The American Recovery and Reinvestment Act of 2009 (ARRA)

NIAID Plans for ARRA Funds

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National Institute of Allergy and Infectious Diseases (NIAID)
National Institutes of Health (NIH)

Scientific Opportunity

Research in
- Immunology
- Microbiology
- Infectious Diseases

- HIV/AIDS
- Biodefense
- Emerging Microbes
- Immune-mediated Diseases
- Global Health

Public Health Needs

Vaccines
Diagnostics
Drug Development
Other Interventions (e.g., prevention strategies)
NIAID Research: A Dual Mandate

Maintain and “grow” a robust basic and applied research portfolio in microbiology, infectious diseases, immunology and immune-mediated diseases

Respond rapidly to new and emerging disease threats

New/Improved Interventions
American Recovery and Reinvestment Act of 2009 (ARRA): Funding Goals

- Stimulate the economy
- Create and preserve jobs
- Advance biomedical research
NIH Plans for ARRA Funds

$10.4B to be spent over two years (FY 2009/FY 2010)

NIH will distribute among 27 ICs/Offices
- $7.4B - ICs for scientific research priorities
- $800M - NIH Office of the Director (includes $200M for Challenge Grants)
- $1.0B - NCRR for extramural construction, repairs, and alterations
- $300M - NCRR for shared instrumentation and other capital equipment
- $500M - NIH buildings and facilities
- $400M - Comparative Effectiveness Research
NIAID Plans for ARRA Funds

- NIAID allocation of ARRA Funds: $1.11B
- Support unfunded RPGs from FYs 2008-2009
- 1-2 years of funding
- R01 or Bridge Award
  - 12th to 25th percentile
- R21/R03
  - 200 priority score
- Participation in NIH-wide ARRA programs
- NIAID Signature Projects
NIAID Participation in NIH-wide ARRA Programs

- Challenge Grants
  - Explore the earliest events in HIV infection
  - Develop diagnostics and drugs for MDR/XDR TB
  - Develop drugs for neglected tropical diseases
  - Explore novel methods in mucosal immunology
  - Characterize human immune response to infection/immunization

- Grand Opportunities ("GO" Grants)
  - Develop medical countermeasures for radiological/nuclear threats
NIAID Signature Projects

- Stopping the HIV Pandemic
- Protection of Human Health by Immunology and Vaccines
- Biodefense and Emerging Infectious Diseases:
  - Expanding Research Capacity through the Regional Centers of Excellence
  - Developing Partnerships to Translate Research into Products
NIAID Signature Projects

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Adults and Children Estimated to be Living with HIV, 2007

Global Total: ~33 million

Source: UNAIDS, 7/2008
HIV/AIDS in the United States

- 562,793 cumulative deaths
- ~1.1 million living with HIV
  - 21% unaware of their infection
- ~56,300 new infections in 2006
  - 53% male-to-male sexual contact, 31% heterosexual contact
  - 45% blacks, 35% whites, 17% Hispanics
  - incidence rate among blacks 7 times higher than whites

Source: CDC, Includes 50 states and District of Columbia
HIV/AIDS in Washington, DC

- ~3% of adults and adolescents in District living with HIV/AIDS, end-2007

- An underestimate, as between 1/3 and 1/2 of DC residents may be unaware of their HIV infection status

Report released 3/16/2009
Proportion of Washington, D.C. Adults and Adolescents Living with HIV/AIDS by Race and Sex, End-2007

- White Females: 0.2%
- Hispanic Females: 0.7%
- Black Females: 2.6%
- White Males: 2.6%
- Hispanic Males: 3.0%
- Black Males: 6.5%

Threshold for generalized/severe epidemic: 1.0%
Overall DC HIV/AIDS Prevalence among Adults and Adolescents: 3.0%

National Average: 1.0%

Source: DC Dept. of Health, 2009; MMWR, 10/3/2008
A Policy Cocktail for Fighting HIV

By Anthony S. Fauci

Three-pronged approach to curbing HIV/AIDS pandemic:

- Pre-exposure prophylaxis of high-risk individuals with antiretroviral therapy (PrEP)
- Universal, voluntary testing/immediate antiretroviral therapy (“test and treat” approach)
- Cure/functional cure research
The Promise of Pre-Exposure Prophylaxis (PrEP)

- Well-established tool for preventing other infectious diseases, e.g. malaria
- ARVs proven to prevent mother-to-child HIV transmission, and as post-exposure prophylaxis
- Generally positive NHP data with tenofovir +/- emtricitabine, drugs with long-half lives, good safety profiles, high genetic barrier to resistance (tenofovir)
- Promise of good acceptability -- PrEP inhibits HIV without requiring change in sexual habits
Voluntary “Test and Treat” Concept

Universal Voluntary HIV Testing with Immediate Antiretroviral Therapy as a Strategy for Elimination of HIV Transmission: a Mathematical Model

RM Granich et al.

- Model indicates that universal and annual voluntary HIV testing followed by immediate antiretroviral therapy treatment (irrespective of clinical stage or CD4 count) could reduce new HIV cases by 95% within 10 years

- Concerns: feasibility, protection of individual rights, drug resistance, toxicity, financing
The Main Obstacles to a Cure for HIV Disease

- HIV hides from the immune system
- HIV forms a latent reservoir protected from drug therapy
NIAID Signature Projects

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Protection of Human Health by Immunology and Vaccines

- New collaborative consortium of Human Immunology Research Centers
- Research to characterize the protective immune response in humans using modern tools (e.g., genomics and proteomics) and other modern technologies, including systems biology approaches
NIAID Signature Projects

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Global Examples of Emerging and Re-Emerging Infectious Diseases

- West Nile virus
- Cryptosporidiosis
- Ebola hemorrhagic fever
- Drug-resistant malaria
- Diphtheria
- Rift Valley fever
- Typhoid fever
- SARS
- E. coli O157:H7
- H5N1 influenza
- Nipah virus
- Hendra virus
- Enterovirus 71
- Chikungunya fever
- Human monkeypox
- Plague
- Anthrax bioterrorism
- Hantavirus pulmonary syndrome
- Dengue
- Yellow fever
- Human African trypanosomiasis
- Cholera
- Marburg hemorrhagic fever
- MDR/XDR tuberculosis
- HIV

Legend:
- Newly emerging
- Re-emerging/resurging
- “Deliberately emerging”
Examples of Human Disease Outbreaks, 2006-2009

- H5N1 avian influenza
- Chikungunya fever
- Dengue
- E. coli O157:H7
- Fusarium keratitis
- Poliomyelitis
- Rift Valley fever
- XDR-TB
- Ebola hemorrhagic fever
- Marburg hemorrhagic fever
- Methicillin-resistant Staphylococcus aureus (MRSA)
- Adenovirus Serotype 14
- Yellow fever
- Salmonella
- 2009 H1N1 influenza
**NIAID Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases**

- **PI – Dr. Samuel Miller**
  University of Washington
  Seattle, WA

- **PI – Dr. John Belisle**
  Colorado State University
  Fort Collins, CO

- **PI – Dr. Olaf Schneewind**
  University of Chicago
  Chicago, IL

- **PI – Dr. Dennis Kasper**
  Harvard Medical School
  Boston, MA

- **PI – Dr. Jay A. Nelson**
  Oregon Health & Science University
  Portland, Oregon

- **PI – Dr. Myron Levine**
  University of Maryland
  Baltimore, MD

- **PI – Dr. Alan G. Barbour**
  University of California
  Irvine, CA

- **PI – Dr. David Walker**
  University of Texas Medical Branch
  Galveston, TX

- **PI – Dr. Samuel Stanley**
  Washington University
  St. Louis, MO

- **PI - Dr. Fred Sparling**
  University of North Carolina
  Chapel Hill, NC
Biodefense and Emerging Infectious Diseases: Developing Partnerships to Translate Research into New Products

Expansion of NIAID initiative to support collaborative projects with academia and industry to advance promising products, including vaccines, therapeutics, and medical diagnostics, e.g.:

- new tools for influenza diagnosis, treatment and prevention
- a vaccine that protects against multiple viral hemorrhagic fever viruses
NIAID Research: A Dual Mandate

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New/Improved Interventions
Unusual Strain of Swine Flu Is Found in People in 2 States

Swine Flu Empties Mexico City's Churches, Streets
Seasonal vs. Pandemic Influenza

Influenza Virus

- Neuraminidase (N)
- Hemagglutinin (H)

Drift

Seasonal Influenza
- Predictable annual occurrence
- Residual immunity in population

Shift

Pandemic Influenza
- Unpredictable rare occurrence
- “Naïve” population
# Influenza Pandemics in the 20th Century

<table>
<thead>
<tr>
<th>Year</th>
<th>Virus Type</th>
<th>Outbreak Name</th>
<th>Death Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918</td>
<td>H1N1</td>
<td>“Spanish Flu”</td>
<td>&gt;50 million deaths</td>
</tr>
<tr>
<td>1957</td>
<td>H2N2</td>
<td>“Asian Flu”</td>
<td>1-2 million deaths</td>
</tr>
<tr>
<td>1968</td>
<td>H3N2</td>
<td>“Hong Kong Flu”</td>
<td>700,000 deaths</td>
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Influenza A (H1N1): Confirmed Cases in the United States, as of May 29, 2009

Total:
8,975 confirmed and probable cases in 49 states
15 deaths in 7 states

Source: Centers for Disease Control and Prevention (CDC)
Global Influenza A (H1N1) Laboratory-Confirmed Cases and Deaths, as of May 29, 2009

- **Total:** 15,510 cases, 99 deaths

Source: WHO
H1N1 Influenza Vaccine Development: A Collaborative Process

- Isolation and Characterization
- Seed Virus
- Pilot Lots Scale-up for Commercial Production
- Clinical Evaluation (e.g. in VTEUs) Commercial production
- Formulation, Filling and Delivery

Influenza Virus

Where we are now

New Vaccine
NIAID’s Network of Vaccine and Treatment Evaluation Units (VTEUs)

Established in 1962

>160 Phase I, II, and III clinical trials since 1995

Trials of
- Seasonal vaccines
- Pre-pandemic vaccines
- Antivirals
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