Duke | Robert J. Margolis, MD Center for Health Policy

Assessing Strategies to Improve the Market for Rapid Diagnostics for Bacterial Diseases

April 18th, 2017 • Washington, DC

Discussion Guide

The rise in antibacterial resistant infections is a major public health threat due, in part, to the overuse and misuse of antibacterial drugs. The availability and adoption of rapid diagnostics could improve the use of antibacterial drugs and help to slow the emergence of drug resistance. The definition of 'rapid' can vary by setting: in outpatient care, a rapid diagnostic could be one that could produce results at the point of care in under twenty minutes; for inpatient care, it may be a diagnostic that provides results in hours rather than days. There are a number of factors that hinder the market success of rapid diagnostics for bacterial diseases, leading to low levels of investment and therefore development of these products. The Duke-Robert J. Margolis, MD, Center for Health Policy is hosting this workshop to explore the challenges associated with bringing a rapid diagnostic device for a bacterial disease to market. The objective of the workshop discussion is to identify potential steps stakeholders throughout the healthcare ecosystem could take to improve the economic viability of these products and support the appropriate use of antibacterial drugs. Workshop participants will be asked to:

- Prioritize the pressing challenges facing developers of diagnostics for bacterial infections,
- Identify potential mechanisms that could be implemented to provide incentives to develop diagnostics for bacterial infections, and
- Characterize the types of evidence needed to demonstrate value of new diagnostic tools.

Funding for this workshop was made possible by the Food and Drug Administration through grant 5U13FD001597. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsements by the U.S. Government.

Introduction

Various groups have called for the development of rapid diagnostic tests to support the appropriate use and stewardship of antimicrobial drugs.[1] Over- and misuse of antimicrobial drugs in clinical care is a key factor contributing to the development of antimicrobial resistance (AMR). During clinical encounters, the time needed for actionable results from diagnostic and sensitivity tests is often multiple days and would require patients to either wait an extended period of time or come back into the office for the results and appropriate treatment, if necessary. Because this would add a significant time and resource burden on patients, their caregivers, and clinical staff, patients are often treated empirically with broader spectrum antimicrobials, which may either be ineffective or unnecessarily expose a wider range of bacteria to the antibiotic and increase the opportunity for further resistance development. As a result of a lack of accurate rapid diagnostics, and patient demand for a prescription, evidence suggests that there are high rates of unnecessary antibiotic use with at least one in three prescriptions for antibiotics not medically necessary.[2] The lack of rapid diagnostics for bacterial infections also hinders the development of new antibacterial drugs because some patients enrolled in the trial ultimately are found not to have the disease caused by the types of bacteria that the investigational drug treats. Without a rapid diagnostic, clinicians must often treat patients before the type of infection is determined, which

may increase the amount of pre-trial or concomitant antibacterial drug therapy that a patient receives, clouding the ability of the trial to assess the effects of an investigational drug.

The availability of rapid diagnostic tests would improve patient care by ensuring that patients receive the most effective treatment quickly and support public health by reducing the emergence of resistance; increased development is needed to meet the needs of physicians treating patients in a broad range of settings. While there are a number of barriers facing the development of these rapid tests, this workshop will focus on challenges with coverage and reimbursement combined with technical and regulatory uncertainties that may limit the potential return on investment for developers.

Technical Challenges of Rapid Diagnostics Development

Various types of diagnostic technology, their unique benefits, and current development and use challenges are presented in a high-level summary in Table 1.

Table 1. Types of diagnostic tests for bacterial infections

Type	Function	Benefits	Challenges
Culture methods	Bacteria can be identified by morphology, growth conditions, and other genotypic and phenotypic characteristics	An accurate test, this method is often considered the gold standard	With some exceptions, this method can generally take several days to produce definitive results, and physicians will prescribe antibiotics empirically
Tests that indicate if infection is caused by bacteria	Often rapid, point-of-care (POC) tests that provide a "yes" or "no" answer	Diagnostic results can be leveraged to reduce the unnecessary prescribing of antibiotics	If the results are not immediate, a physician may prescribe antibiotics, rather than running the test, to save time
Tests that identify the type of bacteria or presence of resistance genes	Diagnostic provides specific information about the infecting pathogen, either the type of bacteria and/or the presence of resistance genes	Tests can provide valuable information about whether certain classes of drug will be effective; can lead to better management of infection and quicker prescription of most effective drug.	Negative results do not necessarily indicate that an infection does not harbor resistance genes, as not all resistance genes are known; presence or absence of resistance does not necessarily predict susceptibility to a drug
Tests that determine susceptibility to a drug	Diagnostic that tests the infection for susceptibility to a certain drug	Diagnostic provides information about the best drug and dose for a particular patient	Drug and device development usually occur independently, and there can be a lag between approval times

Designing diagnostic technologies to detect the cause and treatment options for bacterial infections can be more difficult than for other diseases. Some of the challenges stem from the continuing evolution and emergence of resistance factors; DNA-based methods are limited because measurement of known sequences and older tests will not include new resistance factors. Results from many types of tests may also not help clinicians determine if the bacteria is the infecting pathogen or if it is simply present but not causing the infection. For example, people often carry *S. aureus* or methicillin-resistant *S. aureus* in their nose without signs of infection.[3] Tests may also pick up materials from non-viable cells and result in a false positive for a particular pathogen.

Another hurdle for developers is obtaining access to well-characterized clinical samples to test accuracy, specificity, and sensitivity to validate their diagnostic tools. These types of samples are not always easily accessible, especially if the diagnostic is meant to detect an uncommon resistance gene. The expense for upkeep, patient consent, and degradation of samples over time can make maintaining a specimen bank challenging.

Regulatory Requirements for Diagnostics

FDA regulates diagnostics for bacterial diseases through three different paths. Tests cleared through the 510(k) process are Class II products (and occasionally Class I products) and can demonstrate that they are "substantially equivalent" to an existing predicate test. Clinical trials data are rarely submitted for these types of products, but they often require clinical data to demonstrate equivalence. New tests that do not have a predicate technology but present a low or moderate risk to the patient may be eligible for a *de novo* reclassification as Class II products. Upon submission of a *de novo* application, diagnostic sponsors will need to present evidence that characterizes the risks associated with the device, and propose special controls for risk mitigation. For a *de novo* application, clinical trial data are not required in all circumstances, but could be requested if other data are insufficient.[4]

Tests that cannot be considered substantially equivalent to an existing technology and will also be used to make a critical medical decision (e.g., diagnosis, treatment, or medical management) are considered Class III products and would be required to submit premarket approval (PMA). Diagnostics going through a PMA review typically submit clinical trial data.

Coverage and Reimbursement of Rapid Diagnostics

Many have suggested that inconsistency and lack of predictability in coverage and reimbursement of diagnostics for bacterial diseases may hinder the development of new, innovative rapid diagnostic tools for bacterial infections.[5] There are various levels of coverage and reimbursement decisions by both private and public payers. Typically, for public payers, the first coverage decision is a National Coverage Determination (NCD) issued by the Centers for Medicare and Medicaid Services (CMS). The NCD specifies the conditions that would deem the use of a device to be necessary, and it sets use guidelines for coverage provided by Medicare or Medicare contractors.[6] This evaluation process can take a significant amount of time extending the developers time to market and potential short term financial return.

FDA and CMS recently introduced a parallel approval program that creates a process for both agencies to review the clinical data and evidence simultaneously.[7] A key feature of this process is that manufacturers meet with both FDA and CMS before running the clinical trial in order to receive feedback on the trial design. Upon receiving results from the clinical trial, FDA and CMS provide concurrent, independent reviews. This pathway can potentially save time for manufacturers in two ways. Simultaneous review by both agencies reduces the amount of time that a manufacturer must wait before marketing their product. In some cases, the more critical factor is the opportunity for manufacturers to work with CMS prior to implementation of the clinical trials to design to ensure that their studies will be suitable to support a coverage decisions. To date, only one diagnostic has been approved through this process.[8]

For diagnostic tests, CMS often does not make a NCD. However, the regional Medicare administrative contractors (MACs) may set a Local Coverage Determinations (LCDs).[9] While private payers often make coverage decisions based on the NCD or LCD, this is not always the case. Many private payers conduct individual health technology assessments with recommended coverage based on evidence of effectiveness (as demonstrated by clinical trials), improvement over existing treatments, clinical and

economic outcomes, and the composition of their covered population.[10] There are several coverage decision frameworks available to private payers to help with coverage evaluation, including from the Agency for Healthcare Research and Quality, which oversees private and public evidence-based practice centers.[11]

In practice, LCDs and independent private payer coverage decisions result in national and regional variability in the level of reimbursement that can negatively affect the clinical uptake and utilization of new diagnostics.[12] Inconsistent and uncertain coverage and utilization is a disincentive for innovative development. While the coverage and reimbursement process is similar for all devices, diagnostic developers have indicated that there is greater variability for bacterial diagnostic tools. Developers have noted that more transparency and consistency in payers' evidentiary requirements and policies would create more predictability in the market, and would therefore support new development in this field.

The current process of assigning administrative and claims codes has also raised concerns about the viability of developing rapid diagnostics tools for bacterial infections. Diagnostic developers have noted that the pricing assigned through coding does not reward innovation in diagnostic products.[13] The reimbursement decisions made by CMS are linked to the Current Procedural Technology (CPT) codes created by the American Medical Association (AMA). Medicare assigns a reimbursement amount to a technology once it has received a CPT code. If a newly coded product is similar to one that is currently on the market, it is assigned the same code in a process called "cross-walking". If the new product is not similar to one that is currently available, it is assigned a new code as a "gap-filling" technology.

New cross-walked diagnostics generally receive the same reimbursement as the current product even if they demonstrate significant improvement to the previous technology. Gap-filling diagnostics may allow for higher reimbursement rates, but the assigned reimbursement is not predictable. Developers have cited the unpredictable reimbursement as a key factor discouraging investment in highly innovative products.

There is currently no mechanism in the diagnostic reimbursement decision-making process that factor in the potential downstream benefits to the public health of antimicrobial stewardship to delayed resistance or reductions in transmission. Finding ways to meaningfully measure outcomes related to diagnostics tools that support stewardship could inform a more efficient method for reimbursing clinically significant diagnostics.

Clinical Uptake and Use of Rapid Diagnostics for Bacterial Infections

Even if a diagnostic tool is FDA-cleared and has received payer coverage, it may face challenges in adoption by physicians and provider institutions. For example, new rapid diagnostic tools could improve with the implementation of antimicrobial stewardship programs (ASPs), which are designed to improve patient care and safety through surveillance and judicious use of antimicrobials. However, the use of rapid diagnostics are not explicitly included in the guidelines for these plans and there are not additional reimbursement mechanisms. Education about diagnostic choices and training on use of various diagnostics will still be critical for wide spread adaptation. While both CDC and CMS have recommended the implementation of stewardship programs in hospitals, there are no consistent economic incentives for clinicians and healthcare systems to adopt rapid diagnostics.[14]

Physicians' familiarity and concerns about the validity also play a critical role in the uptake of new diagnostic tools. Beyond the ease of use and readability of the results, concerns about the accuracy, specificity, and sensitivity, as well as how often the test produces false negatives or false positives are key concerns for clinicians. As illustrated in Table 3, several surveys of clinicians on their attitudes towards point-of-care (POC) testing indicate that it is not clear what incentives there are for clinicians to

use new diagnostic tools. While these surveys focused on POC tests, they point to same types of concerns noted about rapid diagnostics. When asked about the qualities of POC diagnostics that would make them attractive for use, clinicians preferred accurate and low cost tests where they felt confident about the result. However, they are often concerned that using these diagnostics may have a negative impact on their ability to provide care because of the length of time needed for testing and disruption of workflow.

Table 3. Summary of clinician attitudes towards point of care diagnostics[15]		
Perceived benefits	**Perceived barriers**	**Clinician preferences**
Diagnostic certainty Improved management of care Improved patient-clinician communication	Lack of accuracy Time to Results Impact on clinical staff Expense/lack of cost-effectiveness	High sensitivity (>90%) Low cost High specificity Time

Recent Efforts to Facilitate Diagnostics Development

Several organizations have recognized the importance of diagnostics to delay antimicrobial resistance and promote appropriate use of antimicrobials, and the U.S. government has taken several concrete steps to enhance development of these tools. The National Institutes of Health (NIH) and the Biomedical Advanced Research Development Authority (BARDA) are funding a prize competition for the development of a POC test to detect antimicrobial resistance.[16] NIH also provides funding to the Antibacterial Resistance Leadership Group (ARLG), which curates a virtual specimen repository, and FDA and CDC have assembled a repository of resistance isolates. These institutions help to facilitate clinical evaluation of diagnostics.

The Presidential Advisory Council on Combatting Antibiotic-Resistant Bacteria (PACCARB) made diagnostics the focus of one of five working groups, which are tasked with providing advice, information, and recommendations.[17] The diagnostics working group made recommendations that would impact all stages of diagnostic development, and importantly, they have emphasized the need for incentives and new mechanisms to reimbursement the development and use of these products.[18]

Assessing Strategies to Improve the Market for Rapid Diagnostics for Bacterial Diseases Workshop Sessions

There are several unique challenges to the development and adoption of diagnostics for bacterial infections. This workshop is focused on the economic factors including improving the predictability of the reimbursement process to increase development in this area. Each session will highlight key topics through the panel discussion for the moderated discussion with all the workshop participants. Sessions will be focused around the questions detailed below.

Session I: Defining the needs of users of diagnostic results

In order to achieve success on the market, diagnostics for bacterial infections must demonstrate the advantages of their product by addressing the needs of their users. The desired characteristics of a test and the evidence needed to demonstrate value vary based on the setting where a patient is treated, which could include acute, inpatient, and outpatient settings as well as for clinical trials. This session will focus on the needs of bacterial diagnostic users, with the goal of understanding the factors that influence use and coverage decisions as well as identifying the types of diagnostics that are most valuable within the clinical setting. Some of the key questions include:

- What are the high-priority diagnostic tools physicians need when they encounter an infection or suspected infection? How do these needs differ in acute care, inpatient care, outpatient, and clinical trials settings?
- What factors shape the decision-making for uptake of diagnostics? How can developers design their diagnostic tools to address the users' needs?
- What measures or data would lead to faster uptake of diagnostics that distinguish viral/bacterial infections? That aid in treatment selection?
- How are coverage decisions influenced by clinical practice?
- What are the potential direct (e.g., timeliness, reimbursement) and indirect (e.g., ease of use and clarity of results) outcomes for the end users of the diagnostic tools that contribute to their value assessment?

Session II: Overcoming the challenges associated with the clinical development of a rapid diagnostic for bacterial diseases

Developers of diagnostics for bacterial infections face unique challenges during the clinical development of their products, which can lead to delayed regulatory approval and market launch. These development costs reduce the potential return on investment for a product, and without financial support or large sales volumes at high prices, the number of companies pursuing innovative rapid diagnostics for bacterial diseases is low. Session II will focus on the challenges faced by developers of diagnostics for bacterial infections during clinical development, aiming to identify approaches or incentives that can help to overcome these barriers. To explore these issues, participants will be asked to discuss the following questions:

- What clinical challenges are most difficult to overcome, and which result in the greatest expense?
- What types of incentives would better balance the cost/risk of diagnostic development?
- Are there new approaches that could reduce the financial burden of clinical trials or clinical validation? If so, what are the barriers to implementation?
- What is the best way to encourage coordinated development of diagnostics and antimicrobials?

Session III: Balancing risk and uncertainty in the development and use of diagnostics

The FDA plays an important role in evaluating the safety and effectiveness of diagnostics for bacterial diseases, and they have recently taken steps to provide guidance on development and reduce the time between approval and coverage decisions. However, there remains uncertainty in weighing what outcome measures (e.g. sensitivity and specificity) mean for the utility and risk profile of a diagnostic. This session will focus on the best way to manage those uncertainties, and will aim to explore how outcomes should be assessed and identify areas where further guidance is needed. Questions for this session include:

- How is the regulatory pathway influenced by scientific challenges?
- Which of these challenges might benefit from additional FDA guidance?
- What factors should be evaluated when determining the thresholds for effectiveness and risk? What considerations contribute to this assessment?

Session IV: Addressing the post-market economic challenges to diagnostics development

Coverage, reimbursement, and uptake by providers contribute to the return on investment for a diagnostic for bacterial diseases. However, the methods used to determine coverage and reimbursement do not always reward innovation, significant improvements on existing technology, or benefits to public health, which is a disincentive for development. At the same time, the cost of a

diagnostic affects utilization by providers. To explore novel approaches to these related issues, this session aims to identify factors that impact return on investment and understand the which outcomes could be best used to assess value.

Questions to address:

- What factors have the greatest impact on diagnostic reimbursement rates? Where are the gaps in evidence?
- Can current payment methods be reformed to provide increased predictability and certainty to diagnostic developers?
- How can reimbursement better reflect the innovation and value that microbial diagnostics bring to the healthcare system?
- How can the value of delaying resistance/preventing infections be measured? Are there other indirect outcomes that should factor into the value calculation?

Session V: Prioritizing actions to incentivize the development of rapid diagnostics for bacterial infections

Building on the discussion from the previous sessions, the panel will be asked to identify priority programmatic and policy solutions. Workshop participants will then be asked for their input on how best to prioritize these activities to address the challenges to promoting diagnostic development, uptake, and reimbursement. The goal of this session will be to put forward short-term, actionable items as well as identify issues that require more in-depth analysis or long-term planning. Potential solutions may include policy incentives, infrastructure development, or new payment approaches.

---

[1] The President's Council of Advisors on Science and Technology. 2014. Report to the President on Combating Antibiotic Resistance. Retrieved online at: [https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/PCAST/pcast_carb_report_sept2014.pdf]; Institute of Medicine. 2003. Microbial Threats to Health: Emergence, Detection, and Response. Retrieved online at: [http://nationalacademies.org/hmd/~/media/files/report%20files/2003/microbial-threats-to-health-emergence-detection-and-response/microbialthreat8pgfinal.pdf]; Pew Charitable Trusts. 2014. A Path to Better Antibiotic Stewardship in Inpatient Settings. Retrieved online at: [http://www.pewtrusts.org/~/media/assets/2016/04/apathtobetterantibioticstewardshipininpatientsettings.pdf]

[2] Cole, A. GPs feel pressurised to prescribe unnecessary antibiotics, survey finds. BMJ 349, g5238–g5238 (2014). Retrieved online at:[http://www.bmj.com/content/349/bmj.g5238]; Fleming-Dutra, K. E., Hersh, A. L., Shapiro, D. J., Bartoces, M., Enns, E. A., File, T. M., Finkelstein et al. 2016. Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011. Jama, 315, 17, 1864. Retrieved online at: [http://jamanetwork.com/journals/jama/fullarticle/2518263]

[3] Centers for Diseases Control and Prevention. Methicillin-resistant Staphylococcus aureus (MRSA). Retrieved online at: [https://www.cdc.gov/mrsa/tracking/]

[4] Hogan J. The De Novo Classification Process: A Work in Progress. Med Device Online. Retrieved online at: [https://www.meddeviceonline.com/doc/the-de-novo-classification-process-a-work-in-progress-0001]

[5] Caliendo, A. M. et al. Better Tests, Better Care: Improved Diagnostics for Infectious Diseases. Clin. Infect. Dis. 57, S139–S170 (2013). Retrieved online at: [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3820169/]; Chantal Morel et al. Ensuring innovation in diagnostics for bacterial infection. (European Observatory on Health Systems and Policies, 2016). Retrieved online at: [http://www.euro.who.int/__data/assets/pdf_file/0008/302489/Ensuring-innovation-diagnostics-bacterial-infection-en.pdf?ua=1]; Four diagnostic strategies for better-targeted antibiotic use. (Wellcome Trust, 2016). Retrieved online at: [https://wellcome.ac.uk/sites/default/files/diagnostic-strategies-for-better-targeted-antibiotic-use-wellcome-jul15.pdf]; The Value of Diagnostics, Innovation, Adoption and Diffusion into Health Care. (2005). Retrieved online at: [https://dx.advamed.org/sites/dx.advamed.org/files/resource/Lewin%20Value%20of%20Diagnostics%20Report.pdf]

[6] Centers for Medicare and Medicaid Services. "Medicare Coverage Determination Process." Retrieved online at: [https://www.cms.gov/Medicare/Coverage/DeterminationProcess/]
[7] U.S. Food and Drug Administration. "Payer Communication Task Force (PCTF)." Retrieved online at: [https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHInnovation/ucm456149.htm]
[8] Regulatory Affairs Professional Society. "FDA and CMS Parallel Reviews of Devices to Continue." Retrieved online at: [http://raps.org/Regulatory-Focus/News/2016/10/21/26052/FDA-and-CMS-Parallel-Reviews-of-Devices-to-Continue/]
[9] Chantal Morel et al. Ensuring innovation in diagnostics for bacterial infection. (European Observatory on Health Systems and Policies, 2016). Retrieved online at: [http://www.euro.who.int/__data/assets/pdf_file/0008/302489/Ensuring-innovation-diagnostics-bacterial-infection-en.pdf?ua=1]
[10] ISPOR Global Health Care Systems Road Map - USA: In-Vitro Diagnostics. (2010). Retrieved online at: [https://www.ispor.org/HTARoadMaps/USMD.asp]
[11] Chantal Morel et al. Ensuring innovation in diagnostics for bacterial infection. (European Observatory on Health Systems and Policies, 2016). Retrieved online at: [http://www.euro.who.int/__data/assets/pdf_file/0008/302489/Ensuring-innovation-diagnostics-bacterial-infection-en.pdf?ua=1]
[12] Chantal Morel et al. Ensuring innovation in diagnostics for bacterial infection. (European Observatory on Health Systems and Policies, 2016). Retrieved online at: [http://www.euro.who.int/__data/assets/pdf_file/0008/302489/Ensuring-innovation-diagnostics-bacterial-infection-en.pdf?ua=1]
[13] Ibid
[14] Fridkin S, Baggs J, Fagan R, Magill S. 2014. Vital Signs: Improving Antibiotic Use among Hospitalized Patients. Morbidity and Mortality Weekly Report. The Centers for Diseases Control and Prevention. March 7, 2014 / 63(09); 194-200. Retrieved online at: [https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6309a4.htm]; Centers for Medicare and Medicaid Services. Medicare and Medicaid Programs; Hospital and Critical Access Hospital (CAH) Changes To Promote Innovation, Flexibility, and Improvement in Patient Care. Retrieved online at: [https://www.federalregister.gov/documents/2016/06/16/2016-13925/medicare-and-medicaid-programs-hospital-and-critical-access-hospital-cah-changes-to-promote]
[15] Hardy, V. et al. Exploring the barriers and facilitators to use of point of care tests in family medicine clinics in the United States. BMC Fam. Pract. 17, (2016). Retrieved online at: [https://bmcfampract.biomedcentral.com/articles/10.1186/s12875-016-0549-1]; Hsieh, Y.-H. et al. Perceptions on Point-of-Care Tests for Sexually Transmitted Infections: Comparison Between Frontline Clinicians and Professionals in Industry. Point Care J. -Patient Test. Technol. 11, 126–129 (2012). Retrieved online at: [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404836/]; Hsieh, Y.-H. et al. What Qualities Are Most Important to Making a Point of Care Test Desirable for Clinicians and Others Offering Sexually Transmitted Infection Testing? PLoS ONE 6, e19263 (2011). Retrieved online at: [http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0019263]; Jones, C. H. et al. Primary care clinicians' attitudes towards point-of-care blood testing: a systematic review of qualitative studies. BMC Fam. Pract. 14, (2013). Retrieved online at: [http://bmcfampract.biomedcentral.com/articles/10.1186/1471-2296-14-117]; Ditkowsky, J., Shah, K. H., Hammerschlag, M. R., Kohlhoff, S. & Smith-Norowitz, T. A. Cost-benefit analysis of Chlamydia trachomatis screening in pregnant women in a high burden setting in the United States. BMC Infect. Dis. 17, (2017). Retrieved online at: [https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-017-2248-5]
[16] National Institutes of Health. Announcement of Antimicrobial Resistance Rapid, Point-of-Care Diagnostic Test Challenge Competition. Retrieved online at: [https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-137.html]
[17] Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria. "About Us." Retrieved online at: [https://www.hhs.gov/ash/advisory-committees/paccarb/about-paccarb/index.html]
[18] Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria. Report Out: PACCARB Working Groups. Retrieved online at: [https://www.hhs.gov/sites/default/files/report-out-paccarb-working-groups.pdf]