Non-compliance at UNL

Office of Science Policy,

Please find attached to this email a report of non-compliance with the NIH Guidelines related to work being conducted without approval by the IBC.

Please contact me if further information is required or with questions/comments.

Sincerely,

Matt

IN OUR GRIT, OUR GLORY.

Matthew A. Anderson, PhD, RBP(ABSA), CBSP(ABSA)
Biosafety Officer/ARO
University of Nebraska–Lincoln
Environmental Health & Safety
3630 East Campus Loop
Lincoln, NE 68583-0824
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Tel: 402.472.9554
Fax: 402.472.9650

"Wisdom is not a product of schooling but of the lifelong attempt to acquire it." — Albert Einstein

National Institutes of Health
Office of Science Policy

Web: http://osp.od.nih.gov
Address: 6705 Rockledge Dr #750, Bethesda, MD 20817
Phone: (301) 496-9838

Template for Reporting Incidents Subject to the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* to the National Institutes of Health Office of Science Policy (OSP)

April, 2019

Instructions for Completing this Template

The *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (*NIH Guidelines*) states that "...any significant problems, violations of the *NIH Guidelines*, or any significant research-related accidents and illnesses" must be reported to NIH within 30 days. Certain types of incidents must be reported on a more expedited basis. Spills or accidents occurring in Biosafety Level (BL) 2 laboratories resulting in an overt exposure must be immediately reported to NIH. Spills or accidents occurring in high containment (BL3 or BL4) laboratories resulting in an overt or potential exposure must be immediately reported to NIH. Relevant incidents would include spills and accidents which result in overt exposures to organisms containing recombinant or synthetic nucleic acid molecules in the laboratory, rather than serious adverse events that may occur in the conduct of human gene transfer research.

This template is intended to facilitate the reporting of incidents that occur during the conduct of research subject to the *NIH Guidelines*. Please complete all fields as fully as possible. The use of this template is not required and other formats for submitting reports may be acceptable.

Completed reports may be sent to OSP via email at NIHGuidelines@od.nih.gov

Does this incident involve research subject to the *NIH Guidelines*?	☑YES ☐NO If no, this incident does not require reporting to OSP
Institution Name:	University of Nebraska, Lincoln
Date of Report:	February 11, 2020
Reporter name and position:	Matthew Anderson, Biosafety Officer
Telephone number:	402-742-9554
Email address:	manderson11@unl.edu
Reporter mailing address:	3630 East Campus Loop Lincoln, NE 68588-0824
Date of incident:	Incident discovered on 2/5/2020, upon interview with the PI, the work started in March 2018.
Name of Principal Investigator:	Shi-Hua Xiang
Is this an NIH-funded project?	☑YES ☐NO If yes, please provide the following information (if known) *NIH grant of contract number:* 1 R21 AI126299-01A1 *NIH funding institute or center:* DHHS-NIAID *NIH program officer (name, email address):* Michael W. Fato (michael.fato@nih.gov) *Program Official:* Patricia Repik (prepik@nsaid.nih.gov)

What was the nature of the incident?	☐ Failure to follow approved containment conditions ☑ Failure to obtain IBC approval ☐ Incomplete inactivation ☐ Loss of containment ☐ Loss of a transgenic animal ☐ Personnel exposure ☐ Spill ☐ Other (please describe):
Did the Institutional Biosafety Committee (IBC) approve this research?	☐ YES ☑ NO If yes, date of approval: IBC will review the research at the scheduled meeting in March 2020.
What was the approved biosafety level of the research?	☐ BL1 ☑ BL2 ☐ BL2+ (describe specific enhancement in report) ☐ BL3 ☐ BL3+ (describe specific enhancement in report) ☐ BL4
What section(s) of the *NIH Guidelines* is the research subject to?	III-E-1
Has a report of this incident been made to other agencies? If so, please indicate No report has been made to other agencies	☐ CDC ☐ Funding agency/sponsor ☐ USDA ☐ State or local Public Health ☐ FDA ☐ Law enforcement ☐ EPA ☐ Other (please describe): ☐ OSHA
Nature of recombinant or synthetic material involved in incident (strain, attenuation, etc.)	HIV-1 derived genes in a plasmid (pSG3Δenv or pNL4-3-Luc-R-E) were used and co-injected into a HEK-293 cell with a pcDNA3.1 plasmid containing Marburg virus envelope glycoprotein M78. This resulted in production of HIV virions pseudotyped with GP M78 on the surface and no transgene cargo. The virions were used in experiments testing novel peptide inhibitors of viral entry.

Please provide a narrative of the incident including a timeline of events. The incident should be described in sufficient detail to allow for an understanding of the nature and consequences of the incident. **Include the following information as applicable.**

A description of:

- The incident/violation location (e.g. laboratory biosafety level, vivarium, non-laboratory space)
- Who was involved in the incident/violation, including others present at the incident location?

  Note – please do not identify individuals by name. Provide only gender and position titles (e.g., graduate student, post doc, animal care worker, facility maintenance worker)
- Actions taken immediately following the incident/violation, and by whom, to limit any health or environmental consequences of the event
- The training received by the individual(s) involved and the date(s) the training was conducted
- The institutional or laboratory standard operating procedures (SOPs) for the research and whether there was any deviation from these SOPs at the time of the incident/violation
- Any deviation from the IBC approved containment level or other IBC approval conditions at the time of the incident/violation
- The personal protective equipment in use at the time of the incident/violation
- The occupational health requirements for laboratory personnel involved in the research
- Any medical surveillance provided or recommended after the incident
- Any injury or illness associated with the incident
- Equipment failures

DESCRIPTION OF INCIDENT: (use additional space as necessary)

In November 2017, Dr. Xiang was approved by the institutional IBC for work to create a pseudotyped HIV virus containing the Ebola virus glycoprotein using the plasmids indicated above in this document. It was proposed that this pseudovirus would be produced in HEK-293T cells for subsequent viral entry inhibition experiments *in-vitro*.

Following a Pathogen Inventory review in on Feb 5th, 2020, creation of an HIV pseudovirus containing the Marburg GP was discovered and confirmed. The PI was **not** approved for experiments with the Marburg envelope GP. An email was immediately sent to the PI requesting cessation of the unapproved work pending submission of an amended IBC protocol.

All pseudotyping experiments were performed at the UNL laboratory of Dr. Xiang, under approved BSL-2 containment. His graduate students assisted with pseudovirus production. These experiments began in March 2018 and continued until enough virions were created to complete the inhibition experiments.

Dr. Xiang received NIH Guidelines training in 2012 in addition to refresher training in 2018 and 2019.

Dr. Xiang submitted an updated amendment on 2-5-2020 that included the Marburg env GP gene and the experiments described above. This work will be reviewed by the IBC at the March 9th IBC meeting.

Has the IBC reviewed this incident?	☑YES ☐NO
Please describe the root cause of this incident:	PI was not aware that all new genes of interest to be used in recombinant experiments must be registered with the IBC, even if they are related by taxonomic family.

Describe measures taken by the institution to mitigate any problems identified (e.g. training, modifying protocols, use of additional safety equipment). For measures identified but not yet taken, please include a timeline for their implementation (use additional space as necessary):

As mentioned above, the PI has already submitted an amendment to his IBC protocol to cover the work.

PI was provided refresher training about research under the purview of the IBC, protocol maintenance, sections of the NIH guidelines that require IBC approval prior to initiation and non-compliance policy on 6/18/2019.

The IBC was notified of the non-compliance at the February 10, 2020 meeting and the committee determined that the PI will be required to complete the full EHS Biosafety Research Compliance training module by Feb 18, which covers the above topics in more detail and also outlines Roles and Responsibilities.

- **Additional information may be requested by NIH OSP after review of this report depending on the nature of the incident.**
- **Submitting this completed template to NIH OSP does NOT fulfill the reporting requirements of other agencies. You should verify with the other parties to whom you must report whether the use of this template is acceptable.**