Expectations
Bioterrorism - a real and present danger
Anthrax attacks in the United States, 2001
Time to Implement Changes and Unexpected Consequences
**The Facts:** Scientists are able to manipulate biological systems to better understand molecular mechanisms of health and disease.

**The Promise:** These advances offer the cures and treatments and vaccines of tomorrow.

**The Issue:** Yet these techniques and discoveries can be misused and could pose a biologic threat to public health and/or national security.
How to Address the Issue

Security-Threat-Vulnerability-Risk Assessment

- What is it to be protected?
- Where is it?
- What is it to be protected against?
- Is what your doing actually protecting it against what you think might happen?
Striking the Right Balance

- Less risk
- More Secure
- Classified
- Limited analysis and critique
- Not available to the research enterprise
- Slower pace of discovery

- More Risk
- Less secure
- Not classified
- Open to analysis and critique
- Available to the research enterprise
- Faster pace of discovery
Biodefense Research Challenges

Culture of responsibility

- Scientists
- Editors of Journals
- National Science Advisory Board for Biosecurity

Classified research-restricted publications

- National Security Decision Directive 189*

Security-Biosecurity

- Facilities, people, research products and resources

*Recent survey by AAU/COCR reported 138 instances of the use of the 7000 clause or other publication or foreign national restrictions
Life Science Research:
USG - National Biosecurity Initiatives

- USA PATRIOT Act of 2001
- Public Health Security and Bioterrorism Preparedness and Response Act of 2002
- Agricultural Bioterrorism Protection Act of 2002
- Promoting and conducting research on the development of countermeasures for biologic threats
Phased in Implementation

Published: December 13, 2002
Effective date: February 7, 2003
Phase-in of new requirements:
- March 12, 2003 - New transfer provisions
- April 12, 2003 – Security Risk Assessments for individuals submitted
- June 12, 2003 – Developed security plan
- Sept. 12, 2003 – Implemented security plan
- Nov. 12, 2003 – Full compliance for registration
What Needed to Be Done?

- Conduct safety and security training
- Maintain records:
  - Inventories
  - Access to agents
  - Access to areas where agents are stored or used
  - Transfer documents
- Develop an emergency response plan
- Provide notification of theft, loss, or release of a select agent or toxin

Security

  - Access
    - “The freedom or ability to obtain or make use of”
    - The physical ability to lay your hands on a select agent or toxin

  - Restricting Access
    - Physical barriers
      - Locks on doors and storage containers
      - Card or key pads
    - Escorted and continually monitored by an authorized and approved person
Oversight - Inspection- Audits

Examination of Records

- Inspection results from annual inspection conducted by Responsible Official (Section 73.10(b))
- Biosafety Plan:
  - Site-specific, agent-specific biosafety manual
  - Chemical Hygiene plan
- Security plan
- EA-101 transfer records – Form 0.1318 records
- Training program and records
- Equipment records (e.g., BSC and fume hood certifications; HEPA filter certifications from BSL3 laboratories)
- Emergency response plan
- Select Agent inventory records
- Personnel access records
PENALTIES

- The Innocent/Accidental/Unintended
- The Fear
- The Realities

  - Civil
    - Up to $250,000 for an individual for each violation
    - Up to $500,000 for an organization for each violation
  - Criminal
    - Imprisonment for up to 5 years, a fine, or both for:
      - Transfer of a select agent to an unregistered person
      - Possession of a select agent by an unregistered person
      - Knowingly making a false statement

- The Gap
Modification of the award process to include Select Agent review and appropriate terms of award

Gaps in international effort required new procedures and costs in collaborations with DOJ, FBI, CJIS CDC, & others

* For details on information requested, see the select agent terms of award.
Select agent terms of award applied to international awards

* For details on information requested, see the [select agent terms of award](#).
Separate Unintended Consequence

From research institutions responding to the survey:

- 76% reported declines from China
- 58% reported declines from India
- 47% reported declines from Korea
- 33% reported declines from Taiwan
- 30% reported a decline from Europe

*Information from a survey conducted by COGS*
Biodefense Research Challenges

- Culture of responsibility
- Classified research-restricted publications
- Security-Biosecurity
  - facilities, people, research resources
Establish the National Science Advisory Board for Biosecurity (NSABB) to advise and guide the government on these initiatives.
The Issue: “Dual Use” Research

Dual use research includes life sciences research:

- with legitimate scientific purpose
- that may be misused to pose a biologic threat to public health and/or national security.
**Goals of Biosecurity Initiatives:**

- to enhance biosecurity protections for life sciences research
- ensure that any impact to the free flow of scientific inquiry is minimized.
Develop and Promulgate:

- National guidelines for local (e.g. IBCs) and federal oversight
- A code of conduct for scientists and laboratory workers in research.
- Education and training in biosecurity
- Guidelines for the appropriate communication of dual use research methodology and research results
- Foster the extension of these biosecurity policies to the international arena.
Institutional and IBC Issues, Anxieties, and Unknowns

- Transition time
- Costs and additional burden
- Lack of enough local expertise
- Reality that research is discovery and can potentially yield unexpected results
- Guidance versus requirements
# Personal Impact

**Security.nih.gov**

*Your central source for security information at NIH*

## Requirements for Code Red

**Employees**
- ALL Red Alert Critical personnel will be permitted access to NIH facilities
- Two primary entrances
- Two government issued IDs required (includes one photo ID)
- Valid NIH parking tag required
- Vehicle inspection

**Commercial Vehicles**
- ONLY commercial vehicles cleared by NIH Chief Security Officer (CSO) will be permitted access on NIH property
- Single gate entrance
- Two IDs required
- Truck/yvan inspected
- Business transaction and destination verified and recorded
- Loading dock access controlled
- Escort may be required

**Patients/Patient Visitors**
- ONLY visitors cleared by NIH Chief Security Officer (CSO) will be permitted access on NIH property
- Single gate entrance
- Vehicle inspection
- Two government issued IDs required (includes one photo ID)
- Sign-in required in buildings
- Screened through metal detector
- All bags/packages searched
- Escort to and from destination within buildings

## Requirements for Code Orange

**Building**
- Separate entrance

**Commercial Vehicles**
- Entrance through commercial vehicle gate
- Valid photo ID required
- Truck/yvan inspected
- Business transaction and destination verified and recorded
- Loading dock access controlled

**Visitors**
- Must enter through visitor gates
- Car inspected
- Two government issued IDs required (includes one photo ID)
- Sign-in required in buildings
- Screened through metal detector
- All bags/packages searched
- Escort to and from destination within buildings

**Additional Security Measures**
- Limited entrance points for all buildings on campus except buildings 10, 31, 38, and 45

**Useful Links**
- Guidelines for Code Yellow
- Guidelines for Code Red

## Code Yellow

**Commercial Vehicles**
- Entrance through commercial vehicle gate
- One photo ID required
- Vehicle inspected
- Loading dock access controlled
- May be subject to sign-in at buildings
- May be screened through metal detector
- May be subject to screening of bags/packages

**Patients/Patient Visitors**
- Must enter through visitor gates
- Vehicle inspected at perimeter and underground garages
- One photo ID required
- May be subject to sign-in at buildings
- May be screened through metal detector
- May be subject to screening of bags/packages

**Visitors**
- Must enter through visitor gates
- Vehicle inspected at perimeter and underground garages
- One photo ID required
- May be subject to sign-in at buildings
- May be screened through metal detector
- May be subject to screening of bags/packages
Impacts

Negative

- Increased operating costs
- Additional time required to enter campus
- Patient access to the clinical center

Positive

- More secure facilities
  - 50-75% decrease in the number of reported thefts and cost on campus.
Unexpected consequences
Examples of Emerging and Re-Emerging Diseases

- Vancomycin-resistant Staphylococcus aureus
- Cryptosporidiosis
- Multidrug-resistant tuberculosis
- Drug-resistant malaria
- E. coli O157:H7
- Lyme disease
- West Nile virus
- v-CJD
- Typhoid fever
- Rift Valley fever
- HIV
- Marburg virus
- Nipah virus
- Vancomycin-resistant Staphylococcus aureus
- Hantavirus pulmonary syndrome
- Dengue hemorrhagic fever
- Hepatitis C
- Cholera

Special Cases:
- Human monkeypox
- SARS
- H5 – Bird Flu
- Lassa fever
- Ebola hemorrhagic fever
- Plague
The Worst Bioterrorist May Be Nature Itself

By Frederick M. Cohan

While we are under siege by microbes spread by terrorists, we face what is probably a worse threat from pathogens that we encounter naturally as part of our human ecology. This important fact is getting overlooked in the national panic over anthrax.
Come Join the National Effort
Welcome to the Funding section of the National Institute of Allergy and Infectious Diseases Web site, providing funding, policy, and other timely information to NIAID's extramural research community.

**Initiatives and Budget**

See NIAID's high-priority funding areas and concepts for RFAs, RFPs, and PAs; special announcements; paylines and budget; and advisory Council. More...

**Grants and Contracts**

View our popular “All About Grants” tutorials, annotated R01 application, quick facts on grants, and other grant information such as our international site. Our contracts site has RFPs and proposal instructions. More...

**Special Research Areas**

Find information and links for human subjects, stem cell and fetal tissue, research animals, rDNA, and biodefense. More...

**Training and Career**

Get advice about training and career development awards for every career stage. More...

**Small Business**

See an annotated SBIR application, and get advice about SEIR and STTR grants, including our high-priority areas of interest. More...

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**Funding News**

*New FY 2004 Paylines*

*Notice of Limited Competition: NCMHD Endowment Program*

*NIH Roadmap Initiatives*

Read more Special Announcements

**NIAID Funding News -- March 5, 2004**

*News Center, Subscribe, Search, Feedback*

**News Articles**

- Only Our Name Has Changed
- Final FY 2004 Budget Picture
- Inflation Will Likely Overtake Biomedical Funding
- e-SNAP Expands to New Members

**Funding Opportunities and Resources**
Welcome to the **Funding** section of the [National Institute of Allergy and Infectious Web site](http://www.niaid.nih.gov/ncn/), providing funding, policy, and other timely information to NIAID's extramural research community.

**Initiatives and Budget**

See NIAID's [high-priority funding areas](http://www.niaid.nih.gov/ncn/) and [concepts for RFAs, RFPs, and PAs; special announcements; paylines and budget; and advisory Council](http://www.niaid.nih.gov/ncn/). More...
Thank You for Your Time

Questions and Comments Welcomed
NIAID Biodefense Research

About Biodefense
- Director's Statement
- National Biodefense Effort
- NIAID's Role
- Leadership
- Careers

For Researchers
- Strategic Plan
- Funding
- Resources
- Upcoming Meetings

For the Public & the Media
- Fact Sheets and Overviews
- Clinical Trials
  - Biocontainment Lab Tour
- News Releases
- Resources

http://biodefense.niaid.nih.gov
Personal Observation

Security.nih.gov

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Impacts

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- Additional time required to enter campus
- Patient access to the clinical center

Positive

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  - 50-75% decrease in the number of reported thefts and cost on campus.
Building 33 – Main NIH Campus

**Occupancy:**
FY 2006

**Size:**
65,000 nsf of lab space

**Cost Design/Construction:**
$186.1 M

**Research Areas:**
Anthrax, poxviruses, TB, TBEV/dengue, tularemia, hantavirus, influenza, botulism, host-parasite interactions

**Features:**
High security; capability for BSL-3 on every floor; vivarium; multi-level parking garage
Building 33 Construction, Jan. 21, 2004
Unexpected consequences

Colorado State University

University of Missouri

University of Chicago

University of Pittsburgh

Boston University

University of Medicine and Dentistry of New Jersey

Duke University

University of Tennessee

University of Alabama, Birmingham

University of Texas Medical Branch, Galveston

Tulane University

NBLs (BSL-4)

RBLs (BLS-3)
Topics for Discussion

- What is Project Bioshield?
- How is it coordinated between DHS and DHHS?
- What are the major roles within DHHS?
- What is the progress to date in developing countermeasures?
- How does this tie into the NIAID mission?
Biodefense: Complementary Roles within DHHS

NIH
- Build Research Infrastructure
- Conduct Basic Research
- Develop Medical Countermeasures

OASPHEP

FDA
- Regulatory Approval
  - Vaccines
  - Therapeutics
  - Diagnostics

CDC
- Strategic National Stockpile (DHS)
- Train Local Response Teams
- Surveillance and Detection
Release of BioShield Funds

- Interagency Approval of Requirement
- Findings by Secretaries of DHS and HHS
  - Determination of material threat
  - Suitability of countermeasure
  - No significant commercial market
  - Numbers of doses required and cost
- Approval by the President
NIH Biodefense Research Pathway

Basic Research

Industry

Pathogen Biology Host Response Target Identification Preclinical Development Clinical Evaluation

Research Resources

Academia

Procurement via BioShield

Bioshield
NIAID Ebola Vaccine Enters Human Trial

The first human trial of a vaccine designed to prevent Ebola infection opened today. Scientists from the Vaccine Research Center (VRC) at the National Institute of Allergy and Infectious Diseases (NIAID), one of the National Institutes of Health (NIH), designed the vaccine, which was administered to a volunteer at the NIH Clinical Center in Bethesda. The vaccine does not contain any infectious material from the Ebola virus.
MVA Development Highlights

- Three year contracts awarded to Acambis Inc. and Bavarian Nordic A/S, Feb. 2003
  - Up to $20M first year funding
  - Production of >10,000 doses completed
  - FDA Animal Rule efficacy studies initiated in monkeys and mice
  - Phase 1 human trials underway
  - Trials in HIV+ patients planned for late 2004

- RFP 04-49 (released to public on Dec. 4, 2003)
  - Follow-on awards to be made in summer of 2004
  - Designed to continue fast-paced product development
  - Production of 3M doses of licensure-grade vaccine
  - Continued testing in animal models in fulfillment of FDA Animal Rule
  - Completion of extended Phase 2 safety trials
  - Production plan for 50M doses of MVA
Plague and Tularemia Vaccine Development

Plague:
RFP issued for Development, Testing and Evaluation of Candidate Vaccines Against Plague. Proposal receipt date was 12/2003.

Tularemia:
Collaborative research project between DoD and NIAID for live vaccine strain development against Tularemia

- DoD to provide product
- NIAID to provide testing
  - Animal toxicity
  - IND filing
  - Phase I clinical trial
## Category A Agents

### Vaccine Development Status

<table>
<thead>
<tr>
<th>Agent</th>
<th>Current Initiatives</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthrax</td>
<td>FY02 (development and testing) FY03 (advanced development)</td>
<td>In human trials Underway</td>
</tr>
<tr>
<td>Smallpox</td>
<td>FY03 (development and testing) FY04 (advanced development)</td>
<td>In human trials Underway</td>
</tr>
<tr>
<td>Botulinum Toxin</td>
<td>FY03 (development) FY06 (advanced development/combination)</td>
<td>Pilot production of individual serotypes</td>
</tr>
<tr>
<td>Plague</td>
<td>FY04 (development and testing)</td>
<td>-</td>
</tr>
<tr>
<td>Tularemia</td>
<td>FY04 (development and testing) FY05 (advanced development)</td>
<td>-</td>
</tr>
<tr>
<td>Rift Valley Fever</td>
<td>FY06 (development and testing)</td>
<td>-</td>
</tr>
<tr>
<td>Ebola – VRC</td>
<td>FY06 (advanced development)</td>
<td>In human trials (VRC)</td>
</tr>
</tbody>
</table>
Example - DHHS Next Generation (rPA) Anthrax Vaccine Program

- Three-stage contracting strategy
  - Stage 1: Research and Early Development (NIAID)
  - Stage 2: Advanced Development (NIAID)
  - Stage 3: Large-scale Production & Acquisition (HHS)
- Aggressive timelines; milestone-driven
- Competitive contracts
- Goal: licensable product
- Licensing strategy will utilize the FDA “Animal Rule”
A Comprehensive Biodefense Research Agenda

NIH

Infectious Diseases

Radiological Threats

Chemical Agents

DHS
EPA
DOE
DoD
FDA
USDA
etc.
NIAID is a Global Organization

NIAID funds research in > 241 countries
Deadly Ebola, Avian Influenza Re-emerging

The World Health Organization announced Wednesday that two particularly deadly viruses have been reemerged: Ebola and an unusual form of avian influenza that is lethal to humans.
Examples of Emerging and Re-Emerging Diseases

- Vancomycin-resistant Staphylococcus aureus
- Cyclosporiasis
- E. coli O157:H7
- Lyme disease
- West Nile virus
- Hantavirus pulmonary syndrome
- Dengue hemorrhagic fever
- Hepatitis C
- Cryptosporidiosis
- Multidrug-resistant tuberculosis
- Drug-resistant malaria
- E. coli O157:H7
- V-CJD
- Typhoid fever
- Rift Valley fever
- HIV
- Marburg virus
- Nipah virus
- Human monkeypox
- Plague
- Ebola hemorrhagic fever
- Lassa fever
- Cholera
Spread of Bird Flu in Asia Worries Officials

By LAWRENCE K. ALTMAN, M.D.

For a small number of bird watchers, the question is not how many species they can spot but what viruses infect the birds. In recent weeks, these bird-watching virologists have become worried about what they and the World Health Organization say is the "unprecedented" simultaneous appearance of an avian influenza virus in a number of countries.
Examples of Emerging and Re-Emerging Diseases

- Vancomycin-resistant Staphylococcus aureus
- Cryptosporidiosis
- Multidrug-resistant tuberculosis
- Drug-resistant malaria
- SARS
- E. coli O157:H7
- H5N1 avian influenza
- Vancomycin-resistant Staphylococcus aureus
- Nipah virus
- Hendra virus
- Enterovirus 71
- Human monkeypox
- Lassa fever
- Ebola hemorrhagic fever
- Plague
NIAID Responds to Emerging Health Needs (examples)

West Nile Virus

Use of biological agents in terrorist attacks
West Nile Virus – An Example

Source – CDC – Sept. 2002
West Nile Virus – An Example

Source – CDC – Sept. 2002
West Nile Virus – An Example

Source – CDC – Sept. 2002
West Nile Virus – An Example

Source – CDC – Sept. 2002
West Nile Virus – 2003 – October 10
**DFARS 252.204-7000**

**Disclosure of Information**

When the Contractor will have access to or generate unclassified information that may be sensitive and inappropriate, include the clause DFARS 252.204-7000.

A. The Contractor shall not release to anyone outside the Contractor’s organization any unclassified information, regardless of medium (e.g., film, tape, document) pertaining to any part of this contract or any program related to this contract, unless –

1. The Contracting Officer has given prior written approval; or

2. The information is otherwise in the public domain before the date of release
B. Requests for approval shall identify the specific information to be released, the medium to be used, and the purpose of the release. The Contractor shall submit its request to the Contracting Officer at least 45 days before the proposed date for release.

C. The Contractor agrees to include a similar requirement in each subcontract under this contract. Subcontractors shall submit requests for authorization to release through the prime contractor to the Contracting Officer.
In accordance with Title 8 U.S.C. 1324a, local Foreign Disclosure Officers (FDOs) may approve access by foreign nationals working on unclassified public domain contracts for the duration of the contract, provided the foreign nationals have appropriate work authorization documentation.

In those instances where foreign nationals are required to perform under any resultant contract and employment eligibility documentation was not submitted with an awardee’s proposal, the employment eligibility documentation specified at 8 CFR 24a.2 shall be submitted to the Contracting Officer at least two weeks prior to the foreign national’s performance for review and approval. Awardees not employing foreign nationals in performance of any resultant contract may disregard this clause.
For the purpose of this clause,

- **Foreign person** is any person who is not a citizen or national of the U.S. or lawfully admitted to the U.S. for permanent residence under the Immigration and Nationality Act, and includes foreign corporations, international organizations, and foreign governments;

- **Foreign representative** is anyone, regardless of nationality or citizenship, acting as an agent, representative, official, or employee of a foreign government, a foreign-owned or influenced firm, corporation or person;

- **Foreign sources** are those sources (vendors, subcontractors, and suppliers) owned and controlled by a foreign person.