



# **The DHHS Response to Bioterrorism Advanced Development and Acquisition of Medical Countermeasures**

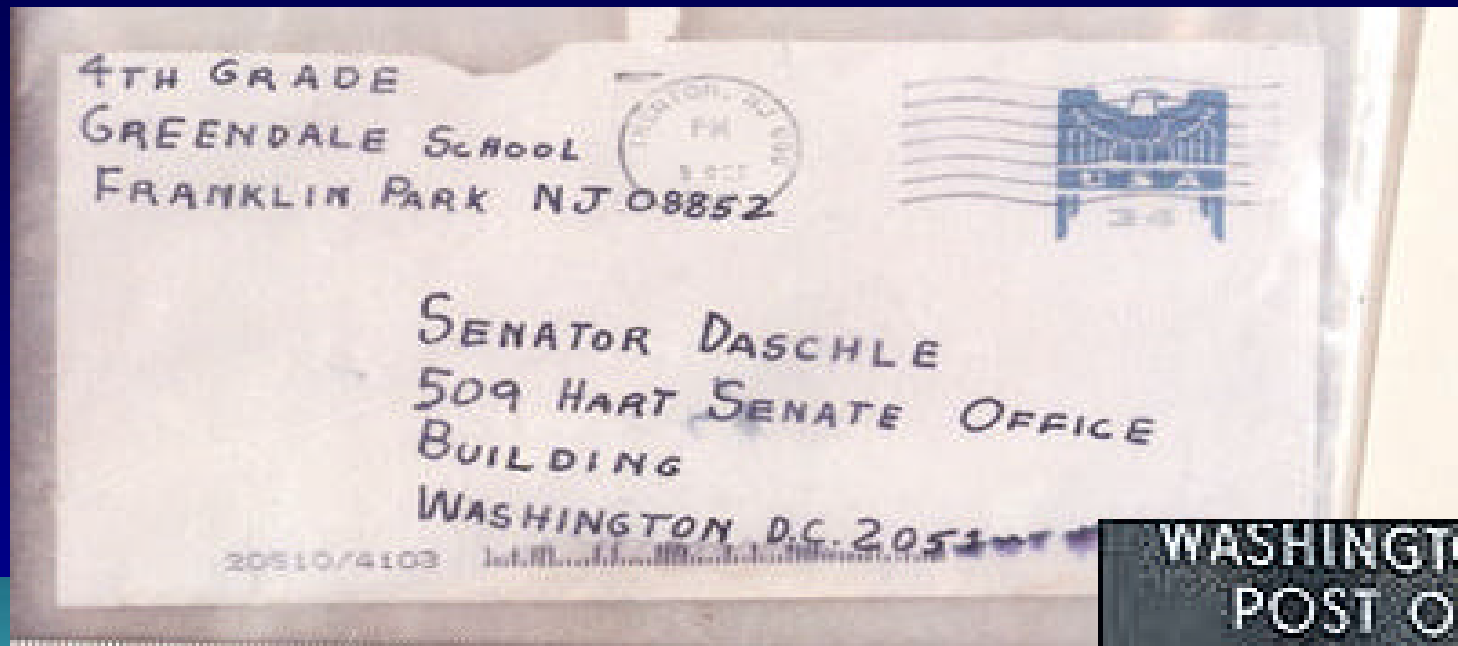
**Monique K. Mansoura, Ph.D.**  
**17 January 2003**



**U.S. Department of Health and Human Services  
Office of the Assistant Secretary for Public Health Emergency Preparedness**

# No longer a theoretical threat

## Anthrax Bioterrorism in the United States, 2001

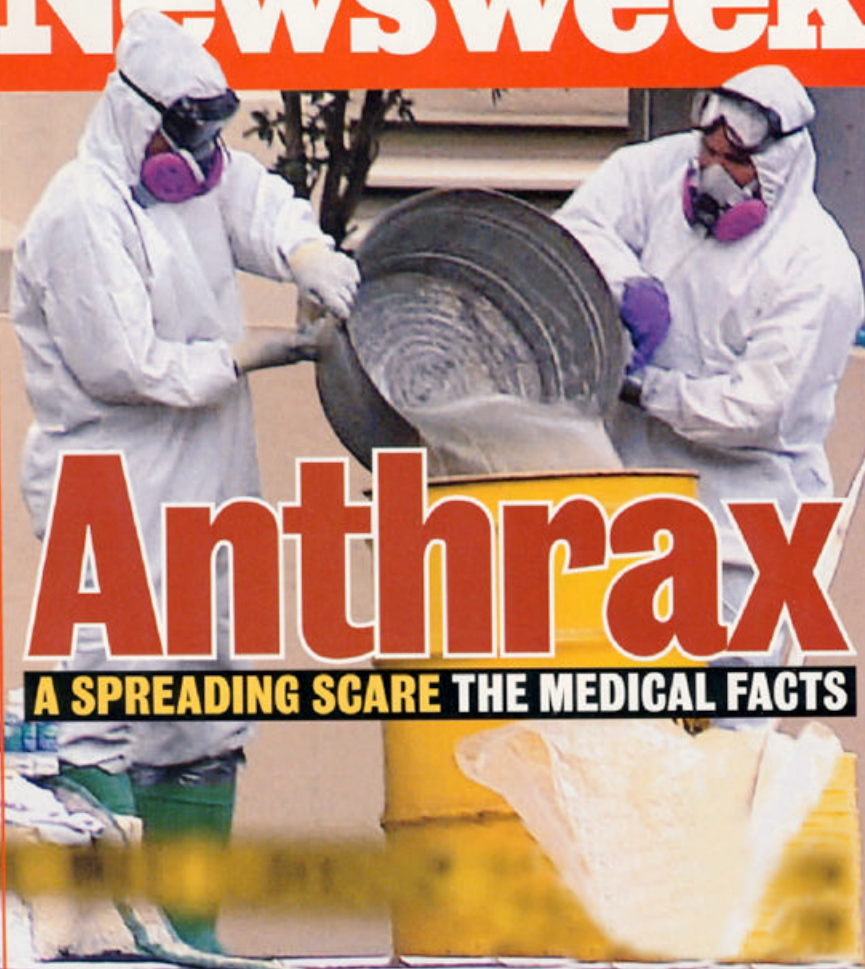




**AFTER THE AIR WAR**

October 22, 2001 • \$3.95

**Newsweek**



# Anthrax

**A SPREADING SCARE THE MEDICAL FACTS**

Fire-and-rescue Special Operations unit at work after the anthrax attack in Boca Raton, Fla.

newsweek.msnbc.com

OCTOBER 22, 2001

www.time.com AOL Keyword: TIME

**AFGHANISTAN: INSIDE THE GROUND WAR**

# TIME

## THE FEAR FACTOR

Anthrax letters. FBI warnings. Bin Laden's videotapes. Bombarded by threats real and imagined, a nation on edge asks, What's next?

# Office of the Assistant Secretary For Public Health Emergency Preparedness: Organizational Structure

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- Office of Planning and Emergency Response
- Office of Emergency Response
- Office of State and Local Preparedness
- **Office of Research and Development**





# **Office of the Assistant Secretary For Public Health Emergency Preparedness: Office of Research and Development**

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- Identify HHS requirements and gaps in medical countermeasures needed to respond to biological or chemical terrorism
- Coordinate with NIH, CDC, FDA and other agencies if necessary to ensure that appropriate research & development and acquisition of medical countermeasures occurs in a timely fashion.
- Provide coordination with DOD and other agencies on issues relating to R&D and acquisition of medical countermeasures
- Maintain a Readiness Report detailing the existing and projected supplies of vaccines and antibiotics in the National Pharmaceutical Stockpile

# Biodefense: Complementary Roles within DHHS

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**CDC**



- Surveillance and Detection
- Train Local Response Teams
- Maintain Vaccine/Antimicrobial Stockpiles

**NIH**



- Conduct Basic Research
- Develop Medical Interventions

**FDA**



- Regulatory Approval
  - Vaccines
  - Therapeutics
  - Diagnostics

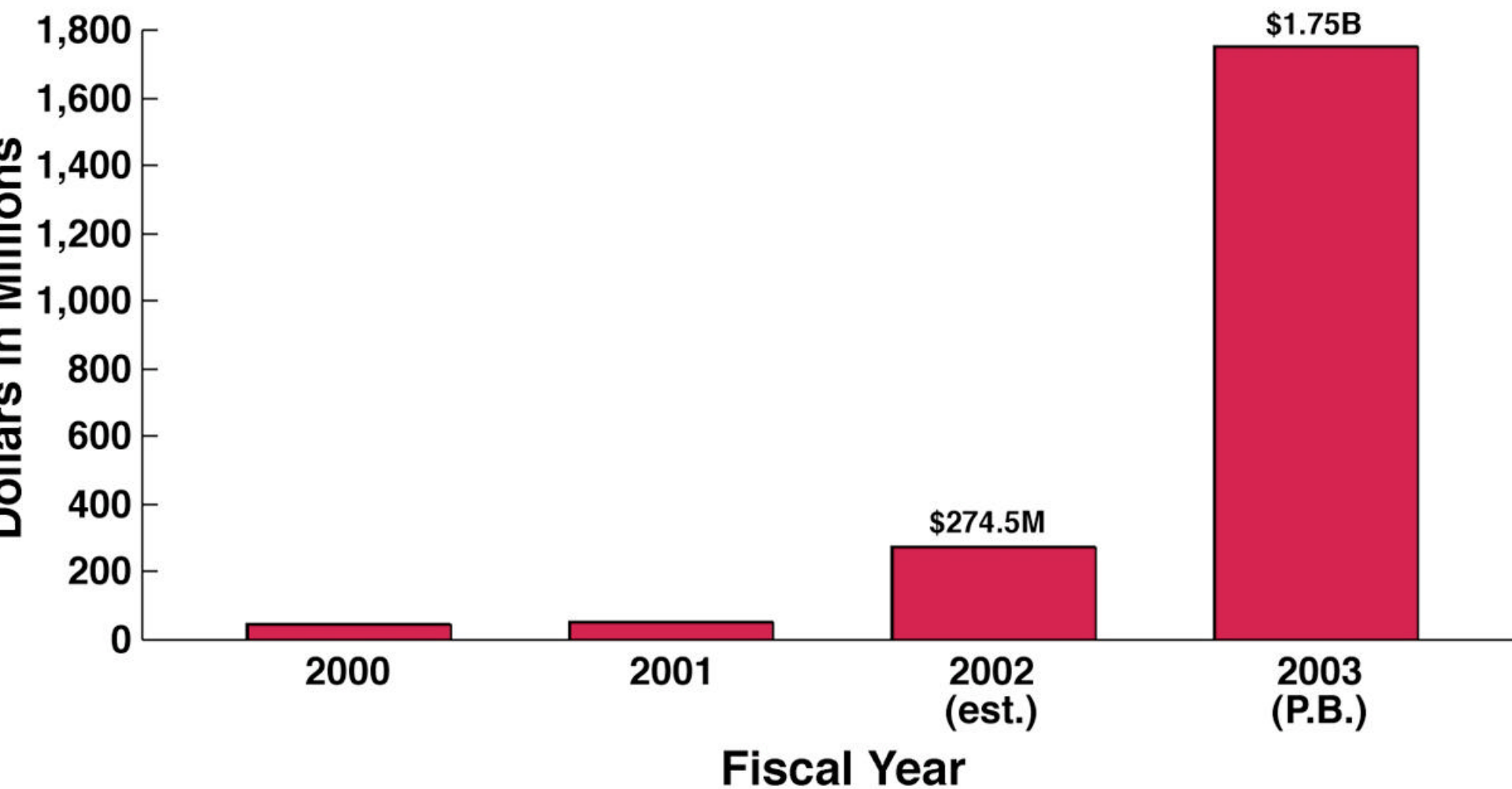
**OEP**



- Mobilize Resources to Coordinate State/Local Response



# NIH Biodefense Research Funding, FY 2000-2003



# **NIH Biodefense Research Funding, FY 2003 (President's Budget)**

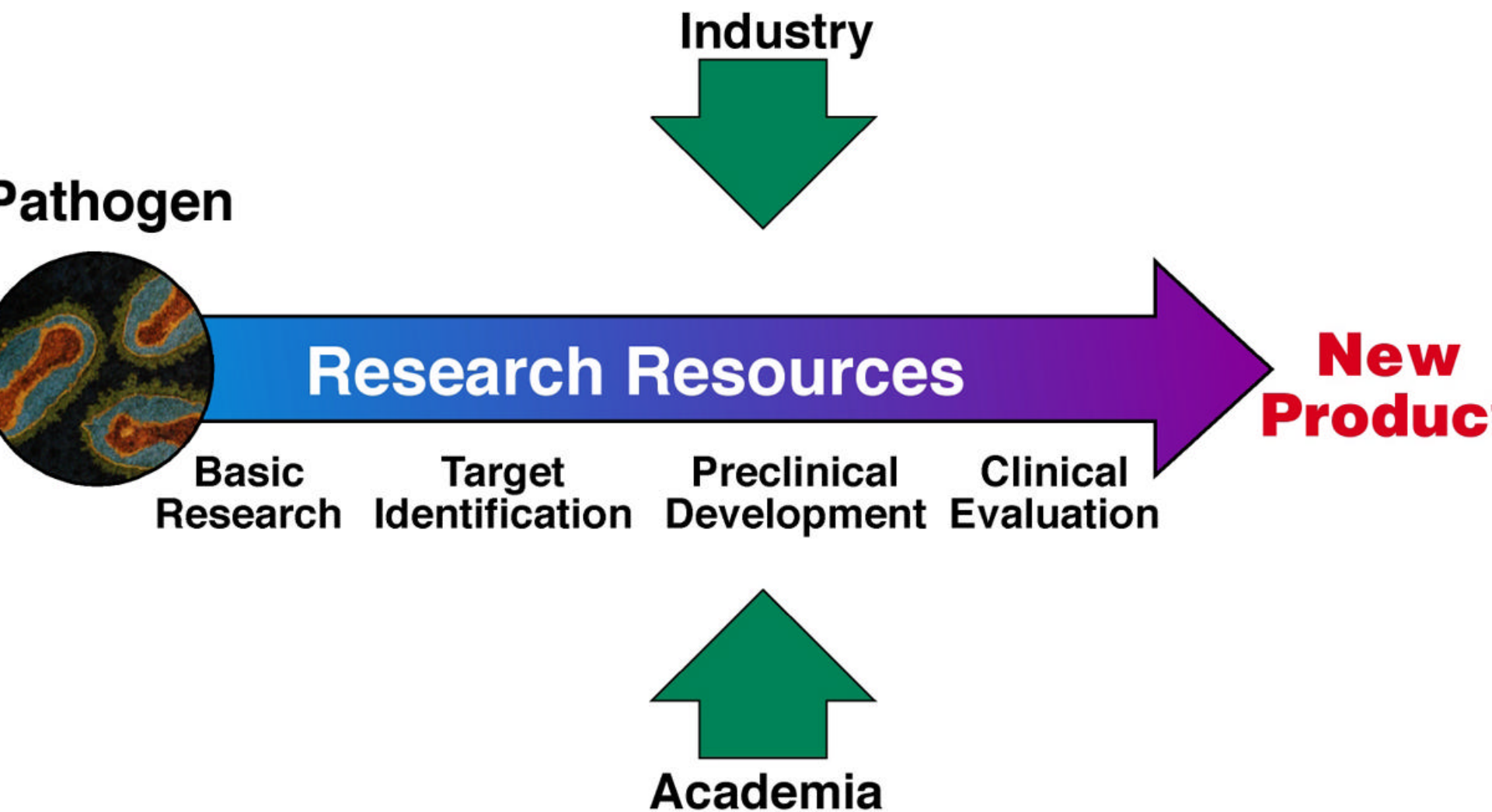
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<b>Basic Research and Development</b>	<b>\$440.6M</b>
<b>Drug/Vaccine Discovery and Development</b>	<b>\$591.9M</b>
<b>Clinical Research</b>	<b>\$194.3M</b>
<b>Research Facilities Construction*</b>	<b>\$521.1M</b>
	<hr/>
	<b>\$1,747.9M</b>

**Research Facilities in FY 2003: \$150M extramural, \$371M intramural**



# NIH Biodefense Research Pathway



# **NIAID Blue Ribbon Panel on Biodefense and Its Implications for Biomedical Research**

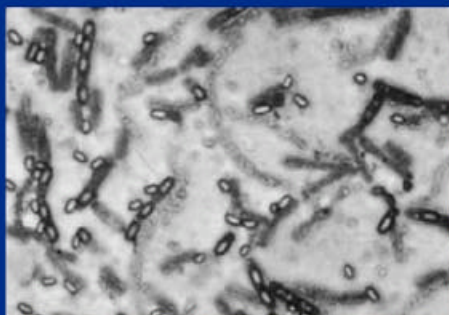
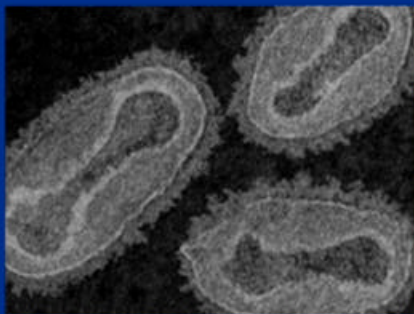
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- **Feb. 4-5, 2002 - Focus on Category A Diseases/Agents, i.e. anthrax, botulism, plague, smallpox, tularemia, hemorrhagic fever viruses**



February 2002

## NIAID Strategic Plan for Biodefense Research



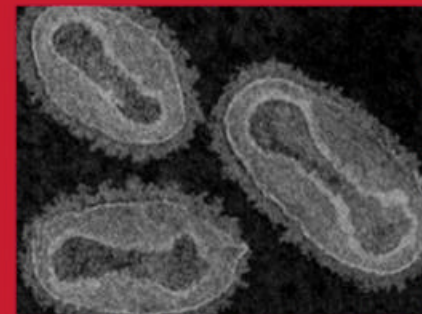
Responding  
Through  
Research



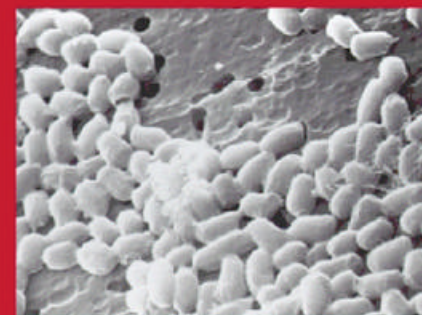
National Institute of Allergy and Infectious Diseases  
NATIONAL INSTITUTES OF HEALTH

February 2002

## NIAID Biodefense Research Agenda for CDC Category A Agents



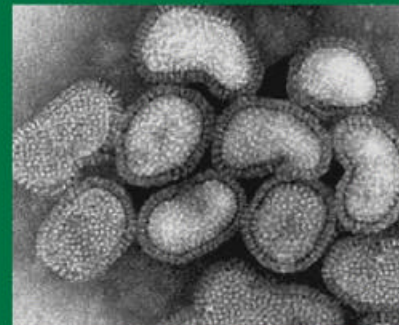
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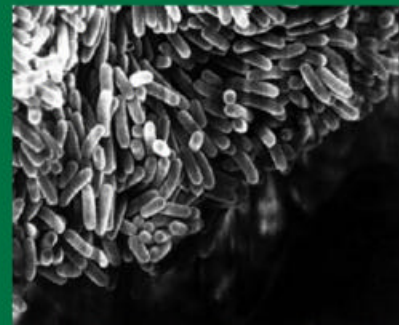
National Institute of Allergy and Infectious Diseases  
NATIONAL INSTITUTES OF HEALTH

January 2003

# The NIAID Biodefense Research Agenda for Category B and C Priority Pathogens



Responding  
Through  
Research



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES



National Institute of Allergy and Infectious Diseases  
NATIONAL INSTITUTES OF HEALTH



# Newsweek

October 14, 2002

newsweek.msnbc.com

## Operation: Smallpox

Inside the  
Emergency  
Plan to  
Inoculate  
Every  
American

How Real  
Is the  
Threat?



# **President Bush Announces U.S. 'Pre-Event' Smallpox Vaccination Program, December 13, 2002**



# Smallpox Vaccine: Availability by Mid-2003

	<u># of Doses</u>
■ 15.4 million doses of Dryvax diluted 1:5	77 million
■ Contracts for cell culture-derived vaccine	209 million
■ Vaccine from Aventis Pasteur Inc. diluted 1:5	> 75 million (> 375 million)
Total	> 363 million (> 663 million)



# **Smallpox Vaccine: Adverse Event Rates Among Primary Vaccinees (Per Million Vaccinations)**

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**Deaths**

**1 - 2**

**Life-threatening adverse events**

**14 - 52**

**Serious, but not**

**life-threatening adverse events**

**49 - 935**

**Minor reactions**

**up to 50% of vaccinees**



# **Contraindications to Smallpox Vaccine**

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- History of eczema or atopic dermatitis (AD), irrespective of severity or disease activity; household contacts with eczema or AD**
- Other skin disorders – herpes, varicella zoster, burns, impetigo, psoriasis, severe acne, contact dermatitis, wounds**
- HIV infection, AIDS, cancer, immunosuppression, oral and topical steroids, inhaled steroids (depending on dose and frequency)**
- Pregnancy**
- Conjunctival or corneal disease**
- Hypersensitivity to vaccine components: polymyxin B, streptomycin, neomycin, chlortetracycline**

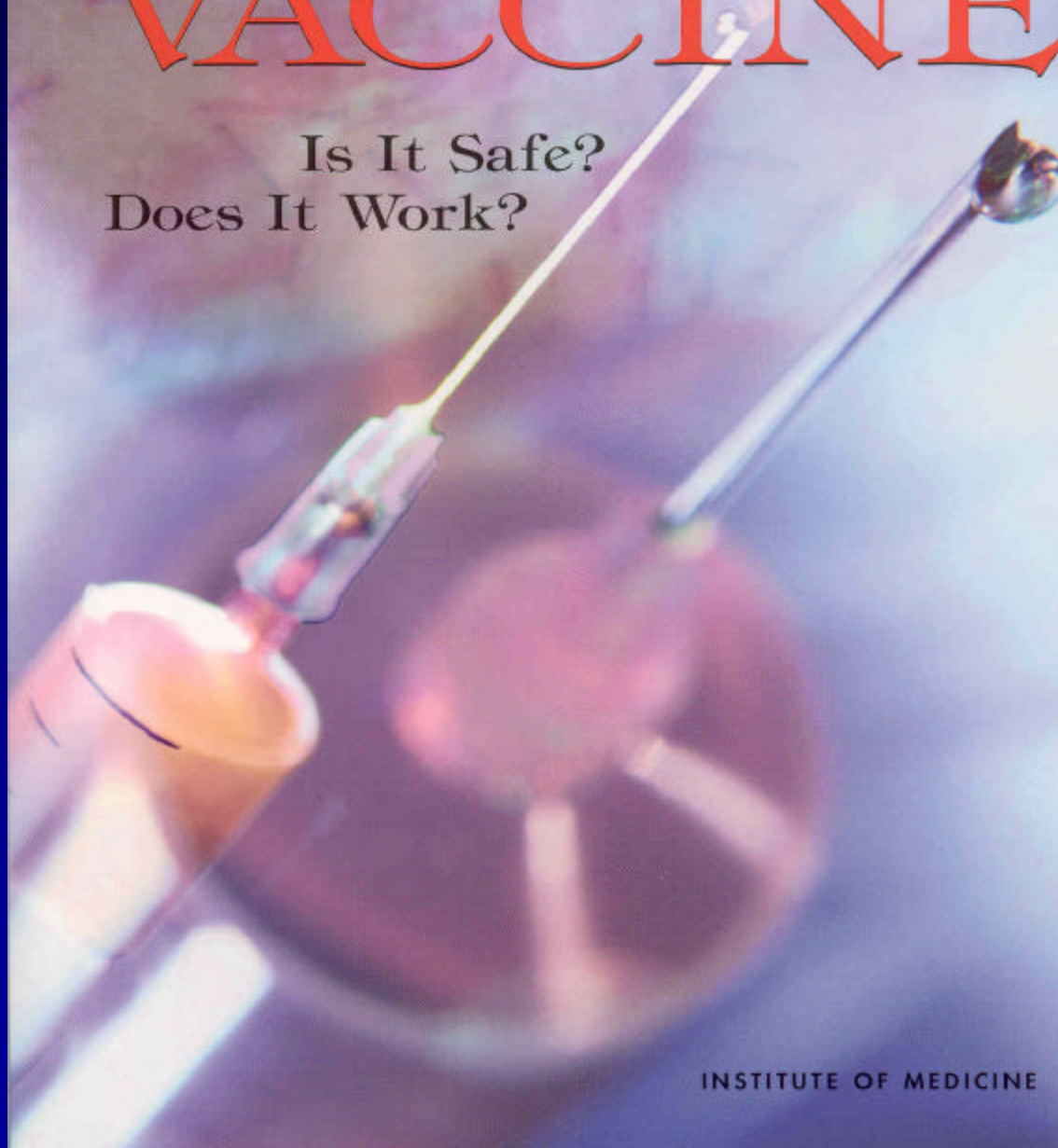
# **A “Next-Generation” Smallpox Vaccine: Modified Vaccinia Virus Ankara (MVA)**

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- **Highly attenuated vaccinia virus**
- **Cannot replicate in most mammalian cell lines, however in animal models elicits a significant immune response**
- **Historically, good safety profile, including at-risk groups**
  - **German smallpox vaccination experience (n= ~120,000)**
  - **Experimental cancer, HIV vaccines**
- **Intramuscular injection rather than scarification**
- **Several candidates in development; most promising will be tested by NIAID at Vaccine Research Center and in network of Vaccine and Treatment Evaluation Units**

# THE ANTHRAX VACCINE

Is It Safe?  
Does It Work?



INSTITUTE OF MEDICINE



**Executive Summary from the 2001 IOM report**  
***The Anthrax Vaccine – Is it Safe? Does it Work?***

**Anthrax Vaccine Adsorbed (AVA)**

**CONCLUSIONS REGARDING EFFICACY**

- AVA as licensed is an effective vaccine for the protection of humans against anthrax, including inhalational anthrax, caused by any known or plausible engineered strains of *B. anthracis*

**FUTURE NEEDS**

- Current events in both the military and civilian arenas highlight and confirm the important of ensuring both the availability and the quality of the nation's anthrax vaccine



# **Executive Summary from the 2001 IOM report** ***The Anthrax Vaccine – Is it Safe? Does it Work?***

## **NEW ANTHRAX VACCINE DEVELOPMENT**

- The current anthrax vaccine, AVA, is:
  - difficult to standardize
  - incompletely characterized
  - relatively reactogenic, and
  - the dose schedule is long and challenging
  
- An anthrax vaccine free of these drawbacks is needed, and such improvements are feasible.

# NIAID FY2003 Biodefense Plan

## Drug/Vaccine/Diagnostics Discovery & Development

- **Test and develop candidates for next-generation anthrax vaccine**
- Engage industry through challenge grants
- Establish repositories for diagnostic and drug reagents
- Develop animal models, establish high-containment facilities and services

# Features of the HHS rPA Program

Science base ripe for advanced development of candidates

Two-stage contracting strategy

- Stage 1: Advanced Development
- Stage 2: Production & Acquisition

Aggressive timelines; milestone-driven

Competitive contracts with harmonization of protocols (laboratory assays, animal studies, clinical trials) to allow for direct comparisons

Goal: licensable product that supports licensure strategy

Licensing strategy will utilize the FDA “Animal Rule”

# Next Generation Anthrax Vaccine Timeline

**2002**

- Jan 8: NIAID reviewed the Dec '01 SAIC report about rPA technologies
- Feb 7: NIH guide announces draft RFP
- Feb 21: Manufacturers' responses to draft RFP due
- **Apr 22: RFP 02-26 issued**  
<http://www.niaid.nih.gov/contract/archive/RFP0226.pdf>
- Jun 6: Proposals due
- Jul 15: Proposal review
- **Sep 30: Contracts awarded**



FOR IMMEDIATE RELEASE  
Thursday, October 3, 2002

## **HHS Announces Contracts for Developing a New Anthrax Vaccine**

HHS Secretary Tommy G. Thompson today announced that the National Institute of Allergy and Infectious Diseases (NIAID) has awarded two companies contracts designed to spur development of a new anthrax vaccine.

“There is an urgent need to devise more effective measures to protect U.S. citizens from the harmful effects of anthrax spores used as instruments of terror,” said Secretary Thompson. “These awards represent the first step toward our goal of securing an initial 25 million doses of an improved anthrax vaccine for our emergency stockpile.”

# NIAID Anthrax Vaccine Contracts - Overview

- Contracts were awarded to:
  - **Avecia**, of Manchester, United Kingdom,
  - **VaxGen Inc.**, of Brisbane, California
- The two contracts total \$22.5 million through fiscal year 2003.
- Requirements include:
  - Recombinant protective antigen (rPA) adsorbed to alum
  - Immunization series not more than 3 doses
  - Pursuit of licensure for pre-exposure prophylaxis and post-exposure immunization

# HHS/NIH/NIAID rPA Contracts - Milestones

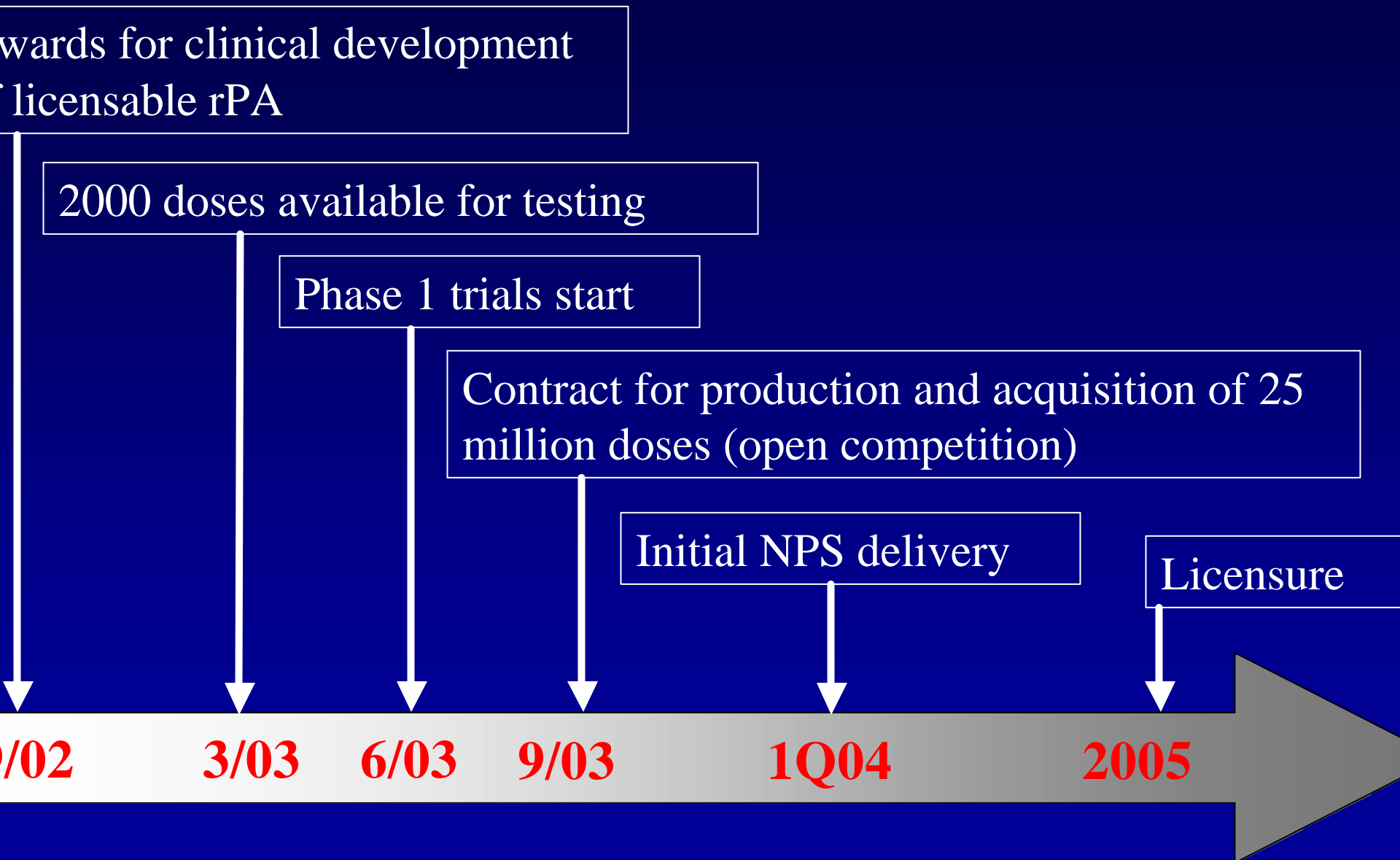
## 2002

- **Sep 30: Contracts awarded**
- Dec 31: Milestone 1
  - Complete bulk manufacture of 2,000 doses

## 2003

- Mar 31: Milestone 2
  - Fill and Finish 2,000 doses
- Mar 31: Milestone 3
  - Submit clinical development plans and Phase 1 protocol
- Dec 31: Milestone 4
  - Complete Phase 1 and begin Option B (Phase 2)
- Sep 30: Milestone 5
  - Deliver a **manufacturing feasibility plan** for up to 25M dose
- **May 15: Issue RFP 03-29 to manufacture up to 25M doses for an emergency-use stockpile**

# Timeline for Anthrax rPA Vaccine Development







**Genomics**



**Basic Research**



**Antimicrobials**



**Diagnostics**



**Vaccines**



**Expansion of  
Research  
Capacity**



# **Summary of NIAID Biodefense Initiatives**

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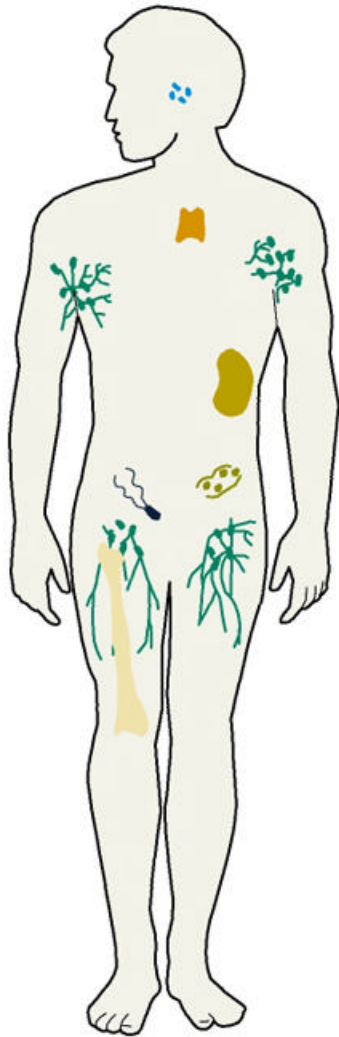
- Combined total of 36 research initiatives in FY 2002 and FY 2003**
- 7 new initiatives awarded in FY 2002 (some in late September)**
- 25 new FY 2003 initiatives have been announced**
- 4 additional FY 2003 initiatives are in final stages of development**
- Expansions to 4 existing NIAID research programs in FY 2002; 12 planned expansions in 2003**

# Genomic Sequencing of Potential Bioterror Agents: Selected NIH Projects Completed or Nearing Completion

Agent	Disease	NIAID Category
<i>Bacillus anthracis</i> (multiple strains)	Anthrax	A
<i>Brucella suis</i>	Brucellosis	B
<i>Burkholderia mallei</i>	Glanders	B
<i>Clostridium perfringens</i>	Gas gangrene	B
<i>Coxiella burnetii</i>	Q fever	B
<i>E. coli</i> 0157:H7	Hemolytic uremic syndrome	B
<i>Mycobacterium tuberculosis</i>	Tuberculosis	C
<i>Rickettsia typhi</i>	Typhus	C
<i>Staphylococcus aureus</i>	Bacteremia, endocarditis	B
<i>Yersinia pestis</i>	Plague	A
<i>Variola major</i>	Smallpox	A

# Biodefense Progress and Priorities: Immunology/ Host Response

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- Innate immunity
- Adaptive immunity
- Immunotherapy
- Vaccinology
- Mapping of protective epitopes



# **Biodefense Therapeutics Research Progress and Priorities**

**Screening**

**New Targets**



**Drug  
Resistance**

**Broad-Spectrum  
Therapies**

# Medical Diagnostics for Biodefense

*In vivo* molecular  
imaging

Inhaled biological  
radiotracers



Integrated systems/platforms  
for screening and detecting  
multiple agents

Nanotechnology

# **“Traditional” Mechanisms of NIH Research Support**

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- Grants**
- Cooperative Agreements**
- Contracts**
- SBIRs**
- CRADAs**

# New Models

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- **Challenge Grant Mechanism**
- **Partnership Programs**
- **Vaccine Production Contracts**
- **NIAID Vaccine Research Center**
- **Increased Emphasis on Research Resources**
  - e.g. reagent repositories, genomic databases, animal models, clinical trials support



# 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



**NIAID  
BIODEFENSE**  
Preparing Through Research

<http://biodefense.niaid.nih.gov>