



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

May 18, 2016

Mr. Kevin McKoskey
Director, Sponsored Projects
University of Minnesota
450 McNamara Alumni Center
200 Oak Street SE
Minneapolis, MN 55455-2070

RE: 2 R01AI089728-06

Dear Mr. McKoskey:

Thank you for your correspondence of April 15, 2016, regarding the October 17, 2014 White House announcement of a U.S. Government-wide pause on certain gain-of-function (GoF) experiments and its potential impact on your research (<http://www.whitehouse.gov/blog/2014/10/17/doing-diligence-assess-risks-and-benefits-life-sciences-gain-function-research>). The research funding pause pertains to GoF research projects that may be reasonably anticipated to confer attributes to Influenza, MERS, or SARS viruses such that the resulting virus would have enhanced pathogenicity and/or transmissibility in mammals via the respiratory route.

NIAID reviewed the original grant application, and the additional information provided by you, and made the following assessments regarding Subaim 2.1 of the above-referenced grant:

- NIAID is in agreement that the work you proposed under Experiments 1, 2, and 3 is not subject to the GoF research funding pause. This determination is based on the fact that the work will be carried out using either recombinant proteins or replication-deficient pseudoviruses, and will not involve the generation of a replicating SARS-CoV variant with enhanced pathogenicity and/or transmissibility via the respiratory route.
- NIAID's determination is that the work proposed under Experiment 4 to generate SARS-Like viruses with enhanced affinity for human receptors (via both reverse genetics and serial passaging) is subject to the GoF research funding pause, and therefore may not be conducted under this grant. Given the lack of empiric evidence that increased receptor binding alone is insufficient to increase pathogenicity, NIAID has determined that the proposed work is reasonably anticipated to result in a SARS-Like virus with enhanced pathogenicity. NIAID acknowledges that in lieu of generating SARS-Like viruses with enhanced affinity for human receptors you will pursue alternative strategies using *loss-of-function* mutations, or mutations targeting the ACE2 receptor. NIAID also acknowledges your statement that if any mutant

viruses you generate demonstrate either enhanced virus growth >1 log compared to the wildtype parental backbone strain or more efficient growth in primary human airway epithelial cells, you will immediately stop all experiments with the mutant and notify NIAID and the IBCs at the University of Minnesota and the University of North Carolina at Chapel Hill of these results

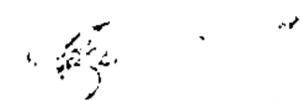
Please remember that the institution must comply in full with all terms and conditions placed on this grant. If your research evolves to include experiments that may be subject to the GoF research funding pause or you observe enhanced pathogenicity and/or transmissibility of SARS or SARS-Like viruses in mammals via the respiratory route at any time during the course of conducting these experiments, you must immediately stop these research activities and provide the NIAID Program Officer and Grants Management Specialist with the relevant data and information related to these unanticipated outcomes

As indicated above, NIAID determinations are based on information from multiple sources, but primarily on our communication with you about the details of your proposed experiments and your research results. Should NIAID's determination change based on information obtained through the U S Government GoF deliberative process, described here <http://www.phe.gov/s3/dualuse/Documents/gain-of-function.pdf>, you will be notified, however, until such time, or until the GoF research funding pause is lifted, NIAID's determination, indicated above, is final

Please let us know if you have any questions, or if you require additional information

Sincerely,


Devon Bumbrey-Quarles
Grants Management Specialist
NIAID/NIH/DHHS


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