**The National Academies of Sciences, Engineering, Medicine**
**Committee on Dual-Use Research of Concern: Options for Limited Communication**
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I would like to thank the Committee for inviting me to provide my assessment of some of the challenges facing the current US Government (USG) approach to the communication of dual-use research of concern (DURC) as well as possible options for addressing this issue moving forward. I would like to begin by emphasizing that the goal of a DURC communication policy should not be to impede the free flow of the results of fundamental research. Instead, the goal should be to limit communication or dissemination only in those very *rare* instances when the risks of particular research results or methods clearly outweigh the potential benefits, posing significant risks to public health. I say "rare" instances based on the actual record to date. Since its creation more than a decade ago, the National Science Advisory Board for Biosecurity (NSABB) has been asked by the USG to review only six manuscripts to determine whether any limitations should be placed on the communication of the methods or results. (NIH Table, attached)

As far as is known, in the same timeframe, there have been only two instances in which journal editors have rejected manuscripts when concerns about the need to redact sensitive information could not be resolved with the authors. The first manuscript, which was published by the author elsewhere, described a process by which the smallpox virus could be made to evade diagnostic tests. The second manuscript focused on modeling anthrax attacks from the air and in buildings. [1] In two other instances, manuscripts were published by *the Journal of Infectious Diseases* after the authors agreed to remove the sequence data from articles on a new botulinum toxin serotype that was resistant to currently available antisera.[2]

That is not to say that there won't be more highly consequential manuscripts in the future, as science and technology continue to advance. But I believe that the number of manuscripts that raise significant risks will continue to be relatively small.

[1] Stuart Nightingale, "Dual-Use Research of Concern (DURC) Review at American Society for Microbiology Journals and its Effect on Other Organizations," *mBio* 6(5) (September-October 2015), http://mbio.asm.org/content/6/5/e01512-15.full

[2] David A. Relman, ""Inconvenient Truths" in the Pursuit of Scientific Knowledge and Public Health," *Journal of Infectious Diseases* 209 (2) (January 15, 2014): 170-172, http://jid.oxfordjournals.org/content/209/2/170.full

**Key challenges of the current USG approach to communication of DURC:**

Definitions: The current USG communication guidance is part of the broader USG policies for oversight by government agencies and by research institutions of DURC, which the USG defines as: "life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be *directly misapplied* [emphasis added] to pose a significant threat with broad potential consequences…" for humans, plants, animals, the environment or national security.[3] But significant threats can result from more than just individuals such as terrorists who could *directly misapply* life sciences research methods or results to deliberately cause harm. Even the most well-intentioned researchers can also make mistakes that can *unintentionally* pose significant threats to public health.

This is demonstrated by the first ever USG report on select agent incidents, which recently revealed that during 2015, there were 201 potential releases of select agents, including 199 incidents involving the potential exposure of laboratory workers. As a result, 908 laboratory workers were provided occupational health services, including medical assessments, diagnostic testing and, as necessary, prophylaxis.[4] Although none of these potential releases resulted in illness, death, or agent transmission outside of the laboratory, the numbers demonstrate that laboratory accidents with dangerous pathogens can and will happen.

Scope of application: The current USG policies for government and institutional oversight of DURC formally do not apply to: 1) classified research; 2) research that does not involve one of 15 specific select agents; or, 3) research at institutions that do not receive USG funding for life sciences research. Classified research by its nature is not published openly, so does not pose a risk of deliberate misuse. But the other two exempted categories could result in research methods or results that could be misused directly or deliberately and cause a significant threat. All three exempted categories of research also could lead to research methods or results the use of which could inadvertently or unintentionally pose a significant risk to public health.

Inconsistent requirements: The current USG DURC policy for government agencies and the policy for research institutions appear to have different requirements for when risk benefit assessments and the development of risk mitigation plans, including plans for communicating research responsibly, must be carried out. The 2012 policy outlining government oversight responsibility clearly applies not only to research that already was being funded at the time the policy was announced but also "proposed

[3] See, for example, *United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern* (Washington, D.C., March 2012), http://www.phe.gov/s3/dualuse/Documents/us-policy-durc-032812.pdf

[4] U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, and U.S. Department of Agriculture, Animal and Plant Health Inspection Service, "2015 Annual Report of the Select Agent Program," June 2016, http://www.selectagents.gov/resources/FSAP_Annual_Report_2015.pdf. A breach in containment involving a select agent is considered a "potential" exposure by the select agent program. To be "confirmed" requires demonstration: (1) of seroconversion or infection, and (2) that seroconversion or infection occurred at the entity.

research" that a government entity has not yet funded or conducted. The 2014 policy on institutional oversight only addresses research that already has been funded, in that the risk mitigation plan that an institution must develop to guide the conduct and communication of the research is to be submitted to the USG agency that is funding the research for approval. It is not clear how these inconsistent requirements are to be implemented by researchers and research institutions. It also is not clear that communication issues are formally being considered early enough in the research process under the 2014 policy for institutional oversight.

Knowledge and experience: The USG communication guidance is intended to be used by researchers, institutional review entities (IREs) and journal editors. But past surveys raise serious questions about whether these parties have the necessary expertise to identify, assess and mitigate communication risks. Between 2004 and 2008, British researchers carrying out interactive seminars with some 3,000 life scientists in Europe, North and South America, and Asia found that very few scientists had thought about the potential dual-use implications of their research or believed that developments in life sciences research might contribute to biological threats.[5] A 2011 survey of life sciences journal editors found that only 11 out of 127 editors serving some 292 life sciences journal had any experience with biosecurity review.[6]

Conflicts of interest: Under the current USG oversight policies, all of the parties expected to identify, assess, and mitigate risks from DURC have a vested interest in conducting and publishing the work: researchers want to pursue ground breaking research, which is critical to securing funding and to career advancement; members of IREs may not wish to complicate another investigator's research plans for fear the same could happen to them;[7] journal editors see possible publication restrictions as an assault on a basic tenet of science – the sharing and replication of results.

USG funding agencies, which the USG communication guidance identifies as a further "optional" source of advice on DURC communication issues, also have a conflict of interest, in that they may be reluctant to place limitations on research they have solicited or funded. Even the NSABB has a conflict of interest, as it is funded and staffed by NIH, which sponsors much of the relevant research.

Harmonization: The USG communication guidance is "optional," which means that individual researchers, IREs and journal editors are not required to follow a uniform approach. The absence of a harmonized approach means that research raising similar communication concerns at different institutions or different journals will be treated differently. Harmonization is important both on a national basis and internationally, as consequential life sciences research is taking place around the

[5] Simon Whitby and Malcolm Dando, "Effective Implementation of the BTWC: The Key Role of Awareness Raising and Education," Bradford Review Conference Paper No. 26, November 2010, http://www.brad.ac.uk/acad/sbtwc/briefing/RCP_26.pdf

[6] David Patrone, David Resnick, and Lisa Chin, "Biosecurity and the Review and Publication of Dual-Use Research of Concern," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice and Science* 10(3) (September 2012): 290-298.

[7] There is also a question as to whether all IREs will comply with DURC review requirements, given the dismal results reported in a past survey of IBC compliance with the NIH Guidelines. See, Sunshine Project, "Mandate for Failure: The State of Institutional Biosafety Committees in an Age of Biological Weapons Research," October 2004.

world, with a corresponding risk of both deliberate misuse and inadvertent harm from the misapplication of sensitive research methods or results that have been disseminated.

Journal focus: The current USG communication guidance focuses heavily on the final stage in the research process – submission of a paper to a journal. But researchers have multiple opportunities throughout the research process for communicating DURC – when a proposal is being drafted, when it is submitted for funding, during the research phase, and when a paper describing methods and results is submitted to a journal. Moreover, over the life of a project, DURC can be conveyed in conversations, emails or other informal communications; in presentations or abstracts at scientific meetings; in postings on online sites; or in formal peer-reviewed journals.

Competing priorities: Two of the six manuscripts previously considered by the NSABB described the creation of modified H5N1 viruses capable of respiratory transmission between mammals. These manuscripts, one originating in a Dutch lab and the other in an American one, were also the focus of an international meeting convened by the World Health Organization (WHO). In their deliberations, both the NSABB and WHO were concerned that limiting access to the H5N1 research results could jeopardize implementation of the 2011 Pandemic Influenza Preparedness Framework, under which countries had agreed after years of debate to share samples of influenza viruses with human pandemic potential for research purposes.

**Options for Limited Communication**

Funding conditions: Some former members of the NSABB have argued for focusing on communication issues much earlier, from inception of the research plans, instead of relying so heavily on journals to evaluate the risks of publication.[8] The USG could clarify its policy for institutional oversight of DURC to explicitly require the inclusion of risk benefit assessments and risk mitigation measures such as communication plans in proposed funding submissions to USG agencies. Federal funders could also include provisions for prepublication review of manuscripts in their funding arrangements with researchers and research institutions although, as discussed below, this likely would result in the research being considered not "fundamental research" and thus subject to US export control requirements.

Journal editors' policy: Since the 2003 statement by journal editors and researchers, a few journal groups (American Society for Microbiology, Nature Publishing Group, NRC Research Press) have developed policies for reviewing dual use research.[9] But according to the 2011 survey cited earlier, only 11 out of 127 journal editors reported that their journal had a written policy covering the review and publication of DURC. Moreover, 9 in 10 journals without a dual-use policy reported they had no plans to develop one in the future.[10]

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[8] Arturo Casadevall, Terence S. Dermody, Michael J. Imperiale, Rozanne M. Sandri-Goldin, and Thomas Shenk, "Dual Use Research of Concern (DURC) Review at American Society for Microbiology Journals,"*mBio* 6(4) (July-August 2015), http://mbio.asm.org/content/6/4/e01236-15.full

[9] Patrone, Op. Cit.

[10] Ibid.

At the same time, nearly 75% of the respondents agreed that they had a responsibility to consider biosecurity threats when reviewing manuscripts. Some one-third also agreed that some sort of "censorship" might be required for national security reasons.[11] These views are consistent with the position of the Council of Science Editors, which in a 2012 White Paper stated that editors have a responsibility to identify dual-use research and to develop guidelines and procedures for evaluating "the possible risks of communicating information with dual use potential."[12]

One option that has been proposed for doing this is for scientists to work with international publishing organizations to develop a uniform set of dual-use policies for use by all life sciences journals.[13] Editors could agree not to publish research that has bypassed national or international risk benefit assessment and risk mitigation requirements or that has not adhered to previously agreed communication plans. This would reinforce other efforts to prevent sensitive research from being disseminated prior to submission to a journal. Editors could also agree to seek voluntary prepublication redaction of problematic information, as was done by the *Journal of Infectious Diseases* in 2013. This could help prevent different journals from treating sensitive manuscripts differently.

Export control policy: In the U.S., the 15 select agents listed in the USG policies for oversight of DURC are subject to the Commerce Department's Export Administration Regulations (EAR). However, *information* related to these agents is exempt from the EAR's export control licensing requirements if, among other things, the information results from "fundamental research." But in order to meet the definition of "fundamental research," the research results and methods must be published and broadly shared among scientists. Restricting access to or redacting scientific information could result in the requirement for an export control license before such information can be shared with non-US scientists in the US or other scientists outside the US. Some EU member states, such as Germany and the UK, make a similar distinction between what is called "basic research," which is publicly available, and research whose dissemination is restricted.[14]

Although researchers, institutions and journals are likely to oppose having redacted information subject to export controls, it is important to point out that requiring an export license does not mean that the redacted information will not be approved for transfer. Rather, it provides an orderly, legally-based process for assessing whether, in the very rare instance in which DURC information is redacted because it could threaten public health, that information should be shared and, if so, with whom. An interesting precedent regarding export controls is the Dutch H5N1 paper, which was barred by the Dutch government from being sent to a U.S. journal until the primary author applied for and received an export license.

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[11] Ibid.

[12] Council of Science Editors, "CSE's White Paper on Promoting Integrity in Scientific Journal Publications, 2012 Update," 7-8, http://www.councilscienceeditors.org/wp-content/uploads/entire_whitepaper.pdf

[13] David B. Resnick, "Can Scientists Regulate the Publication of Dual Use Research?" *Studies in Ethics, Law and Technology* 4(1) (May 2010), http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3134283/pdf/nihms-247995.pdf

[14] Christos Charatsis, "Setting the Publication of 'Dual-Use Research' Under the Export Authorization Process: The H5N1 Case," *Strategic Trade Review* 1(1) (Autumn 2015), http://www.str.ulg.ac.be/wp-content/uploads/2016/01/5.-Setting-the-Publication-of-Dual-Use-Research-Under-the-Export-Authorisation-Process-The-H5N1-Case.pdf

National advisory body: In 2014, following the H5N1 controversy, two former members of the NSABB as well as the chair of the ASM Journals Board issued a public call for a more organized process for managing DURC, including the dissemination of research results. They argued that because institutional review bodies and journal editors may not have sufficient knowledge or experience to determine whether research meets the definition of DURC or whether limitations should be placed on its dissemination, a national advisory board, similar to the RAC, should be created to assist journal editors and others in this process.[15] Another former NSABB member has called for an independent Presidential Commission with a diversity of scientific and other expertise and the authority to convene itself and set its own agenda, separate from any federal department of agency.[16]

International guidance: At the NSABB's 2008 international roundtable, journal editors discussed the need for an international consensus on how to identify and manage DURC, including its publication. They also discussed the problems facing journals that do not have access to biosecurity experts or that have limited resources for reviewing manuscripts. Participants agreed that an international advisory board could be an important resource for editors to turn to for help in assessing high risk manuscripts. Other resources that could be made available on-line were identified, such as lists of relevant experts, information on best practices, and a database on the outcome of various DURC cases.[17] Participants in WHO's consultations on the H5N1 papers also identified the lack of global guidance or a global framework for identifying and managing the risks from DURC as a critical gap, noting that WHO could play a vital role in convening a forum where key stakeholders, governments and international organizations could develop a globally harmonized approach. [18] This could include an agreed definition of DURC that acknowledges both intentional and unintentional threats, and that captures all relevant research, irrespective of funding source or classification.

International review body: In the aftermath of the H5N1 controversy, two former members of the NSABB called for an international group of scientific experts, "free of conflicts of interest," as well as security experts to make decisions on the conduct of DURC.[19] Bruce Alberts, the then editor-in-chief of *Science*, went even further, calling for a "comprehensive international system" responsible for assessing and handling DURC, including providing access on a need to know basis to information that cannot be

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[15] Arturo Casadevall, Terence S. Dermody, Michael J. Imperiale, Rozanne M. Sandri-Goldin, and Thomas Shenk, "On the Need for a National Board to Assess Dual Use Research of Concern," *Journal of Virology* 88(12) (June 2014): 6535-6537, http://jvi.asm.org/content/early/2014/03/27/JVI.00875-14.short

[16] Susan A. Ehrlich, "H5N1: a cautionary tale," *Frontiers in Public Health* 2(117) (August 12, 2014), http://journal.frontiersin.org/article/10.3389/fpubh.2014.00117/full

[17] National Science Advisory Board for Biosecurity, 3rd International Roundtable, "Sustaining Progress in the Life Sciences: Strategies for Managing Dual Use Research of Concern," November 5-6, 2008, http://osp.od.nih.gov/sites/default/files/Report%20from%203rd%20Rt_Final_18%20May%202009.pdf

[18] World Health Organization, "Report of the WHO Informal Consultations on Dual Use Research of Concern," Geneva, Switzerland, February 26-27, 2013, http://www.who.int/csr/durc/durc_feb2013_full_mtg_report.pdf

[19] Michael T. Osterholm and David A. Relman, "Creating a Mammilian-Transmissible A/H5N1 Influenza Virus: Social Contracts, Prudence, and Alternative Perspectives," *Journal of Infectious Diseases* 205(11) (June 2012): 1636-1638, http://jid.oxfordjournals.org/content/205/11/1636.long

communicated openly.[20] Such an approach would avoid the perception that the USG was trying to impose its own DURC oversight policies on other countries, or that it was seeking to deny other countries access to research information. Lessons could be learned about how an international review body might operate from the US and other governments, who have experience controlling access to sensitive information, and from the US, UK, Canada, Denmark and Israel, who have developed processes for vetting researchers who wish to have access to dangerous pathogens.

In closing, I would like to emphasize that no single option described above addresses the full range of challenges facing current USG policies on the communication of DURC. As a general rule, those toward the end of the list have the greatest potential to ameliorate the challenges discussed in this paper. They also are the most difficult to implement, in that they would require serious and sustained efforts to engage a broad range of actors, both on a national and international basis, to work through many complex technical, legal, political and practical issues. But because the conduct of DURC and the communication of DURC are inextricable linked, the end result would be not only a more effective approach to the issue that is the focus of this committee but, also, a much more effective DURC oversight policy here in the US and globally.

[20] Bruce Alberts, "H5N1," Science 336(6088) (June22, 2012): 152, http://science.sciencemag.org/content/336/6088/1521

# Manuscripts reviewed by NSABB

| Manuscript received by NSABB | Date received by NSABB | NSABB conclusions/recommendations | Outcome |
|---|---|---|---|
| Tumpy [sic] et. al., *Characterization of the reconstructed 1918 Spanish influenza pandemic virus.*<br><br>Taubenberger, et. al., *Characterization of the 1918 influenza virus polymerase genes* | September 2005 | • The papers should be published<br>• The authors should add language to elaborate on the public health benefits of the research<br>• The USG should examine the issue of biocontainment practices for 1918 viruses<br>• A communication plan, including an editorial to accompany the publications, should be developed | The manuscripts were published in *Science* and *Nature* with an accompanying editorial |
| Esposito, et. al. *Genome Sequence Diversity and Clues to the Evolution of Variola virus* | November 2005 | • Communicate with addition of appropriate contextual information (e.g., biosafety measures, public health benefits, rationale for decision to communicate). | The manuscript was published in *Science* |
| Garufi, et. al. *Sortase-conjugation generates a capsule vaccine that protects guinea pigs against Bacillus anthracis* | November 2011 | • As written, the findings described in the manuscript may indeed meet the criterion for dual use research of concern. However, NSABB noted significant scientific deficiencies with the methodology and with the interpretation of the results of the research, and concluded that if the scientific deficiencies were appropriately addressed, the manuscript would likely not raise significant dual use concerns.<br>• The Board noted potential for the manuscript as written to be sensationalized and raise public concerns.<br>• NSABB provided additional observations and suggestions for possible revisions to the manuscript, | The manuscript was published in *Vaccine* |

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| | | intended to help mitigate the potential for misunderstanding and sensationalism. | |
| Imai, M., et al., *Haemagglutinin mutations that confer human-type receptor recognition and support respiratory droplet transmission of H5N1 influenza A virus in ferrets*<br><br>Herfst, S., et al., Aerosol transmission of avian influenza A/H5N1 virus | November 2011 | November 2011, after NSABB's review of originally-submitted manuscripts, the Board recommended:<br><br>• Neither manuscript be published with complete data and experimental details.<br>• The conclusions of the manuscripts be published but without experimental details and mutation data that would enable replication of the experiments.<br>• Text be added describing: 1) the goals of the research, 2) the potential benefits to public health (including informing surveillance efforts, pandemic preparedness activities, and countermeasure development and stockpiling efforts), 3) the risk assessments performed prior to research initiation, 4) the ongoing biosafety oversight, containment, and occupational health measures, 5) biosecurity practices and adherence to select agent regulation, and 6) that addressing biosafety, biosecurity, and occupational health is part of the responsible conduct of all life sciences research.<br>• The authors to submit a special communication/commentary letter to the journals regarding the dual use research issue.<br><br>March 2012, after review of revised manuscripts, NSABB recommended:<br><br>• The revised Kawaoka manuscript should be communicated in full.<br>• The data, methods, and conclusions presented in the revised Fouchier manuscript should be communicated, but not as currently written.<br>• The U.S. Government should continue | Revised manuscripts were published and *Nature* and *Science* |

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| | | to develop national, and participate in the development of international, policies for the oversight and communication of dual use research of concern.<br>• The U.S. Government should expeditiously develop a mechanism to provide controlled access to sensitive scientific information. | |

Source: NIH Office of Science Policy, 7-1-2016