

THIS WEEK



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Publishing risky research

Imperfect global biosafety standards and a threat to researchers' motivations from biosecurity concerns are among the significant risks in current flu research.

This week sees the online publication of the paper 'Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets' by the Japanese-US team headed by Yoshihiro Kawaoka at the University of Wisconsin-Madison (M. Imai *et al.* *Nature* <http://dx.doi.org/10.1038/nature10831> (2012). See also pages 7 and 13, and H.-L. Yen and J. S. M. Peiris *Nature* <http://dx.doi.org/10.1038/nature11192>; 2012). Kawaoka's paper was one of two submitted last August, reporting mammalian transmissibility of avian flu as a result of artificial genetic manipulation, the principal scientific interest of which arises from the small number of mutations found to be necessary. The other paper, by a team headed by Ron Fouchier at the Erasmus Medical Centre in Rotterdam, the Netherlands, is expected to appear soon in *Science*.

As has been much discussed in *Nature*, both papers were independently assessed by the US National Science Advisory Board for Biosecurity (NSABB) while being considered by the journals. The NSABB's recommendation, communicated to the journals in November last year, was not to publish the essential methods and data. Although such a recommendation has no statutory force, it makes any researcher or publisher pause. There followed months of public debate and two two-day meetings involving flu experts and other stakeholders, one held by the World Health Organization (WHO) and the other by the NSABB. After the second, at the end of March, the NSABB essentially reversed its position, and *Nature* made its own decision to proceed.

LESSONS LEARNED

As the economist John Maynard Keynes reportedly said: "When the facts change, I change my mind." But the essential scientific elements in the Kawaoka paper were unchanged between the first and second NSABB deliberations. It is now clear that the committee's original deliberations were too limited, especially given the enormous implications for flu research of a recommendation against publication. Yet as a body that aims to anticipate and scrutinize the security risks of biological research, the NSABB is unique worldwide, and it is desirable to have such a forum. The discussion that followed the board's first decision would not have been as valuable or as prompt had it concerned hypothetical cases. Yet there are justified concerns among the research community about the NSABB's processes, and these processes should be reviewed.

Some lessons have emerged that point to actions and policies for the future. First, it was worth deliberating at length on the possibility of redacting the key findings of the paper instead of simply rejecting it. (Rejection has long been an option if *Nature* is advised by security experts that the risks of publication exceed the benefits.) There was also the option that the full paper might be distributed by some third party, to selected recipients only. Having now considered these matters in depth, the editors of this journal have decided that we will not consider either alternative for papers in *Nature* in the foreseeable future. A paper that omits key results or methods disables subsequent

research and peer review. Furthermore, after much internal and external deliberation, we cannot imagine any mechanism or criterion by which to sensibly judge who should or should not be allowed to see the work. Nor do we believe that any restricted information distributed to university laboratories would stay confidential for long.

We are aware that the lack of an option for restricted publication has its own risks in a discipline in which results might be both beneficial to the public benefit and a threat to security. We will willingly explore ways out of this dilemma.

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One major risk amid these discussions is that younger researchers might be discouraged from entering a field that is subject to security constraints. But the attitudes of biosecurity experts are more encouraging than is widely appreciated.

As far as *Nature* is aware, formal assessments by security agencies have led to recommendations that the Kawaoka paper be published.

This includes an independent assessment that we commissioned from a non-US biological-defence agency, whose advice can be found at go.nature.com/wglsea. In subsequent discussions with biosecurity researchers, there has been a striking unanimity: where there is a benefit to public health or science, publish! It has been enlightening to see how scientists in this secretive arena see the open scientific enterprise as their best recourse in times of potential trouble.

The third most important lesson is about biosafety. Here there are real concerns: humans lack immunity to flu viruses with an H5 haemagglutinin protein, and an accidental release of a mammalian-transmissible H5 virus would have the potential to cause a pandemic were it to transmit between humans. A key component of the second round of NSABB deliberations was a clear presentation by Kawaoka of his team's very rigorous security processes and set-up, including physical arrangements, training and due diligence exercised with personnel.

Such a reassuring picture is not globally applicable. The standards of these labs (fully described in the Kawaoka paper) were widely quoted as biosafety level (BSL) 3 enhanced. The WHO discussion considered such standards essential, and worried that to require the distinctly more demanding BSL-4 standard would shut down the research. However, 'BSL-3 enhanced' is not a formally established standard. What is more, not every country may have sufficient regulatory systems and robust laboratory cultures of safety. This is a key issue as the self-imposed moratorium on work by flu-transmissibility researchers continues.

The WHO will soon release guidelines about international standards for biosafety. The signs are that these will highlight key issues and aspects of good governance, but will not themselves provide a framework for strengthened implementation. The absence of such a framework is an urgent concern for all researchers working with dangerous organisms, and for all who fund and publish their work. ■