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EDITORIAL

Consensus is needed at a global level concerning dual-use research

Dual-use research in biomedical science is a long-term unresolved issue. Dual-use refers to meritorious science that would benefit mankind but that might be misused, as with bioterrorism or nuclear warfare. The debates focus on the balance between advancement of science and promotion of biosecurity. In the past, there have been many dual-use research controversies in life science, such as the IL-4 superstrain mousepox [1], the de novo synthesis of polio virus [2], and the reconstruction of the 1918 Influenza virus [3]. In 2012, there again emerged heated debates on the publication of two studies on mutant H5N1 strains, a highly pathogenic avian influenza virus. Yoshihiro Kawaoko's team created a hybrid virus with genes from both H5N1 and the H1N1 strains [4], while Ron Fouchier's team created a new virus with only five mutations, using traditional passaging technology [5]; both viruses are highly transmissible via the airborne route among ferrets. The months-long scientific debate and controversy further highlights the importance of establishing a mechanism to guide and regulate dual-use research. In this issue, Du *et al*. have reviewed established biosafety-related protocols for influenza A virus research and provide potential strategies to improve biosafety protocols for dual-use research on the highly pathogenic avian influenza viruses and other emerging infectious pathogens.

Science may act as a double-edged sword. Nuclear science can be used in medicine and as an energy source but also represents a threat to humankind and the environment if it is mismanaged and misused. The nuclear bomb was used twice in war, but biological weapons were used many times during World War II [6]. Even though one should never underestimate the risk of bioterror, well-documented bioterrorist attacks rarely occur with the notable exception of the 2001 anthrax attack [7]. Far more damage has been caused by lab accidents due to malpractice or faulty management in dual research on highly pathogenic organisms than has been caused by bioterrorism; these laboratory infections and leaks of various pathogens have included smallpox, anthrax, ebola, SARS coronavirus, and others [8,9]. Therefore, the public risk for dual-use research contains at least three components: biosafety, biosecurity, and prevention of bioterror. Prevention of bioterror mainly calls for action and counter-measures from the government. Researchers and the science community are concerned more with biosafety and biosecurity, which are the focus of the discussion of this editorial.

Biosafety focuses on actions to prevent harm to laboratory workers. Biosecurity focuses on preventive measures to reduce the risk of transmission outside of the lab. Bioterrorism or biological warfare is the deliberate use of an organism as a weapon. There is a consensus on strengthening biosafety measures at both national and global levels. The US government and health agencies as well as WHO have taken a lead and developed detailed strategies and technical protocols to improve biosafety. This topic has been discussed in detail by Du in this issue. Learning from the lessons of the SARS epidemic, the State Council of China has passed the "Regulation on the Bio-safety Management of Pathogenic Microbe Labs" [10] to strengthen biosafety oversight in the biomedical research laboratories in the country. In a follow-up measure, the Ministry of Health passed two related national regulations to strengthen laboratory certification and sample shipping for highly pathogenic microbes [11,12]. While research had been somewhat slowed down due to the extra regulation, there have been no severe lab accidents that have happened since the imposition of these regulations. We should always make public health security a priority when dealing with the balance between biosafety and research convenience.

In the USA, dual-use research debates focused on biosecurity and bioterrorism after September 11, 2001. The numerous national consultations resulted in the establishment of the National Science Advisory Board for Biosecurity (NSABB) in 2004 to provide oversight of US-sponsored dual-use research. The NSABB initially recommended not to publish the essential methods and data of the two

H5N1 papers in November 2011 but reversed its position under pressure from the WHO committee and the research community [13]. The two papers were published in mid-2012 with full results and detailed methodology. This shows how difficult and complicated efforts are to solve the dilemma; as Dr. Anthony Fauci of the National Institutes of Health pointed out: "There is no perfect solution. There is not even a good solution" [14].

Science research is a vital part of human advancement and should not be compromised. A Chinese saying goes, "We cannot give up eating for fear of choking." Nevertheless, we cannot underestimate the misuse of dual-use technology in the era of synthetic biology and globalization of the 21st century. We need to cooperate to reach consensus on such important issues as dual-use research representing legitimate concerns affecting global public health security. The scientific community as a whole should obtain the support of civil society and communicate with governments to balance the benefits of science with concerns for security for the good of mankind.

We have had valuable experiences in similar endeavors in the past, such as establishment of the International Atomic Energy Agency to mobilize global efforts towards the peaceful use of nuclear technology. WHO has had a historic role in the management of the global mandate to control the international spread of diseases. Recent examples of such roles by WHO include the establishment of a panel to oversee the final destruction of variola virus stocks and the rapid revision of International Health Regulations after the SARS epidemic [15]. In addition to strengthening oversight of dual-use research plans at the stage of funding by research institutions and review by national funding agencies, the international community should authorize WHO, through the World Health Assembly, to establish an international panel to review dual-use publications and to establish a database to archive the most sensitive, detailed research methods. Through the WHO database and review mechanism, dual-research papers could be published with minimal delays because the most sensitive methodological details can be withheld. These dual-use research methods could, however, be accessed by any legitimate researcher, research organization, or pharmaceutical company through WHO's review panel of scientists, ethicists, and public policy experts. Such an arrangement can both support the integrity of valid, ethical dual-use research and still manage risks to public security. This arrangement is a solution, if imperfect, (like the Brady Bill in US gun control) and would represent an important step forward in global science policy.

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