

## DUAL USE RESEARCH POLICY IMPLEMENTATION

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### I. INTRODUCTION

On February 21, 2013, the U.S. Government released two proposed policy documents: the U.S. Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (Oversight Policy)<sup>1</sup> and the Framework for Guiding U.S. Department of Health and Human Services Funding Decisions about Research Proposals with the Potential for Generating Highly Pathogenic Avian Influenza H5N1 Viruses that are Transmissible among Mammals by Respiratory Droplets (H5N1 Funding Framework Policy).<sup>2</sup> These documents were published almost a year after the U.S. Government Policy for Oversight of Life Sciences Dual Use Research of Concern was released on March 29, 2012 (DURC Policy) and were meant to provide guidance for research institutions on implementation of the DURC Policy.<sup>3</sup> In the proposed policies, the U.S. Government is not prescriptive regarding entities within research institutions that should be responsible for implementation of this oversight. For many, however, the logical choice is the already overextended Institutional Biosafety Committees (IBCs),<sup>4</sup> in part because IBCs are federally mandated to provide review for

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1. United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern, 78 Fed. Reg. 12369-70 (proposed Feb. 22, 2013).

2. U.S. DEP'T OF HEALTH & HUMAN SERVS., FRAMEWORK FOR GUIDING FUNDING DECISIONS ABOUT RESEARCH PROPOSALS WITH THE POTENTIAL FOR GENERATING HIGHLY PATHOGENIC AVIAN INFLUENZA H5N1 VIRUSES THAT ARE TRANSMISSIBLE AMONG MAMMALS BY RESPIRATORY DROPLETS (2013), <http://www.phe.gov/s3/dualuse/Documents/funding-hpai-h5n1.pdf>.

3. United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern, 78 Fed. Reg. at 12370.

4. Letter from David A. Relman, M.D., FIDSA President, Infectious Diseases S. of Am., to Franca R. Jones, Assistant Director, Office of Sci. & Tech. Policy 2 (Apr. 23, 2013) (on file with authors).

research involving “recombinant or synthetic nucleic acid molecules,”<sup>5</sup> and at least some of this research will involve such agents. Further, most institutions have tasked IBCs with oversight of all research-related activities with potential biohazards beyond their original mandate.<sup>6</sup> Review at the institutional level of research with dual use potential may also involve export control compliance.

Consistently, comments on the proposed policies expressed anxiety over logistics, costs, and compliance, particularly when it came to restricting the flow of scientific information.<sup>7</sup> As for compliance, the burden placed on Principal Investigators (PIs) to determine and remain vigilant throughout the research cycle about the potential for dual use of their research seemed unrealistic since most PIs were never trained or conditioned to make such determinations, and this emphasis on PIs raised concerns about how blame would be placed if, in fact, an incident happened.<sup>8</sup> There were also questions as to whether the Oversight Policy applied to only whole versions of the listed organisms or to subcomponents as well,<sup>9</sup> and whether it should apply to other organisms or other types of life sciences research.<sup>10</sup> Concerns were also expressed regarding how resource-intensive the institutional role would become, and whether the DURC Policy should be expanded into a broader class of experiments or agents.<sup>11</sup> Since organisms thus far listed in the DURC Policy are all Select Agents,<sup>12</sup> the additional scrutiny might be unnecessary to begin with.<sup>13</sup> Concerns were expressed regarding how institutions would handle requests for actual assessment documents made

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5. NAT’L INST. OF HEALTH, NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT OR SYNTHETIC NUCLEIC ACID MOLECULES (2013).

6. See Letter from David Relman to Franca Jones, *supra* note 4, at 2.

7. Letter from Judith S. Bond, President, Fed’n of Am. Soc’ys for Experimental Biology, to Franca R. Jones, Assistant Director, Office of Sci. & Tech. Policy (Apr. 12, 2013) (on file with authors).

8. Letter from Samuel Evans, Visiting Professor & Academic Coordinator, Univ. of Cal., Berkeley, to Franca R. Jones, Assistant Director, Office of Sci. & Tech. Policy (Apr. 23, 2013) (on file with authors).

9. Letter from Alan I. Leshner, Chief Executive Officer & Executive Publisher, Am. Ass’n for the Advancement of Sci., to Franca R. Jones, Assistant Director, Office of Sci. & Tech. Policy (Apr. 17, 2013) (on file with authors).

10. Letter from Samuel Evans to Franca Jones, *supra* note 8. See also Letter from David Relman to Franca Jones, *supra* note 4, at 2 (recommending a focus not on a specific set of pathogens but to focus “oversight on the seven identified categories of experiments”); Carrie D. Wolinetz, *Implementing the New U.S. Dual-Use Policy*, 336 SCI. 1525, 1526 (2012).

11. Letter from Hunter R. Rawlings III, President, Association of Am. Univs. and Anthony P. DeCrappeo, President, Council on Gov’t Relations, to Franca R. Jones, Assistant Director, Office of Sci. & Tech. Policy 1 (Apr. 23, 2013) (on file with authors).

12. 42 C.F.R. § 73.3 (2013); 7 C.F.R. § 331.3 (2013); 9 C.F.R. § 121.3 (2013).

13. David Malakoff & Martin Enserink, *New U.S. Rules Increase Oversight of H5N1 Studies, Other Risky Science*, 339 SCI. 1025, 1025 (2013); Wolinetz, *supra* note 10, at 1526.

under the Freedom of Information Act (FOIA) and sunshine laws in certain states.<sup>14</sup> Finally, questions arose regarding the transparency of funding decisions and whether there would be an appeals process.<sup>15</sup> It was also suggested that there was a need for an appeals process at the institutional level regarding classification of research prior to submission to the funding agency.<sup>16</sup> In conclusion, additional guidance, clarification, and training materials all seem critical in order to move forward.

The H5N1 Funding Framework Policy requires additional review at the funding agency level for proposals anticipating to generate Highly Pathogenic Avian Influenza (HPAI) H5N1 viruses transmissible among mammals by respiratory droplets, which could add to the already protracted review process by the National Institute of Health (NIH) and ultimately discourage researchers from attempting certain experiments that could be beneficial from a public health point of view.<sup>17</sup>

Despite these widespread concerns over the new and proposed policies, certain advocates for stricter biosecurity oversight feel that the new requirements are still not stringent enough.<sup>18</sup>

## II. HISTORY OF OVERSIGHT OF DUAL USE RESEARCH

The concept of dual use research is not new, and in the past, the scientific community has demonstrated its ability to self-regulate when it came to responsible development of new technologies. After the Asilomar Conference in 1975, scientists designed and followed a set of guidelines for work with recombinant DNA, then a novel technology of unexplored potential.<sup>19</sup> This led to the publication of the NIH Guidelines for Research Involving Recombinant DNA Molecules.<sup>20</sup> Later, the Centers for Disease Control and Prevention (CDC) and NIH collaborated on the Biosafety in Microbiological and Biomedical Laboratories (BMBL).<sup>21</sup> These two documents have been highly successful in protecting individual

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14. Letter from Alan I. Leshner to Franca Jones, *supra* note 9.

15. *Id.*; Letter from Hunter Rawlings and Anthony P. DeCrappeo to Franca Jones, *supra* note 11, at 2-3.

16. Letter from Hunter Rawlings and Anthony P. DeCrappeo to Franca Jones, *supra* note 11, at 4.

17. See Letter from David Relman to Franca Jones, *supra* note 4, at 1; Wolinetz, *supra* note 10, at 1526.

18. Malakoff & Enserink, *supra* note 13, at 1025.

19. COMM. ON RESEARCH STANDARDS & PRACTICES TO PREVENT THE DESTRUCTIVE APPLICATION OF BIOTECHNOLOGY, NAT'L RESEARCH COUNCIL, BIOTECHNOLOGY RESEARCH IN AN AGE OF TERRORISM 30 (2004) [hereinafter FINK REPORT].

20. NAT'L INST. OF HEALTH, *supra*, note 5.

21. U.S. DEP'T OF HEALTH & HUMAN SERVS., BIOSAFETY IN MICROBIOLOGICAL AND BIOMEDICAL LABORATORIES 3-4 (5th ed. 2009).

biotechnology workers and the public. However, in the wake of the September 11, 2001 attacks, letters containing anthrax bacteria were mailed to several news media offices and to two U.S. Senators, killing five people and sickening seventeen others.<sup>22</sup> Less than one year later, two pieces of legislation were signed into law: The Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of October 2001, (Patriot Act)<sup>23</sup> and The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Bioterrorism Response Act).<sup>24</sup> These laws regulated who, for what purpose, and in what circumstances individuals could possess and transfer any biological agent, specifically addressing a list of restricted agents known as Select Agents, a term coined at the time the Antiterrorism and Effective Death Penalty Act of 1996 was enacted.<sup>25</sup>

Subsequent to the 2001 and 2002 legislations, the Department of Health and Human Services (HHS) and the U.S. Department of Agriculture (USDA) developed the Select Agents Regulations.<sup>26</sup> Another consequence of these events was the infusion of billions of dollars into infectious disease research, which, perhaps ironically, encouraged and increased the study of Select Agents by researchers.<sup>27</sup>

While they provided the official impetus for these new legislations, the events of September 2001 alone did not raise awareness of the potential for misuse of biotechnology. Although bioweapons had been used since antiquity, only earlier that year, a pest control experiment conducted by an Australian researcher reminded the scientific community and the public of the inherent dangers of life sciences research.<sup>28</sup> In an attempt to render

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22. JEANNE GUILLEMIN, *AMERICAN ANTHRAX: FEAR, CRIME, AND THE INVESTIGATION OF THE NATION'S DEADLIEST BIOTERROR ATTACK*, xx-xxi (Henry Holt & Co. 2011).

23. Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism (Patriot Act) Act of 2001, Pub. L. No. 107-56, 115 Stat. 272 (2001) (codified in various sections of the United States Code).

24. Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Pub. L. No. 107-188, 116 Stat. 594 (2002).

25. Antiterrorism & Effective Death Penalty Act of 1996, Pub. L. No. 104-132, § 511, 110 Stat. 1214, 1284. See also *About Us*, NAT'L SELECT AGENT REGISTRY, ANIMAL & PLANT HEALTH INSPECTION SERV. & CTRS. FOR DISEASE CONTROL & PREVENTION, <http://www.selectagents.gov/AboutUS.html> (last updated June 11, 2013).

26. 7 C.F.R. pt. 331 (2012); 9 C.F.R. pt. 121 (2012); 42 C.F.R. pt. 73 (2012).

27. Jerry Jaax, *Administrative Issues Related to Infectious Disease Research in the Age of Bioterrorism*, 46 *INST. FOR LABORATORY ANIMAL RES. J.* 8, 8-9 (2005). See Public Health Security & Bioterrorism Preparedness & Response Act of 2002, Pub. L. No. 107-188, § 125, 116 Stat. 614.

28. See Ronald J. Jackson et al., *Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox*, 75 *J. OF VIROLOGY* 1205 (2001).

female mice sterile by having them mount an immune response against their own eggs, researchers used the mousepox virus as a delivery system for the self-antigens.<sup>29</sup> Unfortunately, the recombinant virus, which also carried immune-modulatory genes, depressed rather than stimulated the immune response of the mice to the mousepox virus, which subsequently died, even if they had been vaccinated and even if the mice used were of a mousepox-resistant.<sup>30</sup> This raised concerns that if similar modifications were made to the smallpox virus, the vaccine could become ineffective.<sup>31</sup>

In 2002, Dr. Eckard Wimmer, a German American virologist, synthesized the full genome of the poliovirus and used it to produce infectious polioviruses *de novo*, raising concerns that individuals who may not have otherwise access to them could use similar techniques to produce more dangerous organisms.<sup>32</sup> Finally, also in 2002, it was found that genetic manipulations of the vaccinia virus, normally relatively harmless to humans, but a close relative of the virus causing smallpox, could perhaps render vaccinia as virulent as smallpox.<sup>33</sup> Due to these and similar instances, the research community became engaged in a debate on how to deal with life sciences research with potential for dual use.<sup>34</sup>

In 2004, the National Research Council's Committee on Research Standards & Practices to Prevent the Destructive Application of Biotechnology published a report entitled, *Biotechnology Research in An Age of Terrorism: Confronting The "Dual Use" Dilemma* (Fink Report).<sup>35</sup> The recommendations of the Fink Report included an enhanced oversight system, initially based on current legislation, for seven types of "Experiments of Concern," which would be those that:

- (1) Would demonstrate how to render a vaccine ineffective.
- (2) Would confer resistance to antibiotics or antivirals.
- (3) Would enhance a pathogen's virulence or render a non-pathogen virulent.
- (4) Would increase a pathogen's transmissibility.
- (5) Would alter a pathogen's host range.

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29. *See id.*

30. *Id.* at 1208.

31. *See id.*

32. Eckard Wimmer, *The Test-tube Synthesis of a Chemical Called Poliovirus*, 7 EUR. MOLECULAR BIOLOGY ORG. REP. (SPECIAL ISSUE) S3, S8 (2006).

33. Ariella M. Rosengard et al., *Variola Virus Immune Evasion Design: Expression of a Highly Efficient Inhibitor of Human Complement*, 99 PROC. OF THE NAT'L. ACAD. OF SCI. 8808, 8808 (2002).

34. Wolinetz, *supra* note 10, at 1525.

35. *See* FINK REPORT, *supra* note 19.

(6) Would enable evasion of diagnostic tests.

(7) Would enable weaponization of pathogens and toxins.<sup>36</sup>

At the publication stage, this oversight would rely on self-governance of scientists and scientific journals.<sup>37</sup> Other recommendations focused on the need for education of the scientific community about the potential for the dual use of certain research endeavors and its moral responsibility to help mitigate these risks.<sup>38</sup> It also advocated for better communication channels internationally, as well as between the scientific community and law enforcement agencies.<sup>39</sup> Most significantly, the Fink Report advised the creation of the National Science Advisory Board for Biodefense (NSAAB) by HHS to provide guidance and leadership for oversight of research with dual use potential.<sup>40</sup>

As suggested by the Fink Report, NSABB was soon established and had its first meeting in 2005.<sup>41</sup> Its current role is to advise the U.S. Government on how to minimize the risk from:

[R]esearch that, based on current understanding, can be reasonably anticipated to provide knowledge, products, or technologies that could be directly misapplied by others to pose a threat to public health and safety, agricultural crops and other plants, animals, the environment or material, defined as 'Dual Research of Concern' or 'DURC.'<sup>42</sup>

The threshold for being DURC takes into account scope (breadth of consequences) and immediacy (whether results can be directly misapplied) of potential threat. NSABB is staffed with subject matter experts from scientific and security communities — *ex officio* government representatives.<sup>43</sup> NSABB has several working groups including: international engagement, synthetic genomics, culture of responsibility/personnel reliability, code of conduct, communications, dual use criteria, and an ad hoc H5N1 working group.<sup>44</sup> These groups have helped publish background and educational material on the Office of Biotechnology's website that is aligned with the mission of NSABB.

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36. *Id.* at 113, 114-15.

37. *Id.* at 8.

38. *Id.* at 113-15.

39. *Id.* at 111.

40. FINK REPORT, *supra* note 19, at 123.

41. Dana A. Shea, CONG. RESEARCH SERV., RL33342 OVERSIGHT OF DUAL-USE BIOLOGICAL RESEARCH: THE NATIONAL SCIENCE ADVISORY BOARD FOR BIOSECURITY 2, 4 (2007).

42. *National Science Advisory Board for Biosecurity – Frequently Asked Questions*, NAT'L. INSTS. OF HEALTH, OFF. OF BIOTECH. ACTIVITIES, [http://oba.od.nih.gov/oba/faqs/NSABB\\_FAQs\\_NEW\\_FINAL.pdf](http://oba.od.nih.gov/oba/faqs/NSABB_FAQs_NEW_FINAL.pdf) (last viewed Oct. 16, 2013).

43. Shea, *supra* note 41, at 3.

44. *Id.* at 3-4.

Before NSABB had its first meeting, a controversial manuscript was published describing how a minute quantity of botulinum toxin dispersed at one dairy plant could kill 400,000 people.<sup>45</sup> With NSABB not yet operational, the author of the manuscript and the Proceedings of the National Academy of Sciences (PNAS) resisted pressure from HHS not to publish it.<sup>46</sup> PNAS's rationale was that the public should be aware of the danger and that free and open scientific inquiry ultimately makes the public safer.<sup>47</sup> The author later stated that he would have welcomed the advice of NSABB had it been provided at that time.<sup>48</sup>

In September of 2005, there was a closed NSABB session to consider the publication of manuscripts about the reconstructed 1918 influenza virus,<sup>49</sup> which was subsequently added to the list of Select Agents.<sup>50</sup> The 1918 pandemic flu caused up to 50 million deaths worldwide, but since viruses of the same sub-type had been in circulation since, it was believed that the vast majority of the world population would have sufficient cross-immunity to fight the 1918 virus.<sup>51</sup> Of note, this belief was challenged during the time of the A(H1N1)pdm09 virus (swine flu), although it was later demonstrated that the vaccine against swine flu would likely be protective against the 1918 pandemic flu.<sup>52</sup> After considering the significance of the information to the scientific community and public health, the risk of the information being misused, the benefits of communicating the information, and the consequences of restricting the information so that the public would not have access to it, NSABB recommended the publication of the manuscripts with some modifications that would emphasize the public health benefits of the research and the precautions that were taken during the

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45. See Lawrence M. Wein & Yifan Liu, *Analyzing a Bioterror Attack on the Food Supply: The Case of Botulinum Toxin in Milk*, 102 PROC. OF THE NAT'L. ACAD. OF SCI. 9984, 9985, 9987 (2005) (discussing the controversial manuscript by authors Lawrence Wein & Yifan Liu).

46. Bruce Alberts, *Modeling Attacks on the Food Supply*, 102 PROC. OF THE NAT'L. ACAD. OF SCI. 9937, 9937 (2005) (editorial from the President of the National Academy of Sciences).

47. Meeting Minutes, Nat'l Sci. Advisory Bd. for Biosecurity, Summary of Second NSABB Meeting 15 (Nov. 21, 2005) (on file with the Office of Biotechnology Activities).

48. *Id.*

49. *Id.*

50. 42 C.F.R. § 73.3(b) (2012).

51. Letter from Michael T. Osterholm, Dir., Minn. Ctr. of Excellence for Influenza Research and Surveillance to Amy P. Patterson, Assoc. Dir. for Sci. Policy, Nat'l. Insts. of Health 6 (Apr. 12, 2012).

52. Rafael A. Medina et al., *Pandemic 2009 H1N1 Vaccine Protects Against 1918 Spanish Influenza Virus*, NATURE COMM'NS, June 15, 2010, at 1, 2, <http://www.nature.com/ncomms/journal/v1/n3/full/ncomms1026.html>.

research to protect the researchers and the public.<sup>53</sup> This example set an informal precedent for the deliberations that took place regarding the publication of two manuscripts discussing the making of mammalian-aerosol transmissible HPAI viruses of the H5N1-subtype six years later, which ultimately triggered the enactment of the U.S. Government policies discussed herein.<sup>54</sup> Of note, HPAI had never been known to be transmissible between mammals, except inefficiently in a close contact ferret model.<sup>55</sup> The studies led by Dr. Ron Fouchier, Ph.D., at Erasmus Medical Center in Rotterdam, Netherlands, and Dr. Yoshihiro Kawaoka, Ph.D., at the University of Wisconsin-Madison, were first presented at the European Scientific Working Group on Influenza in Malta in September 2011.<sup>56</sup> Not surprisingly, the research attracted a lot of attention, and in November 2011, NSABB met to debate whether two resulting manuscripts submitted to *Science* and *Nature* should be published.<sup>57</sup> “After deliberating amongst themselves and talking with both papers’ lead authors, the 23 NSABB members voted unanimously to recommend the two journals redact key parts of the manuscripts, allowing the sensitive portions to be made available to researchers only on a need-to-know basis.”<sup>58</sup> “Although under no legal obligation to do so, the journals and researchers agreed....<sup>59</sup>” However, “*Science* stipulated that the U.S. government would need to provide a ‘written, transparent plan’ for making the redacted information available for ‘all those responsible scientists who request it’ as part of their work.”<sup>60</sup>

By December 2011, the controversy became public knowledge, and a heated debate ensued “across the Internet, in the media, and at conferences” about the appropriateness and communication of the

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53. Meeting Minutes, Nat’l Sci. Advisory Bd. for Biosecurity, Summary of Second NSABB Meeting 15 (Nov. 21, 2005) (on file with the Office of Biotechnology Activities).

54. See, e.g., Michael T. Osterholm & David A. Relman, *Creating a Mammalian-Transmissible A/H5N1 Influenza Virus: Social Contracts, Prudence, and Alternative Perspectives*, 205 J. INFECT. DIS. 1636, 1636 (2012).

55. Amy P. Patterson et al., *A Framework for Decisions about Research with HPAI H5N1 Viruses*, 339 SCI. 1036, 1036 (2013); Hui-Ling Yen et al., *Inefficient Transmission of H5N1 Influenza Viruses in a Ferret Contact Model*, 81 J. VIROLOGY 6890, 6897 (2007).

56. INFLUENZA TIMES, European Scientific Working Group on Influenza (ESWI), Malta, Sep. 11-14, 2011, [http://labs.fhcrc.org/cbf/Papers/H5N1\\_docs/FEIC\\_news\\_from\\_Malta.pdf](http://labs.fhcrc.org/cbf/Papers/H5N1_docs/FEIC_news_from_Malta.pdf).

57. See Press Release, Nat’l Institutes of Health, NSABB Review of H5N1 Research (Dec. 20, 2011) (on file with authors).

58. Wendee Holtcamp, *One Study, Two Paths The Challenge of Dual-Use Research*, 120 ENVTL. HEALTH PERSP. A239, A240 (2012).

59. *Id.*

60. *Id.* at A240 (quoting Statement by Dr. Bruce Alberts, Editor-in-Chief, Sci., Regarding Publication of H5N1 Avian Influenza Research, (Dec. 20, 2011), [http://www.aaas.org/news/releases/2011/media/1220herfst\\_statement.pdf](http://www.aaas.org/news/releases/2011/media/1220herfst_statement.pdf)).

researchers' work, the risks associated with the work, potential partial or complete censorship of scientific publications, and DURC in general.<sup>61</sup> After NSABB's decision, "39 influenza researchers, including Dr. Fouchier and Dr. Kawaoka, voluntarily agreed to a 60-day moratorium on H5N1 research," which was later informally extended to a year.<sup>62</sup> "With the research moratorium in place and the papers delayed, scientists and public health officials convened at several international meetings to debate the dilemma."<sup>63</sup> Then, "a February 2012 meeting convened at the [World Health Organization] WHO headquarters in Geneva culminated in a letter signed by 22 scientists and public-health officials from 11 nations calling for full publication of the H5N1 papers — in contrast to NSABB's recommendation" — after biosecurity and communications issues were addressed.<sup>64</sup> Subsequently, the U.S. Government had NSABB reconsider their original decision based on the WHO consultation, which yielded more details about the two studies.<sup>65</sup>

Dr. Kawaoka<sup>66</sup> had not used a full H5N1 virus. He had used one gene (coding for the hemagglutinin (HA) protein — a surface receptor) from the HPAI H5N1 virus out of eight.<sup>67</sup> The other seven genes were from the pandemic 2009 virus, a virus already adapted to humans.<sup>68</sup> Out of four mutations generated in the H5N1 HA gene, three of these were generated through *in vitro*, and one of these was generated through live infection in ferrets, a technique called passaging that was first used by Louis Pasteur in the nineteenth century.<sup>69</sup> Two of these mutations affected receptor specificity that is critical for transmissibility amongst humans, one affected replication in the nose, which is also critical for transmissibility by aerosol, and another affected fusion of viral particles to human cells.<sup>70</sup> The resulting virus

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61. *Id.*

62. *Id.*; Patterson et al., *supra* note 55, at 1036.

63. Holtcamp, *supra* note 58, at A240.

64. *Id.*; WORLD HEALTH ORG., REPORT ON TECHNICAL CONSULTATION ON H5N1 RESEARCH ISSUES (Feb. 16-17, 2012) (on file with authors).

65. Holtcamp, *supra* note 58, at A240.

66. Donald G. McNeil, Jr., *Scientist Plays Down Danger of Flu Strain*, N.Y. TIMES, Jan. 25, 2012, at A16.

67. Masaki Imai et al., *Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets*, 486 NATURE 420, 420 (2012).

68. *Id.* at 423; Yo Han Jang et al., *Cold-Adapted Pandemic 2009 H1N1 Influenza Virus Like Vaccine Elicits Cross-Reactive Immune Responses against Seasonal and H5 Influenza A Viruses*, 86 J. VIROLOGY 5953, 5953 (2012).

69. Imai et al., *supra* note 67, at 420. See also Louis Pasteur et al., *De l'attenuation des virus et de leur retour a la virulence*, 92 LES COMPTES RENDUS DE L'ACADÉMIE DES SCIENCES [C.R. ACAD. SCI.] 430-35 (1881) (Fr.).

70. *Id.* at 422-24.

attached to human upper respiratory cells, successfully infected ferrets, and was transmissible by aerosol between ferrets.<sup>71</sup> The infections caused lesions and weight loss, but no deaths.<sup>72</sup> Furthermore, the resulting virus reacted with the current H5N1 vaccine, which was only made in limited quantities.<sup>73</sup> Provided the vaccine would elicit a sufficient immune response, it may be protective against a virus with this mutated HA gene.<sup>74</sup> Of note, there are currently H5N1 viruses circulating which are only three mutations away from this version of the H5N1 HA gene.

Dr. Fouchier, on the other end, started with a different, but whole HPAI H5N1 virus.<sup>75</sup> He created five mutations, four in the HA gene, and one in the PB2 gene, which affects with viral replication.<sup>76</sup> Passaging in ferrets generated two of these mutations.<sup>77</sup> The resulting virus attached to human upper respiratory cells, successfully infected ferrets, and was transmissible by aerosol between ferrets.<sup>78</sup> Again, the infections caused lesions and weight loss, but no deaths.<sup>79</sup> The resulting virus reacted with the current H5N1 vaccine, and was also sensitive to Oseltamivir, an antiviral medication that considered effective against avian influenza, although some instances of resistance have already occurred.<sup>80</sup> Again, there are currently circulating H5N1 viruses that are only one mutation away from this version of the hemagglutinin gene.

It is important to clarify that wild type HPAI H5N1 viruses are lethal in ferrets as was the mutated virus in Dr. Fouchier's experiment when he administered it directly into the trachea, not a natural mode of infection.<sup>81</sup> Similarly, intranasal administration of these viruses in their wild type form causes morbidity and sometimes mortality; however, no mortality was observed with Dr. Fouchier's virus when administered in this manner.<sup>82</sup> Prior studies have shown that HPAI H5N1 viruses can be transmitted by direct or indirect contact exposure, including via respiratory droplets, but the results

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71. *Id.* at 422, 426.

72. *Id.* at 424, 426-27

73. *Id.* at 427.

74. Imai et al., *supra* note 67, at 427.

75. Sander Herfst et al., *Airborne Transmission of Influenza A/H5N1 Virus Between Ferrets*, 336 *Sci.* 1534, 1536 (2012).

76. *Id.* at 1539.

77. *Id.* at 1540.

78. *Id.* at 1537-40.

79. Herfst et al., *supra* note 75, at 1540.

80. *Id.*

81. *Id.*

82. John A. Lednicky et al., *Ferrets Develop Fatal Influenza After Inhaling Small Particle Aerosols of Highly Pathogenic Avian Influenza Virus A/Vietnam/1203/2004 (H5N1)*, *J. VIROLOGY* J. 231, 1 (2010), <http://www.virologyj.com/content/7/1/231>.

are inconsistent.<sup>83</sup> What sets the two contentious experiments apart is the fact that the transmissions observed not only occurred efficiently, but by strictly natural means, such as when ferrets were exposed to the sneezing of other ferrets infected by experimental means.<sup>84</sup> Another essential point is that the mutations identified in Dr. Kawaoka's and Dr. Fouchier's studies, while yielding similar results, were not identical, and neither were the wild type viruses which were used as starting points.<sup>85</sup> This suggests that different lineages of HPAI H5N1 viruses and different mutations could yield airborne-transmissible viruses.<sup>86</sup>

On March 29-30, 2012, NSABB reconsidered its initial decision<sup>87</sup> in light of the additional information suggesting that the research may not have been as dangerous as initially feared, that it would be of value to surveillance efforts, and that it had been conducted at an appropriate biosafety level.<sup>88</sup> NSABB voted — although not unanimously in the case of Dr. Fouchier's study — in favor of publication of both revised papers in full.<sup>89</sup> Another factor in their decision was the lack of an established process to share the most sensitive information contained in the manuscripts solely on a "need to know" basis and the wish to avoid the perception that the U.S. may withhold information critical to HPAI surveillance.<sup>90</sup> NSABB members who still opposed the decision felt that a focus on these particular viruses and mutations for surveillance would be misguided and that airborne-transmissible HPAI should only be studied at Biosafety Level (BSL) 4 certified labs/facilities, the highest biosafety level available.<sup>91</sup> Interesting to note, Dr. Kawaoka's and Dr. Fouchier's studies were performed only at enhanced BSL-3 labs/facilities.<sup>92</sup> Nonetheless, Dr. Kawaoka's and Dr.

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83. Hui-Ling Yen et al., *supra* note 55, at 6897.

84. Herfst et al., *supra* note 75, at 1539; Masaki Imai et al., *supra* note 67, at 429.

85. Sander Herfst et al., *Supplementary Materials for Airborne Transmission of Influenza A/H5N1 Virus Between Ferrets*, *SCI.* (June 22, 2012), [www.sciencemag.org/cgi/content/full/336/6088/1534/DC1](http://www.sciencemag.org/cgi/content/full/336/6088/1534/DC1) (providing supplementary materials for Herfst et al., *supra* note 75); Imai et al., *supra* note 67, at 420-21.

86. MAURA SULLIVAN ET AL., *RISK MGMT. SOLUTIONS INC., INFLUENZA PANDEMIC RISK THE CONTRIBUTION OF LABORATORY PATHOGENS TO EXCESS MORTALITY RISK 4* (2013).

87. NAT'L SCI. ADVISORY BD. FOR BIOSECURITY, *FINDINGS AND RECOMMENDATIONS MARCH 29-30 at 1* (2012).

88. *Id.* at 2-3, 5.

89. *Id.* at 2-3.

90. *Id.* at 3-4.

91. *Id.* at 4-5. See also Michael J. Imperlale & Michael G. Hanna, *Biosafety Considerations of Mammalian-Transmissible H5N1 Influenza*, 3 *MBIO* 1, 1 (2012), <http://mbio.asm.org/content/3/2/e00043-12>.

92. Imai et al., *supra* note 67, at 427.

Fouchier's experiments were published in their entirety in May 2012 and June 2012, respectively.<sup>93</sup>

While NSABB finalized its deliberations regarding these manuscripts, HHS released the DURC Policy on March 29, 2012.<sup>94</sup> The scope of the DURC Policy was limited to HPAI H5N1 viruses, the reconstructed 1918 pandemic virus, and Tier 1 Select Agents, which require additional precautions and training of personnel.<sup>95</sup> The DURC was applicable to the seven categories of experiments of concern originally defined in the Fink Report.<sup>96</sup> The DURC Policy defines responsibilities for federal agencies to conduct a review of funded projects and devise risk mitigation plans, which span the entire research life cycle from funding through publication.<sup>97</sup> The responsibilities of the PIs and research institutions are not clearly delineated in the DURC Policy beyond collaborating on the risk mitigation plan and implementation, reviewing emerging research findings for DURC, and as the case may be, notifying the funding agencies.<sup>98</sup> After the DURC Policy went into effect, "NIH conducted a review of its grants and found 381 extramural and 404 intramural projects [using pathogens or toxins] covered by th[e] policy."<sup>99</sup> Ten of the extramural projects were designated as DURC, including seven influenza experiments, and the others used anthrax, plague, and botulism.<sup>100</sup> A mitigation plan was devised in each case.<sup>101</sup>

This first policy was followed approximately one year later by two additional and preliminary pieces of legislation; the goal of which was to provide additional details regarding DURC oversight by research institutions<sup>102</sup> and funding of airborne-transmissible H5N1 HPAI.<sup>103</sup> In the proposed Oversight Policy the roles and responsibilities of the PIs, research institutions, funding agencies, and U.S. Government were more clearly

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93. Herfst et al., *supra* note 75, at 1534; Imai et al., *supra* note 67, at 428.

94. *Biological Security: The Risk of Dual-Use Research: Hearing before the S. Comm. on Homeland Sec. & Gov't Affairs*, 112 Cong. 7 (2012) (testimony of Anthony Fauci, Director, Nat'l Inst. of Allergy & Infectious Disease, Nat'l Inst. of Health, U.S. Dep't of Health & Human Servs.). See also U.S. DEP'T OF HEALTH & HUMAN SERVS., UNITED STATES GOVERNMENT POLICY FOR OVERSIGHT OF LIFE SCIENCES DUAL USE RESEARCH OF CONCERN (2012).

95. U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 93, at 2-3 (2012). See also 7 C.F.R. § 331 (2012); 9 C.F.R. § 121 (2012); C.F.R. § 73 (2012).

96. FINK REPORT, *supra* note 19, at 114-15.

97. U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 93, at 3.

98. *Id.*

99. FRANK GOTTRON & DANA A. SHEA, CONG. RESEARCH SERV., R42606, PUBLISHING SCIENTIFIC PAPERS WITH POTENTIAL SECURITY RISKS: ISSUES FOR CONGRESS 14 (2013).

100. *Id.*

101. *Id.*

102. U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 93, at 4.

103. U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 2, at 1.

defined.<sup>104</sup> For instance, the Oversight Policy states that PIs should conduct regular assessments of their work to determine whether it falls under the scope of the DURC Policy, be knowledgeable and aware of the risks of dual use research, provide DURC education for their personnel, and be compliant with institutional and federal policies, as well as with any risk mitigation plan decided for their projects by funding agencies and their institution.<sup>105</sup> It goes on to state that research institutions should “provide education and training on DURC,” regularly assess the effectiveness of their DURC policies, provide an appeal mechanism for affected PIs, and remain in compliance with federal funding agencies regarding determination of DURC and “implementation of risk mitigation plan[s].”<sup>106</sup> However, the DURC Policy does not dictate which entity within research institutions will be responsible for compliance.<sup>107</sup> Federal funding agencies should be there as a resource to PIs and research institutions, but their most important role is to determine DURC at the funding stage, devise mitigation plans which cover the entire life cycle of the research from funding through publication, and respond to reports of non-compliance from research institutions.<sup>108</sup> Finally, the U.S. Government’s role is to develop training and outreach tools and materials to be used by funding agencies, research institutions, and PIs to “periodically assess the impact of the DURC policy on life sciences research” and biosecurity,<sup>109</sup> as such assessment could lead to eventual revisions of the policy.

Regarding mitigation plans, decisions affecting communication of the research are the most likely to cross into uncharted territory, as they could call for modification of content (with either addition of contextual information, or removal of substantive information), timing (publication could be delayed), or distribution (with restrictions or even classification). In the proposed H5N1 Funding Framework Policy, an additional two-tiered (funding agency and department-level) review beyond scientific merit and DURC is required for projects involving HPAI H5N1 viruses that are transmissible among mammals by respiratory droplets.<sup>110</sup> The goal of this additional step is to ensure that generated viruses could be the result of a natural evolution process and, therefore, be relevant to real life scenarios, that adequate safety precautions are set in place, that research stands to

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104. See U.S. DEP’T OF HEALTH & HUMAN SERVS., *supra* note 93, at 4 (defining the roles of various entities in DURC oversight).

105. *Id.* at 9-10.

106. *Id.* at 10, 12.

107. See *id.* at 11.

108. *Id.* at 13.

109. U.S. DEP’T OF HEALTH & HUMAN SERVS., *supra* note 93 at, 13, 14.

110. U.S. DEP’T OF HEALTH & HUMAN SERVS., *supra* note 2, at 1.

significantly contribute to public health and biosecurity, and that no viable alternatives exist to obtain the same answers.<sup>111</sup>

### III. CHALLENGES WITH IMPLEMENTATION OF DUAL USE RESEARCH POLICIES

Comments elicited by the Oversight Policy express significant concerns regarding the ability of research institutions to achieve and remain in compliance.<sup>112</sup> As noted in the introduction, IBCs, created specifically to oversee research involving DNA recombinant or synthetic nucleic acid molecules, are already overburdened and underfunded because they also assume responsibility for oversight of all activities with biohazards, including compliance with Select Agents Regulations.<sup>113</sup> Tasking them with DURC oversight seems logical and efficient, but may not be practical for some institutions. IBCs may have to create separate committees or hire outside entities, which has the potential for a significant slowdown of the research enterprise that is already besieged with regulations, even if justifiably so. The American Association for the Advancement of Science (AAAS), in collaboration with the “Association of American Universities (AAU), Association of Public and Land-grant Universities, and the Federal Bureau of Investigation” held a meeting that focused on sharing best practices of existing institutional program review and oversight of DURC.<sup>114</sup> The fact that necessary expertise for DURC review may not be available in current IBCs or within certain institutions increases the chances that consulting with outside bodies will be necessary. However, the requirement for a mechanism for review on demand at any time a PI identifies DURC potential<sup>115</sup> makes the involvement of external entities difficult since the university “may have little control over when the review body is available.”<sup>116</sup> Therefore, there is a possibility that these additional layers of regulations and compliances ultimately discourage individual researchers and institutions from

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111. *Id.*

112. See *generally* Letter from Jeffery Miller, President, American Society for Microbiology et al., to Dr. Franca Jones, Assistant Director, Chemical & Biological Countermeasures, Office of Sci. & Tech. Policy (Mar. 27, 2013) (noting the need to balance oversight of DURC in order to “not discourage critical research or place an undue burden on life sciences research conducted in the United States”). See also United States Gov’t Policy for Institutional Oversight of Life Sciences Dual Research of Concern, 78 Fed. Reg. 12369 (Feb. 22, 2013).

113. See *generally* Letter from David Relman to Franca Jones, *supra* note 4, at 2 (explaining that IBCs are already overextended).

114. AM. ASS’N FOR THE ADVANCEMENT OF SCI., BRIDGING SCIENCE AND SECURITY FOR BIOLOGICAL RESEARCH: A DISCUSSION ABOUT DUAL USE RESEARCH AND OVERSIGHT AT RESEARCH INSTITUTIONS 17 (2012).

115. U.S. DEP’T OF HEALTH & HUMAN SERVS., *supra* note 93, at 11.

116. Letter from Hunter Rawlings and Anthony P. DeCrappeo to Franca Jones, *supra* note 11, at 2-3.

undertaking research that would enhance U.S. biosecurity, or they may simply increase chances of unintentional non-compliance.<sup>117</sup>

There is also the distinct possibility that DURC regulations, as enacted or currently proposed, are not sufficient to serve their purpose. As experience amply demonstrated,<sup>118</sup> research with DURC does not necessarily involve Select Agents or HPAI. Even seemingly innocuous research could have dual use implications, if not immediately, at some point in the future. One example is a 1997 study that resulted in the design of a more efficient delivery system for aerosolized medicines, carrying them deep into the lungs, with nefarious potential that did not become evident until the anthrax scare of 2001.<sup>119</sup> Another example is in 1943, botany student Arthur Galston published his thesis on chemicals that were used to hasten the development of flowering plants.<sup>120</sup> Military researchers read and then used Galston's findings to develop the defoliant Agent Orange, a chemical that was used in the Vietnam War and has caused human health problems ever since.<sup>121</sup> There are also those agents, which despite being restricted, can be recovered from the environment or animals in endemic regions, or that can be made in the laboratory.<sup>122</sup> While regulations limit access to these agents through regular channels, they certainly do not prevent motivated individuals from acquiring or making them.<sup>123</sup> Another issue is that species are not as well delineated in the microbial world as would be necessary to exclude the possibility that two different species belong to the same genus.<sup>124</sup> The bottom line is that list-based regulations may be completely insufficient if they are to prevent misuse of research results.<sup>125</sup> It is possible that certain future federal funding opportunities will focus on dual use research with acceptance of the funds contingent upon pre-publication review and other

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117. Wolinetz, *supra* note 10, at 1526.

118. Roland Jackson et al., *Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox*, 1205 J. OF VIROLOGY 1205-1210 (2011); Eckard Wimmer, *The Test-Tube Synthesis of a Chemical Called Poliovirus*, 7 EUROPEAN MOLECULAR BIOLOGY ORG. (SPECIAL ISSUE) 53-59 (2006).

119. Wen-I Li & David A. Edwards, *Aerosol Particle Transport and Deaggregation Phenomena in the Mouth and Throat*, 26 ADVANCED DRUG DELIVERY REVIEWS 41, 42, 46 (1997).

120. Holtcamp, *supra* note 58, at A241.

121. *Id.*

122. Arturo Casadevall & David Relman, *Microbial Threat Lists: Obstacles in the Quest for Biosecurity?*, 8 NATURE REVIEWS MICROBIOLOGY 149, 150 (2010).

123. *Id.* at 150.

124. *Id.* at 151.

125. See Wolinetz, *supra* note 10, at 1525 (discussing the insufficiency of list-based regulations to prevent misuse of research results).

restrictive measures consistent with the proposed policies.<sup>126</sup> It is important to note that this will not resolve the fact that many projects will still carry the potential for DURC, even if they are not identified by the funding agency as such at the beginning of the research cycle or preselected in response to funding opportunities.

According to the DURC Policy already in place, federal DURC oversight begins when a project is considered for funding, which may be too late in some cases considering that much communication about the research takes place prior to grant submission, including when preliminary experiments are shared at the occasion of scientific conferences.<sup>127</sup> In any event, the U.S. Government funds only about 31% of the total research and development efforts in the U.S.<sup>128</sup> Research funded by entities other than the U.S. Government may involve academia, industry (including small start-up companies), non-profit organizations, contract research organizations, trade associations, industry consortia, investors, and may be performed in a variety of settings, even in private homes in the case of self-funded *home experimenters*. This leaves many projects flying under the federal radar until publication, and increases the likelihood of untimely incomplete, or even unenforceable stopgap measures after the research is already done and the results disseminated.

Research covered under the new policies requires a considerable need for self-policing on the part of institutions and PIs, and because of that, there is much room for error. There is a need for a more bottom-up approach to complete, or in many cases replace, top-down oversight by the U.S. Government. Another limitation of relying too much on top-down oversight is a lack of working relationships and trust between life sciences research and security communities. Life scientists, unlike their counterparts in nuclear physics and cryptography, are accustomed to readily sharing, and in-turn gaining, access to information. However, the flow of information with security experts is one-directional, although they may use that information to make decisions regarding enforcement of DURC policies with little or no input from the scientific community. This culture chasm makes it difficult for scientists to adjust to the new and still evolving *status quo*. Yet WHO reported that both communities needed each other's expertise to make effective decisions and policies regarding DURC.<sup>129</sup>

Good will and cooperation on the part of the scientific community is all the more critical since the government generally has no authority to classify

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126. GOTTRON & SHEA, *supra* note 98, at 15-16.

127. *Id.* at 16.

128. *Id.* at 22.

129. WORLD HEALTH ORG., REPORT OF THE WHO INFORMAL CONSULTATION ON DUAL USE RESEARCH OF CONCERN 7 (2013).

information unless it was produced within a certain pre-agreed framework, usually in government laboratories or in fulfillment of government contracts.<sup>130</sup> The only two exceptions are information related to nuclear weapons, which is “born classified,” and information received as part of a patent application.<sup>131</sup> Beyond classification, limiting general access to research results is new territory, and there is not a mechanism to identify this information in a timely manner nor an entity that could store and distribute it according to criteria that does not yet exist. Establishing clear guidelines as to when information needs to become restricted and what penalties would follow, if either primary or secondary dissemination occurred, would need to be articulated and then enforced.

In fact, the DURC Policy geared at limiting the dissemination (publication) of dual use research contradicts existing federal regulations and policies related to export controls and fundamental research.<sup>132</sup> Both the Export Administration Regulations<sup>133</sup> and the International Traffic in Arms Regulations<sup>134</sup> contain exclusions for fundamental research. To qualify as “fundamental research,” basic and applied science and engineering research activities must be those ordinarily published and shared broadly within the scientific community.<sup>135</sup> They must also be free from pre-publication review, except for determining whether patent rights are being compromised or proprietary information is being divulged.<sup>136</sup> This “Fundamental Research Exclusion” (FRE) is the primary means by which U.S. universities engage in research related to dual use technologies without the need for export control licenses.<sup>137</sup> Such licenses are costly and the process takes considerable time. The cost and time barriers prevent universities from engaging in export controlled projects without the availability of exclusions and exemptions. This is especially true in the case of *deemed exports*, which essentially make granting access to export-controlled technological information (not physical items) to a foreign national (person) in the U.S. the same as if they were in their home country. Such limitations on the free exchange of ideas and research activities present both practical and philosophical challenges to universities. In many instances, universities have

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130. See 1 S.K. PRASAD, *BIOLOGICAL WAR* 206 (2009).

131. *Id.*

132. GOTTRON & SHEA, *supra* note 98, at 15-16; Mark S. Frankel, *Regulating the Boundaries of Dual-Use Research*, 336, *SCI.* 1523, 1524 (2012).

133. 15 C.F.R. § 734.8 (2013).

134. 22 C.F.R. § 123.16 (2012).

135. 15 C.F.R. § 734.8 (2013).

136. 15 C.F.R. § 734 (Supp. 1 2013).

137. See CAROL T. CARR, *NEGOTIATING THE MINE FIELD: THE CONDUCT OF ACADEMIC RESEARCH IN COMPLIANCE WITH EXPORT CONTROLS*, NAT’L ASS’N OF COLL. & UNIV. ATT’YS 12 (2006).

implemented policies and procedures that limit research projects to those that qualify as fundamental research and/or would otherwise not require preventing or limiting the involvement of foreign nationals.<sup>138</sup> As a result, most federally funded research conducted on U.S. university campuses is unrestricted and exempt from export controls.<sup>139</sup> Moreover, federal funding agencies encourage publication and presentation of the research findings. Prevailing best practice in university export control compliance is oriented toward seeking out any contract clause or side deal that may prohibit or limit public dissemination (e.g., pre-publication review) for fear that this would invalidate the FRE. This is an example of how regulations sometimes limit the scope of the research enterprise in the U.S.

Several scientific journals have performed pre-publication review of scientific manuscripts for DURC content voluntarily since 2003. This review is a response to their own risk analysis rather than that of an external entity, and their conclusions may differ substantially from those of NSABB or the U.S. Government. During Dr. Kawaoka's and Dr. Fouchier's controversy, both *Science* and *Nature* made it clear that their actions to delay publication and their considerations of changing the content were completely voluntary and would not be repeated in the future in similar circumstances.<sup>140</sup> Journals do not have the infrastructure or mechanisms in place to limit the dissemination of information to a restricted audience beyond withholding publication or redaction, and doing so goes directly against their primary purpose.

#### IV. CONCLUSION

The requirement for self-policing at the institutional and individual levels, combined with presumably heavy financial and possibly legal penalties in the event of non-compliance, is understandably troublesome to many. In this regard, DURC policies, as enacted or proposed, differ from those covering research with recombinant DNA, which is accomplished by a combination of local self-regulation and limited federal oversight.<sup>141</sup> In the event of non-compliance with these guidelines, the penalties are strictly financial at the individual or institutional level. Non-compliance with DURC policies, on the other hand, would be more consequential, due in part to the applicability of

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138. See *id.* at 6.

139. See *id.*

140. GOTTRON & SHEA, *supra* note 98, at 11; Editorial, *Publishing Risky Research*, 485 NATURE 5, 5 (2012).

141. See NAT'L INST. OF HEALTH, NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT OR SYNTHETIC NUCLEIC ACID MOLECULES (NIH GUIDELINES) 24, 24-31 (2013) (discussing the self-regulation of research labs that focus on covering research with recombinant DNA, and the lack of government oversight as a result).

Select Agents Regulations in many cases, and in all instances due to the implications for national security, similar to the significant civil and criminal penalties for violating the export control laws. Therefore, it is likely that institutions would want to involve a separate body to make final decisions, such as a federal entity like NSABB, or another independent entity, but without giving up complete control at the institutional level.

Many institutions are not planning to review research for DURC potential due to the current scope of existing or proposed DURC policies, simply because they do not conduct Select Agents research. This may be imprudent considering the intent of DURC policies, which makes it likely that their scope will be expanded in the future. However, a number of institutions have already implemented institutional-level DURC policies.<sup>142</sup> Some institutions review only research with Select Agents for DURC potential, while others review all research proposed by and conducted at the institution for associated DURC risks<sup>143</sup> with compiled data from three different IBC surveys at public and private research institutions, hospitals, and clinics with response rates ranging from 29.2%–45.1%.<sup>144</sup> Over 50% of the respondents indicated that IBCs reviewed research for potential DURC, and another 15% considered doing so.<sup>145</sup> However, the survey indicated that only 37% of IBC members were being trained on dual-use risks.<sup>146</sup> Considering the sharp rise in the number of IBCs in the U.S. from 397 in 2002, to 799 in 2010,<sup>147</sup> and assuming a learning curve for newly formed IBCs and their members, it is difficult to ascertain whether IBCs across the U.S. are, in fact, qualified to the extent needed to ensure compliance with DURC policies for PIs and institutions, especially when DURC review is not their primary responsibility.

Perhaps sharing the above concerns, some institutions have convened a committee separate from the IBC to review research involving Select Agents with DURC potential, but they are a small minority.<sup>148</sup> These separate committees include scientific, medical, security, and safety experts.<sup>149</sup> Examples of such committees exist at Boston University and the University of Wisconsin-Madison.<sup>150</sup> At Boston University, the formal review process starts

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142. AM. ASS'N FOR THE ADVANCEMENT OF SCI., *supra* note 112, at 12-13.

143. *Id.* at 20.

144. Raymond W. Hackney, Jr. et al., *Current Trends in Institutional Biosafety Committee Practices*, 17 APPLIED BIOSAFETY 11, 12 (2012).

145. *Id.* at 14.

146. *Id.* at 15.

147. *Id.* at 12.

148. AM. ASS'N FOR THE ADVANCEMENT OF SCI., *supra* note 112, at 20 (this is Boston University and University of Wisconsin-Madison).

149. *Id.*

150. *Id.* at 14-15.

with the researchers responding to eight specific questions, which are designed to identify the seven types of experiments of concern.<sup>151</sup> In this regard, this is similar to how proposals are identified as needing export control review.<sup>152</sup> If warranted, the DURC review committee discusses the research with the PI, and a mitigation plan is designed in consultation with university officials and with NSABB.<sup>153</sup> Because information gained during the course of any research might raise new questions or concerns regarding DURC, and to ensure buy-in of its community, Boston University preceded implementation of its institutional DURC Policy with a preliminary phase, which has consisted, since 2009, of diligent awareness and an education program for all research personnel and administrators.<sup>154</sup>

The University of Wisconsin-Madison has a similar process with a heavy educational component.<sup>155</sup> Identification of research with DURC potential does not necessarily start with the PI, however, it may also be initiated by any committee reviewing the research or by a funding agency.<sup>156</sup> If such determination is made, the PI and relevant personnel meet with officials responsible for Select Agents and Toxins Regulations compliance for information gathering.<sup>157</sup> This information is then forwarded to an IBC subcommittee to perform another interview with the PI to assess DURC potential of the research, and write a report to be presented to the entire IBC.<sup>158</sup> The IBC conducts a vote, and if warranted, the report is forwarded to a separate committee, the Biosafety Task Force, for further discussion and vote, which includes input from the PI, until a consensus is reached regarding a mitigation plan.<sup>159</sup> This plan is forwarded, along with the review process, to the funding agency for further guidance.<sup>160</sup>

Research institutions differ by size, sector, funding sources, scientific expertise, and interests influencing the type of review and oversight process that may work best for them. The Boston University and University of Wisconsin-Madison examples illustrate that each institution should ideally come up with its own system to review and oversee DURC locally, but also suggests that best practices would include participation by an entity separate

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151. *Id.* at 14.

152. *See id.*

153. *See* AM. ASS'N FOR THE ADVANCEMENT OF SCI., *supra* note 112, at 14.

154. *Id.*; *Dual Use Research of Concern (DURC)*, BOS. UNIV., <http://www.bu.edu/orc/initiatives/durc/> (last visited Aug. 15, 2013).

155. AM. ASS'N FOR THE ADVANCEMENT OF SCI., *supra* note 112, at 15.

156. *Id.*

157. *Id.*

158. *See id.*

159. *Id.*

160. *Policies, Responsibilities, and Procedures*, UNIV. OF WI-MADISON, <http://www.grad.wisc.edu/research/policyrp/rcr/index.html> (last visited Aug. 18, 2013).

from the IBC. While these two institutions formed separate committees internally, we believe that it would be highly beneficial to the research enterprise in the U.S. and abroad to adhere to a set of best practices, which would be reviewed on a regular basis by an independent accrediting body, operating internationally. We base this belief on several reasons. First, such an entity would be a source of additional expertise for institutions, as well as a means to ensure consistency in the identification, communication, and mitigation of those risks associated with DURC. This review body would not impose additional pressures or burdens on the research community, but would provide a source of non-punitive, confidential oversight. Furthermore, such a process would be consistent with the position taken during the WHO meeting held on February 26-28, 2013, where it was agreed that global guidance on DURC issues was badly needed.<sup>161</sup>

There is a precedent in the research community for an independent accrediting body, which provides accreditation to research institutions committed to following best practices: the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC). AAALAC is a "private, nonprofit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs."<sup>162</sup> Its "purpose is to provide an open, fair, and impartial peer-evaluation that results in valuable suggestions and information organizations can use to improve their programs."<sup>163</sup> To encourage "forthright dialogue that results" in significant improvements, "AAALAC assures its program participants that none of the details of their evaluations are made public," and it does not share information with the public obtained through the accreditation process, except regarding whether or not the organization is accredited.<sup>164</sup> "More than 880 companies, universities, hospitals, government agencies, and other research institutions in 37 countries have earned AAALAC accreditation,<sup>165</sup> demonstrating their commitment" to excellence and the wide acceptance of this accrediting body. These institutions volunteer to participate in AAALAC's program, in addition to complying with the local, state, and federal laws that regulate animal research.<sup>166</sup> Through accreditation, these institutions demonstrate that they go beyond meeting minimum standards required by law and go the extra

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161. WORLD HEALTH ORG., *supra* note 128, at 6.

162. *About AAALAC*, ASS'N FOR ASSESSMENT & ACCREDITATION OF LAB. ANIMAL CARE INT'L, <http://www.aaalac.org/about/> (last visited Aug. 18, 2013).

163. *Accreditation*, ASS'N FOR ASSESSMENT & ACCREDITATION OF LAB. ANIMAL CARE INT'L, <http://www.aaalac.org/accreditation/policies.cfm?printPage=1&> (last visited Aug. 16, 2013).

164. *Id.*

165. See ASS'N FOR ASSESSMENT & ACCREDITATION OF LAB. ANIMAL CARE INT'L, *supra* note 161.

166. *Id.*

step to implement best practices. The U.S. Government and federal funding agencies recognize AAALAC accreditation and have different reporting requirements for institutions that are accredited.

We believe that implementing a system of voluntary accreditation for research institutions performing research with DURC potential would maximize compliance with DURC policies and encourage adoption of the most effective and least burdensome practices. It would also improve the understanding of DURC issues by individual institutions without increasing the need for additional regulations. Most importantly, it would demonstrate a culture of scientific responsibility to the public.