

Controversial research on modifying A(H5N1) influenza viruses in the laboratory

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United States Advisory Board changes its position.

New US government guidance on handling dual use research in the life sciences.

In the autumn of 2011 a United States Government body, [the National Science Advisory Board for Biosecurity \(NSABB\)](#) established under the National Institutes of Health considered two scientific papers describing experimental work manipulating avian influenza A(H5N1) viruses to help determine their pandemic potential for humans.(1-3) Both the research teams that prepared the papers used ferrets as an animal model as these are often considered the best readily available animal model for how influenza behaves in humans.(4). The two papers, lead authors Yoshihiro Kawaoka (University of Wisconsin, USA) and Ron Fouchier (Erasmus University, the Netherlands) had already been accepted by prominent scientific journals. The NSABB's opinion was that publication of the papers represented a threat to health and biosecurity because of the potential for Dual Use that is biological research with legitimate scientific purpose that may be misused to pose a threat to public health and/or national security concerning which the US Government has recently issued new guidance.(5) The NSABB's opinion then was that the papers should only be published with considerable 'redaction', that is removal of or obscuring of certain text.(1)

The NSABB's was accepted by the US government which set in train a series of consequences because of the threat it posed to the scientific process of publication and the implementation of the newly negotiated Pandemic Influenza Preparedness (PIP) framework agreed by all nations at the 2011 World Health Assembly.(3) Indirectly it also led to a global moratorium on all similar research despite its importance for virological risk assessments.(1,3)

The World Health Organization (WHO) was especially concerned over the implications for the PIP framework and risk assessment and convened a technical consultation which came to very different conclusions from the NSABB. The WHO meeting (on February 16th and 17th 2012) noted the importance of the issues raised by NSABB but came to different conclusions.(1,6) In its consensus the WHO consultation specifically recommended that

- The redaction option was not viable for the two papers under discussion in view of the urgency of public health needs,
- The papers should be published in full though some critical issues needing to be addressed before publication of the papers were:
 - There should be a focused communications plan to increase public awareness and understanding of the significance of these studies and the rationale for their publication,
 - There was a need for a review of the essential biosafety and biosecurity aspects of the newly developed knowledge.

Subsequent to this the US Government (the Department of Health and Human Services) NSABB was asked to revisit its position on the paper and did so looking at somewhat revised papers on March 29th-30th 2012. That meeting concluded that the NSABB:

- strongly supported the unrestricted communication of research information unless that information could be directly misused to pose a significant and immediate risk to public health and safety;
- did not now feel the data in the manuscripts provided information that would immediately enable misuse of the research in ways that would endanger public health or national security (though this was by a majority vote for the Fouchier paper);
- emphasised the importance of understanding specific mutations that may improve international surveillance and public health and safety;
- understood that global cooperation, critical for pandemic influenza preparedness efforts, is predicated upon the free sharing of information and was a fundamental principle in evaluating these manuscripts.

The Board's recommendations were informed by the newly released United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern.(5) This policy applies to US federally funded life sciences research and will ensure that dual use concerns are addressed during evaluation of ongoing and future research on A/H5N1 influenza virus.

ECDC Comment (3 April 2012):

The fact that the US Board has changed its views neither means that this issue is over nor that the papers will be published straight away and the moratorium lifted. The statement on March 30th is only advisory and so it now has to be seen if the US Government endorses the advice. Hopefully that is a technicality but the moratorium on research remains in place and both the WHO consultation and the Board recommended a number of actions that need to be undertaken and will be relevant to Europe. This includes decisions on what exactly are the right levels of biosafety for this kind of work including defining what BSL-3+ means operationally, focused communications to increase public awareness and understanding of the significance of these studies and the rationale for their publication.(1) There may also need to be a review of some of the rules for EU research in the light of the American publication. (1,5) Finally it should be remembered that despite all of the concern expressed in the media over the modified viruses the indications to date are that in ferrets they are neither very transmissible nor very pathogenic. (4,7) Though because the papers remain unavailable there must be some doubt on even that.

1. [US National Institutes of Health NIH Statement on H5N1, 20 January 2012](#)
2. [ECDC Risk Assessment Laboratory-created A\(H5N1\) viruses transmissible between ferrets, 29 February 2012](#)
3. [ECDC Scientific advance: Application of Virological Risk Assessments: US Department of Health and Human Services \(HHS\) sponsors clinical trials of a vaccine targeted to a novel A\(H3N2\)v influenza strain, 12 January 2012](#)
4. [ECDC Scientific advance: Ferrets as experimental models of influenza in humans Scientific Advance, 7 March 2012](#)
5. [United States government policy for oversight of life sciences dual use research of concern, 29 March 2012](#)
6. [WHO Report on technical consultation on H5N1 research issues Geneva, 16–17 February 2012.](#)
7. [Kawaoka H H5N1: Flu transmission work is urgent, Nature Comment 25 January 2012, DOI:10.1038/nature10884](#)

