

UPDATED: Avian flu controversy comes to roost at WHO

International meeting seeks to chart a way forward for mutant flu research.

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UPDATE: *The meeting of flu experts convened by the World Health Organization has concluded that both mutant flu studies should be published in full.*

Almost two dozen experts kicked off a two-day international meeting this morning at the World Health Organization (WHO) in Geneva, in a bid to find ways to move forward in the controversy over two studies that have created strains of the H5N1 avian flu virus that are transmissible in ferrets. The meeting may reach some consensus on a few immediate issues, such as what parts of the studies should be published, and who might qualify for access to the full papers on a 'need-to-know' basis.

But the narrowness of the expertise of those taking part means that the meeting will not even begin to address the far bigger issue of whether such research should be allowed at all in the future, and if so, how it should safely proceed. Key to that question is an assessment of the relative public-health benefits, compared to the risks that a proliferation of such research in labs worldwide would increase the risk of an accidental or intentional release of the lab strains. Ferrets are a good proxy for how flu behaves in other mammals, including humans, so any release could itself spark a H5N1 pandemic, with potentially catastrophic consequences given the virus's likely high mortality rate (see '[Death-rate row blurs mutant flu debate](#)').

The list of experts attending the meeting — which the WHO [made public](#) this morning — shows that the panel is overwhelmingly stacked with academic flu researchers, almost all of whom are strongly in favour of such research, and many of whom would like to see it proceed unfettered. By contrast, there are almost no public-health officials of international stature attending, nor experts in risk assessment, biosafety or biosecurity.

The WHO [has explained](#), however, that the participants were limited to "people who have direct involvement or knowledge about these two studies, their review or oversight, or potential dissemination of results", and that this meeting has the very limited remit of clarifying "key facts about the two research studies and the most urgent related issues".

The WHO sees this meeting as the start of a much longer, and more inclusive, broadening of the discussion over the H5N1 studies to a more international level, as anticipated in my Q&A on this with Anthony Fauci, the director of the US National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, who is also taking part in the WHO meeting (see '[Open the debate on flu research](#)').

To provide some breathing space for discussion — and perhaps avert a ban on such research — researchers on 20 January also declared a voluntary pause in research on making avian flu viruses more transmissible (see '[Scientists call for 60-day suspension of mutant flu research](#)'). But the process of international discussion and arbitration that may ultimately create a framework for international oversight of such research will undoubtedly take far longer than this, so that pause will probably need to be extended. Future meetings will also need to enlarge the debate to include many other interested parties, far beyond the narrow confines of flu researchers.

The two researchers at the centre of the controversy are attending the meeting: Ron Fouchier, a flu virologist at Erasmus Medical Center in Rotterdam, the Netherlands, and Yoshihiro Kawaoka of the University of Wisconsin–Madison. In a study submitted to *Science*, a team led by Fouchier found that just five mutations allowed avian H5N1 to spread easily among ferrets. In a study submitted to *Nature*, Kawaoka and his colleagues also succeeded in making the virus transmissible in ferrets, by creating a virus that has the H5 haemagglutinin (HA) surface protein from the H5N1 virus, with all the remaining genes coming from the 2009 pandemic H1N1 virus (see '[Pandemic 2009 H1N1 virus gives wings to avian flu](#)').

Also attending the meeting are Philip Campbell, editor-in-chief of *Nature*, and Barbara Jasny, an editor at *Science*, as well as Paul Keim, director of pathogen genomics at Northern Arizona University in Flagstaff, and chair of the US National Science Advisory Board for Biosecurity (NSABB). It was on the advice of the NSABB that the US government in December asked *Science* and *Nature* to publish only the broad conclusions of the two studies, and not to reveal the scientific details, so as to limit the risk of uncontrolled proliferation

of such research that might lead to accidental or intentional release of similar mutant viruses. (For NSABB's reasoning see ['Policy: Adaptations of avian flu virus are a cause for concern'](#) and for Keim's own thoughtful perspective see ['Q&A: Reasons for proposed redaction of flu paper'](#).)

Nature and *Science* have agreed to the redaction requested by NSABB, provided that a suitable mechanism is established to disseminate the data to flu researchers and public-health officials on a need-to-know basis. Although the WHO has not yet released a meeting agenda, discussion of any mechanism is almost certainly going to be a high priority. Whether any consensus will be reached is another matter.

What seems clear is that the data need to be made available to the H5N1 flu virus surveillance community, in some form, so that they can monitor whether such combinations of mutations appear in the wild. This could, for example, result in intensifying the culling of poultry and other control measures. Genetic surveillance for H5N1 is currently extremely poor: very few viral isolates are collected and even fewer are sequenced, often only after months or years. Just 160 H5N1 isolates were submitted to GenBank last year (see ['Caution urged for mutant flu work'](#)). But we should be increasing the surveillance of H5N1 — and other animal and poultry flu viruses with these mutations — to assess their pandemic potential, even if such knowledge is of little practical benefit at present given the lack of surveillance, in particular in pigs. Better funding of real-time surveillance is also needed in affected countries.

But although this data could be useful for surveillance, we should not lose sight of the harsh reality that the next pandemic virus — if it occurs in the next few years — will not be detected in advance, but is likely to be, just as during the 2009 pandemic, present in many countries before we even detect the first case. And even were we to get an early warning, it would mean nothing to the 80% of the planet who will not have access to vaccines.

How to get the data from the two papers disseminated out to those doing the surveillance might be a task that the WHO and the UN Food and Agriculture Organization are well placed to accomplish. Much of the H5N1 surveillance effort is done in collaboration with their networks, such as the WHO's global influenza surveillance and response system ([GISRS](#)) laboratories.

Complicating matters overall is the fact that sharing of avian flu isolates, genetic sequences and other data is a politically charged issue. In 2005, Indonesia refused to continue to supply these to the WHO flu lab networks, on the very good grounds that it saw nothing in return, in terms of intellectual property, access to vaccines and drugs and technology transfer. It was only after six years of negotiations that the WHO succeeded last year in getting agreement on a ['Pandemic influenza preparedness Framework'](#), which provides for countries supplying viruses to have material benefits in return. It does not want the present controversy over sharing data to jeopardize that hard-won system — it's no surprise, therefore, that there are three representatives of Indonesia attending the WHO meeting, and that this issue is likely to be a major element in the discussions.

But ultimately answering the question of who should have access to the data from these papers seems inextricably linked to the far bigger question of how such research should be regulated in the future to avoid unnecessary proliferation of such strains, and of what will happen to data from any future studies. Moreover, the Fouchier and Kawaoka papers have already been seen by many researchers, and many labs that are competent in this area would be capable of replicating the work even without having the data from the two papers. So the far more important question is how to develop a framework for regulating this research.

The short-term public benefits of such flu research appear slim (see ['Facing up to flu'](#)), whereas the risks of an accidental lab release are not negligible, and the consequences could be a public-health disaster. There is therefore no need to rush headlong into more research to create mammalian-transmissible avian flu virus, and the international community must take the time needed to figure out whether and how such research can be allowed to proceed safely, and how best its proliferation can be checked. It is important that, in considering how this research goes forward, we bear in mind our present inability to deal with any H5N1 pandemic. As such, any proliferation of such research would, as veteran flu researcher Robert Webster at St. Jude Children's Research Hospital in Memphis, Tennessee, [puts it](#), create an "unacceptably high level of risk to humanity should mammalian-transmissible H5N1 virus be accidentally or intentionally released".

This week's meeting at the WHO will not even begin to address such wider issues. But one can hope that it will provide for a serious and thoughtful analysis of the studies and the issues they raise, which will help inform wider debate. As Fauci points out: "We need to get people in the same room discussing the pros and cons rather than having duelling soundbites. That doesn't help anybody."

See also our [web special on the H5N1 controversy](#).

Updates

Updated: A two-day meeting of 22 experts convened in Geneva by the World Health Organization has now ended, concluding that the two [controversial flu studies should be published in full](#). However, the panel also agreed to extend a voluntary 60-day moratorium to allow broader discussions on the biosafety aspects of how such work could best be carried out. See *Nature's* [news blog](#) for more details.