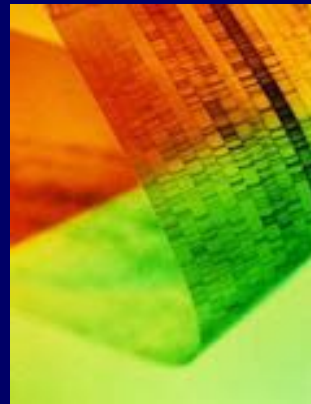
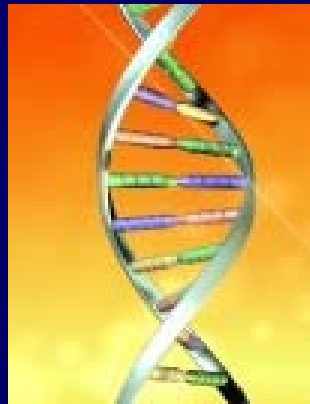


# Dual Use Research of Concern: Recent Policy Developments



**Amy P. Patterson, M.D.**  
**Associate Director for Science Policy**  
**National Institutes of Health**

**Presentation to the**  
**Advisory Committee to the Director, NIH**  
**June 14, 2012**



# Overview



- **What is “dual use” research?**
- **Case study: H5N1 research**
- **New USG Policy for Oversight of Life Sciences Dual Use Research of Concern (March 2012)**
- **Development of USG Policy on Institutional Oversight of Dual use Research**
- **Issues and challenges in policy development**

# The “Dual Use” Dilemma



- ***Life sciences research underpins:***
  - **Biomedical and public health advances**
  - **Improvements in agriculture**
  - **Safety and quality of food supply**
  - **Environmental quality**
  - **Strong national security and economy**
- ***However, good science can be put to bad uses***

# DUR vs. DURC



- **Dual use research (DUR)** = legitimate research that yields information or technologies that could be misused for malevolent purposes
  - NOTE: Most life sciences research conceivably could be considered DUR in that it has *some* potential to generate information that could be eventually misused
- Goal is to identify the subset that has highest potential for generating information that could be readily misused = **DUR of concern (DURC)**

# Dual Use Research of Concern (DURC) Defined



**“Life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.”**

# DURC: Risk Mitigation Strategies



- **Management of DURC may entail a variety of possible strategies, for example:**
  - **Changes in the design or conduct of research**
  - **Applying specific biosecurity and/or biosafety measures**
  - **Monitoring of research for findings with additional DURC potential**
- **In some rare instances, it may be appropriate to restrict communication of experimental details or other specific information**

# Weighing Risks and Benefits



## Restricting Dissemination

### ■ Benefits

- Keeping DURC information from terrorists

### ■ Risks

- Slowing scientific progress, preparedness efforts
- Being unprepared for a disease outbreak



## Full, Open Communication

### ■ Benefits

- Rapidly furthers validation of findings and scientific progress
- Provides information needed for preparedness

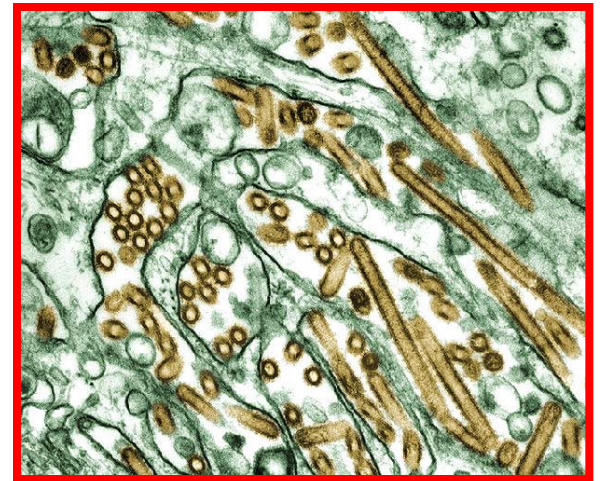
### Risks

- Increases ease of misuse

# Case in Point: H5N1 Research



- Results of two NIH-funded studies on respiratory transmission of H5N1 were submitted for publication in two major scientific journals
- The manuscripts raised dual use research questions over whether they contained information that could be utilized to create a potentially human-transmissible form of H5N1 that, in the wrong hands, could be intentionally released to threaten public health and security

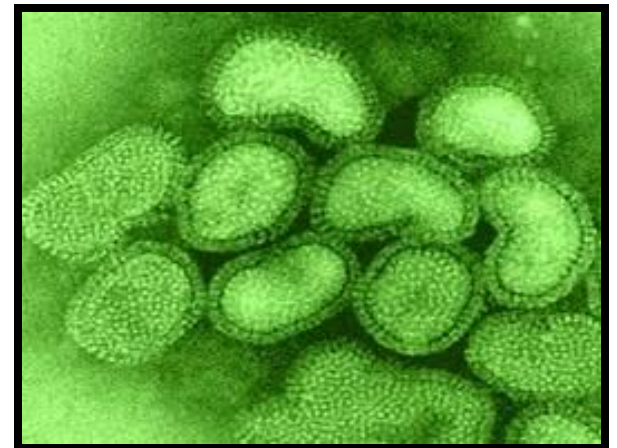




# NSABB and H5N1 Research



- **US Government charged National Science Advisory Board for Biosecurity (NSABB) with:**
  - **Assessing the dual use research implications of two as-yet-unpublished manuscripts on the avian influenza A/H5N1 virus**
  - **Considering the risks and benefits of communicating the research results**
  - **Providing findings and recommendations regarding the responsible communication of the research**



# NSABB Findings and Recommendations – November 2011



- Noted the importance of the general findings in these manuscripts as they relate to public health preparedness, as well as significant concerns about the potential for the misuse of the specific experimental information
- Recommended that the conclusions of the manuscripts be published **without experimental details and mutation data that would enable replication of the experiments**
  - Unprecedented recommendation for an unprecedented scenario

# Diverse Public Perspectives



## The New York Times

**An Engineered  
Doomsday**  
...the research should  
never have been  
undertaken because the  
potential harm is so  
catastrophic

## NewScientist

**One mistake away  
from a worldwide  
flu pandemic**

AFTER a hard day at  
the lab, a biologist  
travels home on the  
subway. Later that  
evening...

## the Atlantic

**Hope or Fear: The  
Opposing Ideas of  
H5N1 Bird Flu  
Researchers**

By Hans Villarica  
Jan 20 2012, 12:06  
PM ET

*After the government  
asked journals to cut  
two studies, concerns  
about censorship took  
center stage, but what  
does it mean for  
research?*

## Los Angeles Times

**Fear gone viral**  
Despite government alarms  
bells, recent research with  
ferrets didn't create flu strains  
that threaten the world....there's  
really not much cause for alarm.

## nature

**Don't censor life-saving  
science**

Controlling who is allowed  
access to information about  
mutations in the H5N1 bird  
flu virus is unacceptable

# Response of the Influenza Research Community

## ■ Voluntary pause on the conduct of H5N1 research

Scienceexpress

Letter

### Pause on Avian Flu Transmission Research

Ron A. M. Fouchier,<sup>1\*</sup> Adolfo Garcia-Sastre,<sup>2</sup> Yoshihiro Kawada,<sup>3</sup> Wendy S. Barclay,<sup>4</sup> Nicole M. Bourke,<sup>5</sup> Ian H. Brown,<sup>6</sup> Haria Capua,<sup>7</sup> Hsiang Chen,<sup>8</sup> Richard W. Compans,<sup>9</sup> Robert B. Couch,<sup>10</sup> Nancy J. Cox,<sup>11</sup> Peter C. Dolery,<sup>12</sup> Ruben O. Donis,<sup>13</sup> Heinz Feldmann,<sup>14</sup> Yi Guan,<sup>15</sup> Jacqueline Katz,<sup>16</sup> H. D. Klenk,<sup>17</sup> Gary Kobinger,<sup>18</sup> Jimma Liu,<sup>19</sup> Xinfan Liu,<sup>20</sup> Anice Lowen,<sup>21</sup> Thomas C. Mettenleiter,<sup>22</sup> Albert D. M. E. Osterhaus,<sup>23</sup> Peter Palese,<sup>24</sup> J. S. Malik Peiris,<sup>25</sup> Daniel E. Perez,<sup>26</sup> Jürgen A. Richt,<sup>27</sup> Stacey Schultz-Cherry,<sup>28</sup> John Swoell,<sup>29</sup> Kanta Subbarao,<sup>30</sup> David E. Swayne,<sup>31</sup> Toru Takimoto,<sup>32</sup> Masato Tashiro,<sup>33</sup> Jeffrey K. Taubenberger,<sup>34</sup> Paul G. Thomas,<sup>35</sup> Ralph A. Tripp,<sup>36</sup> Terrence M. Tumpey,<sup>37</sup> Richard J. Webby,<sup>38</sup> Robert G. Webster<sup>39</sup>

<sup>1</sup>Department of Virology, Erasmus MC, 3000CA Rotterdam, 3015GE Rotterdam, Netherlands; <sup>2</sup>Department of Microbiology, Mount Sinai School of Medicine, New York, NY 10029, USA; <sup>3</sup>Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, WI 53711, USA; <sup>4</sup>Department of Medicine, Imperial College, London, UK; <sup>5</sup>Division of Infectious Diseases and Department of Microbiology, Mount Sinai School of Medicine, New York, NY 10029, USA; <sup>6</sup>Virology Department, Animal Health and Veterinary Laboratories Agency, Addiscombe, KT11 5LJ, UK; <sup>7</sup>Istituto Zooprofilattico Sperimentale della Venezia, 35020, Padova, Italy; <sup>8</sup>Harbin Veterinary Research Institute, CAAS, Harbin 150001, China; <sup>9</sup>Influenza Pathogenesis and Immunology Research Center, Emory University, School of Medicine, Atlanta, GA 30322, USA; <sup>10</sup>Department of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, TX 77030, USA; <sup>11</sup>Centers for Disease Control and Prevention, Influenza Division, Atlanta, GA 30333, USA; <sup>12</sup>Department of Immunology, St. Jude Children's Research Hospital, Memphis, TN 38105, USA; <sup>13</sup>Molecular Virology and Vaccines Branch, Influenza Division, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA; <sup>14</sup>Laboratory of Virology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rocky Mountain Laboratories, Hamilton, MT 59840, USA; <sup>15</sup>State Key Laboratory of Emerging Infectious Diseases, The University of Hong Kong, Hong Kong SAR, China; <sup>16</sup>Immunology and Pathogenesis Branch, Influenza Division, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA; <sup>17</sup>Institut für Virologie, 35043 Marburg, Germany; <sup>18</sup>National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, Manitoba R3E 3R2, Canada; <sup>19</sup>Department of Preventive Veterinary Medicine, China Agricultural University, Beijing, China; <sup>20</sup>Animal Infectious Disease Laboratory, School of Veterinary Medicine, Yangzhou University, Yangzhou, Jiangsu 225009, China; <sup>21</sup>Department of Microbiology and Immunology, Emory University School of Medicine, Atlanta, GA 30322, USA; <sup>22</sup>Friedrich-Loeffler-Institut, D-17499 Greifswald-Insel Riems, Germany; <sup>23</sup>Department of Virology, Erasmus MC, Rotterdam, Netherlands; <sup>24</sup>Department of Microbiology, Mount Sinai School of Medicine, New York, NY 10029-6574, USA; <sup>25</sup>Department of Microbiology and HKU-Pavlov Research Centre, The University of Hong Kong, Pokfulam, Hong Kong SAR; <sup>26</sup>Department of Veterinary Medicine, University of Maryland, College Park, College Park, MD 20742, USA; <sup>27</sup>College of Veterinary Medicine, Kansas State University, Manhattan, KS 66506, USA; <sup>28</sup>Department of Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN 38105, USA; <sup>29</sup>Department of Microbiology and Immunology, Emory University, School of Medicine, Atlanta, GA 30322, USA; <sup>30</sup>Emerging Respiratory Virus Section, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892-3203, USA; <sup>31</sup>Southeast Poultry Research Laboratory, USDA/Agricultural Research Service, Athens, GA 30605, USA; <sup>32</sup>Department of Microbiology and Immunology, University of Rochester Medical Center, Rochester, NY 14642, USA; <sup>33</sup>National Institute of Infectious Diseases, Influenza Virus Research Center, Tokyo, 208-001, Japan; <sup>34</sup>Viral Pathogenesis and Evolution Section, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892-3203, USA; <sup>35</sup>Department of Immunology, St. Jude Children's Research Hospital, Memphis, TN 38105-3678, USA; <sup>36</sup>Department of Infectious Diseases, College of Veterinary Medicine, University of Georgia, Athens, GA 30602, USA; <sup>37</sup>Influenza Division, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA; <sup>38</sup>Department of Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN 38105-3678, USA; <sup>39</sup>Division of Virology, Department of Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN 38105, USA.

\*To whom correspondence should be addressed. E-mail: r.fouchier@erasmusmc.nl

The continuous threat of an influenza pandemic represents one of the biggest challenges in public health. Influenza pandemics are known to be caused by viruses that evolve from animal reservoirs, such as in birds and pigs, and can acquire genetic changes that increase their ability to transmit in humans. Pandemic preparedness plans have been implemented worldwide to mitigate the impact of influenza pandemics. A major obstacle in preventing influenza

pandemics is that little is known regarding what makes an influenza virus transmissible in humans. As a consequence, the potential pandemic risk associated with the many different influenza viruses of animals cannot be assessed with any certainty.

Recent research breakthroughs identified specific determinants of transmission of H5N1 influenza viruses in swine. Responsible research on influenza virus transmission



ScienceInsider

Breaking news and analysis from the world of science policy

## In Dramatic Move, Flu Researchers Announce Moratorium on Some H5N1 Flu Research, Call for Global Summit

by David Malakoff and Martin Enserink  
20 January 2012, 12:42 PM

Stung by a growing global controversy over the potential dangers of experiments involving the H5N1 avian flu virus—and worried about heavy-handed government regulation—the world's leading H5N1 researchers have agreed to a 60-day moratorium on a controversial category of studies "to allow time for international discussion."



# World Health Organization



## Roundtable Geneva – February 16-17, 2012

- **Goal:** Establish a common understanding around H5N1 research, especially for pandemic flu preparedness
- **New information made available**
  - Additional data and clarifications from authors
  - New non-public epidemiological information
- **Conclusions:**
  - Studies provide an important contribution to public health surveillance of H5N1 viruses
  - Delayed publication of full manuscripts preferable to urgently publishing redacted manuscripts

# Revised Manuscripts



- **Based on research conducted prior to the voluntary “pause,” as well as input from the external reviewers, the authors revised their manuscripts to incorporate:**
  - **Additional data**
  - **Clarifications of findings in the original Fouchier manuscript**
    - **Virus produced after ferret passaging was not highly lethal when transmitted by aerosol**

# New Charge to the NSABB



- **“Taking into account the additional information in the revised manuscripts, epidemiological information presented during the meeting, and the security information that will be presented in the classified briefing:**
  - **Assess the dual use research implications of two unpublished, revised manuscripts on the transmissibility of avian influenza A/H5N1 virus;**
  - **Consider the risks and benefits of communicating the research results; and**
  - **Develop findings and recommendations regarding whether or not the information should be communicated, and if so, to what extent.”**

# NSABB Recommendations

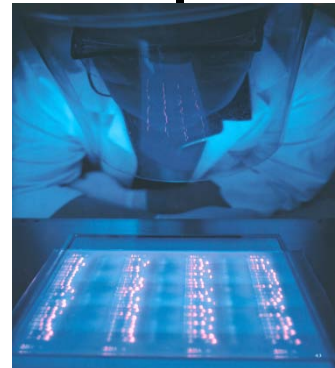
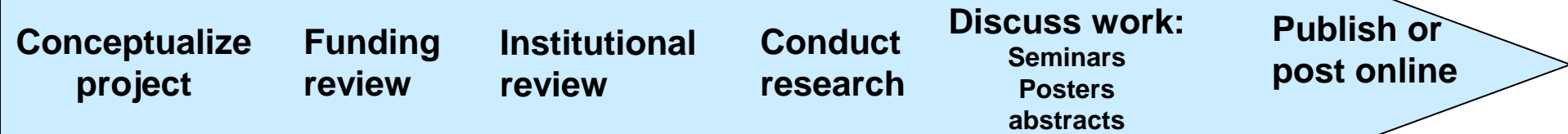
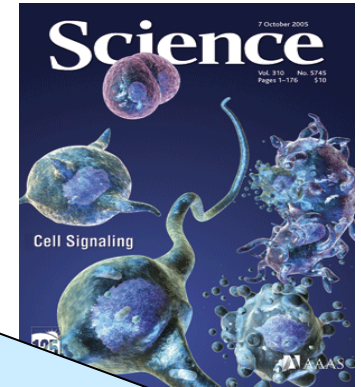
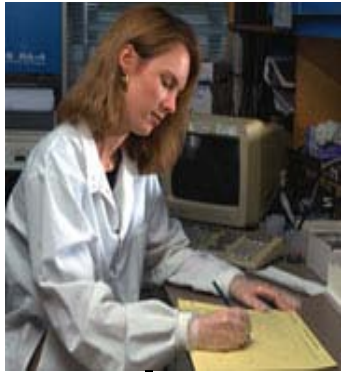
## March 30, 2012



- Revised Kawaoka manuscript should be communicated in full (unanimous; published online May 2, 2012)
- Data, methods, and conclusions presented in revised Fouchier manuscript should be communicated, but not as currently written (12-to-6)
- The U.S. Government should
  - Continue to develop national, and participate in development of international, policies for oversight of dual use research of concern
  - Develop a mechanism to provide controlled access to sensitive scientific information



# Proposed Oversight Approach: Comprehensive Coverage of Research Process



# **“It takes a village”**



- **To deal with the issue effectively:**
  - **Responsibility must be shared among the researcher, publishers, institutional officials, local oversight bodies, and the Federal government**

# USG Policy on Oversight of DURC



- **Issued by** the Administration on March 29, 2012
- **Purpose:** To establish regular review of USG funded or conducted research with certain high-consequence pathogens and toxins for its potential to be DURC in order to:
  - mitigate risks where appropriate; and
  - collect information needed to inform the development of an updated policy, as needed, for the oversight of DURC

# USG Policy on Oversight of DURC



- **Aim:** To preserve the benefits of life sciences research while minimizing the risk of misuse of the knowledge, information, products, or technologies provided by such research.
- **Complements existing regulations and policies** governing the possession and handling of pathogens and toxins.
- **Will be updated**, as needed, following domestic dialogue, engagement with international partners, and input from interested communities

# Step 1: Identification of research involving any of the 15 agents or toxins listed



1. Avian influenza virus (highly pathogenic)
2. *Bacillus anthracis*
3. Botulinum neurotoxin
4. *Burkholderia mallei*
5. *Burkholderia pseudomallei*
6. Ebola virus
7. Foot-and-mouth disease virus
8. *Francisella tularensis*
9. Marburg virus
10. Reconstructed 1918 Influenza virus
11. Rinderpest virus
12. Toxin-producing strains of *Clostridium botulinum*
13. Variola major virus
14. Variola minor virus
15. *Yersinia pestis*

## **Step 2:** Identification of research that produces, aims to produce, or is reasonably anticipated to produce any of the listed effects



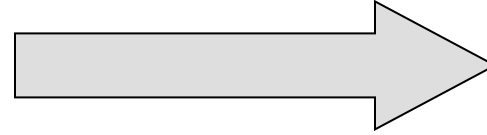
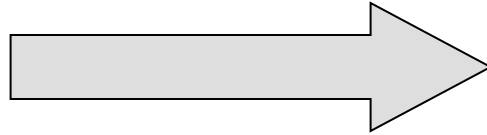
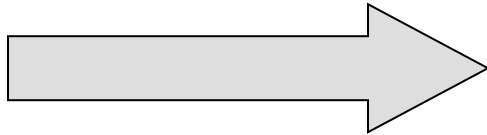
- 1. Enhances the harmful consequences of the agent or toxin;**
- 2. Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical and/or agricultural justification;**
- 3. Confers to the agent or toxin resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitates their ability to evade detection methodologies;**
- 4. Increases the stability, transmissibility, or the ability to disseminate the agent or toxin;**
- 5. Alters the host range or tropism of the agent or toxin;**
- 6. Enhances the susceptibility of a host population to the agent or toxin; or**
- 7. Generates or reconstitutes an eradicated or extinct agent or toxin listed in Section III.1**

## **Step 3: Determination of whether the research is DURC**

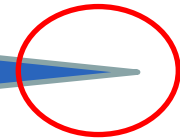


### ***Dual Use Research of Concern***

**Life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.**



**Federally Funded Life Sciences Research**



**Requires additional  
Federal and local  
oversight and risk  
mitigation strategies to  
address dual use concerns**



# Risk Assessment



- For projects that fall within the scope and that are determined to meet the definition of DURC, departments and agencies will:
  - Assess the **risks and benefits** of such projects, including how research methodologies may generate risks and/or whether open access to the knowledge, information, products, or technologies generates risk
  - Develop, in collaboration with the institution or researcher, a **risk mitigation plan** to apply any necessary and appropriate risk mitigation measures



# Current Risk Mitigation Measures



- **Biosafety**
  - NIH Guidelines for Research Involving Recombinant DNA Molecules
  - Biosafety in Microbiological and Biomedical Laboratories (BMBL)
  - Select Agent Rules
- **Biosecurity**
  - Personnel Reliability Programs
  - Select Agent Rules
- **Occupational Health and Safety**

# USG Policy on Institutional Oversight of DURC



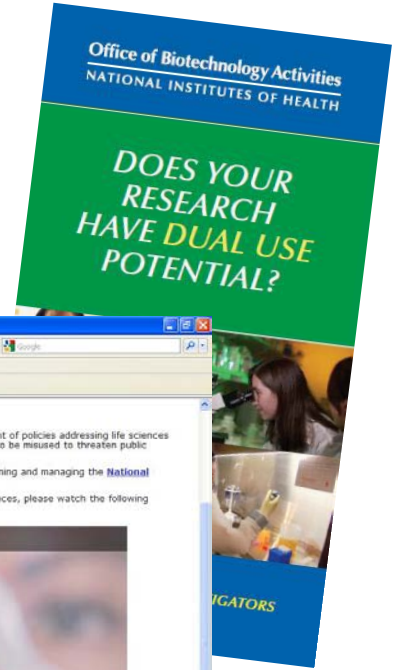
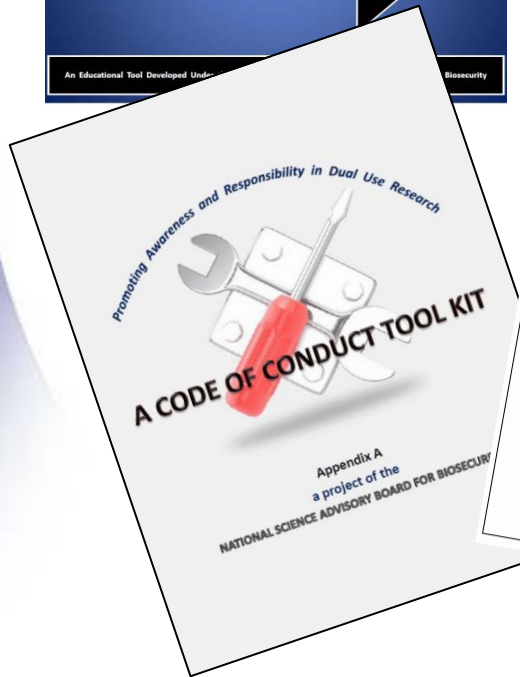
- **Proposed Policy**
  - Under development
  - Will define roles and responsibilities of research institutions and investigators funded by the USG
  - Will be issued for public comment
- **Companion document** - Tools to assist institutions in implementing policy, including:
  - Risk/benefit assessment tool
  - Guidance for responsible communication of DURC
  - Tool for developing a code of conduct

# USG Policy Development: Examples of Challenges



- **Determination of whether research meets the dual use research of concern criteria is more of a judgment call than:**
  - **Animal research**
  - **Human subjects research**
  - **Recombinant DNA research**
- **Traditional life sciences training does not include how to assess**
  - **Ways in which life science research could be misused**

# Current Educational Tools on DURC



<http://oba.od.nih.gov/biosecurity/biosecurity.html>

# USG Policy Development: Examples of Challenges



- **Minimizing the possibility of misuse of research while promoting the responsible advancement of science – concerns:**
  - **Restricting the open communication of science**
  - **Stigmatizing certain areas of research**
  - **Discouraging new investigators to enter these fields**
  - **Inhibiting science to the detriment of public health and security**

# Other considerations



- **Management of “threshold-crossing” dual use information**
  - **Role of classification**
  - **Controlling access to sensitive information in the absence of classification**
- **International cooperation**
  - **Science and public health are global concerns**
  - **Nexus of US policies and practices with those of international partners**

# International Engagement



## ▪ Objectives

- Raise awareness of DURC internationally
- Learn from and foster international programs, activities, and strategies for dealing with DURC
- Create an international network of individuals and organizations interested and engaged in DURC





# International Engagement Activities of USG



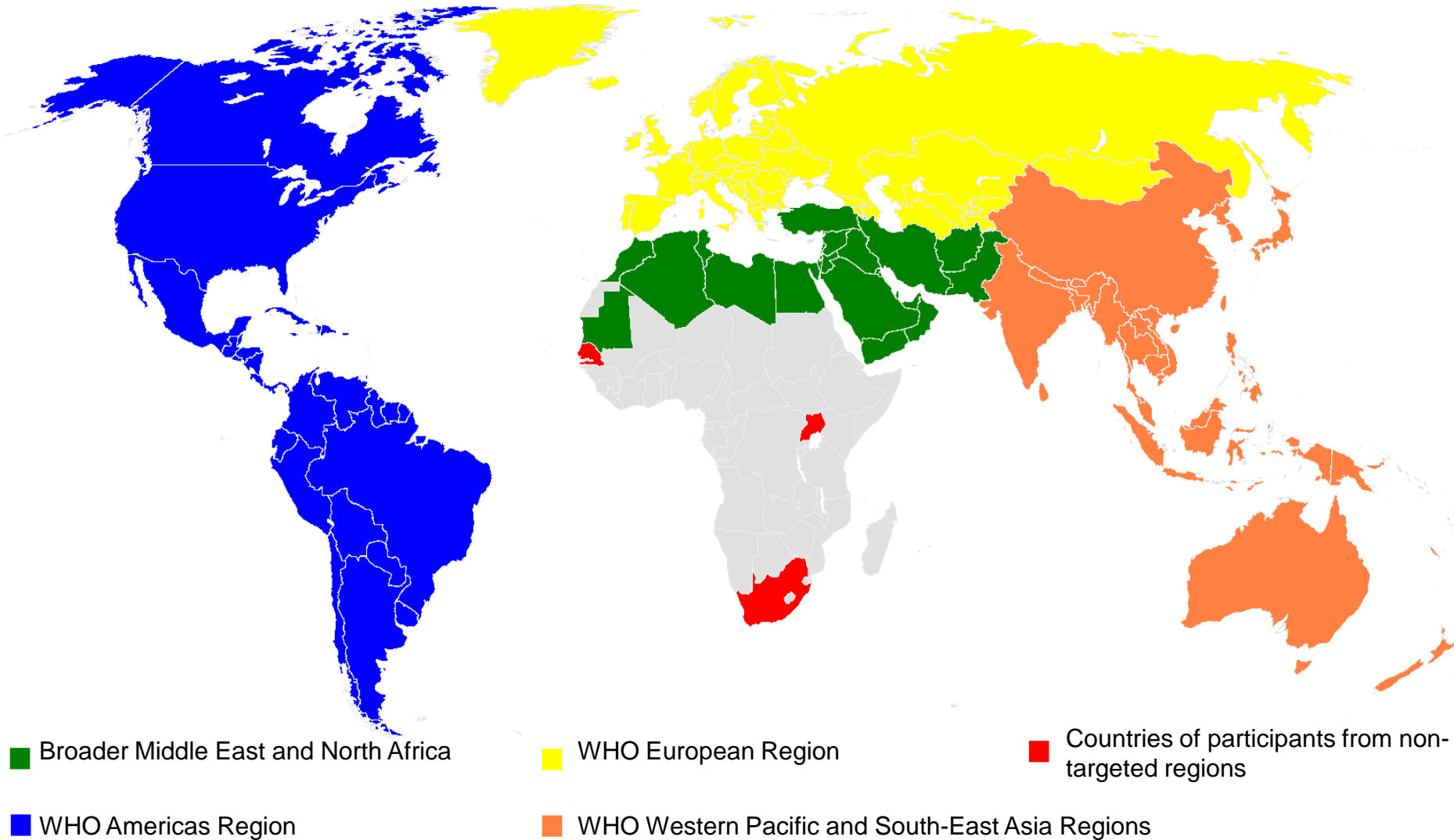
## ■ Modes of Engagement

- International Roundtables (Bethesda, Maryland)
- Interactive Webcasts (Regional)
- Video-teleconferences (Regional and global audiences)
- International Workshops (Regional)

## ■ Participants

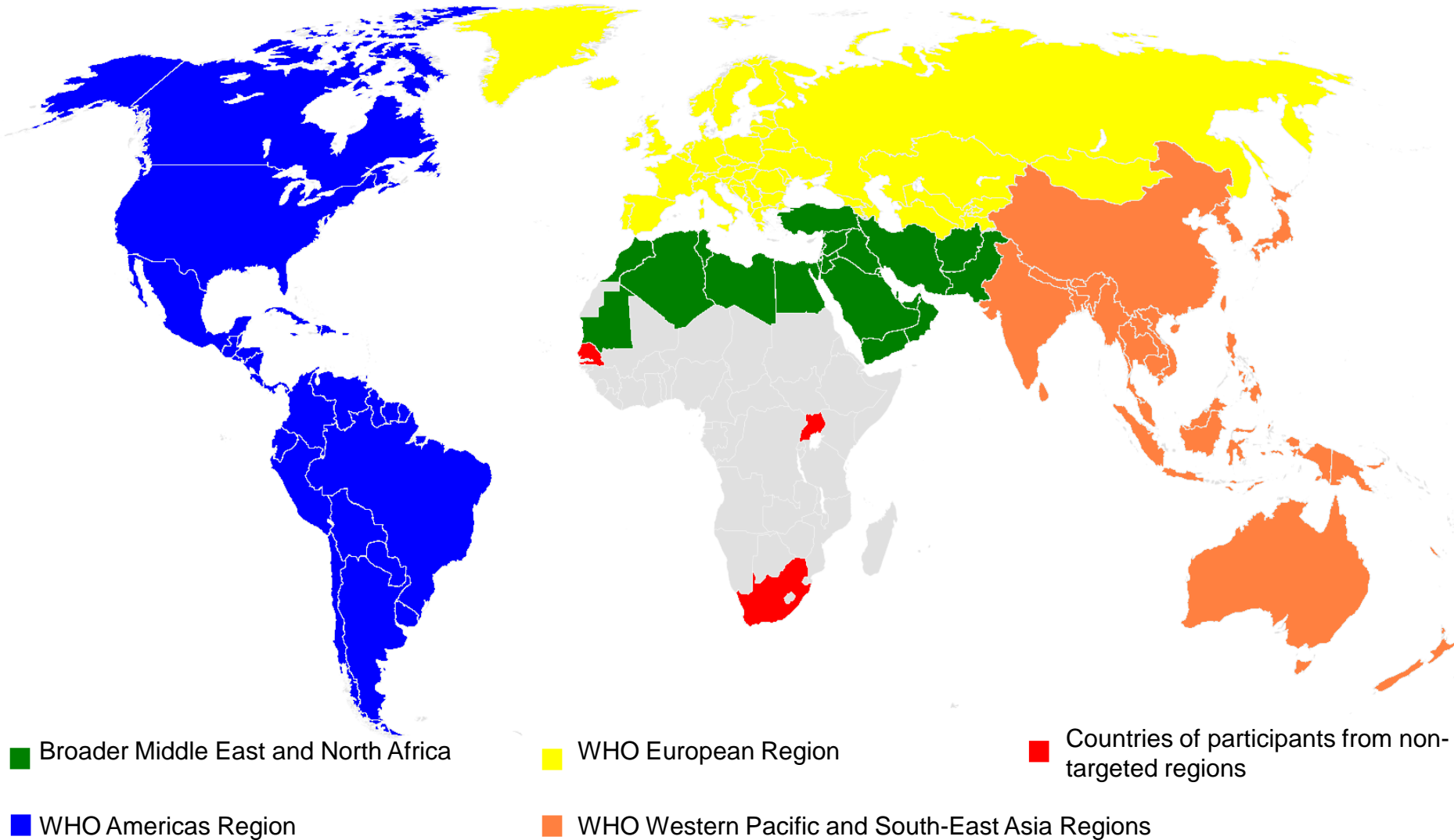
- Health and science ministries globally
- Intergovernmental organizations (FAO, OECD, UNESCO, WHO, etc.)
- Philanthropic organizations
- Scientific associations and international societies

# Regions Engaged through International Outreach\*



\*Organized by NIH Office of Science Policy in collaboration with USG agencies, NSABB, international partners

# Regions Engaged through International Outreach\*



\*Organized by NIH Office of Science Policy in collaboration with USG agencies, NSABB, international partners



- **Logistics**
  - Geneva; early 2013
  - Participants: Broad range of stakeholders and interested parties from around the globe
- **Meeting Objectives**
  - Identify key perspectives, issues and concerns around DURC;
  - Assess gaps in current strategies for managing DURC; and
  - Identify options for improving ways to address DURC
- **Outcomes**
  - Report that summarizes opportunities and challenges, and articulates options for moving forward

# Discussion



- **A lot is at stake:**
  - Public health
  - National security
  - Public trust
- **Getting oversight right:**
  - Amount
  - Locus
  - Mechanisms
  - Measuring impact
  - Adjusting as needed
- **Your input on these matters is needed**

# Discussion



- **Questions?**
- **Comments?**