



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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October 21, 2014

Transmitted via e-mail to:  
[michael.king@mssm.edu](mailto:michael.king@mssm.edu)

Dr. Michael J. King  
Director, Grants and Contracts Office  
Icahn School of Medicine at Mt. Sinai  
One Gustave L. Place, Box 3500  
New York, NY 10029

Subject: **NOTICE OF PARTIAL STOP WORK ORDER**, Contract HHSN272201400008C  
"NIAID Centers of Excellence for Influenza Research and Surveillance"

Dear Dr. King:

On October 17, 2014, the US Government issued a Research Funding Pause on selected gain-of-function research on influenza, MERS and SARS viruses (<http://www.phc.gov/s3/dualuse/Documents/gain-of-function.pdf>). The scope of this Research Funding Pause has been defined to include any gain-of-function experiments that may be reasonably anticipated to confer attributes to any influenza, MERS, or SARS viruses such that the virus would have enhanced pathogenicity and/or transmissibility in mammals via the respiratory route. NIAID has interpreted this Research Funding Pause to also include any experiments utilizing influenza viruses previously generated that exhibit enhanced transmissibility in mammals via the respiratory route. The Research Funding Pause does not apply to characterization or testing of naturally occurring influenza viruses, unless the experiments are reasonably anticipated to increase transmissibility and/or pathogenicity.

Contracts are used by the US Government to acquire goods and services for its direct benefit. While this Research Funding Pause is in place, goods and services tied to gain-of-function research on influenza, MERS and SARS are no longer a government requirement. Thus, experiments that fall under the scope of this Research Funding Pause will not be conducted under any NIAID contract. This action is being taken in accordance with FAR 52. 242-15 [Stop Work Order (August 1989) with Alternative I (April 1984)] incorporated under Article F.4. of the subject contract.

NIAID has determined that the following projects in your contract, HHSN272201400008C, may contain gain-of-function experiments that fall under the Research Funding Pause.

**Project 1: MIT Surveillance and Surveillance-Related Research**  
SPECIFIC AIMS POTENTIALLY IMPACTED:

- Aim 1.* How does reassortment in LPPI impact their pandemic potential?
- Aim 2.* How does variation in receptor binding affect host specificity?

Project 2: Avian, swine and human H5N1 influenza virus surveillance activities in Asia and the Middle East

SPECIFIC AIMS POTENTIALLY IMPACTED:

*Aim:* Identification of novel virulence determinants.

Project 3: Phenotypic Characterization of Influenza Viruses

SPECIFIC AIMS POTENTIALLY IMPACTED:

*Aim.* Reverse genetics assays

Project 4: Host Factors and Disease Outcome

SPECIFIC AIMS POTENTIALLY IMPACTED:

*Aim 2.* To assess the antiviral mechanism(s) of Mx proteins

*Aim 2.3:* Selection of influenza viruses with increased resistance to MxA or Mx1 by introduction of random mutations.

Project 5: Host Factors and Virus Tropism

SPECIFIC AIMS POTENTIALLY IMPACTED:

*Aim 1:* Host specific inhibition of innate immunity by NS1.

*Aim 1.3.* Impact on virus replication, pathogenesis and host tropism

*Aim 2:* Host specific interactions of NEP.

*Aim 2.1:* Species-specific interactions of the NEP:

*Aim 2.3:* Impact on virus replication, pathogenesis and host tropism

*Aim 3:* Host adaptive polymerase mutations

*Aim 3.1:* Identify and characterize polymerase mutations that emerged during H5N1 passaging in ferrets:

*Aim 3.3:* Examine new polymerase polymorphisms and their role in promoting virus replication through interaction with essential human host factors.

*Aim 4:* Virus specific interactions with myeloid cells.

*Aim 4.3:* NS1 mediated inhibition of DCs and macrophages.

Project 6: HA Determinants of Virus Phenotype: Antigenicity, Virulence, and Transmission

SPECIFIC AIMS POTENTIALLY IMPACTED:

*Aim 1.* To identify molecular determinants of antigenic properties in HA

*Aim 2.* To identify molecular determinants of virulence in HA

*Aim 3.* To identify airborne transmission determinants of H5 HA

*Aim 4.* To identify airborne transmission determinants of H1 HA

*Aim 5.* To identify host determinants of transmission in guinea pigs and ferrets.

Project 7: Mechanisms of Interspecies Transmission of H9 and H7 Viruses

SPECIFIC AIMS POTENTIALLY IMPACTED:

*Aim 1.* Determine the tissue tropism, receptor binding preference, and growth kinetics of parental and transmissible viruses in ex vivo tissue explants (EXTE).

*Aim 2:* Quantify differences in viral shedding, determine mutation frequencies in virus populations, and determine the Aerosol Infectious Dose50 (AID50) of the H9 and H7 parental viruses and the respiratory transmissible viruses in ferrets.

*Aim 3:* Define the phenotypes of changes in each gene from transmissible H9 and H7 viruses, and test their pathogenesis and spread in animals.

*Aim 4:* Determine if the molecular changes required for respiratory transmission can be transferred to influenza isolates from the same subtype

If these projects contain any work as described under the Research Funding Pause, it must stop effective immediately upon receipt of this Notice. In addition, should any other applicable research that is being conducted with NIAID contract funding fall under the Research Funding Pause it too must stop immediately. Within 14 days of the date of this letter please respond to this partial stop work notice with a detailed list of the projects and experiments that you have halted. You should contact your COR to discuss re-direction of the research that has been stopped. This partial stop work order will remain in effect for ninety (90) calendar days from the date of this letter or until you are otherwise notified.

You shall take the following steps related to cessation of work:

- 1) Evaluate all projects for experiments in question; stop all identified gain-of-function experiments that can enhance pathogenicity and transmissibility of any influenza virus; within 14 days of receipt of this Notice provide a detailed list of projects and experiments that have been halted, and contact COR to discuss redirection of contract activities.
- 2) Keep adequate records of your compliance with #1), above, showing the:
  - (a) Effective date of the Partial Stop Work Order;
  - (b) Evaluation of projects for GOF experiments
- 3) Furnish notice of stop work to each immediate subcontractor, consultant and supplier that will be affected by this Partial Stop Work Order. In this notice:
  - (a) Specify your Government contract number;
  - (b) State that the contract is under a Partial Stop Work Order;
  - (c) State the effective date of the Partial Stop Work Order;
  - (d) Provide instructions to stop work required;
  - (e) Request that similar notices and instructions be given to its immediate subcontractors.

Matters not covered by this notice should be brought to the attention of the undersigned.

**bijan.mansoury@nih.gov**

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On behalf of Michael C. Finn  
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