

Biosafety Implications of Synthetic Genomics Technology: US Policy Development



February 27, 2008



Background

DNA synthesis technology is rapidly advancing. Can be used to synthesize partial or, in some circumstances, whole genomes *de novo*, without needing access to natural sources of organisms or their nucleic acids.

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Open availability of DNA sequence data of pathogens

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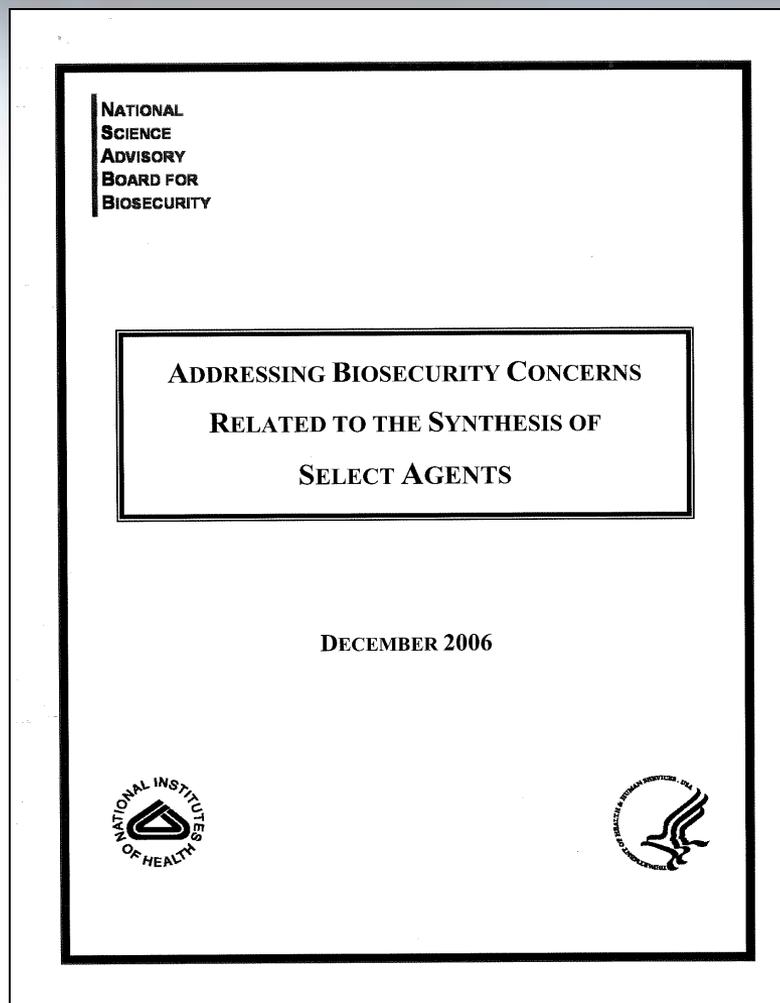
Concerns that this technology and information could be misused to make dangerous pathogens to threaten public health

Charge to NSABB on Synthetic Genomics

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

NSABB Report

www.biosecurityboard.gov



Selected Findings and Recommendations of NSABB

- Increase awareness among investigators and service providers about their responsibility to know what they possess, manufacture and/or transfer
- Need for 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**

Selected Findings and Recommendations of NSABB

- **Some practitioners of synthetic genomics are:**
 - **Educated in disciplines that do not routinely entail formal training in biosafety; and**
 - **Uncertain about when to consult an Institutional Biosafety Committee (IBC)**
- **There is a need for biosafety principles and practices applicable to synthetic genomics**

U.S. Government Consideration of NSABB Recommendations

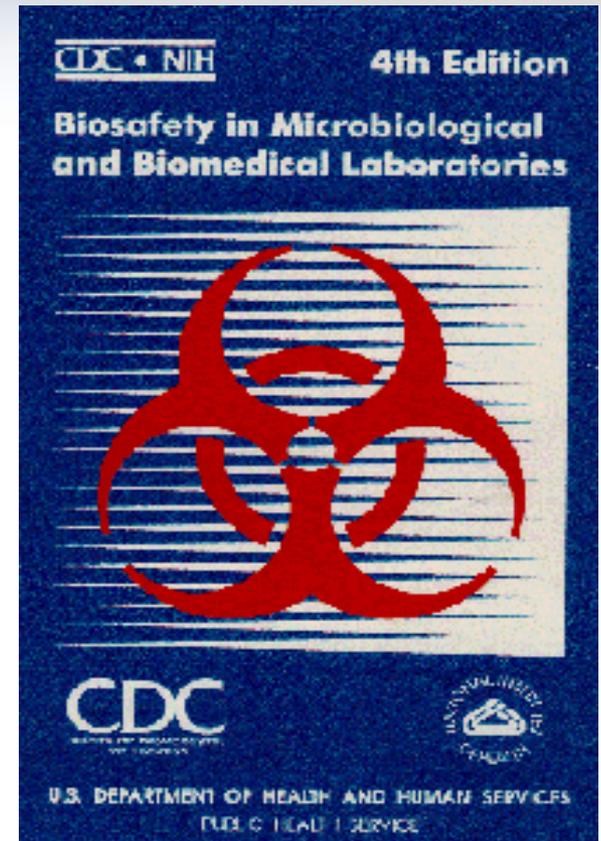
- **NSABB recommendations were considered through a trans-federal policy coordination process**
 - **Led by the White House Homeland Security Council and Office of Science and Technology Policy**
- **Recommendation on need for biosafety guidance accepted by USG with understanding that implementation would be through modification of existing guidelines as appropriate**

U.S. Government Policy Decisions

- HHS should update and revise as appropriate the *NIH Guidelines and Biosafety in Microbiological and Biomedical Laboratories*
- Develop guidance for investigators and laboratory workers that addresses the unique safety issues related to work with certain synthetic nucleic acids and offers practical and effective options for managing risks to personnel and public health associated with such research

Current Biosafety Guidance

- **Biosafety in Microbiological and Biomedical Laboratories Manual (BMBL)**
 - Agent specific, not technology driven
 - References the *NIH Guidelines*



Current Biosafety Guidance

- ***NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)***
 - ❑ **Molecules that are constructed outside living cells by joining natural or **synthetic** DNA segments to DNA molecules that can replicate in a living cell, or**
 - ❑ **Molecules that result from the replication of those described above**

NIH Guidelines

<http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html>

Amendment Effective July 26, 1994, Federal Register, August 5, 1994 (59 FR 40170)
Amendment Effective April 17, 1995, Federal Register, April 27, 1995 (60 FR 20726)
Amendment Effective December 14, 1995, Federal Register, January 19, 1996 (61 FR 1482)
Amendment Effective March 1, 1996, Federal Register, March 12, 1996 (61 FR 10004)
Amendment Effective January 23, 1997, Federal Register, January 31, 1997 (62 FR 4782)
Amendment Effective September 30, 1997, Federal Register, October 14, 1997 (62 FR 53335)
Amendment Effective October 20, 1997, Federal Register, October 29, 1997 (62 FR 56196)
Amendment Effective October 22, 1997, Federal Register, October 31, 1997 (62 FR 59012)
Amendment Effective February 4, 1998, Federal Register, February 17, 1998 (63 FR 3052)
Amendment Effective April 30, 1998, Federal Register, May 11, 1998 (63 FR 26019)
Amendment Effective April 29, 1999, Federal Register, May 11, 1999 (64 FR 25365)
Amendment Effective October 2, 2000, Federal Register, October 10, 2000 (65 FR 60339)
Amendment Effective December 28, 2000, Federal Register, January 5, 2001 (66 FR 1149)
Amendment Effective December 11, 2001, Federal Register, December 11, 2001 (66 FR 64051)
Amendment Effective December 19, 2001, Federal Register, November 19, 2001 (66 FR 57970)
Amendment Effective January 10, 2002, Federal Register, December 11, 2001 (66 FR 64052)
Amendment Effective January 24, 2002, Federal Register, November 19, 2001 (66 FR 57970)

NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT DNA MOLECULES (NIH GUIDELINES)

April 2002

Visit the OBA web site at:
<http://www4.od.nih.gov/oba>

For current information on Guidelines, Protocols, Principal Investigator Meetings,
and information about upcoming Gene Therapy Policy Conferences

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)

These NIH Guidelines supersede all earlier versions and shall be in effect until further notice.

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NIH Recombinant DNA Advisory Committee (RAC)

- Federal advisory committee providing advice and recommendations to the NIH Director and Secretary of HHS regarding recombinant DNA research
- Unique public forum for the discussion of science, safety, and ethics of recombinant DNA research

NIH RAC Expertise

- **Virology**
 - **AdV**
 - **RV**
 - **HSV**
 - **AAV**
- **Biosafety**
- **Immunology**
- **Genetics**
- **Bioethics**
- **Public representative**
- **Internal Medicine**
- **Pediatrics**
- **Infectious Disease**
- **Cardiology**
- **Pulmonology**
- **Metabolism**
- **Hematology**
- **Oncology**
- **Neurology**
- **Clinical Trial Design**
- **Clinical Data Monitoring**
- **Law**

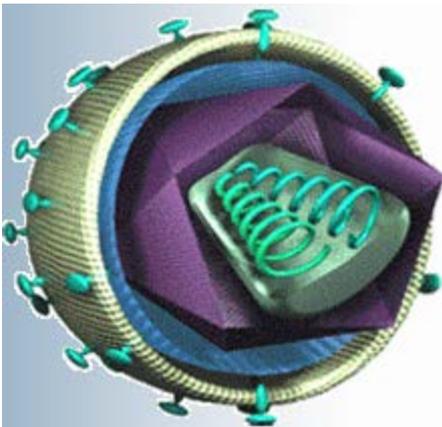
RAC and rDNA Research

- **Reviews over 60 human gene transfer protocols per year and selects approximately a dozen protocols per year for public discussion**
- **Provides NIH with advice and expertise on emerging policy issues related to rDNA research and biosafety**
- **Includes *ex-officio* representation from other agencies include the FDA, CDC, USDA and OHRP**
- **Provides the scientific community and public opportunity to participate in quarterly meetings**

The RAC: *NIH Guidelines and Biosafety*



- **Recommendations to NIH on selected research that raises important public health issues**
 - Introduction of tetracycline resistance into *Chlamydia* *sps.*
 - Introduction of chloramphenicol resistance into *Rickettsia conorii* and *typhi*
- **Safety Symposia and Guidance**
 - *Safety Considerations in Recombinant DNA Research with Pathogenic Viruses*
 - *Biosafety Considerations for Research with Lentiviral Vectors*
 - *Designation of research strains of Ecoli as RG 1 agents*



RAC

Biosafety Working Group

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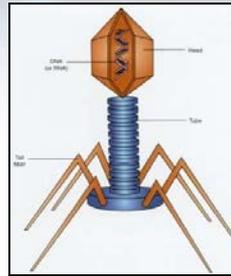
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Charge to the RAC

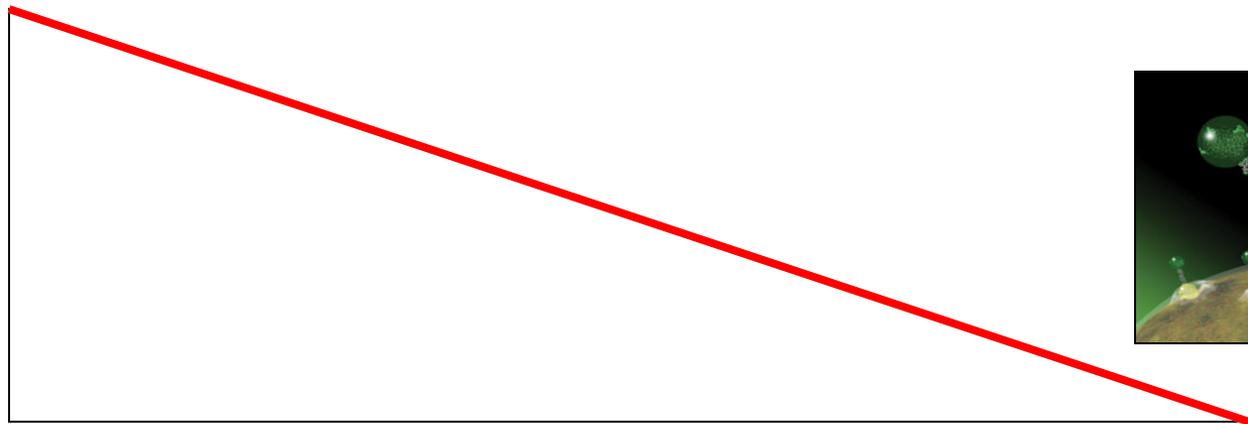
Synthetic biology:

- **Consider the applicability of the *NIH Guidelines for Research Involving Recombinant DNA Molecules* to synthetic biology:**
 - ❑ **To what degree is this technology covered?**
 - ❑ **Does the scope need to be modified to capture synthetic biology?**
- **Develop draft recommendations regarding principles and procedures for risk assessment and management of research involving synthetic biology**

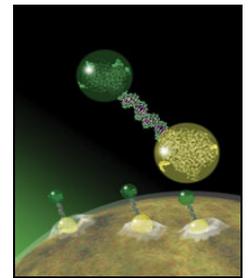
Revisiting the Current Risk Assessment Paradigm



**Data
Underpinning
Biosafety
Level
Designation**



**Known
Agent**



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Review of Revised *NIH Guidelines*

- **Draft work products will be reviewed and approved by full RAC**
- **Recommendations to be published in Federal Register and opportunity for public comment**
- **Recommendations ultimately conveyed to NIH Director and HHS leadership**