NEWS IN FOCUS

S. DAS/AP/PRESS ASSOCIATION IMAGES

Upgrading the biosafety level for studies on mutant avian influenza could put a stranglehold on the work.

BIOSECURITY

Flu meeting opts for openness

Controversial virus studies should be published and oversight of such work strengthened, conference concludes.

BY DECLAN BUTLER

After weeks of debate, two controversial papers describing forms of the H5N1 avian influenza virus capable of transmitting between mammals should be published in full. That was the unexpected outcome of a meeting convened last week in Geneva, Switzerland, by the World Health Organization (WHO), which also promised to create a more rigorous oversight system for such research.

The decision goes against a recommendation from the US National Science Advisory Board for Biosecurity (NSABB), which the US government has adopted as its official position. In December 2011, the board said that experimental details of the two studies should be redacted from any publications, because of concerns that the information could be used in a bioterror attack. The board also feared that publishing the details would prompt more laboratories to work on the viruses, making an accidental release more likely.

The studies, which created forms of H5N1 that can spread between ferrets through airborne transmission, are likely to be published in a few months. The 22 experts at the meeting, mainly flu researchers, believe that the delay is needed to explain the benefits of the work to the public, and allay concerns about its safety. Meanwhile, a 60-day moratorium on similar research will be extended until a system is put in place to review levels of biosafety and biosecurity. To that end, the WHO intends to convene international discussions among regulators and other bodies in the next few months.

The two researchers at the centre of the controversy say that they are pleased with the outcome. "I was pleasantly surprised by the fact that there were unanimous decisions about most issues, and strong consensus on the others," says Ron Fouchier, a flu virologist at Erasmus Medical Center in Rotterdam, the Netherlands, whose study has been accepted by the journal *Science*. Yoshihiro Kawaoka of the University of Wisconsin-Madison, lead researcher on the other study, adds that the meeting allowed him and Fouchier to explain their work, including the potential benefits for surveillance of emerging flu strains (*Nature* **481,** 417–418; 2012) and for vaccine preparation (*Nature* **482,** 142–143; 2012). "We presented why we did these experiments, what we did, what data we obtained, what these data contribute to public health and to the scientific field, and why we think the results should be shared," says Kawaoka, whose paper has been accepted by *Nature*. He adds that data he and Fouchier presented on the evolution of H5N1 in the wild clarified the threat from the virus, although he would not be drawn on the details, citing confidentiality.

Microbiologist Paul Keim, who chairs the NSABB and attended the meeting, did not respond to *Nature*'s request for an interview, but is reportedly "disappointed" by the recommendation to publish the papers.

NATURE.COM
For more, see *Nature*'s mutant flu special:
go.nature.com/mhmibi

Nature and *Science* last year agreed in principle to redact the papers, on the condition that the ▶

US government would develop a mechanism to disseminate the full papers to researchers and health officials on a need-to-know basis. But meeting participants concluded that this was impractical, and that the potential public-health benefits of the work outweighed any risk of publishing the papers in full.

BIOSAFETY FIRST

Many flu researchers have already seen the papers, so there was little to be gained by restricting their dissemination, says Richard Ebright, a molecular biologist and biodefence expert at Rutgers University in Piscataway, New Jersey. It is much more urgent, he says, to put in place strict biosafety, biosecurity and oversight provisions for such research.

David Fidler, an expert in international and national security law at Indiana University in Bloomington, points out that the meeting hasn't actually broken the publication deadlock, because Keim and representatives of the US government still do not agree with publishing the studies in full. "Most of the meeting's participants appear to have rejected the US position," says Fidler, "but [have] agreed to the extended moratorium and publication delay in the hope that the US government will change its mind."

Participants agreed that the mutant viruses should remain in their two containment facilities — rated at 'BSL-3 enhanced', the second-highest level of biosafety — and that both should be reviewed before any work restarts. Didier Houssin, president of the French Evaluation Agency for Research and Higher Education, says that the biosafety review of the work must consider whether studies of this kind should be conducted only in labs with the highest biosafety rating of BSL-4, a restriction imposed this month by Canada. Houssin, who attended the meeting, notes that imposing such a restriction globally would curtail similar work because there are just a few dozen BSL-4 labs worldwide. The safety level of BSL-3 labs is very variable, he says, and so any facilities working on such viruses would need to be rigorously assessed.

Fidler and other experts note that the meeting did not address the overall risks and benefits of the work, or how similar research might be overseen in future. Keiji Fukuda, WHO Assistant Director-General for Health Security and Environment, explains that later meetings will deal with these topics and will have wider participation.

Meanwhile, the meeting agreed that it was "critical" for the WHO to form a communications plan over the next few months to increase public awareness and understanding of the importance of the flu work, and to alleviate public anxieties. But Peter Sandman, a risk-communications consultant in Princeton, New Jersey, advises against any attempt by the WHO to "educate" the public out of its concerns. As a strategy, he says, it "is thoroughly discredited, because it doesn't work". ■ SEE EDITORIAL P.439

EPIDEMIOLOGY

Growing pains for children's study

Door-to-door recruitment abandoned for US project.

BY MEREDITH WADMAN

A proposed 15% budget cut is making for a troubled adolescence at the National Children's Study (NCS), an ambitious US government project that aims to chart biological, environmental and social influences on the health of 100,000 American children from before birth to age 21 years.

The study's managers at the National Institute of Child Health and Human Development (NICHD) in Bethesda, Maryland, say that they can cope with the White House's budget proposal, released on 13 February. This would cut funding for the programme by US$28 million, to $165 million in 2013 (see 'Belt tightening'). But their plan to save money, by recruiting study participants through health-care providers rather than by door-to-door recruitment, is worrying some of the study's scientists, who already feel shut out from its planning.

In 2010, a year after it started, the NCS's pilot phase had to expand from seven sites to 37 after recruitment rates fell well short of expectations. As the pilot winds down recruitment this year, it has enrolled only 4,000 subjects. The study, which could be used to probe the roots of conditions such as asthma, autism and diabetes, must therefore accelerate recruitment sharply after its main arm launches in 2013.

NICHD director Alan Guttmacher says that there was "understandable angst" among study-site directors the day the budget was made public. But NCS managers see room for savings, estimating that $30 million was spent on recruitment in 2011 alone. Although door-to-door recruitment is considered a gold standard in epidemiology, study managers believe that subjects can be recruited much more cheaply through health-care-providers' offices, where pilot-study data show that recruiters are much more likely to find eligible women who are pregnant or trying to become pregnant. The household recruitment has another downside, says Guttmacher: "It would take so long it would compromise the study." A "scientifically compelling" study with a budget of $165 million is still possible, he says.

According to one of the study's principal investigators (PIs), however, money is already too tight. "The idea that there are cost savings to be made here is absolutely absurd," says the researcher, who contends that many PIs have yet to receive funding for their data-management systems that was promised by NICHD managers last October. Some are coping by diverting funds from other parts of the study; others have simply stopped entering data for study subjects. The study's managers say that the PIs have been adequately funded.

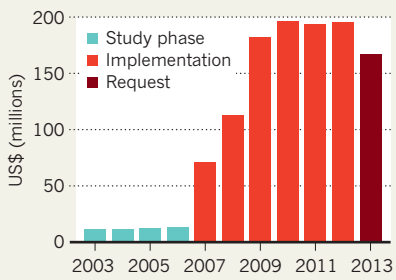
Some PIs are also worried that recruitment at health-care-providers' offices would bias the study and render its findings inapplicable to the wider population. They point to a 2008 Institute of Medicine report that called the household-based sampling approach one of the study's main strengths.

And some scientists complain that they had no input into the decision to change the recruiting strategy, which many failed to hear about even after the budget was announced. "We don't have any full, thorough discussion of this," says Nigel Paneth, a paediatrician at Michigan State University in East Lansing who is PI at the NCS site in Wayne County. "What this study needs is full scientific input, not Bureaucratic Planning Central." Guttmacher notes that government officials cannot talk about White House budget proposals before they are released.

But with many congressional districts hosting study centres, the programme has proved resilient. The administration of former president George W. Bush repeatedly tried to cancel it, but Congress always restored full funding. ■

BELT TIGHTENING

Facing a proposed 15% cut, the US National Children's Study is seeking cheaper ways to recruit its cohort of more than 100,000 children.



SOURCE: NIH