NATIONAL SCIENCE ADVISORY BOARD FOR BIOSECURITY

NSABB Working Group on Synthetic Genomics

Recommendations to the Board

David Relman, M.D.
Working Group Chair
10/25/2006

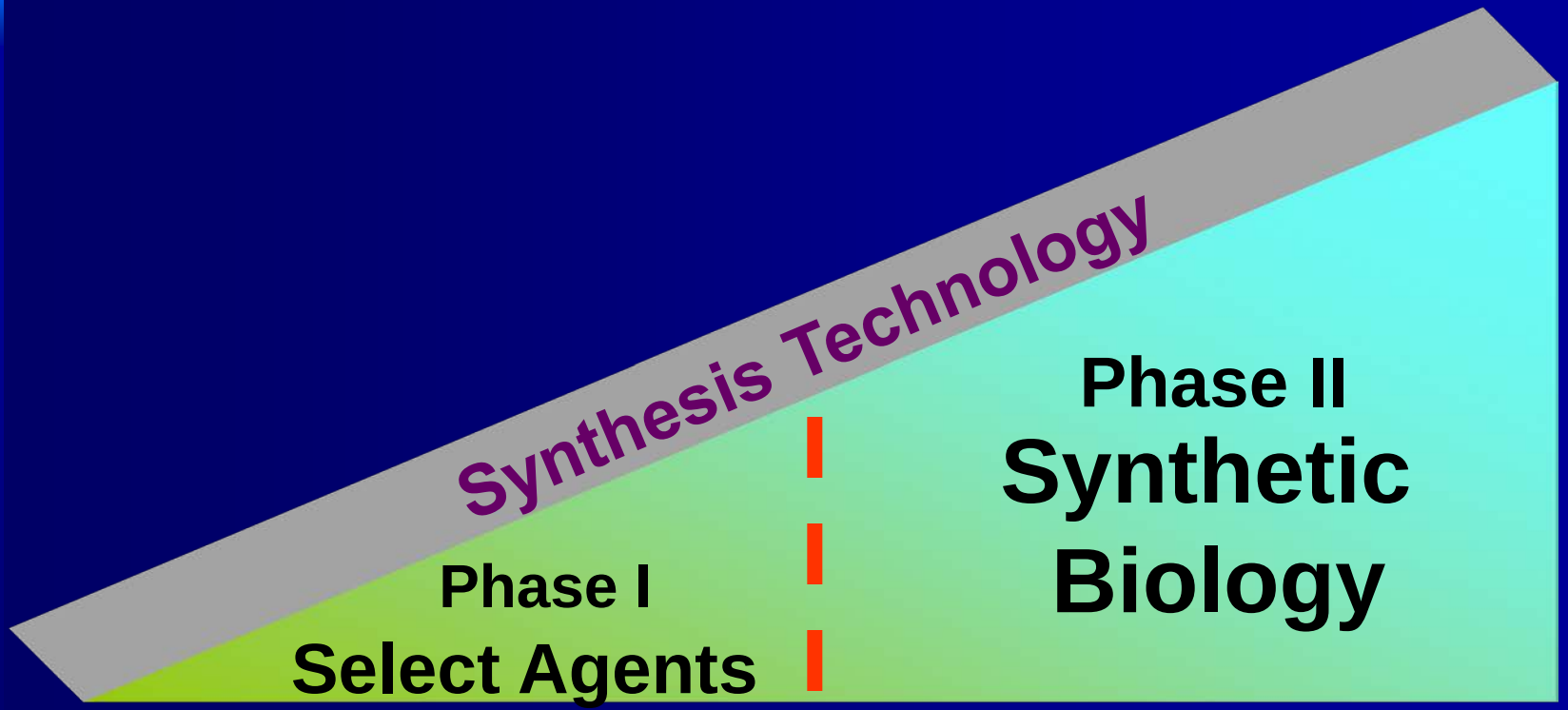
Working Group Charge

Phase 1: Examine 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

Phase 2: Identify, assess, and recommend strategies to address potential dual use concerns that may arise from work being performed in the nascent field of synthetic biology

Working Group Charge: Focus



Approach: Expert Consultations

Examined the state of the science and oversight system via consultations with:

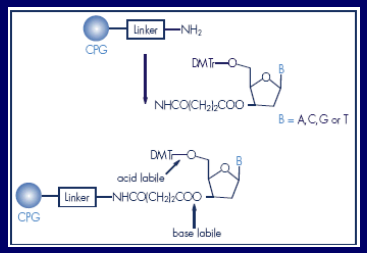
- Industry experts
- Eminent researchers
- U.S. Government (USG) officials
- Other key stakeholders

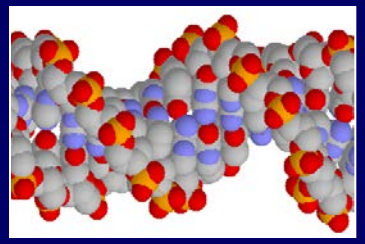
Current Status: Phase I

- Completed first phase of charge
  - Identified biosecurity concerns
  - Developed strategies to address concerns
- Sought input from stakeholders on recommended strategies
- Submitted recommendations to Board

Key Findings

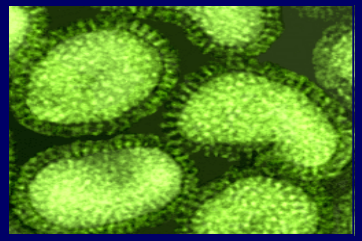
Technological Capability





- **Reagents/equipment for synthesizing DNA are readily available around the globe**
- **Synthesizing oligos accurately up to 120 base pairs (bp) in length is routine and common; beyond 180 bp remains somewhat of an art**
- **Complete genomes of some viruses can be synthesized presently, but not all DNA synthesis companies have this capability**

State of Science



- It is possible to recover/reconstruct from DNA certain SA; however, successful use of such reverse genetic systems currently requires that one be “skilled in the art”

- Researchers have successfully created infectious chimeric viruses using combinations of genomic material from various SA; these novel organisms do not fit current taxonomical classification schemes.

Biosecurity Concerns

Biosecurity Concerns

- Ease of acquisition of synthetic Select Agent nucleic acids
- Need for additional regulatory clarity in specific areas
- Difficulty in developing a suitable regulatory framework

Difficulty Developing Suitable Framework for Pathogenic Agents

- Due to:
  - the lack of consensus among scientists regarding an appropriate approach and methods for identifying/defining Select Agents and for screening sequences; and
  - current capabilities for constructing new pathogens.

Recommendations to U.S. Government

Recommendation 1

Develop and Disseminate Harmonized Guidance

- Clarify what genetic elements or genomes are covered by Select Agent Rules (SAR)
- Increase awareness among investigators and providers about their responsibilities to know what they possess, manufacture and/or transfer in order to comply with the SAR

Recommendation 2

Develop Standards & Practices

- Develop a process for determining the sequences for which to screen (SA or otherwise)
- Develop standards & practices (S&P) for screening orders and interpreting the results
- Draft “Points to Consider” for determining if genomic material is subject to the SAR
- Develop S&P for providers for retaining records of orders for gene-length or genome-length nucleic acids

Recommendation 2 (continued)

Promote Screening

- Require federal grantees/contractors to order from providers that screen and retain information about requests for SA sequences
- Foster an international dialogue regarding best practices/standards for screening sequences

Recommendation 3

Amend Current Laws/Regulations

- Repeal 18 U.S.C. 175(c) because current scientific insight precludes meaningful definition of an agent based solely on sequence homology
- Examine current biosafety guidelines and regulations to ensure they provide adequate guidance for working with synthetically-derived DNA
- Continue to reconcile the genetic elements language in the CCL with that in the SAR

Recommendation 4

Convene Experts

- Examine the SA classification system and determine if current controls can be reconciled with anticipated scientific advances
- Determine if an alternative framework based on predicted features and properties encoded by nucleic acids, can be developed and utilized in lieu of the current finite list of specific agents and taxonomic definitions

Recommendation 4 (continued)

Consider Intl. Implications & Foster Intl. Collaboration

- Consider the potential international implications of any proposed changes to the current oversight framework for synthetic DNA and synthetic genomes
- Foster an international dialogue and collaboration on these issues

Working Group Roster

Voting Members	Federal Representatives
Judge Susan Ehrlich, J.D. Claire M. Fraser-Liggett, Ph.D. John Gordon, GEN. USAF (Retired) Michael Imperiale. Ph.D. Adel Mahmoud M.D., Ph.D. David Relman, M.D. Harvey Rubin, M.D., Ph.D. Thomas Shenk, Ph.D.	Irma Arispe (OSTP) Kenneth A. Cole (DOD) Jerome Donlon (HHS) Maria Giovanni (NIH) Wendy Hall, Ph.D. (DHS) Susan D. Haseltine (DOI) Charles Brokopp (CDC) Maryanna Henkart (NSF) Stuart L. Nightingale (HHS) Tanuja Rastogi (State Dept.) Caird E. Rexroad (USDA) Scott Steele (DOJ) David G. Thomassen (DOE) Ronald A. Walters (Intel. Com.)

Next Steps

- Consider input from the Board
- Seek broader public input on the recommendations, particularly from “part-time” users