Enhancing Biosecurity in the Life Sciences

National Science Advisory Board for Biosecurity

NBSB Meeting
June 18, 2008

The "Dual Use" Issue

- ***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***

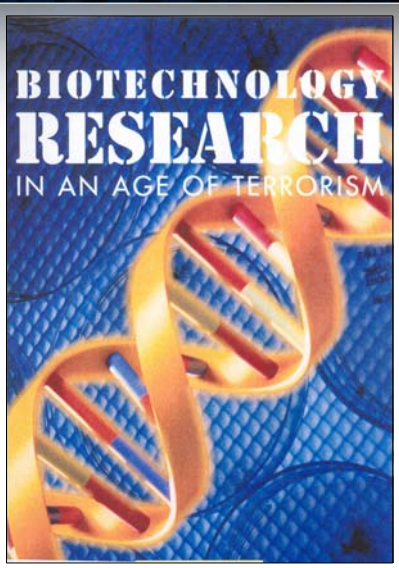
Calls to Action

- **Increasing recognition of need to consider possibility that new information from life sciences research could be subverted for malevolent purposes**
- **Growing global acknowledgment of need to institute new biosecurity measures to minimize this risk**

National Academies Report on Dual Use Research

Report of the National Research Council of the National Academies:

"Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma"
(October 2003)



Journal Editors and Authors Group statement on the consideration of biodefense and biosecurity

We recognize that the prospect of bioterrorism has raised legitimate concerns about the potential abuse of published information, but also recognize that research in the very same fields will be critical to society in meeting the challenges of defense.

Fundamental is a view, shared by nearly all, that there is information that, although we cannot now capture it with lists or definitions, presents enough risk of use by terrorists that it should not be published.

Scientist and their journals should consider the appropriate level and design of processes to accomplish effective review of papers that raise such security issues.

Editorial
Nature 421:771 (2003)

"Do no harm: reducing the potential for the misuse of life science research"

Research institutions and funding agencies need to consider how to build on existing processes for reviewing research projects to ensure that risks of misuse are assessed in an appropriate and timely manner.

2004 Report of the Royal Society-Wellcome Trust

"Science and Security in an Age of Terrorism"

The scientific, engineering, and health research community should work closely with the federal government to determine which research may be related to possible new security threats and to develop principles for researchers in each field.

Alberts, Wulf and Fineberg
Presidents of the National Academies
October 18, 2002

"Risks and benefits of dual-use research"

"It is important to develop clear guidelines about what research is considered sensitive, what is expected of researchers whose work produces dual-use outcomes, and how the government should in practice respond without losing the priceless virtue of open scientific scrutiny."

***Nature* 435:7044 (2005)**

US Government Response

- Agreement that new biosecurity measures warranted
- USG launched a series of biosecurity initiatives, including establishment of National Science Advisory Board for Biosecurity (NSABB)
  - NSABB to recommend strategies for the efficient and effective oversight of dual use life sciences research
    - Consider both national security concerns and needs of the life sciences research community

NSABB Expertise

- Molecular/genomics
- Microbiology
- Clin. ID/diagnostics
- Lab biosafety/security
- PH/epidemiology
- Health physics
- Pharm. production
- Veterinary medicine
- Plant health
- Food production
- Bioethics
- National security
- Intelligence
- Biodefense
- IBCs
- Export controls
- Law, law enforcement
- Scientific publishing
- Perspectives from academia, industry, public, RAC

NSABB: A USG-wide Initiative

- Advisory to heads of all Federal entities that conduct/support life sciences research
- Supported by 15 USG departments and agencies with a role/interest in life sciences research
  - Appoint *ex officio* member(s)
  - Consider recommendations of NSABB when developing and implementing life sciences research programs and policies

NSABB *ex officios*

- Exec. Office of the President
- Department of Health and Human Services
- Department of Energy
- Department of Homeland Security
- Department of Veteran's Affairs
- Department of Defense
- Environmental Protection Agency
- United States Department of Agriculture
- Department of Interior
- National Sciences Foundation
- Department of Justice
- Department of State
- Department of Commerce
- National Aeronautics and Space Administration
- Intelligence community

NSABB Charge

- Criteria for identifying dual use research of concern
- National guidelines for oversight of dual use research at both local and federal levels
- National guidelines on communication and dissemination of dual use research methodology and research results
- A code of conduct for scientists and laboratory workers in life sciences research
- Program for biosecurity education and training for all scientists and laboratory workers at federally funded institutions
- Strategies for promoting international dialogue on dual use research issue
- Other issues as assigned

Modus Operandi

- Working Groups
- Iterative Consultations:
  - Life sciences research community (domestic and international)
  - Life sciences research administrators
  - Security community
  - Scientific and Professional society leadership
  - Public policy groups
  - Bioethics community
  - Biosafety community
  - Scientific publishing community
  - General Public

Concerns

Scientific Community

- Evidence of problem?
- Red tape and restraints on research and communication slow progress
- Restricting communication -- starting down a slippery slope to censorship?

Public

- Need for more effective oversight of dual use research
- Laws and regulations may be necessary

NSABB Considered These Concerns

- **NSABB Deliberations**
  - What is the problem?
  - How big is it?
- **NSABB Conclusions**
  - Threat of misuse exists and consequences could be severe
    - Risks to public health, security
    - Damage to public trust
  - Response to threat of misuse of research findings must be carefully measured
    - Continued rapid progress of life sciences is critical

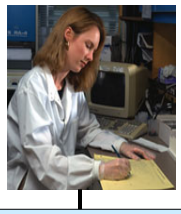
Draft Oversight Framework: Main Elements

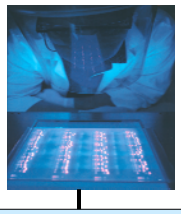
- Guiding principles
- Roles and responsibilities
- Criterion for identifying dual use research of concern
- Risk assessment and management
- Responsible communication of dual use research
- Considerations for code of conduct

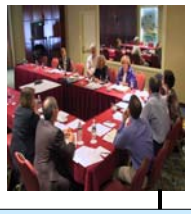
Available on the NSABB website:
www.biosecurityboard.gov

Status: Submitted to USG

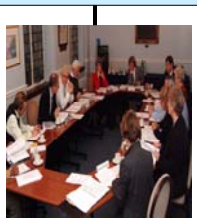
Culture of Awareness and Responsibility Throughout the Research Life Cycle







Conceptualize project → Funding review → Conduct research → Discuss work: Seminars, Posters, abstracts → Peer review → Publish or post online



July 15, 2008 Consultation on Proposed Oversight Framework

- Precious resource in the balance
  - Life sciences vital to health and progress
  - Predicated on public trust
- Input needed to inform the policy decision making process
  - USG sponsored workshop to solicit input from scientific community and general public
    - Specific questions for consultation outlined in Appendix 2 of Oversight Framework

International Engagement

- Science is global
- Hosting a series of international discussions
  - Encourage dialogue and collaboration regarding oversight of dual use research
  - Welcome international input on US approach to oversight of dual use research
- Initiated dialogue with over 50 countries and multiple international organizations
  - USG-WHO International Roundtables on Dual Use Life Sciences Research*

*http://www.biosecurityboard.gov/pdf/1st%20International%20Roundtable%20FINALWeb.pdf
*http://www.biosecurityboard.gov/pdf/Intl%20Roundtable%20Brief%20Summary%20Oct07%20NSABBWeb.pdf

NSABB Charge

- √ Criteria for identifying dual use research of concern
- √ National guidelines for oversight of dual use research at both local and federal levels *(framework)*
- √ National guidelines on communication and dissemination of dual use research methodology and research results
- √ A code of conduct for scientists and laboratory workers in life sciences research
- Program for biosecurity education and training for all scientists and laboratory workers at federally funded institutions *(ongoing)*
- Strategies for promoting international dialogue on dual use research issue *(ongoing)*
- Other issues as assigned *(ongoing)*

Biosecurity Concerns and Synthetic Genomics

Background

DNA synthesis technology is rapidly advancing. Can be used to make organisms *de novo*, without needing access to natural sources of organisms or their nucleic acids.

+

Open availability of DNA sequence data of pathogens

=

Concerns that this technology and information could be misused to make dangerous pathogens to threaten public health

"Revealed: the lax laws that could allow assembly of deadly virus DNA"

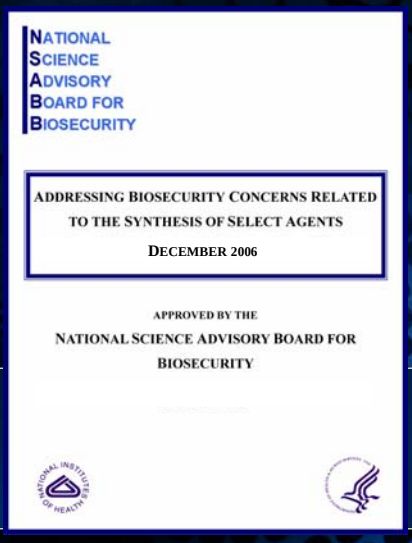
The Guardian
June 14, 2006

- A phial containing an incomplete sequence of smallpox DNA, obtained by the Guardian over the internet.
- Urgent calls for regulation after Guardian buys part of smallpox genome through mail order

Photo: Martin Arles

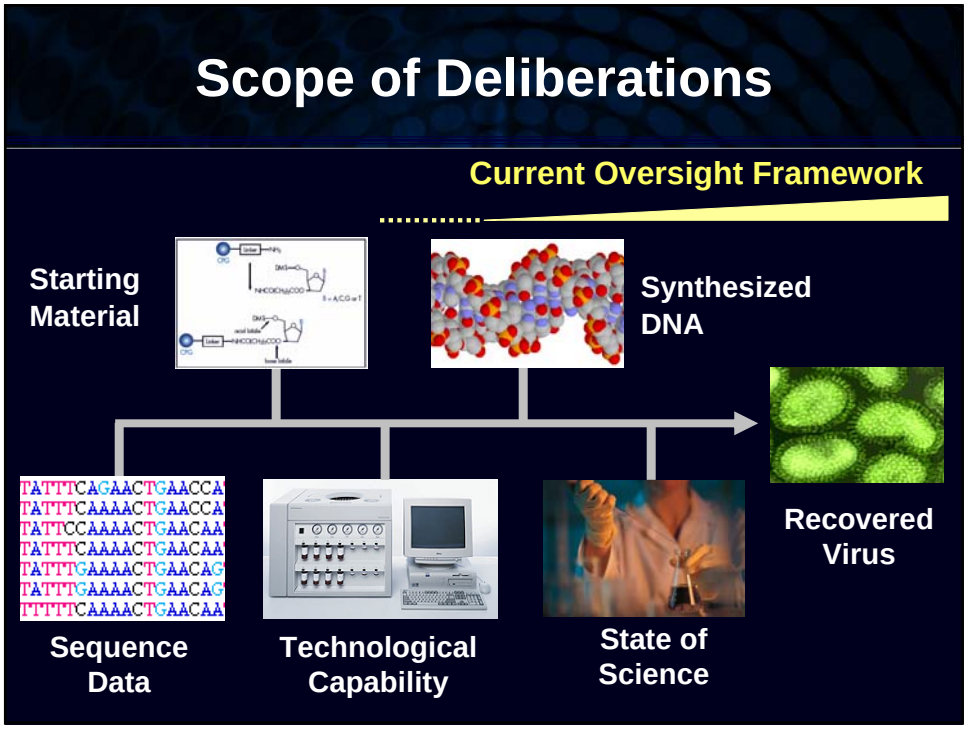
Charge to NSABB

- Identify the potential biosecurity concerns raised by synthesis of Select Agents (SA)
  - Assess the adequacy of the current regulatory and oversight framework
  - Recommend potential strategies to address any biosecurity concerns



Available on the NSABB website: www.biosecurityboard.gov

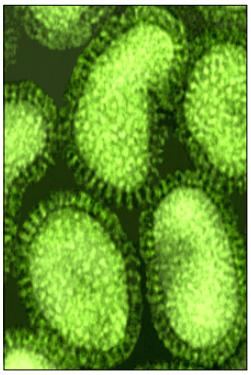
Scope of Deliberations



Scope of Findings

- **State of the science** in a few key application areas, for deriving infectious agents from synthetic nucleic acids
- **State of the technology** for synthesizing nucleic acids
- **State of the oversight framework** for the control of SA

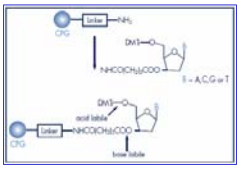
State of the Science

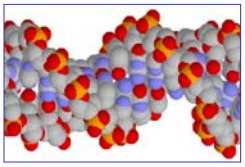


- Possible to recover/reconstruct from DNA certain SA
  - successful use of reverse genetics requires technical skill
- Infectious viruses have been created using combinations of genomic material from various SA
  - these novel organisms do not fit current taxonomic classification schemes

State of Technology

- DNA synthesis reagents and equipment readily available globally.
- Synthesis of DNA up to 120 base pairs (bp) in length (accurately) is routine and common; >180 bp remains somewhat of an art.
- Complete genomes of some viruses can be synthesized *de novo*, but this capability is not yet widely distributed.





State of the Oversight Framework

- **Key components of the SA oversight framework for synthetic SA nucleic acids include:**
  - **Select Agent Rules (SAR)**
  - **Export Controls**
  - **Commerce Control List (CCL)**
  - **18 USC 175c (Variola amendment)**
- **Biosafety guidelines**
  - ***NIH Guidelines for Research Involving Recombinant DNA Molecules***
  - **Biosafety in Microbiological and Biomedical Laboratories Manual (BMBL)**

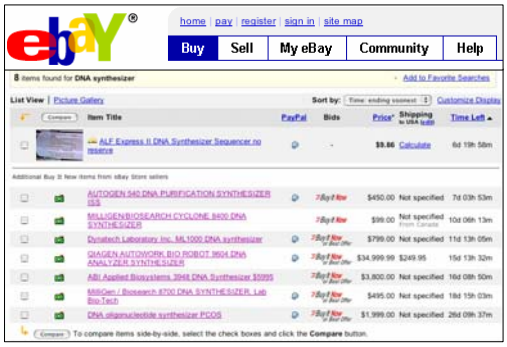
Overview of Biosecurity Issues

- **Synthetic genomics may enable easy acquisition of a SA without authorization from CDC/USDA**
- **Screening sequences**
- **Regulatory ambiguity, inconsistency, and limitations**
- **Challenges to developing alternate regulatory approaches**
- **Biosafety**

Issue: Ease of Acquisition

- **Synthetically derived SA nucleic acids easily acquired**
  - Increasingly feasible to synthesize ≥ gene-length DNA constructs
  - Reagents and machines readily available
  - Methods, technology, sequences in public domain
- **Rapidly expanding global industry largely localized in private sector**
  - No accepted "best practices" in record keeping, sequence tracking, etc.
- **Reports from service providers of requests from customers to not query sequence identity**
  - Invoking "trade secret"

DNA Synthesis: Do It Yourself



Commercial DNA Synthesis Foundries

Rob Carlson, University of Washington; Gerald Epstein and Anne Yu, CSIS

18 July 05. Method: Rough Google search. Thus not a thorough survey. No academic facilities.

Data Source: Rob Carlson, U of W, Seattle
www.synthesis.cc, rob@synthesis.cc

Issue: Regulatory Ambiguity

- **Considerable diversity of interpretation of key laws, regulations and policies and their applicability to synthetic sequences and organisms**
  - **e.g., SAR preamble notes that it is incumbent upon entities that manufacture "substances" to "know what they are manufacturing" and to ensure that they comply with the SAR**
  - **However, <50% of providers surveyed routinely screen sequences**

Issue: Screening Sequences

- Need for better screening tools
- This requires more science and technology
  - Improved sequence databases and software tools;
  - Enhanced understanding of virulence;
  - Improved framework for interpreting sequence screening results

Issue: Difficulty in Developing a Suitable Regulatory Framework

- Synthetic Genomics:
  - Allows expression of agents with the harmful properties of a specific SA, without being clearly identifiable as SA based on their sequence; and
  - Provides or enhances the capability for producing novel agents that pose risks equal to, or greater than, those of naturally-occurring SA
- There currently is no optimized, standardized, or agreed-upon method for screening orders for sequences
- Current scientific understanding inadequate to predict function and behavior of an agent from its genetic sequence
  - Harmful properties of agents often due to combination or interaction of genetic elements rather than one specific gene sequence
  - Agent functional properties depend on biologic context

Issue: Biosafety

- Current risk assessment paradigm based on knowledge of parent agent
  - De novo synthesis of “designer” pathogens with little or no homology to a parent organisms challenges current risk assessment approaches
- Some practitioners of synthetic genomics are:
  - Educated in disciplines that do not routinely entail formal training in biosafety; and
  - Unclear as to the circumstances under which to consult an Institutional Biosafety Committee.

Selected Findings and Recommendations

- Increase awareness among investigators and service providers about their responsibility to know what they possess, manufacture and/or transfer
- Develop additional guidance and tools for screening orders and interpreting results
- Foster international dialogue and collaboration
  - Develop and implement universal standards and preferred practices for screening sequences
- Need to ensure that biosafety guidelines address synthetic nucleic acids
- 18 USC 175c (aka “Variola Amendment”) is highly problematic

USG Response to NSABB Report

- **Trans-federal policy coordination process involving 22 departments and/or agencies led by White House Homeland Security Council and Office of Science and Technology Policy**

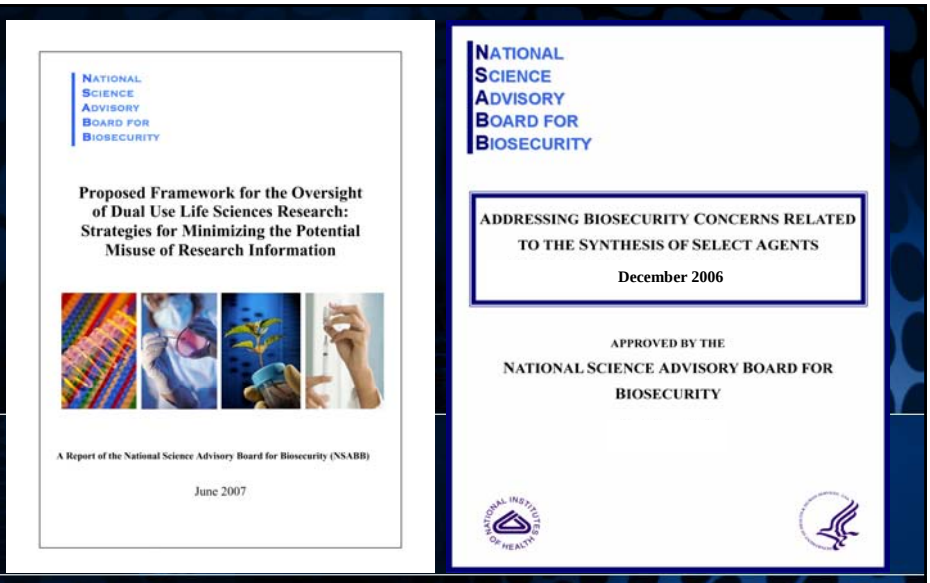
Implementation of USG Policy on Synthetic DNA and Security

1. **HHS and USDA should develop and disseminate harmonized guidance concerning the Select Agent Regulations with respect to synthetically-derived DNA;**
2. **HHS, USDA, DHS et al. should engage stakeholders in industry and academia to identify, evaluate and support establishment of a screening infrastructure for use by commercial providers and users of synthetic nucleic acids.**
   - **In parallel, HHS and USDA should explore the legal options, benefits, and costs associated with the range of implementation options;**
3. **State Dept. should coordinate interagency dialogue, strategy, and international outreach on synthetic biology issues per the general principles outlined in its white paper;**
4. **DoJ should, convene an interagency panel to address the issues raised concerning 18 U.S.C. 175c;**

Implementation of USG Policy on Synthetic DNA and Security

5. HHS should update and revise as appropriate the *NIH Guidelines for Research Involving Recombinant DNA Molecules* and *Biosafety in Microbiological and Biomedical Laboratories*;
6. Commerce Dept., in coordination with HHS and USDA, should explore opportunities for reconciliation of Commerce Control List and SAR language in the context of action 1;
7. Following implementation of actions outlined in 1 and 2, HHS and OSTP should convene a panel to consider the possibility of revision of the SAR to accommodate future advances in synthetic genomics;
8. HHS and OSTP should identify the list of scientific advancements necessary before a predictive oversight system can be postulated, developed, evaluated and potentially implemented.

Assigned agencies are actively carrying out these taskings in accordance with APA and other relevant laws.



Available on the NSABB website:
www.biosecurityboard.gov

Status: Submitted to USG

http://www.biosecurityboard.gov