

# **A PUBLIC HEALTH PERSPECTIVE ON ANTIMICROBIAL RESISTANCE DIAGNOSTICS**

Meeting Summary and Opportunities to Address Challenges

Centers for Disease Control and Prevention and AdvaMedDx

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## EXECUTIVE SUMMARY

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On December 4, 2015, CDC's Division of Healthcare Quality Promotion's Office of Antimicrobial Resistance (OAR) and AdvaMedDx hosted an all-day meeting with industry leaders to forecast the future development of diagnostic tests and look for solutions to challenges that come with the development, uptake and implementation of tests that can improve public health and slow the spread of antibiotic resistance (AR). The meeting—A Public Health Perspective on AR Diagnostics—included more than 80 attendees representing more than 28 companies from diagnostic, academic, policy, patient advocacy and microbiology backgrounds.

Attendees participated in breakout sessions covering opportunities to improve antibiotic use, promote infection control diagnostics in healthcare, improve use of new diagnostics with education and guidance, and collect resistance data in an era of culture-independent diagnostics (CID). Attendee input in the interactive forecasting discussion and breakout sessions has been compiled and synthesized here, resulting in a list of opportunities for industry, government and professional societies to work together and optimize the potential impact of diagnostics to address the problem of antibiotic resistance.

Overall, the day's discussion showed:

- 1. The use of existing diagnostics can be improved.** Provider and patient education is needed to improve understanding of a diagnostic test's value, when and how to properly use it, and how to apply lab results.
- 2. More utilization studies are needed.** Studies should demonstrate the clinical and public health impact of a diagnostic. Clinical trials would also generate data to show facilities the clinical and economic benefit to using diagnostic testing.
- 3. Financial factors are contributing barriers to development of new diagnostics.** Reimbursement to manufacturers, however, may offset those barriers.
- 4. Near-future technologies include whole genome sequencing (WGS) and biomarkers.** Near-future tests will also include point-of-care, direct-from-specimen capabilities and a focus on sepsis and upper respiratory infections.
- 5. Manufacturers are encouraged to engage FDA early.** This will avoid delays in bringing a test to market and use isolates from public health banks during development to ensure that tests detect a full range of pathogens seen in clinical settings.
- 6. Diagnostic testing recommendations can be improved.** Guidelines should be developed across organizations and specialties, and should include specific recommendations for infection control. Development of these recommendations should also be sped up and should quickly follow a test's market release.

- 7. Solutions are needed for collecting resistance data.** This data would help public health assess the threat and implement prevention measures if new or changing resistance develops.

As a result, the following activities were identified by meeting attendees as opportunities to ensure that we use current diagnostics appropriately and optimize the use of next generation diagnostics as they come to market. The activities listed here are offered for consideration to the groups identified and intended to form a framework for future discussion, collaboration and evaluation of AR diagnostics by all parties involved. **Those marked with an asterisk (\*) are already under implementation by CDC.**

**Opportunities to help with innovation and uptake of diagnostics to improve patient care and public health:**

1. Industry and professional societies should expand educational efforts to promote the clinical, public health and/or economic impact of new diagnostics to include doctors as well as laboratorians.
2. Industry and public health should work together to conduct utilization trials that assess the clinical, public health and economic impact of using a diagnostic.\*
3. Where diagnostics are most important for controlling transmission, industry and public health should conduct clinical trials to assess the public health and economic impact of infection control diagnostics.\*
4. Industry and public health should conduct studies to assess the microbiome status as a risk factor for transmission. Use these studies to evaluate prototype diagnostics.\*
5. CDC and FDA should expand, update and improve the FDA-CDC AR Isolate Bank to support industry test development.\*
6. Payers should consider incorporating diagnostic testing as condition of reimbursement when there is a clear benefit of testing, especially when there may be an economic disincentive for testing (i.e., the antibiotic costs less).

**Opportunities to ensure proper implementation of tests we have today and new tests coming to market:**

7. Based upon clinical and public health needs, industry should work to incorporate antimicrobial resistance detection methods into culture-independent diagnostic tests.
8. Professional societies, public health and standards setting organizations should proactively coordinate the development of educational materials, guidance and standards for implementation of new diagnostics; ensure that audience-specific materials are developed (e.g., for providers or laboratorians); establish relevant liaisons or representatives on the appropriate committee for each organization; and ensure materials include “best practice” recommendations for reporting results.\*
9. Professional societies and public health should work together to develop or update treatment guidelines that include best practices for diagnostic testing.\*

10. Professional societies and CDC should monitor the uptake of culture-independent diagnostics and communicate clinical and public health needs for antimicrobial resistance data to industry.\*
11. Where infection control testing is needed to prevent transmission of resistant pathogens, CDC should leverage public health laboratory capacity to ensure state prevention programs have access to testing.\*
12. CDC should expand surveillance for pathogens of public health importance affected by culture-independent diagnostics.\*
13. CDC should pilot reflex culture for *Salmonella* CID-positive specimens. Isolates recovered can be tested for antimicrobial susceptibility, presence of resistance mechanisms, and typed to improve detections of outbreaks.\*

The report that follows provides a more in-depth account of the current state of antibiotic resistance diagnostics, a summary of subject matter leaders' expectations for how their groups will address the problem, a closer look at breakout session discussion points, and ideas for addressing challenges.

## BACKGROUND ON THE PROBLEM

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Antibiotic-resistant pathogens are a public health threat that have the potential to revert medical practice to the pre-antibiotic era. The primary drivers of antibiotic resistance are antibiotic use and the transmission of resistant pathogens. Diagnostic testing holds great promise of positively impacting both of these drivers, resulting in a decrease of resistant infections.

Building upon ideas generated at previous antibiotic resistance meetings, meeting attendees focused on strategies that reflect the clinical and public health benefits of diagnostic testing. Specifically, these ideas were grouped as the following, which also served as breakout session topics:

- Avoiding unnecessary antibiotic use and optimizing antibiotic selection
- Identifying high-risk patients as part of infection control
- Promoting optimal implementation through education
- Collecting public health data in an era of culture-independent diagnostics

### Avoiding Unnecessary Antibiotic Use and Optimizing Antibiotic Selection

Antibiotics are a medical necessity, but too often they are misused. Studies indicate that as much as 50% of the antibiotics used in hospitals are unnecessary.<sup>1</sup> In the outpatient setting, prescription data indicate that United States prescribers write more than two times the number of antibiotic prescriptions per 1,000 persons than some European countries<sup>2</sup>; a finding that suggests a high degree of unnecessary antibiotic use in the U.S. Many factors contribute to inappropriate antibiotic use, including managing patient expectations and clinician uncertainty because diagnostic information is lacking. Improving antibiotic use with diagnostics will require better use of tests that we already have and the development of new tests that produce results faster than our current technology.

CDC is working with government and healthcare partners to help build a healthcare antibiotic stewardship infrastructure. Multiple studies have shown that engaging antibiotic stewardship programs has proven to be an important component of diagnostic test implementation to improve antibiotic use. Planning for this engagement should start now.

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<sup>1</sup> Centers for Disease Control and Prevention (2014). *Overview and evidence to support stewardship: Fast facts*. Retrieved from <http://www.cdc.gov/getsmart/healthcare/evidence.html>

<sup>2</sup> Goosens, H., Ferech, M., Coenen, S., & Stephens, P. (2007). Comparison of outpatient systemic antibacterial use in 2004 in the United States and 27 European countries. *Clinical Infectious Diseases*, 44(9). Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17366456>

## Identifying High-Risk Patients: An Infection Control Perspective

Preventing transmission of antibiotic resistance requires an institutional commitment to good general infection control practices, like consistent handwashing by healthcare workers, and appropriate environmental cleaning of hospital facilities and instruments. Generalized infection control strategies can significantly reduce transmission of antibiotic-resistant infections, but more targeted interventions may be needed for some resistant pathogens or when general infection control practices are not enough. For example, CDC recommends using tests to identify patients asymptomatically colonized with CRE as a tier I intervention when CRE infections are identified in a healthcare facility. Despite this recommendation, few laboratories use such assays because there are few FDA-approved tests on the market and the cost of testing is assumed by an institution's operating expenses. Promoting the uptake of important infection control diagnostics will require overcoming these barriers.

In addition to tests that detect resistant infections or colonization, infection control strategies of the future will focus on preserving or restoring the microbiome. Diagnostics that assess the microbiome status will help determine when interventions are most needed.

## Promoting Optimal Implementation through Education

As new tests come to market, laboratories and end users need education and guidance for optimal implementation. Professional societies, laboratory standards setting organizations and CDC have a role in developing these materials. As testing and prescribing become more complex, it will be essential that these groups develop materials in a timely manner and keep them up to date.

## Collecting Public Health Data in an Era of Culture-Independent Diagnostics (CID)

Diagnostics are moving away from single analyte tests to syndrome-based multi-analyte tests, and away from culture-based methods to molecular or other non-culture technologies. These changes are good for patients, but the result often means that we lose the ability to collect critical antibiotic resistance data. These data are necessary for a robust public health response to resistance. New strategies are needed to collect these data and we are dependent upon diagnostic test manufacturers to help find solutions.

## FINDING SOLUTIONS: FORECASTING SUMMARY

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New diagnostics to address the problem of antibiotic resistance is a top priority for all sectors responding to this public health threat. During the AR Diagnostics meeting, the hosts asked participants from industry, regulations (FDA) and test

development funding (NIH and BARDA) a series of questions about the future of diagnostics. Participants responded via an anonymous audience participation tool, with the intention of encouraging candid responses, and results were viewed as a group and expounded upon by individual volunteers. Although the survey was limited, some clear trends were evident:

- **Improve use of existing diagnostics.** Participants felt that the new global focus on combating antibiotic resistance is resulting in a new era of innovation within the diagnostic industry, but the medical field could do more now to combat antibiotic resistance by using existing diagnostics better. An example discussed was the need for better use of diagnostics to avoid unnecessary antibiotic prescribing for urinary tract infections. CDC data indicates that 50% of all antibiotics prescribed in U.S. health provider offices are either unnecessary or inappropriate; this could be reduced by better use of existing diagnostic tests.<sup>3</sup>
- **Financial factors are barriers to development.** For half of the participants, financial factors are the biggest barriers to bringing the next-generation AR diagnostics to market (i.e., the need for greater investments in diagnostic test development), but the other half thought that the need for financial investment and the need for technological advances are equal barriers to developing next-generation diagnostics.
- **Reimbursement may drive development.** Projected reimbursement rates were identified as the biggest driver of new test development.
- **Technological advances are needed for next-generation tests.** Important technological advances needed are (1) less expensive tests and more automated analysis of sequence data, (2) increasing the concentration of infectious disease agents from a clinical specimen, and (3) single-cell diagnostic testing, like microfluidics.
- **Near-future technologies include WGS and biomarkers.** Participants reported that the technologies to most likely be used in the next 4-10 years are infectious agent DNA detection by whole genome sequencing and testing for a biomarker to measure host reaction to an infectious agent. Most of the audience predicted a bacterial versus viral diagnostic would come to market in the near future and the test(s) would detect the infectious agent and a biomarker.
- **Focus on sepsis and upper respiratory infections.** Participants reported that diagnostic test development is currently most focused on diagnosing sepsis and upper respiratory infections. Few reported some diagnostic test development for lower respiratory infections, urinary tract infections, gastrointestinal disease, and sexually transmitted disease.
- **Expect a direct-from-specimen test soon.** Half of the participants predicted that a direct-from-specimen test that drives definitive therapeutic decisions would come to market in the next 3-5 years.

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<sup>3</sup> Centers for Disease Control and Prevention (2015). *Community antibiotic prescribing rates by state (2013/2014)*. Retrieved from <http://www.cdc.gov/getsmart/community/images/usmap.jpg>



- **Development is only half the battle, need focus on implementation.** Nearly all participants agreed that with the advent of new diagnostics, we need better education of end users, improved use of information technology to report complex results, and antibiotic stewardship programs for translation of results into appropriate therapeutic decisions.

The survey conducted did not capture all complexities anticipated for diagnostic test development, but participants provided thoughtful responses to help put the future in perspective. It is clear that advances in diagnostics are coming, but technological barriers still exist. New tests for important infections like sepsis are in development, but important gaps, like new diagnostics for lower respiratory tract infections, exist. We need to find drivers of diagnostic test development that extend beyond test reimbursement. A key activity here will be conducting studies to measure the impact new diagnostics have on patient outcomes, antibiotic use and preventing transmission of resistant pathogens. It was clear from participants that none of the players expect a single diagnostic test to solve the AR problem; so while new tests are coming, a sustained focus on AR test development and proper implementation is needed by all sectors (industry, academics and government).

## FINDING SOLUTIONS: BREAKOUT SESSION SUMMARY

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During the meeting's afternoon session, participants had the opportunity to attend two of the four breakout groups. The following is a summary of the discussion for each breakout and recommended milestones for next steps.

### Breakout Session #1: Avoiding Unnecessary Antibiotic Use and Optimizing Antibiotic Selection

**The Challenge.** Antibiotic use is the principal driver of antibiotic resistance in pathogenic bacteria. If we want to address the problem of antibiotic resistance we need to improve the use of antibiotics. Hospitals are implementing antibiotic stewardship programs and, in the outpatient setting, guidelines and educational efforts are employed to improve antibiotic use. In addition to these efforts, improved use of existing diagnostics and new diagnostic tests can play a critical role in improving patient outcomes and antibiotic use. There is a growing body of evidence that diagnostics most effectively improve antibiotic use if antibiotic stewardship programs are employed to interpret results and guide therapy. The challenges are (1) ensuring that tests we have now, as well as future tests, are optimally implemented in clinical settings; (2) developing new diagnostics that improve patient care and antibiotic use; and (3) measuring the impact of diagnostics and antibiotic use.

**Discussion.** Breakout participants identified many barriers to the proper use of diagnostics for antibiotic prescribing. Barriers highlighted include:

- Providers may not fully understand what tests to order, may be confused by complex reports (i.e., those requiring comments or qualification), or may develop mistrust in a diagnostic if test performance is not perfect. There is also little incentive to providers to use a diagnostic test when an antibiotic may be cheaper to them or the patient. For example, patients with pharyngitis should be tested for Group A Streptococcus before being prescribed antibiotics. These tests are rapid, easy to perform and highly accurate. However, attendees suggested that providers are not using the test and, if they do and the result is negative, an antibiotic is still prescribed.
- Patients may not understand the value of a diagnostic test when they can often be prescribed an antibiotic without the test, especially when testing takes more time and may delay their access to the antibiotic. In the outpatient setting, it is difficult for patients to understand that financial costs of laboratory testing now are likely less than the future health costs of using an antibiotic when one is not needed.
- Well-powered utilization studies are needed to demonstrate the clinical, public health and economic impact of a diagnostic. Even when the benefits of using a diagnostic are clearly demonstrated, diagnostic testing is rarely included in patient management guidelines, most likely because laboratory expertise is not part of the guideline writing team.

**Moving Forward.** Key groups, represented by those at the meeting, can have an impact on avoiding unnecessary antibiotic use and optimizing selection. First steps may include:

- Industry and Professional Societies – Work together to develop education materials and programs on the proper use of diagnostic tests for doctors prescribing antibiotics, not just for laboratorians.
- Industry and Public Health – Work together to conduct utilization trials that assess the clinical, public health and economic impact of using a diagnostic.
- Professional Societies and Public Health – Work together to develop or update treatment guidelines that include best practices for diagnostic testing.
- Payers – Consider incorporating diagnostic testing as condition of reimbursement when there is a clear benefit of testing, especially when there may be an economic disincentive for testing (i.e., the antibiotic costs less).

## Breakout Session #2: Identifying High-Risk Patients: An Infection Control Perspective

**The Challenge.** Preventing transmission of antibiotic-resistant bacteria is a proven strategy for reducing antibiotic-resistant infections. Generalized infection control strategies can significantly reduce transmission of antibiotic-resistant infections, but more targeted interventions may be needed for some resistant pathogens or when general infection control practices are not enough. In particular, carbapenemase-producing Enterobacteriaceae (CPE) is one of the most significant infection control challenges healthcare facilities face today. These resistant pathogens can colonize the

gastrointestinal (GI) tract and proliferate when the GI microbiome is disrupted by antibiotics. This overgrowth of CPE can result in greater transmission of the resistant pathogen between patients. Prevention and control of a CPE outbreak depends upon being able to detect CPE colonized patients and implement appropriate transmission precautions. The uptake of diagnostics to detect CPE colonization has been slow. Some of the barriers to uptake are the lack of FDA-approved tests and the need of healthcare institutions to assume the cost for infection control testing.

**Discussion.** Breakout participants identified ways forward for identifying and improving infection control among high-risk patients. Discussion highlights include:

- The need for infection control diagnostics was re-affirmed by participants, but participants did not find an easy solution to promoting uptake of infection control diagnostics. In the absence of test-specific reimbursement, facilities need to see a clinical and economic benefit to testing. These kinds of data need to be generated in clinical trials that include all populations at risk for multidrug-resistant organizations transmission and infection (e.g., patients in long-term care facilities). Testing recommendations should be included in prevention guidelines (e.g., the recommendations to test for CPE colonization in the [CDC CRE Toolkit](#)).
- The highest priority infection control tests were (1) tests that detect CPE colonization from rectal or fecal specimens, (2) sequence-based tests that provide molecular epidemiological or typing results that can assist with outbreak detection and response, and (3) tests that can assess the risk of resistant pathogen transmission (e.g., a test that detects GI colonization with a resistant pathogen and assesses the status of the microbiome). Tests that fit description (1) and (2) have been developed or are in development. Tests that assess the microbiome status was a novel idea to many and representatives from industry indicated that an important driver of microbiome test development are studies correlating microbiome status to pathogen transmission.
- The FDA approval pathway for infection control diagnostics were also discussed. FDA encouraged industry to engage them early in test development. Making surveillance isolate collections available to industry can help ensure that tests detect the range of resistant pathogens occurring in clinical specimens.

**Moving Forward.** Key groups, represented by those at the meeting, can have an impact on identifying and improving infection control among high-risk patients. First steps may include:

- Industry and Public Health – Where diagnostics are most important for controlling transmission, conduct clinical trials to assess the public health and economic impact of infection control diagnostics.
- Industry and Public Health – Conduct studies to assess the microbiome status as a risk factor for transmission. Use these studies to evaluate prototype diagnostics.
- CDC – Where infection control testing is needed to prevent transmission of resistant pathogens, leverage public health laboratory capacity to ensure state prevention programs have access to testing.

- FDA and CDC – Expand, update and improve the FDA-CDC AR Isolate Bank to support industry test development.

### Breakout Session #3: Promoting Optimal Implementation through Education

**The Challenge.** There is a new era of diagnostic test innovation and development to address the problem of antibiotic resistance. As new diagnostic tests come to market, the medical community will need to adjust to new kinds of data for patient management. Reporting and interpreting diagnostic tests is already very complicated, but it is likely to become more so with the availability of new tests. Several organizations develop guidance for reporting and interpreting infectious disease tests, including American Society for Microbiology (ASM), Infectious Diseases Society of America (IDSA), Clinical and Laboratory Standards Institute (CLSI), Society for Healthcare Epidemiology of America (SHEA) and the Healthcare Infection Control Practices Advisory Committee (HICPAC), and CDC. The medical community is best served when these organizations work together to develop timely education materials and guidance and keep them up to date.

**Discussion.** Breakout participants identified ways forward for improving the use of new diagnostics with end-user education and expert guidance. Discussion highlights include:

- There is a need for more education of providers so that they can use diagnostic tests appropriately and interpret and apply results correctly. There is a similar need to educate patients about the use and value of diagnostic tests, especially when use of the test may prevent the unnecessary use of antibiotics.
- Often, testing recommendations are developed long after tests come to market. Reason for delay is often the lack of data measuring clinical and public health impact of a diagnostic. These types of studies, if done at all, are usually conducted long after studies for FDA-clearance have concluded. Guidance is needed earlier, even if the guidance outlines areas of uncertainty. Similarly, clinical studies measuring impact are needed earlier in the test development and implementation process.
- Guidelines would benefit from cross-organizational and cross-specialization representation on the guideline writing committee. This coordination will aid in developing comprehensive guidance for multiple audiences.
- Information technology (IT) systems will be critical to promote proper use of a diagnostic (i.e., appropriate ordering), for clearly reporting results to the provider, and to link laboratory results with antibiotic stewardship programs for improved antibiotic prescribing.

**Moving Forward.** Professional societies in particular can have an impact on improving the use of new diagnostics with end-user education and expert guidance. First steps may include:

- Professional Societies, Public Health and Standards Setting Organizations – Proactively coordinate the development of educational materials, guidance and standards for implementation of new diagnostics:
  - Ensure that audience-specific materials are developed (e.g., for providers, laboratorians, and the public).

- Establish relevant liaisons or representatives on the appropriate committee for each organization.
- Ensure materials include “best practice” recommendations for reporting results.

## Breakout Session #4: Collecting Public Health Data in an Era of Culture-Independent Diagnostics

**The Challenge.** More infectious diseases are diagnosed using culture-independent diagnostic (CID) technologies. Examples include gonorrhea, lower respiratory infections, enteric infections, and tuberculosis. Culture-independent methods offer many benefits, such as improved sensitivity, faster turnaround to results, and the ability to test for several etiological agents using one test. With such benefits, the trend toward culture-independent diagnostics cannot and should not be stopped. Unfortunately, in many cases, important clinical or public health information, such as the susceptibility to antibiotics, is not obtained in the absence of a bacterial isolate. With increasing antibiotic resistance, this information can be critical for treating an infection and to identify important public health trends. Other strategies are needed to obtain these data and the strategies are often pathogen-specific. Pathogens of interest include *Salmonella*, *Shigella*, pathogenic *E. coli*, *Campylobacter*, *Mycobacterium tuberculosis*, and *Neisseria gonorrhoeae*.

**Discussion.** Participants agreed: CID are here to stay. These tests are nearly always more sensitive than culture techniques and increased sensitivity means better patient care. If antibiotic resistance data are needed, participants feel that one of three strategies need to be employed:

- Incorporate antimicrobial resistance detection into culture-independent diagnostic tests;
- Collect a specimen for culture-independent tests that is suitable for reflexive testing if the test is positive for a relevant infectious agent; or
- Collect a second (or duplicate) specimen for reflexive culture if strategy B is not possible.

A summary of pathogen-specific points can be found in Table 1.

Strategy A is a decision made by diagnostic test manufacturers and, when developing the test, they must evaluate what the assay needs to detect versus what the test could detect. Diagnostic test manufacturers should develop a test that responds to patient care needs without letting the test become too complex or costly. For each of these pathogens, as the importance of antibiotic resistance data for patient care becomes more important, the evolution of a test to detect resistance should follow.

Strategy B and C describe reflex testing for positive specimens. This is challenging to implement in hospital laboratories, because the second test will probably not be reimbursed, especially if the testing is done for public health purposes

rather than patient care testing. Strategy C describes collecting a second specimen from the patient, a practice that is costly and logistically difficult to implement.

Participants agree that for each of the pathogens, industry, clinicians, hospital microbiologists and public health experts need to work together to monitor evolving antimicrobial resistance and determine when and how resistance testing can be incorporated into commercial CID platforms (Strategy A) or isolated and tested for susceptibility in hospital labs. In the meantime, participants agree that CDC should find solutions for collecting resistance data needed to assess the public health threat and implement prevention measures if new or changing resistance develops.

**Moving Forward.** Key groups, represented by those at the meeting, can have an impact on collecting public health data in a culture-independent diagnostics era. First steps may include:

- Industry – Based upon clinical and public health needs, work to incorporate antimicrobial resistance detection methods into culture-independent diagnostic tests.
- Professional Societies and CDC – Monitor the uptake of culture-independent diagnostics and communicate clinical and public health needs for antimicrobial resistance data to industry.
- CDC – Continue to gather and expand surveillance for pathogens of public health importance affected by culture-independent diagnostics.
- CDC – Pilot reflex culture and susceptibility testing of fecal specimens that test positive for enteric pathogens using CID.

**Table 1. Antimicrobial susceptibility data needs for pathogens commonly detected using culture-independent diagnostics.**

Pathogen	Antimicrobial or Susceptibility Data Needs for Patient Care and Public Health
<i>Salmonella</i>	Data are needed for patient care if the infection is serious or the patient is at risk for developing a serious infection. Multi-drug resistant <i>Salmonella</i> are increasingly common; therefore, AR surveillance data are needed to assess the impact of antibiotic use in animals has on human health. These data are also used to assess the correlation between genotypic detection of resistance and phenotypic susceptibility methods.
<i>Shigella</i>	Data are increasingly important for patient care because new resistance to drugs like azithromycin is making empiric treatment decisions very challenging. It is important that hospital laboratories be able to isolate <i>Shigella</i> and test for antibiotic susceptibility or for resistance markers. More testing is needed in the public health realm to look for new resistance and to assess the correlation between genotypic detection of resistance and phenotypic susceptibility methods.
Pathogenic <i>E. coli</i>	Antibiotics are rarely used to treat infections and antibiotic resistance is still low so data are not needed for patient care at this time. Surveillance for resistance continues in the public health sector to monitor for any concerning changes.
<i>Campylobacter</i>	With increasing resistance in <i>Campylobacter</i> spp., resistance testing for patient management issues is becoming more important and culture-independent tests for resistance can be helpful. More testing is needed in the public health realm to look for new resistance and to assess the correlation between genotypic detection of resistance and phenotypic susceptibility methods.
<i>Neisseria gonorrhoeae</i>	Currently, the only testing for antimicrobial resistance or susceptibility occurs in public health surveillance programs. With increasing resistance, the need for resistance data for patient care will increase. Increased occurrence of highly resistant strains, like those seen outside of the U.S., could accelerate the need for routine testing in healthcare settings. Commercial assays that can detect resistant markers or test for antimicrobial susceptibility would help to slow this growing AR threat.
<i>Mycobacterium tuberculosis</i>	With increasing resistance, the combination of rapid molecular testing for resistance determinants and culture-based phenotypic antimicrobial susceptibility testing are essential for patient care. Rapid molecular tests results are used to guide early treatment decisions but not sufficient to detect all types of resistance, so culture-based methods are still required to guide definitive therapeutic decisions.

## SUMMARY OF ACTIONS TO OPTIMIZE THE USE OF DIAGNOSTICS

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Based on attendee input at the AR Diagnostics meeting, the following activities are offered for consideration to the groups identified to ensure that current diagnostics are used appropriately and that next generation diagnostics are optimized as they come to market.

### **Opportunities to help with innovation and uptake of diagnostics to improve patient care and public health:**

1. Industry and professional societies should expand educational efforts to promote the clinical, public health and/or economic impact of new diagnostics to include doctors as well as laboratorians.
2. Industry and public health should work together to conduct utilization trials that assess the clinical, public health and economic impact of using a diagnostic.\*
3. Where diagnostics are most important for controlling transmission, industry and public health should conduct clinical trials to assess the public health and economic impact of infection control diagnostics.\*
4. Industry and public health should conduct studies to assess the microbiome status as a risk factor for transmission. Use these studies to evaluate prototype diagnostics.\*
5. CDC and FDA should expand, update and improve the FDA-CDC AR Isolate Bank to support industry test development.\*
6. Payers should consider incorporating diagnostic testing as condition of reimbursement when there is a clear benefit of testing, especially when there may be an economic disincentive for testing (i.e., the antibiotic costs less).

### **Opportunities to ensure proper implementation of tests we have today and new tests coming to market:**

7. Based upon clinical and public health needs, industry should work to incorporate antimicrobial resistance detection methods into culture-independent diagnostic tests.
8. Professional societies, public health and standards setting organizations should proactively coordinate the development of educational materials, guidance and standards for implementation of new diagnostics; ensure that audience-specific materials are developed (e.g., for providers or laboratorians); establish relevant liaisons or representatives on the appropriate committee for each organization; and ensure materials include “best practice” recommendations for reporting results.\*
9. Professional societies and public health should work together to develop or update treatment guidelines that include best practices for diagnostic testing.\*
10. Professional societies and CDC should monitor the uptake of culture-independent diagnostics and communicate clinical and public health needs for antimicrobial resistance data to industry.\*



11. Where infection control testing is needed to prevent transmission of resistant pathogens, CDC should leverage public health laboratory capacity to ensure state prevention programs have access to testing.\*
12. CDC should expand surveillance for pathogens of public health importance affected by culture-independent diagnostics.\*
13. CDC should pilot reflex culture for *Salmonella* CID-positive specimens. Isolates recovered can be tested for antimicrobial susceptibility, presence of resistance mechanisms, and typed to improve detections of outbreaks.\*