

**Secretary's Council on Public Health  
Preparedness**

**The NIH Biodefense  
Research Agenda:  
A Progress Report**

**Anthony S. Fauci, M.D.**

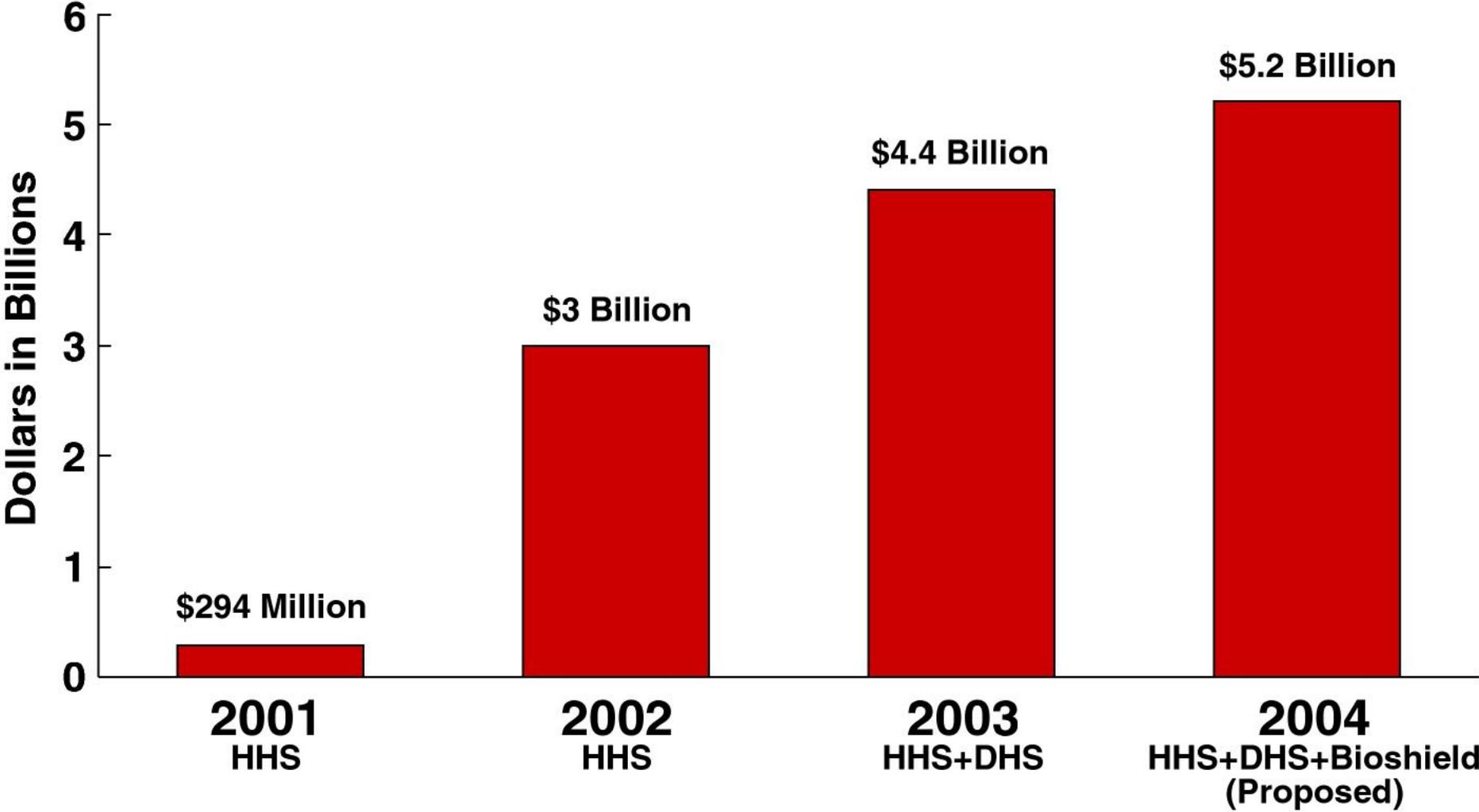
**Director**

**National Institute of Allergy and  
Infectious Diseases**

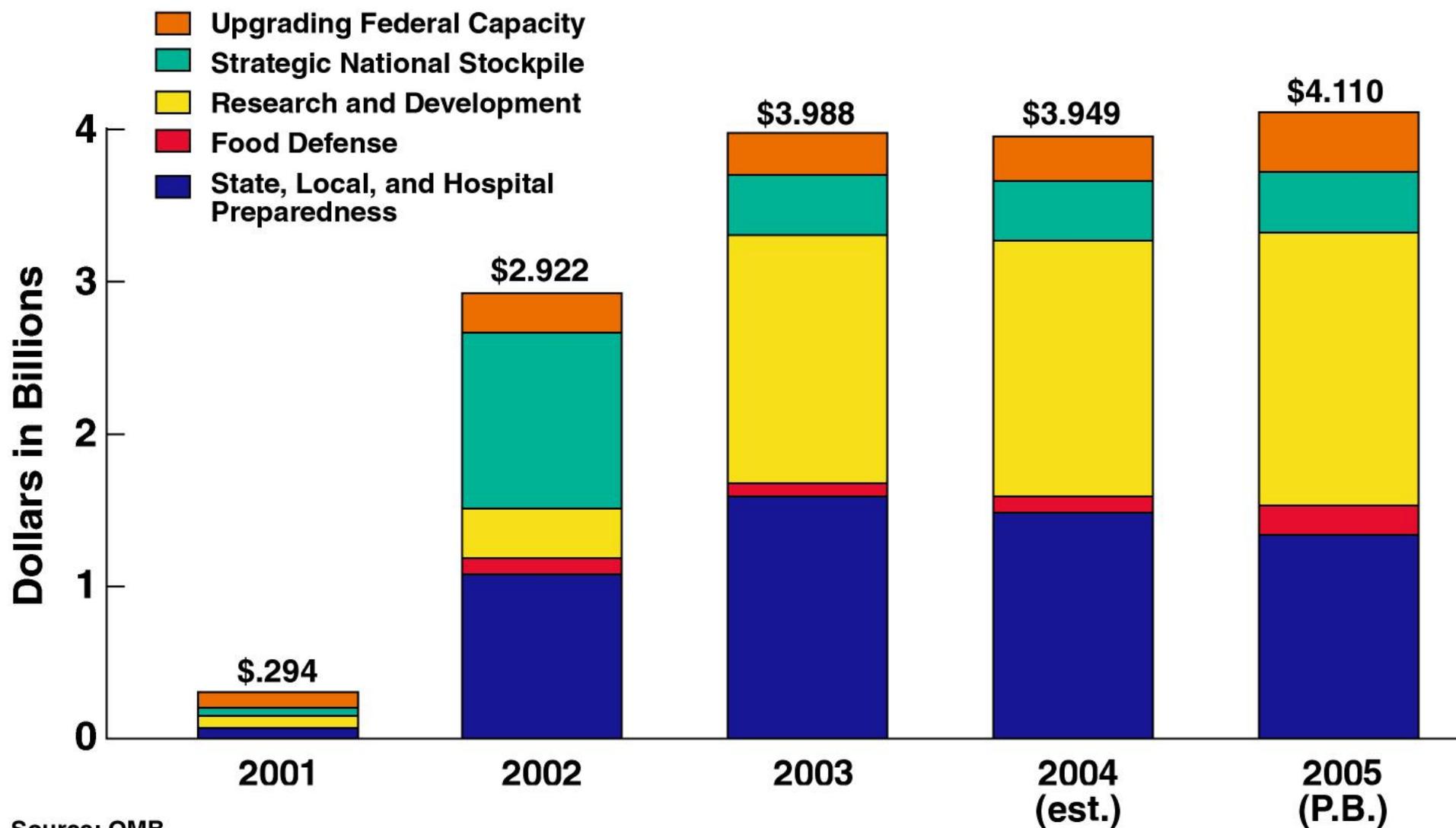
**May 3, 2004**



# Combined HHS and DHS Biodefense Spending



# HHS Biodefense Funding



Source: OMB



**Therapeutics**

**\$276M**

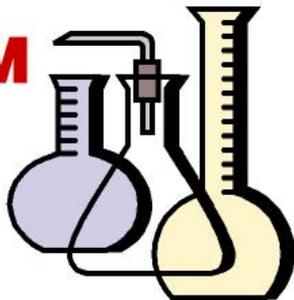


**Diagnostics**

**\$64M**

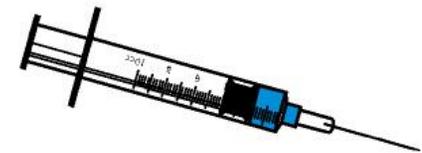
**Biodefense  
Research  
Priorities**

**\$541M**



**Basic Research  
(including Genomics)**

**Fiscal Year  
2004 (enacted)  
Total: \$1.62B**



**Vaccines**

**\$739M**

# **Biodefense R+D Progress, 2004**

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- **The USA now has enough smallpox vaccine to vaccinate everyone in the country if necessary.**
- **New and improved vaccines against smallpox, anthrax, and other potential bioterror agents are being developed and evaluated and will soon enter the national stockpile through Project BioShield.**
- **A fast-acting Ebola virus vaccine is being tested in human volunteers.**
- **NIH-supported scientists have identified antivirals that may play a role in treating smallpox or the complications of smallpox vaccination, as well as new antibiotics and antitoxins against other major bioterror threats.**

# **Biodefense R+D Progress, 2004 (cont'd)**

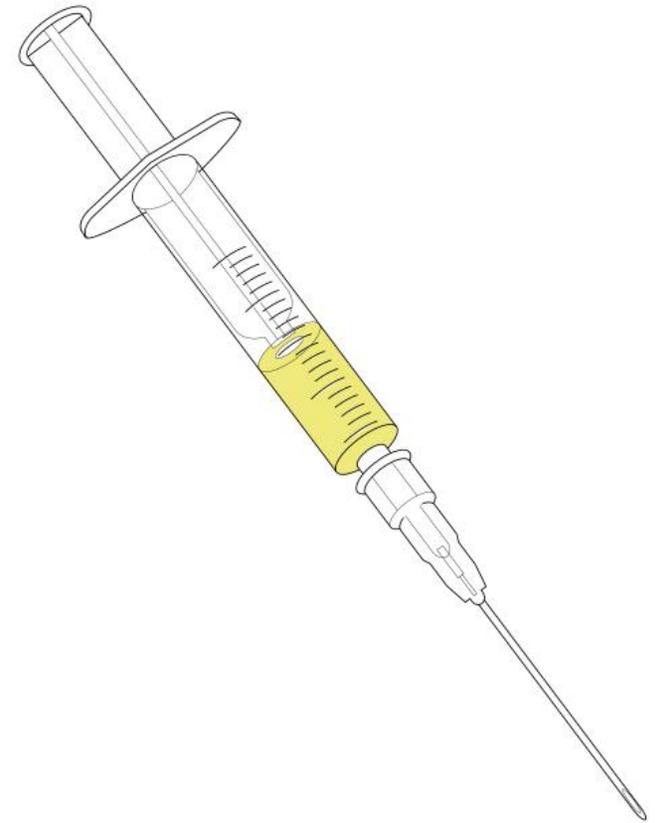
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- **NIH has established eight Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research (RCE).**
- **NIH has funded construction of two National Biocontainment Laboratories (NBLs) and nine Regional Biocontainment Laboratories (RBLs).**
- **Genomic sequencing of representative strains of all bacteria considered to be bioterror threats has been completed, as has the sequencing of genomes for at least one strain of every potential viral and protozoan bioterror pathogen.**

# **Biodefense Vaccine Research: Goals**

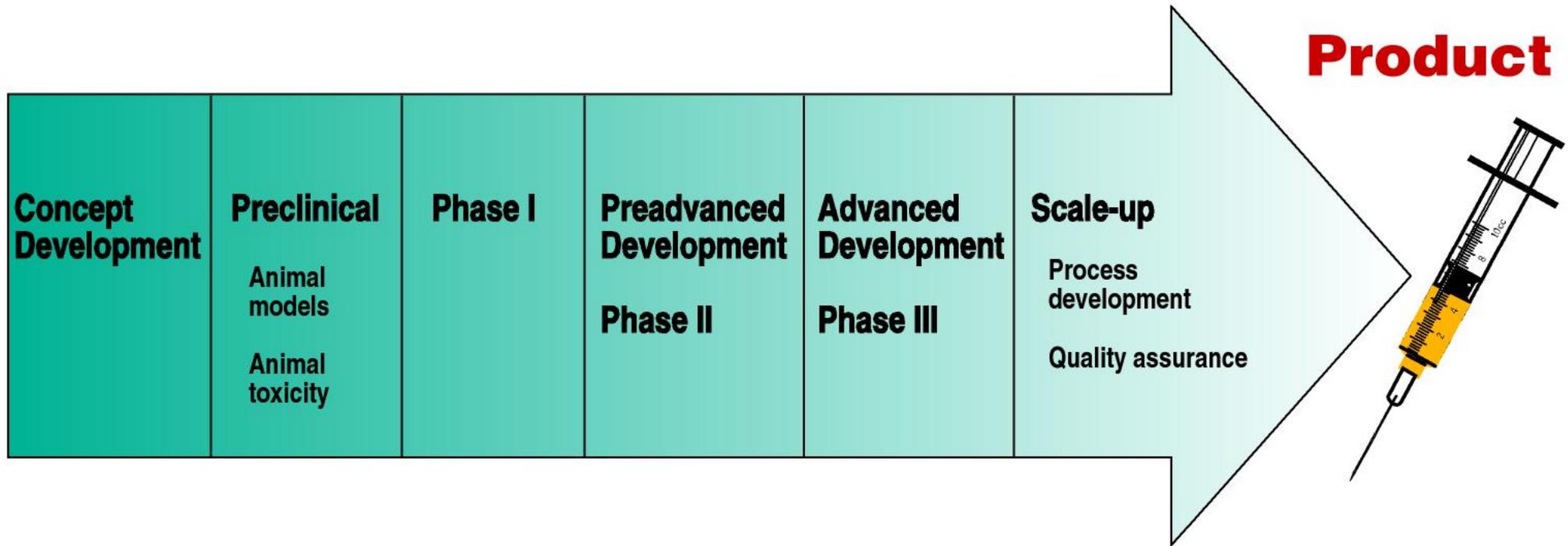
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- **Protect all groups of civilians**
- **Develop improved vaccines against microbes for which vaccines currently exist**
- **Develop new/novel vaccines against microbes for which none currently exist**



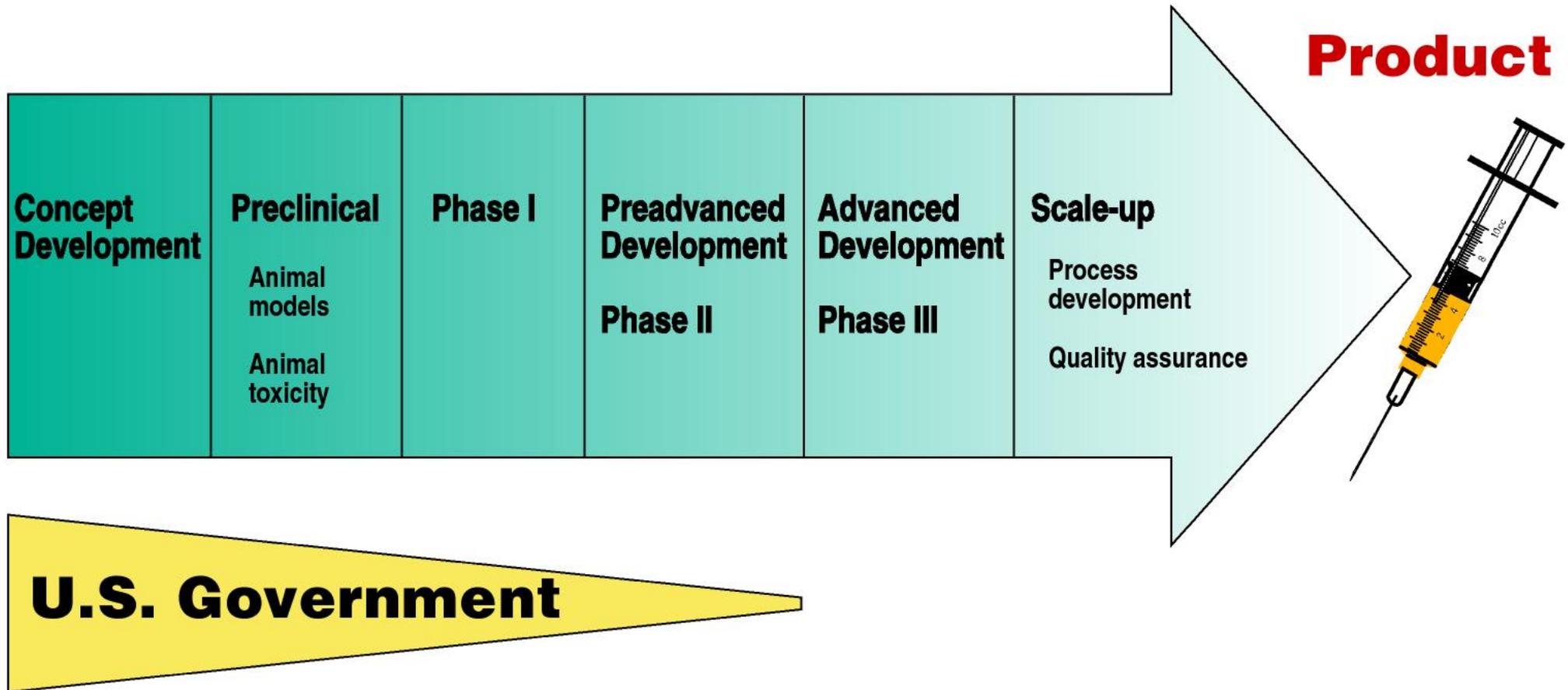
# Vaccine Development: A Changing Paradigm

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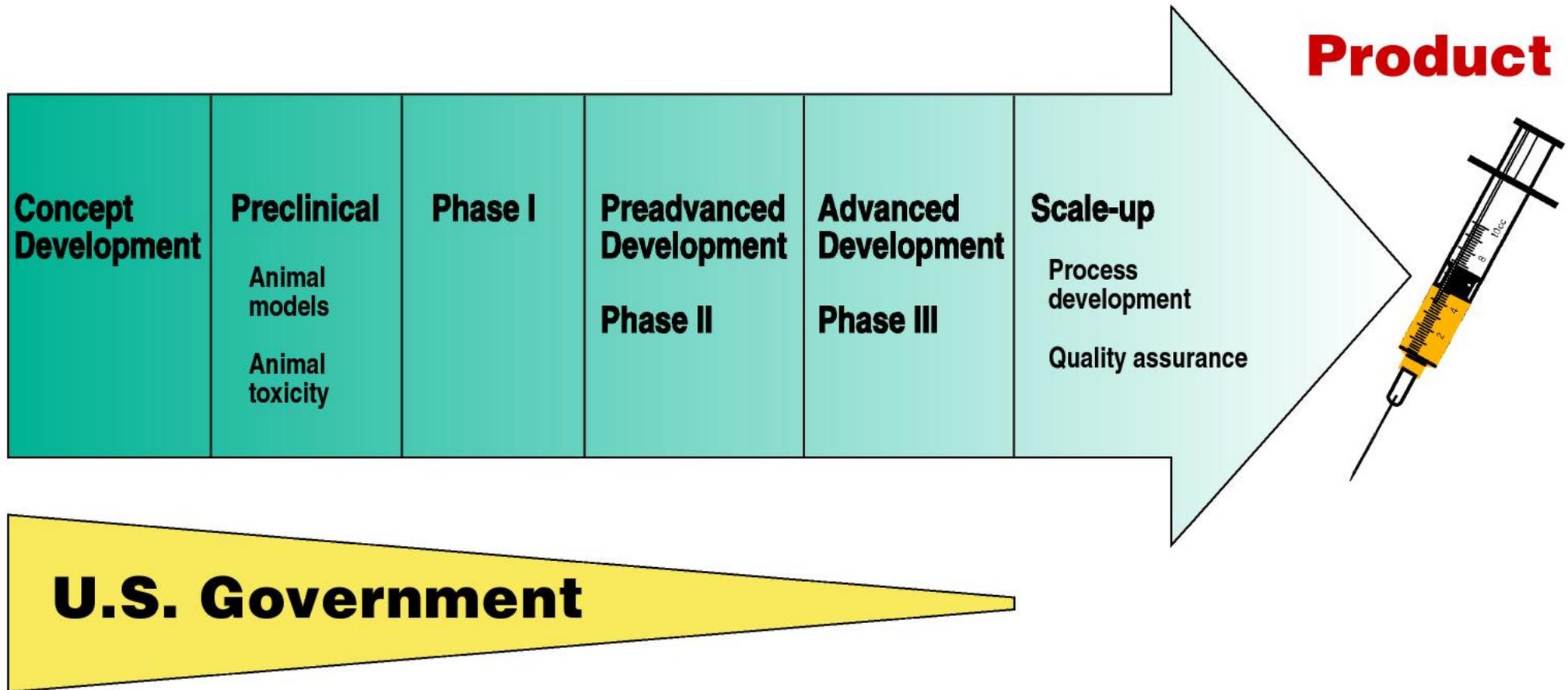
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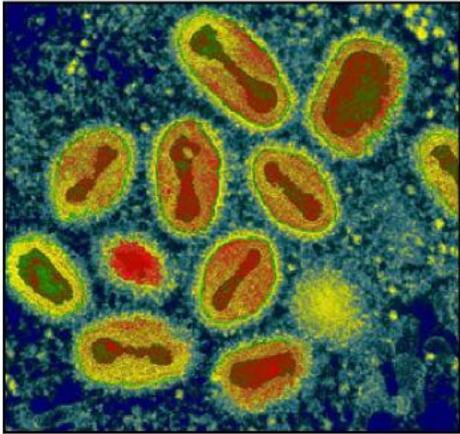
# Vaccine Development: A Changing Paradigm

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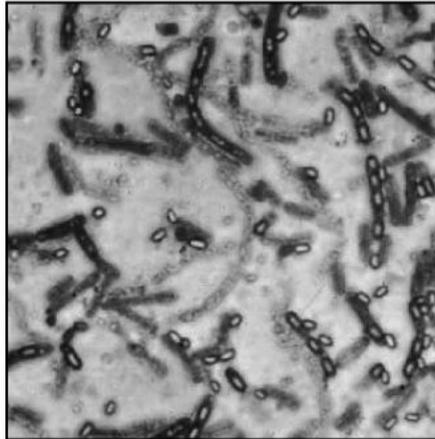


# NIH Progress in Developing Vaccines Against Agents of Bioterrorism

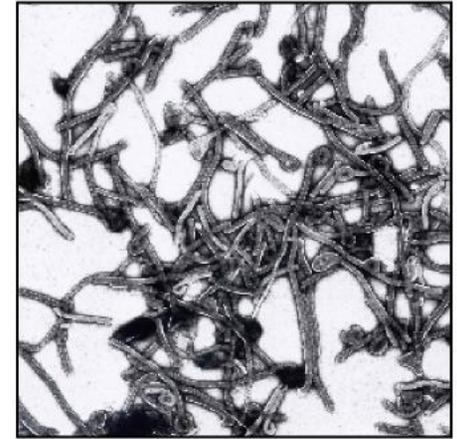
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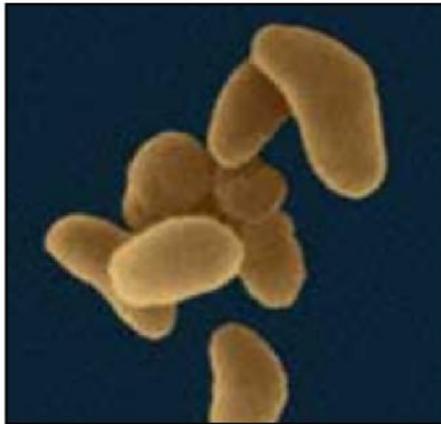
**Smallpox**



**Anthrax**



**Ebola**



**Tularemia**



**Plague**

The Atlanta Journal-Constitution

March 10, 2004

# *Progress Reported on Safer Smallpox Vaccine*

An experimental form of smallpox vaccine made from a highly weakened form of a related virus has shown that it can protect lab animals while producing fewer side effects than the current vaccine.

The work by scientists with the National Institutes of Health and the U.S. Army Medical Research Institute of Infectious Diseases, published today in *Nature* and on the Web site of the Proceedings of the National Academy of Sciences, could pave the way for a safer smallpox vaccine, the researchers said.

11 March 2004

International weekly journal of science

**nature**

940.00

www.nature.com/nature

# **Immunogenicity of a Highly Attenuated MVA Smallpox Vaccine and Protection Against Monkeypox**

Patricia L. Earl, Jeffrey L. Americo, Linda S. Wyatt, Leigh Anne Eller, J. Charles Whitbeck, Gary H. Cohen, Roselyn J. Eisenberg, Christopher J. Hartmann, David L. Jackson, David A. Kulesh, Mark J. Martinez, David M. Miller, Eric M. Mucker, Joshua D. Shamblin, Susan H. Zwiars, John W. Huggins, Peter B. Jahrling & Bernard Moss

March 30, 2004  
vol. 101 | no.13

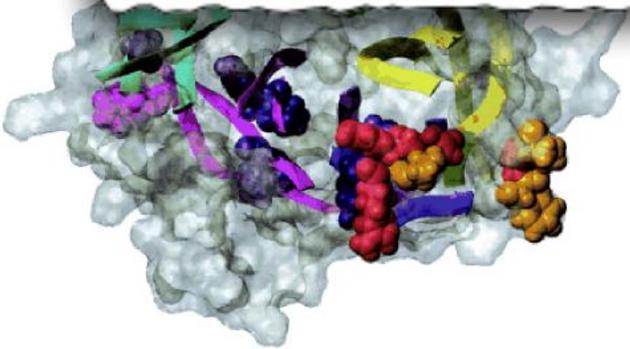
**PNAS**

# **HIGHLY ATTENUATED SMALLPOX VACCINE PROTECTS MICE WITH AND WITHOUT IMMUNE DEFICIENCIES AGAINST PATHOGENIC VACCINIA VIRUS CHALLENGE**

Linda S. Wyatt, Patricia L. Earl, Leigh Anne Eller, and Bernard Moss

# Smallpox DNA Vaccine Protects Nonhuman Primates against Lethal Monkeypox

JW Hooper JW, E Thompson, C Wilhelmsen, M Zimmerman, MA Ichou, SE Steffen, CS Schmaljohn, AL Schmaljohn & PB Jahrling



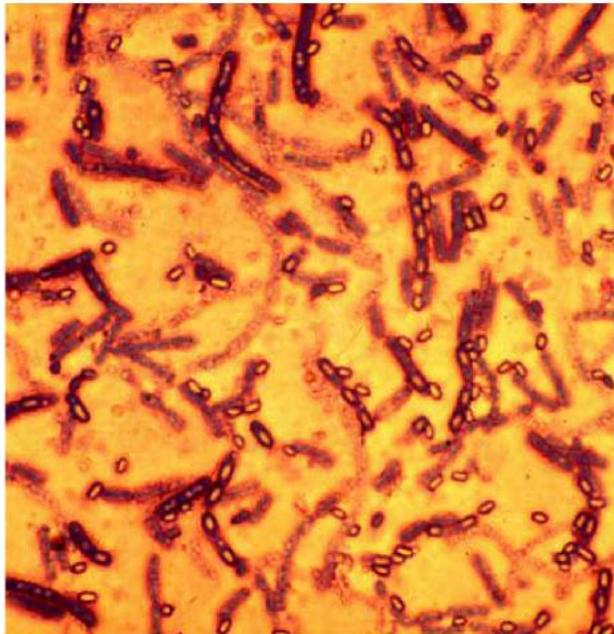
- DNA vaccine consisting of four vaccinia virus genes protected monkeys against severe disease.
- "This is the first demonstration that a subunit vaccine approach to smallpox-monkeypox immunization is feasible."

Journal of  
Virology

April 2004, Volume 78, Number 9

# **Anthrax rPA Vaccine Development**

**Approx. \$182M Awarded by  
NIH for rPA Vaccine  
Development Contracts**



# **Anthrax Vaccine – Phase II Trials Update**

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## **■ VaxGen**

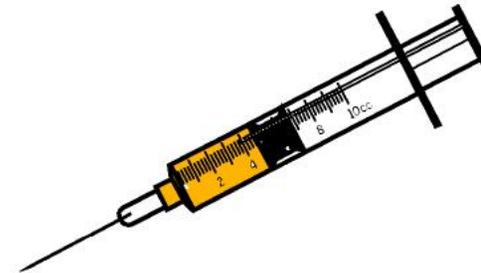
- Phase 2a protocol approved by FDA**
- Phase 2a immunizations began April 26, 2004**

## **■ Avecia**

- Phase 2 protocol to be submitted to FDA for review.**

# **Acquisition of Anthrax Recombinant Protective Antigen (rPA) Vaccine for the Strategic National Stockpile (SNS) RFP-DHHS-ORDC-04-01**

- **Primary purpose of RFP is the acquisition and maintenance of 75 million single dose units of licensed anthrax rPA vaccine for the SNS to protect U.S. citizens against inhalation anthrax.**
- **RFP issued: March 11, 2004**  
**Responses due: April 16, 2004**  
**Awards to be made: ~August 9, 2004**



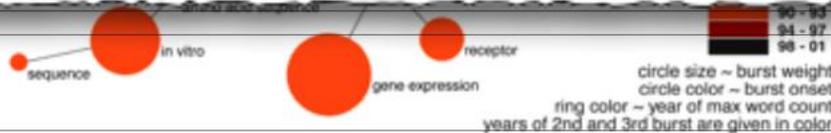
April 6, 2004

PNAS

Proceedings of the National Academy of Sciences of the United States of America

# mAbs to *Bacillus anthracis* Capsular Antigen for Immunoprotection in Anthrax and Detection of Antigenemia

TR Kozel, WJ Murphy, S Brandt, BR Blazar, JA Lovchik, P Thorkildson, A Percival & CR Lyons



The *B. anthracis*  $\gamma$ -D-PGA capsule is a promising target for:

- Active immunization in combination with toxin-based vaccines
- Passive immunization of unvaccinated individuals
- Antigen detection in diagnosis of inhalational anthrax.

January 2004

# Infection & *Immunity*

## **Protection Against Anthrax Toxemia by Hexa-D-Arginine in Vitro and in Vivo**

MS Sarac, JR Peinado, SH  
Leppla, and I Lindberg

March 2, 2004

# PNAS

## **Selective Inhibition of Anthrax Edema Factor by Adefovir, a Drug for Chronic Hepatitis B Virus Infection**

Y Shen, NL Zhukovskaya, MI  
Zimmer, S Soelaiman, P Bergson,  
CR Wang, CS Gibbs, and WJ Tang



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

## Progress Report



April 2004



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
National Institutes of  
Health  
National Institute of Allergy and Infectious  
Diseases

# NIAID Category B Priority Pathogens

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- *Burkholderia pseudomallei* (melioidosis)
- *Coxiella burnetii* (Q fever)
- *Brucella* species (brucellosis)
- *Burkholderia mallei* (glanders)
- Ricin toxin (from *Ricinus communis*)
- Epsilon toxin (of *Clostridium perfringens*)
- Staphylococcal enterotoxin B
- Typhus fever (*Rickettsia prowazekii*)
- Food- and Water-borne Pathogens
  - Bacteria
  - Viruses
  - Protozoa
- Additional viral encephalitides, e.g. West Nile virus, Japanese encephalitis virus

# **NIAID Category C Priority Pathogens**

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- **Emerging infectious disease threats such as Nipah virus and additional hantaviruses**
- **Tickborne hemorrhagic fever viruses, e.g. Crimean Congo Hemorrhagic fever virus**
- **Tickborne encephalitis viruses**
- **Yellow fever**
- **Multi-drug resistant TB**
- **Influenza**
- **Other Rickettsias**
- **Rabies**

April 16, 2004

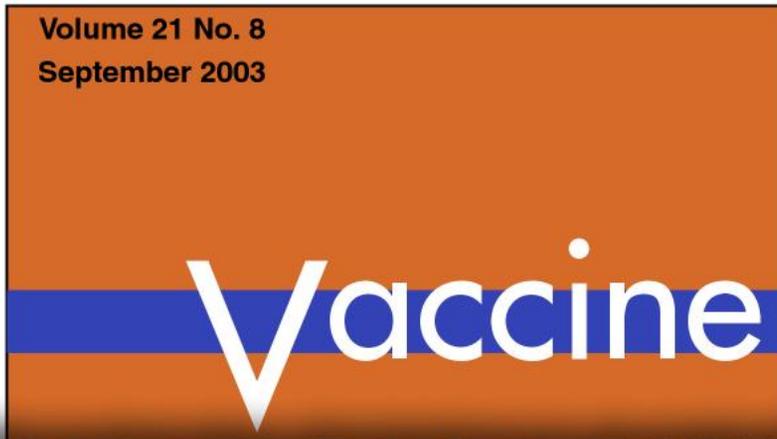
# SCIENCE

## **Complete Genome Sequence of the Apicomplexan, *Cryptosporidium parvum***

MS Abrahamsen et al.

- NIAID Category B priority pathogen; no effective therapy.
- Extremely streamlined metabolic pathways and a reliance on the host for nutrients.
- "Elucidation of core metabolism, including enzymes with high similarities to bacterial and plant counterparts, opens new avenues for drug development."

# Discovery of Antigens and Cross-Protective Immunity May Lead to the Development of Vaccine Against Multiple Species of Rickettsia



## Cross-Protection Between Distantly Related Spotted Fever Group Rickettsia

HM Feng and DH Walker



## Identification of CD8 T-Lymphocyte Epitopes in OmpB of *Rickettsia conorii*

Z Li et al.

May 2003 Volume 41 No. 5

# JOURNAL OF Clinical Microbiology

## **Evaluation of *Coxiella burnetii* Antibiotic Susceptibilities by Real-Time PCR Assay**

RE Brennan and JE Samuel

- ***Coxiella burnetii* is an NIAID Category B Pathogen.**
- **A promising alternative to traditional antibiotic testing methodologies for intracellular bacteria such as *C. burnetii*.**

# Recombinant Japanese Encephalitis Virus Vaccine Developed

Oct. 15, 2003

The Journal of  
Infectious  
Diseases

- Yellow fever virus vaccine as backbone.
- Two phase II trials completed; a third is underway.
- Vaccine appears to be safe and provides protective levels of neutralizing antibody after a single dose.

**Chimeric Live, Attenuated Vaccine Against Japanese Encephalitis (ChimeriVax-JE): Phase 2 Clinical Trials for Safety and Immunogenicity, Effect of Vaccine Dose and Schedule, and Memory Response to Challenge with Inactivated Japanese Encephalitis Antigen**

TP Monath et al.

# San Francisco Chronicle

NORTHERN CALIFORNIA'S LARGEST NEWSPAPER

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FEBRUARY 18, 2002

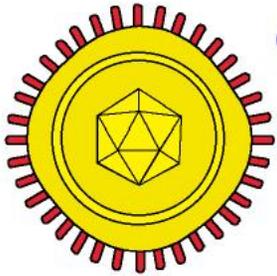
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## *Bioterror Funds a Boon for Public Health*

**Experts say research will apply to  
fighting infectious diseases**

# NIH West Nile Virus Vaccine Development, 2004

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## Chimeric

### Acambis - YF/WNV

- 100% protection in rhesus monkeys
- Phase 1 clinical trials initiated 11/03

### Intramural - Dengue/WNV

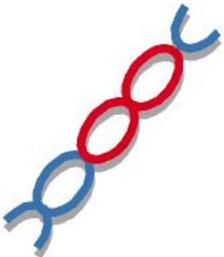
- 100% protection in rhesus monkeys
- Phase I clinical trials to begin summer, 2004



## Subunit Vaccines

### Extramural

- Drosophila-expressed WNV recombinant vaccine for humans
- Baculovirus-expressed WNV recombinant vaccine for humans
- E.coli-expressed WNV recombinant vaccine for horses



## DNA Vaccines

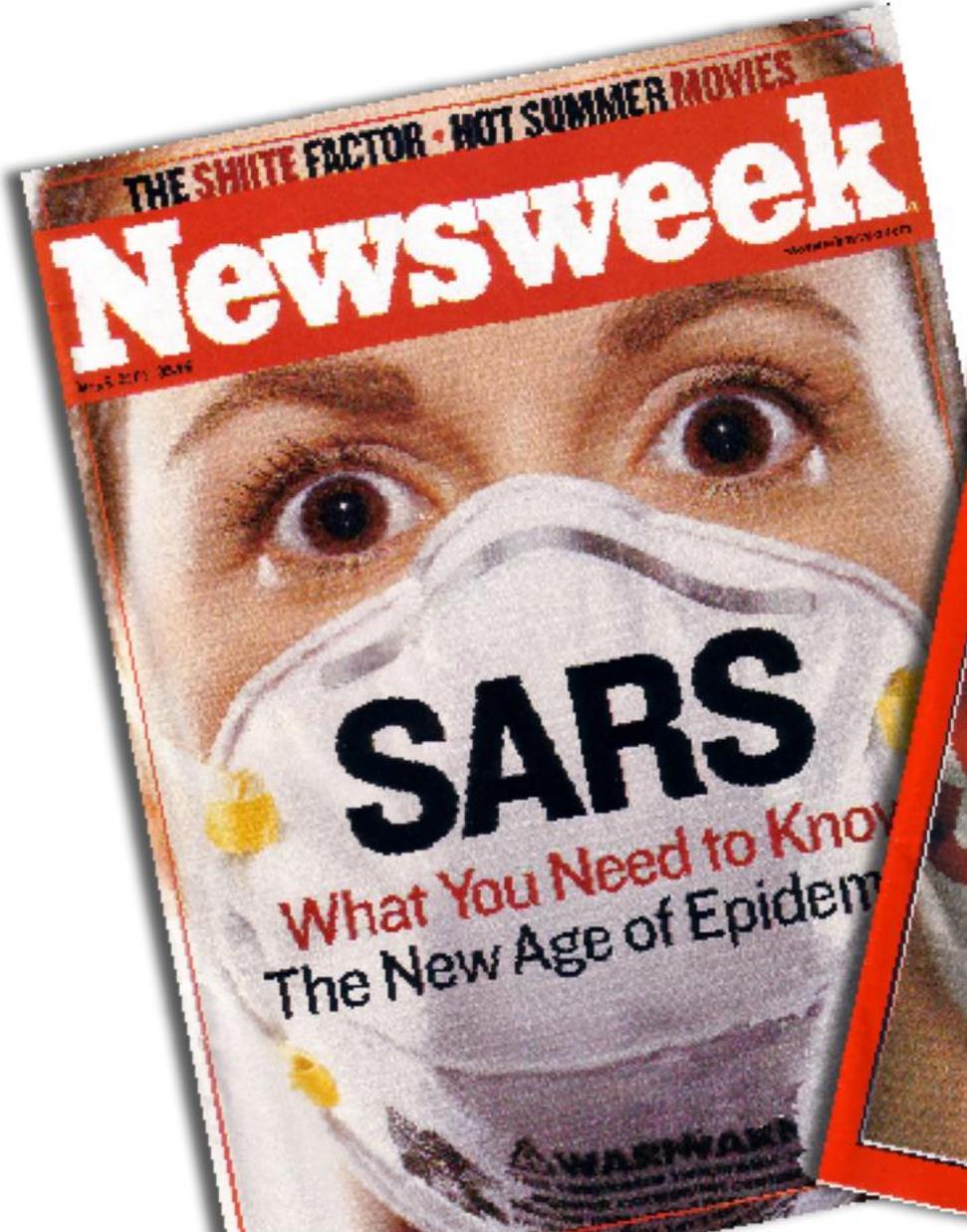
- VRC - phase I clinical trial planned for early 2005
- Extramural - projects in early stage R&D

# **West Nile Virus Intravenous Immunoglobulin Clinical Trial**

**CASG 210 -- A Phase I/II Randomized, Placebo-controlled Trial to Assess the Safety and Efficacy of Intravenous Immunoglobulin G (Omr-IgG-am) Containing High Anti-West Nile Virus Titers in Patients With, or at High Risk for Progression to West Nile Virus Encephalomyelitis**

- **Expected enrollment - 110**
- **Conducted by NIAID-sponsored Collaborative Antiviral Study Group (CASG) at ~35 sites around the U.S. and at the NIH Clinical Center**

# SARS: A New Challenge to Global Health



March 31, 2004

International weekly journal of science

# nature

## **A DNA Vaccine Induces SARS Coronavirus Neutralization and Protective Immunity in Mice**

**Zhi-yong Yang, Wing-pui Kong, Yue Huang,  
Anjeanette Roberts, Brian R. Murphy,  
Kanta Subbarao & Gary J. Nabel**

- **Phase I human clinical trial at NIAID Vaccine Research Center (VRC) to begin by Fall of 2004.**

PNAS

Proceedings of the National Academy of Sciences of the United States of America

**Severe Acute Respiratory Syndrome  
Coronavirus Spike Protein Expressed  
by Attenuated Vaccinia Virus  
Protectively Immunizes Mice**

**H Bisht, A Roberts, L Vogel, A Bukreyev, PL Collins, BR Murphy,  
K Subbarao & B Moss**

# **Confronting the Dual Use Dilemma**

# **The Issue: “Dual Use” Research**

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- **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.**

# **Dual Use Research: Need for Action**

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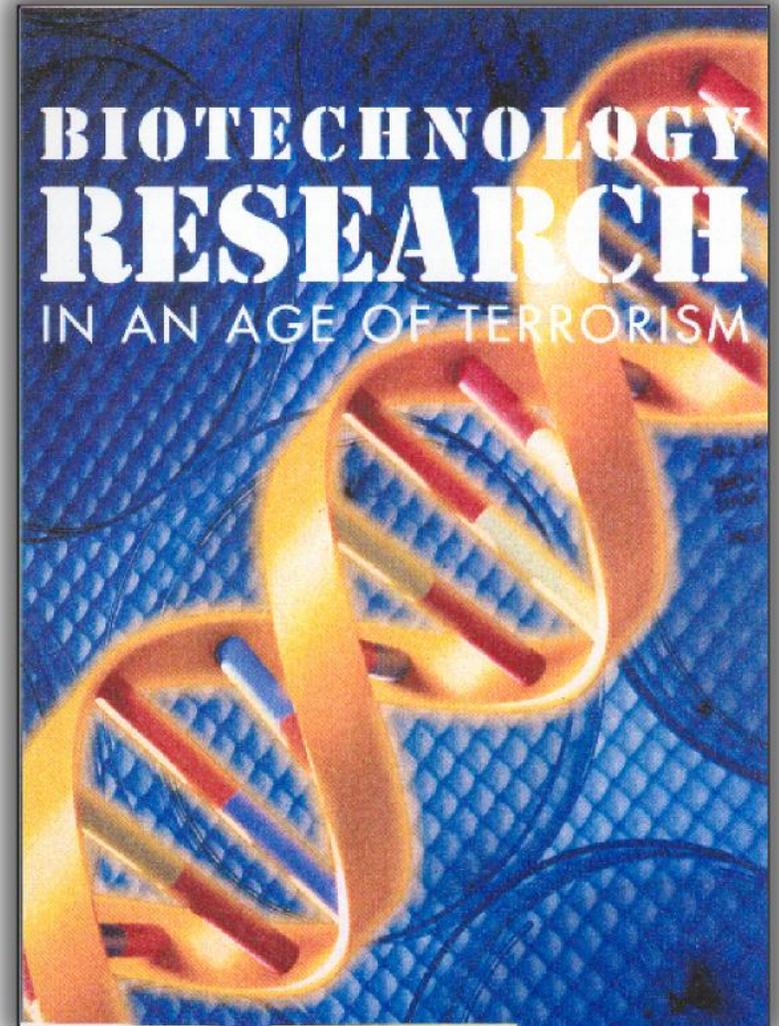
- **“Dual use” potential of certain life sciences research requires consideration of new biosecurity measures.**
- **Goal is to enhance biosecurity protections for life sciences research while ensuring that any impact to the free flow of scientific inquiry is minimized.**

# **NRC Report on Dual Use Research**

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**Report of the National  
Research Council of the  
National Academies:**

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



# **National Science Advisory Board for Biosecurity (NSABB)**

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- **NSABB will provide advice and guidance regarding biological research that has the potential for misuse and could pose a biologic threat to public health or national security.**
- **NSABB will advise HHS Secretary, NIH Director, heads of all Federal entities that conduct/support life sciences research.**
- **<http://www.biosecurityboard.gov>**

# **NSABB Structure/Operations**

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- **25 voting members appointed by Secretary, HHS, after consultation with other Federal Agencies**
- **Meets quarterly and as needed**
- **Meetings open to public, unless otherwise determined by the Secretary, HHS**
- **Will be managed and administered by the NIH**

# **NSABB Expertise**

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- **Molecular/genomics**
- **Microbiology**
- **Clin. ID/diagnostics**
- **Lab biosafety/security**
- **Pub. health/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 *ex officios*

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- 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

