Facilitating Antibacterial Drug Development Outlining the Path Forward

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On behalf of the

Infectious Diseases Society of America

Disclosures

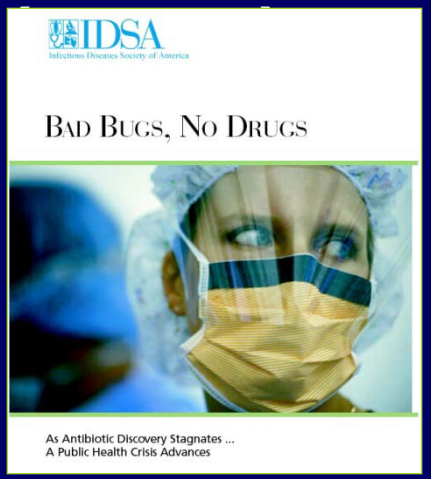
- In the last 12 months, consultant/advisor to:
  - Cerexa
  - Durata
  - Merck (adjudication committee)
  - Rib-X
  - Wyeth/Pfizer (Data safety monitoring committee)

Scientific Challenges

- Lack of sufficient diagnostic tests
  - We need rapid, sensitive, specific, ideally bedside/office tests that directly influence use of antibiotics

- Insufficient research support
  - National Institutes of Health; Public-Private Collaborations - Biomedical Advanced Research and Development Authority

- Need for improved clinical trial infrastructure



Meeting Scientific Challenges
Diagnostic Tests - Path Forward

Clinical Specimen Repository

- **Urine, sputum, blood whose microbial content is known and validated**

WHY a repository ?

- **To collect, save and repurpose samples from clinical trials**
- **So that diagnostic tests can be quickly and easily assessed**
- **Allow researchers (Govt and industry funded) to access samples and conduct new trials**
    - **Validate diagnostic tests quickly**

How to establish a repository?

- **Similar to Cancer Human Bio-Bank established by National Cancer Institute**
- **National Institutes of Health funding initially, goal to become self-sufficient (via charges for access/analysis)**

Meeting Scientific Challenges Diagnostic Tests - Path Forward

Clinical Trials

- Integrate diagnostic development with drug development
- More early and /or point of care diagnostics
  - Enrich clinical trial evaluable population
  - Provide generalizable data

Research Support – some good news
Public Private Collaboration

BARDA

- **Contracts for advanced R&D of Gram-negative active drugs awarded to**
  - **Achaogen ACHN 490**
    - **$27M over the 1st two years; up to $64.5M**
  - **GSK 2251052**
    - **$38.5M over the 1st two years; up to $94M**
  - **Tetraphase TP-434**
    - **$11.4 M 1st year; up to $67.2 M**

Public-Private Collaboration

HHS Medical Countermeasures (MCM) PLAN – Aug, 2010

- Strategic investment firm called for in the Pandemic All-Hazards Preparedness Act (PAHPA) funded through tax dollars, but operates outside of government; to leverage venture capital
  - 1st focus
    - novel antimicrobials for resistant organisms
  - Passed Senate as part of PAHPA
  - We need the House to agree
  - $50 MM proposed FY 13 in President's budget
    - We need more

Research Support – some good news

NIH

- Research funding slowly increasing
- NIAID funds development of new broad-spectrum therapeutics, Oct 2011
  - CUBRC partnership with Tetraphase TP-271
    - $5.7 M, up to $35 M over 5 years
  - Enanta biocyclolides
    - $14.3 M, up to $43 M over 5 years
- Host-Targeted Interventions as Therapeutics for Infectious Diseases (R21/R33) $4 M/yr for 5 years to be funded in May 2012
- Partnerships for Development of Therapeutics and Diagnostics for Biodefense (R01) $9.3 M /yr for 5 years to be funded in January 2013

Paths Forward – New ideas?

National Institutes of Health National Center for Advancing Translational Sciences (NCATS) partnership with Pfizer, AZ and Lilly

- Plan
  - allocate $20 M fiscal 2013
- Pairs researchers with drug companies to repurpose compounds that never moved beyond phase I or II
- Currently includes 3 companies/24 compounds
- Focus
  - rare/genetic disorders/neurological conditions

- Is NIAID involved in this or similar ID-only focused effort?

National Institute of Allergy and Infectious Diseases (NIAID) Clinical Trials Infrastructure on Antibiotic Resistant Bacterial Infections

Purpose

- To do studies that industry can't, or are not willing, to perform
- Build on existing infrastructure (from AIDS Trials Networks, etc.)
- Develop clinical trials leadership group

Timeline

- Earliest start date: December 2013 (FY 2014)

Funding

- Initially 10M USD (the cost of ONE typical early study in patients) – much more $$$ needed!
- IDSA supports a total NIAID commitment of $500 M specific to antibacterial resistance and antibiotic R&D research (including but not limited to the clinical trials infrastructure)

Future goal:

- Clinical trials consortia

More on NIAID
Antibacterial Resistance Strategic Plan

NIAID should form a blue ribbon panel of experts including representatives from

- **Infectious diseases professional societies**
- **Pharmaceutical and diagnostics industries**
- **Others**

Goal:

- **create an antibacterial resistance strategic plan to assist in prioritizing research**

NIAID should continue to improve speed and efficiency of its preclinical services and other resources, including genomic-related services, for both the investigator community and companies that are on a product development timeline

Priority: Recruiting new investigators into antibacterial resistance

Meeting Regulatory Challenges Guidances – Speed is Key!

- Predictable, feasible guidance needed on
  - Standard antibiotic indications – often the initial development pathway
    - FNIH process
    - Feasibility key – consider the "costs" of various options (e.g., inclusion criteria that limit US patient enrollment)
  - Pathways for new Gram-negative antibiotics (e.g., urinary tract, intra-abdominal infections, and pneumonia)
    - For newly-emerging resistant pathogens these studies can't easily be done
    - Tiered approach (PhRMA) or LPAD

Meeting Regulatory Challenges Guidances – Speed is Key!

- Harmonization a key goal
  - Global development programs

- New approaches desperately needed - consider
  - Small studies
  - Clinical trials consortia
  - Patient registries
  - Bacteria- or “organism-specific” rather than disease-specific approval
  - Pathway must permit development of multiple drugs over time

Legislative Solutions

- Public-Private Collaboration (PPC) Report
  - Lead Federal Agency to explore PPCs
    - pursue options with the European Union's Innovative Medicines Initiative
- Biorepository Feasibility Report
- Limited Population Antibiotic Drug (LPAD) Proposal
  - FDA should move quickly to adopt LPAD to the extent possible through regulatory means and through Interim Final Regulation if possible to expedite LPAD's creation

Legislative Solutions

- Generating Antibiotic Incentives Now (GAIN) Act
- Tax incentives
- Transferable R&D tax credits similar to what is available for Orphan Drugs, but with the option of allowing them to be transferable so that small companies without profits can sell them
- IDSA is advocating for strengthened appropriations for BARDA, NIAID and FDA

Our Patients Desperately Need New Antibiotics - The Path Forward

Scientific paths

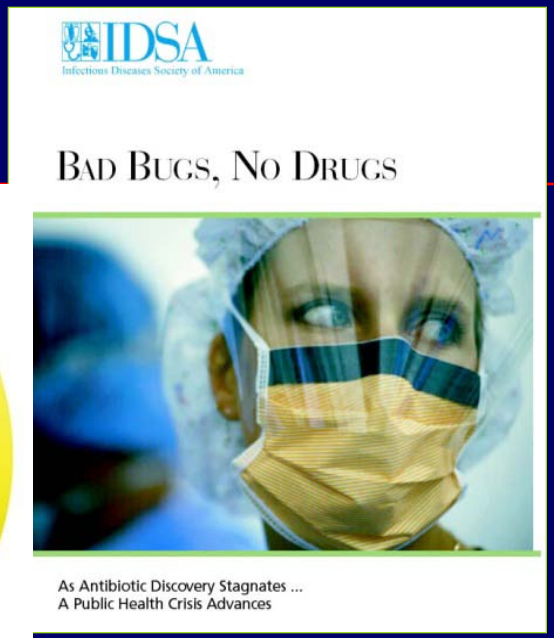
- **Central Clinical Specimen Repository**
- **Research Support – NIH, BARDA, PPCs**
- **Clinical Trials Infrastructure**

Regulatory paths

- **LPAD??**
- **Feasible, predictable FDA Guidances**
  - **Resistant-pathogen "unmet need" guidance a priority**
  - **FNIH, other efforts**
  - **Permit development of multiple drugs over time**

Legislative paths

- **Incentives - GAIN, LPAD, PDUFA**



BAD BUGS, NEED DRUGS
The 10 X '20 Initiative: Pursuing a Global Commitment to Develop 10 New Antibacterial Drugs by 2020

IDSA

Thank You!

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