

Report:
OID-BSC Meeting, December
6-7, 2017

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Clinical Laboratory Improvement Advisory
Committee (CLIAC)
April 10-11 2018 Meeting

OID-BSC Meeting, December 6-7, 2017 Included Reports:

- National Center for Emerging and Zoonotic Infectious Diseases (NCEZID) Update
 - *Focused Discussion:* Building a U.S. Estimate of the Burden of Waterborne Diseases
- Update on the Presidential Advisory Council on Combatting Antibiotic-Resistant Bacteria (PAC-CARB)
- CDC budget update/discussion
- Update from the Center for Global Health (CGH)
- Report from other CDC Infectious-disease related advisory committees
- Report back from the Dec 4-5 meeting of the Food Safety Modernization Act Surveillance Working Group (FSMA SWG)
- Update from the National Center for Immunization and Respiratory Diseases (NCIRD)
- Update from the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP)
 - *Focused Discussion:* Outbreaks of Hepatitis A in the United States

National Center for Emerging and Zoonotic Infectious Diseases (NCEZID) Update

Rima Khabbaz MD

- New NCEZID brochure and Fact Sheet. New brochure on innovative technologies; mobile apps for first responders, accurate *C. auris* test.
 - • Workforce needs: state-level capacity for diagnosis of *C. auris* and other fungal organisms is very limited.
- AMD Day: Advanced Molecular Detection conference with ~400 internal and external partners; rapid field-deployable DNA sequencing.
- Funding Initiatives
 - Antibiotic resistance: \$77M epidemiology and laboratory capacity
 - Research \$9M for 25 investigators; patient strategies; human microbiome and prevention; impact of resistance in water and soil
 - Epidemiology and Lab Capacity grants; program being modernized. EIP grants for 10 states.



Update on the Presidential Advisory Council on Combatting Antibiotic-Resistant Bacteria (PAC-CARB)

Michael Craig, Senior Advisor, Division of Healthcare Quality Promotion, NCEZID

- PACCARB designed to provide advice and recommendations to president vis HHS Secretary.
 - PACCARB includes 15 voting members who are special government employees; 5 non-voting members who represent nongovernmental organizations; and 10 non-voting ex-officio members who represent agencies of HHS, DOD, and USDA.
- Angela Caliendo is the clinical lab person on the committee; though there's only the one.
- 2018 Working Group on infection prevention and stewardship...to take most of the year.
- Working to address some of these issues on a global level; Abx and Dx development with EU and WHO.
- Queries about representation; about global surveillance; about action taken on basis of recommendations.

PAC-CARB Diagnostics Incentives

- 2017 Working groups on incentives; including for diagnostics. Report at <https://www.hhs.gov/sites/default/files/paccarb-final-incentives-report-sept-2017.pdf>

PACCARB Top 10 Recommendations*		
Human Health	Incentives to Develop	Animal Health
<ul style="list-style-type: none"> Provide additional funding for the development of new product pipelines for vaccines that prevent viral or bacterial syndromes that drive antibiotic use Optimize the interactions among sponsors, regulatory agencies (such as FDA), and use policy committees (e.g., the ACIP) Incentivize the uptake of vaccines by influencing behavior, such as reimbursement to ensure "first-dollar coverage"	 Vaccines	<p>Develop and fund a National Policy and Innovation Institute under USDA whose main functions will include the following:</p> <ul style="list-style-type: none"> Supporting basic research on immunology across species for the development of vaccines
<ul style="list-style-type: none"> Include the development of a concomitant AST as part of any new antibiotic funding (or funding for new antibiotics) Provide financial support for diagnostic manufacturers to bring new tests to market Continue funding for clinical trial networks with common rules or shared IRBs	 Diagnostics	<ul style="list-style-type: none"> Promoting educational programs for veterinarians on the use and interpretation of diagnostic tests
<ul style="list-style-type: none"> Develop new economic models (pull incentives) for therapies to support the currently available push incentives	 Therapeutics / Alternatives	<ul style="list-style-type: none"> Providing resources to conduct, evaluate, and create a database of efficacy studies of alternative products

PAC-CARB

Diagnostics Incentives -- Economic

- Issue Statement 1: Following approval of new antibiotics, corresponding ASTs are not immediately available to ensure proper use of the antibiotic.
 - Recommendation: Funding for the development of new antibiotics should always include the development of a concomitant *rapid* AST device.
- Issue Statement 2: Because there is no method to determine the value of a diagnostic test, reimbursement is not aligned with the value of diagnostic tests.
 - Recommendation: A “reimbursement-plus” system for tests of key public health importance (e.g., CRE colonization testing) designed with input from CMS and other public health agencies.
- Issue Statement 3: There is a lack of clinical and economic outcome studies showing that any diagnostic test could prevent the emergence of antibiotic-resistant bacteria and would be cost-effective.
 - Recommendation: Increase funding of diagnostics outcomes studies (e.g., from the Agency for Healthcare Research and Quality [AHRQ], CDC, the Patient-Centered Outcomes Research Institute [PCORI], NIH, and DoD), including those assessing patient outcomes, lengths of stay, changes in antibiotic use, rates of antibiotic use for certain patient populations, and costs of care.
- Issue Statement 4: The high cost of development of diagnostics is a disincentive for diagnostics companies.
 - Recommendation: Tax credit for a portion of the qualified clinical testing expense, potentially modeled after the Orphan Drug Tax Credit.

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Diagnostics Incentives -- R&D

- Issue Statement 1: Rapid point-of-care tests are needed to distinguish between bacterial and viral infections in the outpatient setting.
- Issue Statement 2: There is a need for better biomarker tests to aid clinicians in making decisions regarding when to initiate and discontinue antibiotics in the inpatient setting.
- Issue Statement 3: Tests are needed that rapidly identify or quantify pathogens directly from the clinical specimen and provide rapid susceptibility results.
- Recommendations:
 - Sustained investment in funding mechanisms (e.g., grants) for developing new, cost-effective diagnostic tests and updating existing diagnostic tests (through Small Business Innovation Research [SBIR] and Small Business Technology Transfer grants, among others).
 - Expanded funding for clinical trials networks (e.g., NIH-supported Antibacterial Resistance Leadership Group [ARLG]) and applied innovation networks (e.g., CDC-supported Prevention Epicenters) and assurance that these networks work through a common institutional review board (IRB)
- Issue Statement 4: Collaboration between diagnostics companies and other stakeholders is limited and inconsistent.
 - Recommendation: Federal government agencies (e.g., HHS, FDA, CDC, NIH, DoD, USDA) should come together to create a list of the most critically needed diagnostics for combating AMR.

PAC-CARB

Diagnostics Incentives -- Regulatory

- Issue Statement 1: The regulatory approval clearance process for modifying and improving existing diagnostic tests is complex and expensive.
 - Recommendation: Advancing FDA regulatory efforts for improvements or updates of existing tests that utilize postmarketing study results and real-world evidence to promote development of improved tests.
- Issue Statement 2: The current regulatory process for new diagnostics is time-consuming and costly, posing a disincentive for developers.
 - Recommendations
 - Additional or enhanced clinical trials networks that function with a common IRB to reduce the regulatory burden of test approval.
 - Modification of requirements to simplify process for obtaining Clinical Laboratory Improvement Amendments (CLIA) waivers.
 - Utilization of postmarketing study results and real-world evidence to facilitate the approval process of new diagnostics.
 - Complementary structuring of the FDA-CDC Antimicrobial Resistance Isolate Bank and the ARLG virtual repository to increase diagnostics companies' access to isolates.
- Issue Statement 3: Hospitals are not required to update their microbiology laboratories with newer technologies.
 - Recommendation: CLIA requirements to update microbiology laboratories' technology as part of the accreditation process.

PAC-CARB

Diagnostics Incentives – Behavioral

- Issue Statement 1: Clinicians do not always use diagnostic tests, believe the results, and act on them.
 - Recommendations
 - Evidence-based research, supported by public and private resources, to facilitate a better understanding of the behavior that affects decisions about using rapid diagnostics, with a goal of identifying drivers that prevent adoption.
 - Inclusion of experts in clinical use of diagnostics who can provide information regarding appropriate use of relevant rapid tests on clinical guidelines committees that address prevention, diagnosis, and treatment of infectious diseases.
 - Clinician education on the use and interpretation of diagnostic tests.
 - Development of tools and mechanisms that improve clinicians' abilities to make decisions in the ambulatory setting (e.g., linking antibiotic prescriptions, accompanied by laboratory results, to pharmacy dispensing of antibiotics and antivirals through an electronic medical record).

Other BSC Working Groups

- Working Group on ID Diagnostics
 - Co-chairs: Jill Taylor and Susie Sharp
 - Advanced Molecular Detection (AMD) initiative
 - Culture-independent tests (CIDTs).
 - Some IDLWG members will participate in a May 2-3 meeting hosted by the Research Center that will bring together public and private sector experts to consider the epidemiologic and laboratory implications of increased use of CIDTs.
- Joint Working Group on Vector-Borne Diseases
 - To advance strategic planning to build U.S. capacity to address mosquito-borne and tickborne threats. Need volunteers.
- Antibiotic Resistance
 - Tabled pending development of CDC agenda for this, and assessment of overlap with PAC-CARB.

Report back from other CDC infectious-disease-related advisory committees

- Sheldon Campbell – CLIAC
 - Back to CLIAC: DLS laboratory biosafety people might profit from interfacing with HHS NETEC program: The National Ebola Training and Education Center; funded by HHS-PHE group and CDC.
- Susan Philip – CHAC (CDC-HHS Advisory Committee on HIV/TB/STI)
 - HCV recommendations
 - Recommendation to extend universal HCV screening to pregnant women.
 - Recommendation to extend HCV-RNA testing of exposed infants at 1-2 months of age.
 - Recommendation to extend HCV AB testing to reflex to RNA
 - STI recommendations
 - Name STD as an urgent public health threat
 - Increase STD resources in clinical settings; incl increased screening

Healthcare Infection Control Practices Advisory Committee (HICPAC) Deborah Yokoe, HICPAC Co-chair

- HICPAC has drafted a White Paper to facilitate discussion of issues that are critical to adequate reprocessing of flexible endoscopes. The current evidence base may not be sufficient to recommend a specific microbiologic method for assessing the adequacy of high level disinfection for endoscopes.
- HICPAC might consider addressing:
 - The clinical implications of PCR test results for bacterial infections at hospitals that may indicate colonization rather than infection, e.g. *C. difficile*.

Report back from the Dec 4–5 meeting of the Food Safety Modernization Act Surveillance Working Group (FSMA SWG) Tim Jones, FSMA SWG Chair

- FSMA is federally-mandated group
 - Largely FDA-focused; created BSC working group and Centers of Excellence; CDC is key in evaluating program.
 - Signed into law 2011; sweeping change in FDA authority (incl ability to order food recalls; new!); broad prevention mandate and accountability; import oversight; farm-to-table responsibility.
 - Standards developed, finalized in 2015-16, implementation near-complete.
- Measuring Impact
 - What are meaningful metrics?

FSMA SWG and CIDT

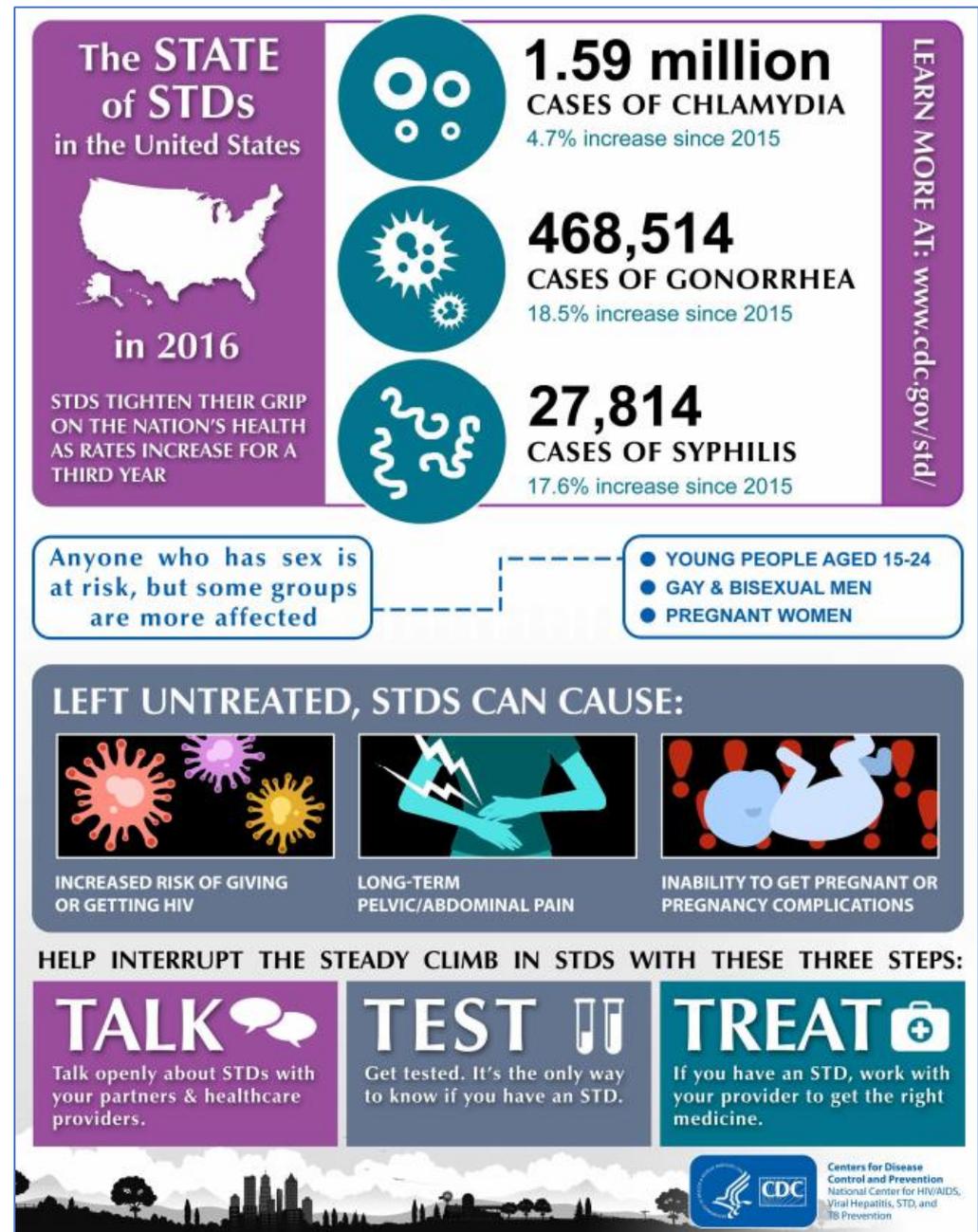
- CIDT pose a special challenge to public health.
- Loss of culture-based techniques to impact ability to detect foodborne outbreaks and foodborne drug resistance.
- CIDT likely also affect estimates of disease incidence and disease trends.
- BSC members commented that:
 - Microbial cultures will always be needed for specific public health purposes, such as characterizing pathogens that cause outbreaks. Immediate concern is loss of the ability to conduct routine strain-typing to detect outbreaks.
- The 2017 Annual Report describes potential ways to address CIDT issues but does not make recommendations. During 2018, the 3-step plan described in the Annual Report might be updated to:
 - Include specific guidance on preserving isolates as a short-term solution (step 1)
 - Document progress in developing a sequence-based infrastructure (step 2)
 - Describe ongoing research efforts to develop metagenomic methods (step 3)
 - Additional investments in metagenomics might speed the development of new diagnostic methods, as suggested at a recent FoodNET meeting.
 - An overlap in use of WGS and metagenomic methods is likely during the transition to metagenomic methods, similar to the overlap use of PFGE and WGS that occurred during the PulseNet transition to WGS.
- The BSC plans to draft recommendations on CIDT issues by early summer, taking into account:
 - APHL's Recommended actions for clinical laboratories and public health agencies (see: APHL CIDT Fact Sheet, February 2015: https://www.aphl.org/programs/food_safety/APHL%20Documents/FS_CIDTFactSheet_Feb2015.pdf)
 - Input from a May 8-9 meeting on CIDTs organized by the Pew Research Center to engage subject matter experts from clinical medicine, industry, and public health.
 - The estimated costs of taking action at the state and local levels (e.g., to conduct reflex testing). The BSC recommendations will include an analysis of the resources required to implement them.

Update from the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP)

- Jono Mermin, Director, NCHHSTP

HIV, HCV, STI

- HIV
 - Vital Signs released on HIV testing
 - One in 2 people with HIV were infected for at least 3 years before diagnosis.
 - Seven in 10 people at high risk for HIV visited a healthcare provider during 2015 but were not tested for HIV. These healthcare visits represent lost opportunities for HIV diagnosis and treatment.
 - Much HIV transmitted by undiagnosed pts (~15% of total); rest by untreated.
 - The US gap between diagnosed and suppressed is the highest in the world.
- HCV
 - HCV infections tripled since 2010; est. 34K new cases; surveillance problematic. Seems to be driven by opioid crisis.
- STI
 - Record high level of STIs; largest total number ever. See infographic.



TB

- 2016 report released.
- Lowest rate ever (last years increase didn't repeat; but 5y trend is level).
- Over 50% of active TB in NY, TX, CA, FL. Focus on working with those states.
- Over 2/3 of active TB, even in foreign-born, are in people who have been in country >5y.
 - Need to focus on latent TB
 - Six to 13 million people in the United States have LTBI. How to identify persons with LTBI who are likely to progress to active TB disease?

Update from the National Center for Immunization and Respiratory Diseases (NCIRD)

Nancy Messonnier, Director, NCIRD

- Bacterial Disease Division – Global Health projects; looking for overlap and synergies.
 - Incl deploying advanced diagnostics
 - TAC (Taqman Array Cards) used to identify causes of death; 100+ RT-PCR rxns; optimized in multiple multiplex format; covering PNA, AFI, meningitis, sepsis, diarrheal dz.
 - Deployed PCR for meningitis confirmation in meningitis belt.
- Disease burden; vaccine-preventables.
 - Technical support incl for lab diagnostic capacity.
- Q&A:
 - Molecular GBS screening; does it decrease incidence of GBS disease? Expensive, ~10% more sensitive. No data, but interesting question to look into.