

NIH's Role in Combating Antibacterial Resistance (CARB)

Dennis M. Dixon, PhD

Division of Microbiology and Infectious Diseases
NIAID, NIH, HHS

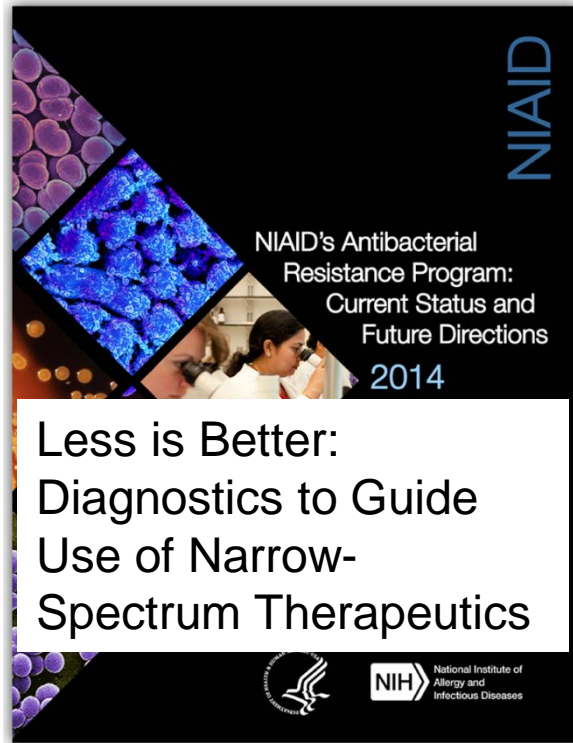
September 29, 2015
CARB Presidential Advisory Council

CARB Goal 3

Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria.

- **Objective 3.1:** Develop and approve new diagnostics including tests that rapidly distinguish between viral and bacterial pathogens and tests that detect antibiotic resistance...

NIAID Antibacterial Resistance Program



- Basic Research
- Translational Research/
Product Development
- Clinical Research



Diagnosis, Prevention and
Treatment

Context: Diagnostics at NIAID

- 12 targeted funding opportunities since 2010 addressing:
 - Healthcare-Associated Infections
 - POC Technologies
 - Drug-Resistant Bacteria
- Workshops:
 - 2011 TATFAR: Challenges and Solutions in the Development of New Diagnostic Tests to Combat Antimicrobial Resistance
 - 2014: Coordinated Development of Diagnostics and Therapeutics (with FDA)

NIAID Support for Platform Technologies



BioFire FilmArray

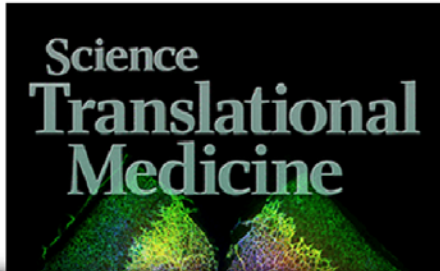
- FDA-Cleared Respiratory Viral Panel
- 2 minutes hands on time; 1 hour to result
- Other panels being developed



Cepheid GeneXpert

- FDA cleared MTB/RIF test
- 2 hours sample to answer
- Other cartridges being developed

Translational/Product Development: Diagnostics Distinguish Viral Respiratory Infection



A Host-Based RT-PCR Gene Expression Signature to Identify Acute Respiratory Viral Infection

AK Zaas, GS Ginsburg et al.

18 September 2013

Vol. 5, Issue 203

- Duke University study, funded by NIAID
- RT-PCR test distinguishes viral from bacterial infection
- 102 emergency department patients, distinguished with 89% sensitivity, 94% specificity
- Could limit inappropriate prescription practices

AS Fauci/NIAID

Antibacterial Resistance Leadership Group

Diagnostics Activities

- Host-based signature to distinguish viral from bacterial respiratory infections (Zaas, cont.)
- Virtual biorepository
- Capability to collect clinical specimens for diagnostics development
- Master protocol for validation of multiple diagnostics simultaneously
- Using procalcitonin levels to identify CAP patients who will not benefit from antibiotics

Recent NIH CARB Activities – Objective 3.1

- Recently funded 9 grants under [RFA-AI-14-019](#), Partnerships for Diagnostics to Address Antimicrobial Resistance of Select Bacterial Pathogens.
- Example projects -- PCR-independent, beyond proof-of-concept, provide ID of species and resistance
 - **GeneFluidics, Inc.:** Fully Integrated CentriFluidic System for Direct Bloodstream Infection PID/AST
 - **BioFire Diagnostics, LLC:** FilmArray Direct: Rapid Diagnosis of Antimicrobial-Resistant Pathogens from Blood
 - **The Broad Institute of MIT and Harvard:** RNA-Based Diagnostics for Rapid Pathogen Identification and Drug Resistance

Challenges

- Scientific
 - Limit of detection (Bloodstream infection)
 - Colonization vs. infection (Pneumonia)
- Other
 - Clinical uptake
 - Reimbursement uncertainty

Recent NIH CARB Activities – Objective 3.1

- NIH and BARDA, with technical and regulatory expertise from CDC and FDA, are developing the AMR Diagnostic Challenge Competition (Prize is \$20 million)
- Request for Comments was issued in Federal Register on June 2, 2015, and obtained stakeholder input from industry, academia, and the public
- Public consultation scheduled for October 7, 2015 in conjunction with ID Week 2015 in San Diego
- Stakeholder comments will be used to develop design and parameters of Challenge competition
- Competition to be announced in early 2016

Thank you

...for your interest

FDA Role in CARB GOAL 3:

Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria

Steven Gitterman, M.D., Ph.D.

Division of Microbiology Devices
OIR, CDRH, FDA

September 29, 2015

Objectives:

3.1 Develop and approve new diagnostics, including tests that rapidly distinguish between viral and bacterial pathogens and tests that detect antibiotic resistance that can be implemented in a wide range of settings.

United States Government departments and agencies will work with domestic and international partners to develop rapid diagnostic tests that can:

- Identify clinical illnesses that may benefit from treatment with antibiotics.
- Detect invasive bacterial pathogens in blood, cerebrospinal fluid, synovial fluid, and urine.
- Provide information to guide decisions on treatment and control of CRE, *Neisseria gonorrhoeae*, and other multidrug-resistant organisms.

Objectives:

3.2 Expand the availability and use of diagnostics to improve treatment of antibiotic resistant bacteria, enhance infection control, and facilitate outbreak detection and response in healthcare and community settings.

Progress in AMR Diagnostics

- A golden era in the development of diagnostics
 - Molecular Multiplex Devices (3.1, 3.2)
 - CSF, GI, Respiratory, TB, Blood, CT/NG
 - All direct specimens except blood
 - Integrated Sample prep
 - Batch and random access
 - Turnaround time 0.5 – 2 hours
 - Can detect select common resistance markers
 - Concerns are cost, infrastructure, throughput
 - Clinical interpretation challenging in certain scenarios

Regulatory Progress for Molecular/Multiplex Devices

- Significant Advances in Regulatory Paradigms
 - Input through Public Workshops, Panel meetings
 - Guidance development
 - Analytical requirements
 - Clinical validation
 - Recommendations continue to evolve in response to accrued experience, presubmission questions
- Reclassifications: Molecular detection of TB, rapid detection of Influenza
- CLIA waived molecular diagnostics
 - Improved performance may alter clinical practice

Direct Detection from Blood

- Increased sensitivity of newer devices through different approaches
- High Negative Predictive Value
 - Important for efficiency of clinical trials
 - Turn-around time still in hours
- Different approaches
 - PCR/Mass-spec
 - PCR/improved detection
 - Others
- Cost, accessibility, volume still factors

Infrastructure Progress

- Biomarker repository
 - CTB² for tuberculosis
 - FDA-CDC Antimicrobial Resistance Isolate Bank
 - Enterobacteriaceae Carbapenem Breakpoint Panel
 - Gram Negative Carbapenemase Detection Panel
 - Enterobacteriaceae Carbapenemase Diversity Panel
- Curated NGS database
 - As diagnostics, NGS not relevant for this meeting as a currently rapid diagnostic but database may be valuable

'Current' Activities

- Guidance on Antimicrobial drug – AST device coordinated development
- Public Workshops
 - 9/28-29: FDA/NLM/CDC Sematic Interoperability Workshop
 - 10/16: FDA Workshop on Non-microbial Biomarkers of Infection for *In Vitro* Diagnostic Use
 - Comparator methods and study designs for diagnostics for viral/bacterial infection URI
 - Comparator methods and study designs for sepsis or SIRS

'Collaboration'

- NIH/BARDA
 - Consultative role on AMR Diagnostic Prize
- Repositories
 - CDC Resistant isolates
 - Essential piece for susceptibility devices
 - TB Alliance
- Close Working relationship with CDC, NIH, NLM, CMS, others
- Very active presubmission process

Thank-you for your attention

CMS Role in CARB GOAL 3:

Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria

Shari M. Ling, M.D.

Centers for Medicare and Medicaid Services

September 29, 2015

Objectives:

3.2 Expand the availability and use of diagnostics to improve treatment of antibiotic resistant bacteria, enhance infection control, and facilitate outbreak detection and response in healthcare and community settings.

FDA-CMS Parallel Review Pilot

- Soliciting nominations from sponsors of innovative medical device technologies to participate in a pilot program for concurrent review of certain FDA premarket review submissions and CMS national coverage determinations
- Sets procedures for voluntary participation and guiding principles that the agencies will follow
- Appropriate New Technology candidates:
 - The sponsor/requestor has had sufficient pre-investigational device exemption interaction with FDA or approved IDE application
 - An original or supplemental application for premarket approval or petition for *de novo* review would be required
 - Within the scope of Part A or Part B Medicare benefit category and are not subject to an NCD
- Published October 7, 2011 (76 FR 62808)
- Effective November 10, 2011 (extended to December 2015)
- <http://www.gpo.gov/fdsys/pkg/FR-2011-10-11/pdf/2011-25907.pdf>

CMS Payments for New Technologies

- Medicare pays for most items and services on a prospective, rather than cost basis
- CMS proposes payment rates and policy changes for the following year
 - Employs rule-making with public comment
 - In some instances CMS holds public meetings to gather input
- Payment systems for acute and ambulatory care settings are the most likely to see introduction of new tech
 - Inpatient acute care hospital
 - New Technology Add-on Payments (NTAP)
 - Hospital outpatient departments & Physician offices
 - New Technology Ambulatory Payment Classifications (APCs)

- Medicare
- Medicaid/CHIP
- Medicare-Medicaid Coordination
- Private Insurance
- Innovation Center
- Regulations & Guidance
- Research, Statistics, Data & Systems
- Outreach & Education

Home > Medicare > Acute Inpatient PPS > New Medical Services and New Technologies

- Acute Inpatient PPS**
- [Wage Index Reform](#)
- [Wage Index](#)
- [Outlier Payments](#)
- [Disproportionate Share Hospital \(DSH\)](#)
- [Direct Graduate Medical Education \(DGME\)](#)
- [Indirect Medical Education \(IME\)](#)
- New Medical Services and New Technologies**
- [Wage Index Files](#)
- [Three Day Payment Window](#)
- [Hospital Value-Based Purchasing](#)
- [Readmissions Reduction Program](#)
- [Hospital-Acquired Condition \(HAC\) Reduction Program](#)
- [Medicare PPS Excluded Cancer Hospitals](#)
- [Acute Inpatient - Files for](#)

New Medical Services and New Technologies

New Technology Town Hall Meeting Information

The annual New Technology Town Hall meeting will be held on Tuesday, February 3, 2015 at CMS in Baltimore. Complete details on the Town Hall meeting can be found in the Federal Register notice published on November 21, 2014. Click the link below "FY 2016 New Technology Town Hall Federal Register Notice."

- To register to attend the New Technology Town Hall meeting **in person** send an email to newtech@cms.hhs.gov if you would still like to attend and have not already registered.
- **Due to changes in the Department of Homeland Security mandate regarding the Real ID Act, CMS will not be implementing the Real ID Act on January 19, 2015, as originally scheduled. The effective date of implementation has been postponed until October 2015.**
- For participants who cannot attend the Town Hall Meeting in person, an open toll-free phone line, (877) 267-1577, has been made available. The meeting number is "993 601 192." **NO PRIOR REGISTRATION IS NECESSARY TO CALL IN.**
- To view a live video/audio stream feed of the new technology town hall meeting, visit <http://cms.gov/live> **NO PRIOR REGISTRATION IS NECESSARY TO VIEW THE TOWNHALL VIA THIS LINK.**
- Users will also be able to watch a live audio/video feed and archived copy of the video/audio stream of the town hall on the CMS You Tube channel at <https://www.youtube.com/watch?v=dn-R5KGQu-M> **NO PRIOR REGISTRATION IS NECESSARY TO VIEW THE TOWNHALL VIA THIS LINK.**
- To participate via webinar, visit <http://webinar.cms.hhs.gov/newtech> **Note:** Users can follow presenters slides via the webinar only. Use the call in number for an audio feed or the links above for a live audio/video feed. **NO PRIOR REGISTRATION IS NECESSARY TO VIEW THE TOWNHALL VIA THIS LINK.**
- An agenda for the meeting can be downloaded in the "Downloads" section below.

Num C

https://www.cms.gov/Medicare/Medicare-Fee-
Payment/HospitalOutpatientPPS/Downloads/new

Process and Information Required for a New Technology Ambulatory Payment Classification (APC) Assignment Under the Hospital Outpatient Prospective Payment System (OPPS)

Please note: For process and information required to apply for transitional pass-through payment status for **drugs and biologicals**, or for assignment and payment for **new pass-through device categories**, go to the main OPPS web page, currently at http://www.cms.gov/HospitalOutpatientPPS/01_overview.asp to see the latest instructions. (NOTE: Due to the continuing development of the new cms.hhs.gov web site, this link may change.)

This guidance describes in detail the process and information required for applications requesting a New Technology APC assignment under the Medicare hospital outpatient prospective payment system (OPPS)



Centers for Medicare & Medicaid Services

Learn about [your healthcare options](#)

Medicare

Medicaid/CHIP

Medicare-Medicaid Coordination

Private Insurance

Innovation Center

Regulations & Guidance

Research, Statistics, Data & Systems

Outreach & Education

Home > Medicare > Hospital Outpatient PPS > Pass-Through Payment Status and New Technology Ambulatory Payment Classification (APC)

Hospital Outpatient PPS

[Device, Radiolabeled Product, and Procedure Edits Archive](#)

[Pass-Through Payment Status and New Technology Ambulatory Payment Classification \(APC\)](#)

[OPPS Guidance](#)

[Program Transmittals](#)

[Hospital Outpatient Program Memoranda](#)

[Hospital Outpatient Regulations and Notices](#)

[Addendum A and Addendum B](#)

Pass-Through Payment Status and New Technology Ambulatory Payment Classification (APC)

This page contains the process and information required to apply for transitional pass-through payment status for drugs and biologicals, or for assignment and payment for new pass-through device categories.

Downloads

[List of Pass Through Payment Device Category Codes - Updated: July 2015 \[PDF, 91KB\]](#)

[For a New Technology Ambulatory Payment Classification \(APC\) Designation Under the Hospital Outpatient Prospective Payment System \(OPPS\) \[PDF, 107KB\]](#)

[To Apply for New Device Categories For Transitional Pass-Through Payment Status Under the Hospital Outpatient Prospective Payment System - Updated 11/13/2014 \[PDF, 108KB\]](#)

[To Determine Eligibility of Drugs and Biologicals for Transitional Pass-Through Payment Under the Hospital Outpatient Prospective Payment System - Updated 12/09/14 \[PDF, 112KB\]](#)



***INNOVATORS’
GUIDE TO
NAVIGATING
MEDICARE***

**Version 3
2015**

New Technology Payment Vehicles

- New Technology Add-on Payments (NTAP)
 - <http://www.cms.gov/Medicare/Medicare-fee-for-service-payment/AcuteInpatientPPS/newtech.html>
- New Technology Ambulatory Payment Categories (APCs)
 - <http://www.cms.gov/Medicare/Medicare-fee-for-service-payment/HospitalOutpatientPPS/Downloads/newtechapc.pdf>
- Transitional pass-through payments
 - http://www.cms.gov/Medicare/Medicare-fee-for-service-payment/HospitalOutpatientPPS/passthrough_payment.html

Thank you

Shari Ling, MD

Shari.ling@cms.hhs.gov

410 786 6841