

**U.S. Government Gain-of-Function Deliberative
Process and Research Funding Pause on Selected
Gain-of-Function Research Involving Influenza,
MERS, and SARS Viruses**

Frequently Asked Questions

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What is “gain-of-function” research?

“Gain of function” refers to any modification of a biological agent that confers new or enhanced activity. Typically, researchers mutate or alter genes and examine the impact of these modifications on a particular property or trait of the organism. For example, some investigators can modify influenza viruses in ways that enhance pathogenicity and/or transmissibility in order to better understand the origins and nature of these traits at the molecular level, as well as their pathogenesis in susceptible hosts. Since influenza viruses constantly evolve in nature, these gain-of-function studies may help predict whether these viruses could evolve naturally over time to acquire these new or enhanced traits, and if so, how the viruses might affect hosts and the kinds of medical countermeasures that might be most effective. Some gain-of-function studies may entail biosafety and biosecurity risks that require unique risk assessment and mitigation measures.

Why is gain-of-function research undertaken?

Gain-of-function studies involving infectious agents help us understand the fundamental nature of host-pathogen interactions and can shed light on the potential for, and mechanisms of, evolution of viruses and other infectious agents to acquire certain properties. Greater insight into the biological processes that contribute to pathogenicity or transmissibility can provide a foundation for identifying and developing effective approaches to prevent or treat human or animal infections. Gain-of-function research may also enable assessment of the pandemic potential of emerging infectious agents, which could inform public health and preparedness efforts, including the development of effective medical countermeasures.

Why is the U.S. government¹ pausing the funding of certain types of gain-of-function studies at this time?

The occurrence this year of laboratory biosafety incidents at U.S. government research facilities have caused the federal government to re-assess the risk/benefit calculus underpinning funding decisions for a certain subset of gain-of-function research involving agents that pose a significant risk to public and animal health. The pause will allow the U.S. government, in partnership with the life sciences community, to conduct a comprehensive assessment of gain-of-function research with the explicit goal of developing a new policy framework to guide future funding decisions.

What is the scope of research covered by the funding pause?

During the pause, the U.S. government will not release new funding for gain-of-function research projects that reasonably may be anticipated to confer attributes to influenza², Middle East Respiratory Syndrome (MERS), or Severe Acute Respiratory Syndrome (SARS)

¹<http://www.whitehouse.gov/blog/2014/10/17/doing-diligence-assess-risks-and-benefits-life-sciences-gain-function-research>

² Any influenza virus, not only highly pathogenic strains

viruses such that the resulting virus has enhanced pathogenicity and/or transmissibility (via the respiratory route) in mammals. This means that the U.S. government will not release new funding for experiments that meet the gain-of-function funding pause criteria. For the small subset of ongoing work that is determined to meet the gain-of-function funding pause criteria, the contract-funded work has been stopped and the grant-funded work is subject to a voluntary pause. The funding pause will not apply to characterization or testing of naturally occurring influenza, MERS, and SARS viruses, unless these tests reasonably are anticipated to increase transmissibility or pathogenicity.

Why is the funding pause limited to only research involving influenza, SARS, and MERS viruses?

These three viruses not only share the characteristic of being human health threats - causing in some instances significant morbidity and mortality - but they also have the potential to cause pandemics because they are transmitted easily by the respiratory route. A pandemic with any of these pathogens could have serious repercussions for health, security, and economics, both nationally and globally. While the U.S. government recognizes that understanding the pandemic potential of these organisms is one of the reasons investigators conduct gain-of-function studies, such experiments entail certain risks to individual and public safety and security. This year's federal laboratory incidents led the government to reassess the risk/benefit calculus underpinning funding decisions for a certain subset of gain of function research, and consequently pause funding for those high-risk gain of function experiments until a comprehensive review of the risks and benefits of gain of function studies could be completed.

How many ongoing research projects involving influenza, SARS, and MERS viruses entail experiments that fit the characteristics of those subject to the funding pause?

The National Institutes of Health (NIH) initially identified 18 projects that might entail experiments subject to the funding pause. Letters were sent to principal investigators on those projects to notify them of the funding pause and to request that they assess the applicability of the pause to their projects. Discussions between NIH and these investigators are currently ongoing and regard specific experimental details and research results in order to determine the applicability of the funding pause to those experiments. Therefore, the number of projects actually affected by the pause may change from the 18 currently identified.

What if I am not sure whether an experiment falls under the funding pause?

In cases where it is not clear whether an experiment involving influenza, MERS, or SARS virus would be subject to the pause, determinations will be made on a case-by-case basis by the funding agency. Investigators who have questions about whether an experiment may be subject to the pause should contact their funding agency.

Are experiments involving isolated genes of influenza, MERS, or SARS virus included in the funding pause?

No. The pause applies to research that would create viruses with certain attributes. If the research does not include production of infectious, replication-competent virus, then it would not be subject to the pause.

Are *in silico* or modeling studies of influenza, MERS, or SARS virus included in the funding pause?

Experiments *in silico* or modeling studies are not covered under the pause unless they also involve work with the actual viruses and meet the criteria.

Will influenza surveillance activities be affected by the funding pause?

The pause is not intended to affect influenza surveillance work generally, and the U.S. government is committed to ensuring the nation is prepared for seasonal and pandemic influenza. Influenza surveillance projects supported by the U.S. government should continue, unless these projects involve the manipulation of naturally occurring isolates such that the resulting viruses have enhanced transmissibility and/or pathogenicity.

What will occur during the pause?

During the pause, a deliberative process will be undertaken in which the potential benefits and risks of gain-of-function research will be evaluated by the life sciences community and federal government. The deliberative process will involve two distinct, but complementary, entities, and is explicitly structured to facilitate robust engagement between the federal government and life sciences community. The National Science Advisory Board for Biosecurity (NSABB) will serve as the official federal advisory body for providing advice on oversight of this area of dual use research, in keeping with federal rules and regulations.

Early in the deliberative process, the National Research Council (NRC) of the National Academies will be asked to convene a scientific symposium focused on the issues associated with gain-of-function. The NRC will also hold a second symposium later in the deliberative process, which will include a discussion of the NSABB draft recommendations regarding gain-of-function research.

The NSABB, informed by discussion at the NRC public consultations, will provide recommendations to the heads of all federal entities that conduct, support, or have an interest in life sciences research. The final NSABB recommendations as well as the outcomes of the NRC symposia will inform the development and adoption of a new U.S. government policy regarding gain-of-function research. The life sciences community will be encouraged to provide input through both the NRC and NSABB deliberative processes.

Will members of the life science community and public have opportunities to provide input to the NSABB and NRC discussions?

Yes. The NSABB and NRC proceedings will employ mechanisms to engage the life sciences community and public at large, who will be encouraged to provide input.

When will the funding pause end?

The funding pause will end when the U.S. government has adopted a federal policy to guide future funding decisions regarding gain-of-function studies on the basis of the deliberative process described above. The objective is for the pause not to be any longer than necessary, and the federal government has launched a process that is intended to take 12 months.

Is there a provision to allow gain-of-function research subject to the funding pause to proceed, for example, if the research is required for public health or national security purposes?

Yes, an exception from the funding pause may be granted by the head of the federal funding department or agency if that official determines in writing that the research is urgently necessary to protect public health or national security.

I believe that my research is indeed urgently necessary to protect public health or national security and should not be subject to the funding pause. What is the process for requesting and receiving an exception?

Principal investigators should begin by contacting the program or contract officer at the agency funding the research in question. Agency staff will then consider whether particular experiments are subject to the funding pause, and if so, whether they meet the exception criterion of being “urgently necessary to protect the public health or national security.” If program staff believe the research in question may meet the exception criterion, the matter will then be referred to the Director of the department or agency that funds the research for a final evaluation and determination. Once the director makes a determination, agency staff will notify the investigator about the outcome of this evaluation in a timely way. While individual experiments and specific evaluation processes will vary, the U.S. government is committed to evaluating potential exceptions and making determinations as expeditiously as possible.

Is the funding pause related to ongoing efforts to respond to the Ebola outbreak in West Africa?

No. The research pause only affects release of new funding for gain-of-function research experiments that reasonably are anticipated to confer attributes to influenza, MERS, or SARS virus such that the resulting virus has enhanced pathogenicity and/or transmissibility via the respiratory route in mammals.