

# Championing Patient and Public Health Needs: IDSA Efforts to Strengthen the Antibiotic Pipeline

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STUART B. LEVY

CENTER FOR INTEGRATED MANAGEMENT  
OF ANTIMICROBIAL RESISTANCE



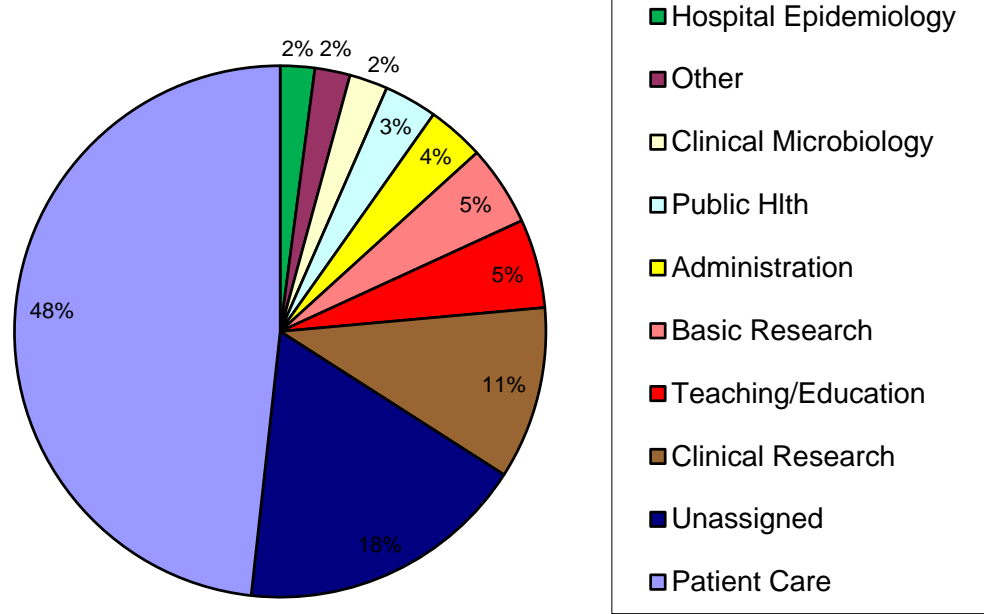
# Disclosures

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- Editor
  - ID Clinics of North America
  - Antimicrobial Agents and Chemotherapy
  - Sanford Guide
- Treasurer, Infectious Diseases Society of America
- Member, ID Board, American Board of Internal Medicine
- Voting Member, Presidential Advisory Council on Combating Antibiotic Resistant Bacteria (PACCARB)

# IDSA Membership

## Primary Professional Activity



**12,000+ strong**

# Agenda

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- **Why patients need new antibiotics (case study)**
- **Progress and persistent gaps**
- **IDSA efforts**
- **IDSA federal policy recommendations**

# **Why Patients Need New Antibiotics**

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Case Study

# Case

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- 60 year old lady with leukemia s/p chemotherapy, in remission
- Developed fever, cough
  - Chest x-ray showed pneumonia
  - Labs showed pancytopenia
- She was on the floor waiting for her blood counts to recover
- The hematologists were optimistic about her prognosis
- Meropenem and vancomycin were started as empirical therapy

# Blood culture results

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## *Elizabethkingia meningoseptica*

- ID consult recommended
- Multi-drug resistant organism
- Plazomicin result  $\geq 512$  ug/mL NIS
- Piperacillin/tazobactam  $\geq 128$  R
- Ceftazidime  $\geq 64$  R
- Ceftriaxone  $\geq 64$  R
- Cefepime  $\geq 64$  R
- Meropenem  $\geq 16$  R
- Amikacin  $\geq 64$  R
- Gentamicin  $\geq 16$  R
- Tobramycin  $\geq 16$  R
- Ciprofloxacin  $\geq 4$  R
- Trimethoprim/Sulfa 80 R
- Ceftazidime/avibactam 32 NIS
- Ceftolozane/tazobactam 32 NIS

NIS = no interpretive standards

# Case (continued)

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- When I sat to deliver this news, my patient said, “how can this be?...surely you’ll find something to treat this”
- Ceftazidime-avibactam and aztreonam were added
- The organism was rushed to Dr. Bonomo’s lab for further testing
- Compassionate use cefiderocol was obtained under IND
  - Arrived 4 days later
- Antibiotic background was changed based on results of testing
  - Minocycline added
- She deteriorated, required ventilatory support, died 10 days later



# Progress & Persistent Gaps

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# Significant Progress Made: Persistent Gaps

## Progress

- 2012 GAIN Act/QIDP
- 2013 ARLG
- 2015 CARB National Action Plan
- 2016 CARB-X
- 2016 21<sup>st</sup> Century Cures Act/ LPAD
- 2020 CARB National Action Plan

## Gaps

- Narrow-spectrum,  
e.g., single-pathogen, drugs
  - Focus of 2016 FDA workshop  
and 2017 FDA Advisory  
Committee Meeting

*The Journal of Infectious Diseases*

MAJOR ARTICLE



## White Paper: Developing Antimicrobial Drugs for Resistant Pathogens, Narrow-Spectrum Indications, and Unmet Needs

Helen W. Boucher,<sup>1</sup> Paul G. Ambrose,<sup>3</sup> H. F. Chambers,<sup>5</sup> Richard H. Ebricht,<sup>6</sup> Amanda Jezek,<sup>7</sup> Barbara E. Murray,<sup>8</sup> Jason G. Newland,<sup>9</sup> Belinda Ostrowsky,<sup>4</sup> and John H. Rex<sup>2,10,11</sup>; on behalf of the Infectious Diseases Society of America

<sup>1</sup>Division of Geographic Medicine and Infectious Diseases, Tufts Medical Center and Tufts University School of Medicine, and <sup>2</sup>CARB-X, Boston, Massachusetts; <sup>3</sup>Institute for

# **IDSA Efforts**

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**Calls to Action and Expert Leadership**

# IDSA Calls to Action on AMR

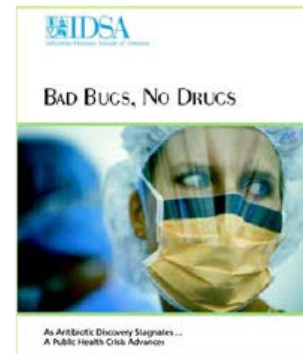
- **Bad Bugs, No Drugs. As Antibiotic Discovery Stagnates ... A Public Health Crisis Brews**
  - Infectious Diseases Society of America. July 2004
- **Bad Bugs Need Drugs: What's in the Development Pipeline? An Update from the Antimicrobial Availability Task Force of the Infectious Diseases Society of America**
  - *Clin Infect Dis* 2006; 42: 657-68

## IDSA REPORT

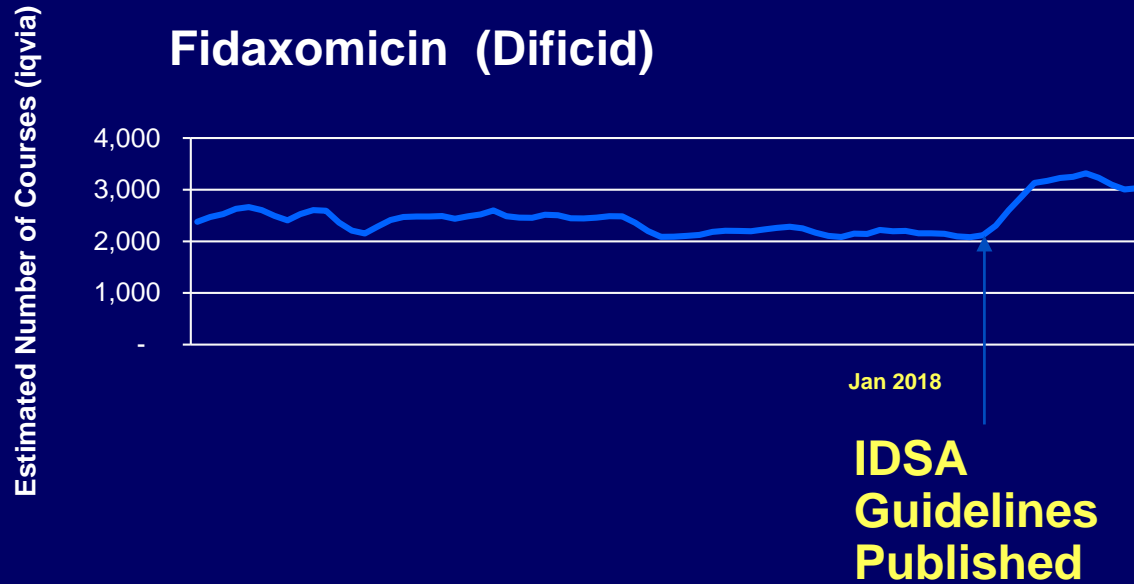
### Bad Bugs, No Drugs: No ESKAPE! An Update from the Infectious Diseases Society of America

Helen W. Boucher,<sup>1</sup> George H. Talbot,<sup>2</sup> John S. Bradley,<sup>3,4</sup> John E. Edwards, Jr.,<sup>5,6,7</sup> David Gilbert,<sup>8</sup> Louis B. Rice,<sup>3,10</sup> Michael Scheld,<sup>11</sup> Brad Spellberg,<sup>5,6,7</sup> and John Bartlett<sup>12</sup>

<sup>1</sup>Division of Geographic Medicine and Infectious Diseases, Tufts University and Tufts Medical Center, Boston, Massachusetts; <sup>2</sup>Talbot Advisors, Wayne, Pennsylvania; <sup>3</sup>Division of Infectious Diseases, Rady Children's Hospital San Diego, and <sup>4</sup>University of California at San Diego, San Diego; <sup>5</sup>Division of Infectious Diseases, Harbor-UCLA Medical Center, and <sup>6</sup>Los Angeles Biomedical



# Guidelines Are Critical For Generating Awareness and Adoption



***How Can New Therapies Find Use When Its Own Specialty Doesn't Support Innovation?***

# IDSA AMR Guidance – September 2020

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## Infectious Diseases Society of America Guidance on the Treatment of Antimicrobial Resistant Gram-Negative Infections

Published by IDSA, 9/8/2020

A Focus on Extended-Spectrum  $\beta$ -lactamase Producing Enterobacterales (ESBL-E), Carbapenem-Resistant Enterobacterales (CRE), and *Pseudomonas aeruginosa* with Difficult-to-Treat Resistance (DTR-*P. aeruginosa*)

Pranita D. Tamma\*, Samuel L. Aitken, Robert A. Bonomo, Amy J. Mathers, David van Duin, Cornelius J. Clancy

<https://www.idsociety.org/practice-guideline/amr-guidance/>

# **IDSA Federal Policy Recommendations**

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**The Time for Action is NOW**

# Consensus for Action

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- **Pull incentives:**
  - **Reimbursement Reform and PASTEUR**
- **Regulatory: Novel Clinical Trial Design, Clinical Trials Networks, LPAD Implementation**
- **Stewardship**
- **Workforce**
- **CARB National Action Plan**



# Broad Agreement: Fix the Antibiotic Pipeline

STAT NEWS FIRST OPINION

Medicare payment rules hinder the  
fight against superbugs

By KEVIN OUTTERSON and  
HELEN W. BOUCHER

APRIL 17, 2019



*W.H.O. Warns That Pipeline for New Antibiotics Is Running Dry*

In two new reports, the global health agency says only government intervention  
can fix the broken market for new antimicrobial drugs

**A Jacobs, New York Times, January 18, 2020**



THE  
HILL

The antibiotic  
market is broken  
and won't fix itself

# Incentives

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## Principles

- Robust, understandable, predictable to motivate industry/private investors
- Target areas of greatest unmet need
- Aligned with efforts to promote stewardship, maintain access

## Continue & Expand Push Incentives

- CARB-X, BARDA, NIH ARLG etc.

## Enact Pull Incentives NOW

- Subscription Model: PASTEUR Act
- Reimbursement Reform

# PASTEUR Act

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## *Pioneering Antimicrobial Subscriptions to End Upsurging Resistance (PASTEUR) Act*

- **Goals:**
  - Support the development of new antibiotics and promote appropriate use of existing ones
  - Limit increase and spread of resistant infections
    - Good stewardship

# **PASTEUR Act**

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- **Subscription program to provide federal payments for critically needed new antibiotics**
- **Payments delinked from sales —provides predictable return on investment that aligns with appropriate use goals**
- **Establishes a new HHS committee to determine details of subscription contracts (including preferred characteristics of drugs that should receive subscription payments); input from advisory group of non-government experts**
- **Payments made after drug's approval over a period of up to 10 years**
- **Establishes new HHS grant program to support hospital implementation of antibiotic stewardship programs and hospital reporting of antibiotic use/resistance data to CDC National Healthcare Safety Network**

# PASTEUR Act

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- **Bipartisan leadership:**
  - **Senators Bennet (D-CO) and Young (R-IN)**
  - **Reps. Doyle (D-PA) and Ferguson (R-GA)**
- **Supported by 40+ organizations, including: IDSA, AdvaMedDx, ASM, BIO Cystic Fibrosis Foundation, Research!America, Society of Critical Care Medicine, Society of Hospital Medicine, Society of ID pharmacists, The Joint Commission, multiple academic centers**
- **Reflects consensus recommendations from multiple expert bodies and reports: PACCARB, UK AMR Review, Duke Margolis Center for Health Policy, PCAST, DRIVE-AB**

# 10 x '20 but Nobody's Buying: The Case for Reimbursement Reform



Adapted from: GH Talbot, A Jezek, BE Murray, RN Jones, RH Ebright, GJ Nau, KA Rodvold, JG Newland, HW Boucher. Clin Infect Dis 2019

# Reimbursement Reform: Initial Steps

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- CMS 2020 Inpatient Prospective Payment Final Rule:  
Good first steps but impacts expected to be limited
  - *NTAP reforms and increases*
  - *Increased severity levels*

# Reimbursement Reform: What's Next

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- Remove QIDP antibiotics from Medicare bundled payment (DRG) to reimburse separately and require hospitals to report antibiotic use and resistance data to CDC (important to track how reimbursement changes impact use and resistance)
- CMS could do under current authority or could also be done legislatively (DISARM); concerns persist that it could drive overuse of antibiotics



# **LPAD: Benefits for R&D and Stewardship But Slow Progress**

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- **LPAD = Limited Population Pathway for Antibacterial Drugs**
- **IDSA led multi-stakeholder advocacy for congressional passage**
- **Allows smaller, more rapid clinical studies of new antibiotics for unmet needs**
- **“Limited Population” labeling = stewardship opportunities**
- **Only 2 LPAD approvals so far**
  - **Bedaquiline for TB**
  - **Aerosolized liposomal amikacin for MAI**

# Stewardship

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- Medicare Condition of Participation Oct 2019
- Fully supported by industry
- One Health approach
- IDSA Leadership: Stewardship Centers of Excellence
- Resources needed to support implementation & workforce
- Focus must be patient outcomes, not cost

# 27 IDSA Advancing Antimicrobial Stewardship

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IDSA Antimicrobial Stewardship  
Curriculum for Fellows



IDWeek: Presenting the Latest in  
Stewardship Research



Antimicrobial Stewardship Centers of  
Excellence



Utilizing Tele-health to Extend the Reach  
of Stewardship Experts

# IDSA ASP Centers of Excellence

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- Recognize facilities that have achieved high standards in their ASP and highlight the value of stewardship
- Core criteria built upon CDC Core Elements
- Inaugural Centers of Excellence included: Tufts Medical Center, Duke University Hospital, University of Michigan, and Northwestern
- Currently 109 hospitals included
- All health systems are welcome to apply for the CoE designation and can learn more about the criteria at: [www.idsociety.org/ascoe](http://www.idsociety.org/ascoe)

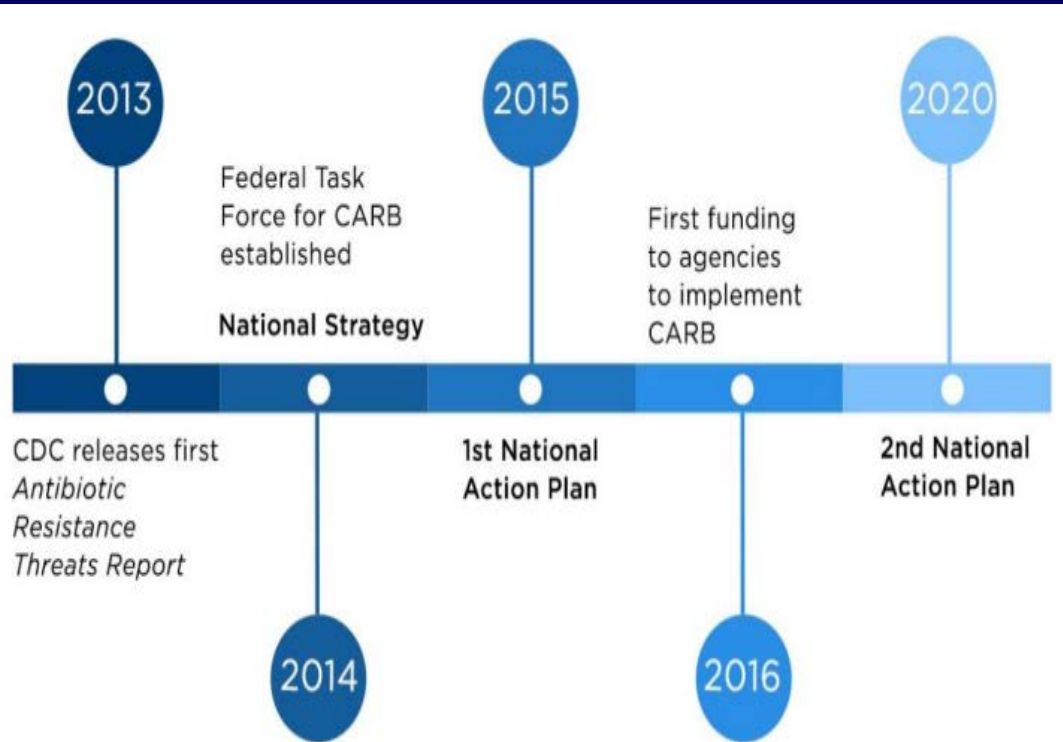


# Strengthening the ID Physician Pipeline

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- Expanding loan repayment opportunities for ID physicians:
  - 2016 - expanded NIH loan repayment for ID physician-scientists
  - 2019 - loan repayment for ID physicians and others who participate in the CDC Epidemic Intelligence Service
- Ensuring fair compensation
  - ID physician compensation is \$100K/year below average for physician specialists (Medscape)
  - Source of disparity: ID physicians perform mainly cognitive (evaluation/management or E/M) work, which is undervalued compared to procedures
  - CMS 2021 Medicare Physician Fee Schedule makes overdue updates to outpatient E/M codes; must update inpatient E/M codes now

# 2020 CARB National Action Plan



## 5 Goals:

- Goal 1: Slow Emergence of AMR and Prevent Spread of Resistant Infections
- Goal 2: Strengthen National One Health Surveillance Efforts
- Goal 3: Advance Development/Use of Rapid and Innovative Diagnostic Tests
- Goal 4: Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines
- Goal 5: Improve International Collaboration and Capacities for Antibiotic-resistance Prevention, Surveillance, Control and Antibiotic Research and Development

# CARB Success Contingent Upon Funds

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- **FY2016, \$379 million in NEW funding to address AMR across federal agencies:**
  - **\$160 million for CDC new AR Solutions Initiative**
  - **\$100 million increase for NIAID AR Research**
  - **\$97 million increase for BARDA**
  - **\$10 million increase for AHRQ AR efforts**
  - **\$9 million increase for FDA AR efforts**
- **Since FY2016, rate of funding growth has been modest**

# 2020 NAP Objectives – Goal 4

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- Expand basic/applied research; target 1000 publications by 2021
- **Rebuild research workforce**
  - **60+ new/early-career investigators by 2021**
- 100 new awards (CARB-X, NIH, and BARDA) for pre-clinical therapeutic R&D by 2024 + additional candidate therapeutics from DoD and Department of Agriculture
- **10 therapeutic candidates in clinical development by 2022**
  - **3 NDAs by 2025**
- 25 preclinical programs for prevention by 2022, plus 2 for agricultural use
- Clarify pathways for preventatives, including vaccines; FDA guidance
- **Promote sustainability of commercial market**



# 2020 NAP Objectives

## Goal 4: Commercial Market Sustainability Initiatives

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1. Support creation of a network of clinical trial sites to reduce barriers to research and establish comprehensive understanding of the safety and effectiveness of new antibiotic agents in challenging clinical settings and indications, to enroll patients by 2023
2. Examine changes in new technology add-on payments (NTAP) under the CMS Inpatient Prospective Payment System (IPPS) Final Rules, starting with the FY 2020 IPPS/long-term care hospital prospective payment system final rule, to inform potential additional actions
3. Strengthen commercial markets for antibiotic products through direct Public Health and National Security purchases by BARDA. This appears to call for more contracts similar to the one BARDA recently awarded to Paratek
4. Support efforts to secure U.S. - based manufacturing infrastructure

# Championing Patient and Public Health Needs: IDSA Efforts to Strengthen the Antibiotic Pipeline

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Considerable work has been done

- Regulatory: LPAD
- Stewardship
- IDSA Guidance
- CARB National Action Plan
- Pull incentives: PASTEUR
  - Addresses goals of advancing both a meaningful pull incentive and stewardship

Time for Action is Now

# Thank You!

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- Antimicrobial Resistance Committee, IDSA
- Cesar Arias
- Sara Cosgrove
- Neil Clancy
- James Hughes
- Amanda Jezek
- Ramanan Laxminarayan
- Kevin Outterson
- John Rex
- Our patients and their families