TB Drug-Susceptibility Testing

Expert Panel Meeting
Summary Report

December 12-13, 2007
Atlanta, GA

This report was produced in cooperation with the Centers for Disease Control and Prevention.
The Association of Public Health Laboratories (APHL) is a national non-profit dedicated to working with members to strengthen laboratories with a public health mandate. By promoting effective programs and public policy, APHL strives to provide public health laboratories with the resources and infrastructure needed to protect the health of US resident and to prevent an control disease globally.

The TB Susceptibility Testing Expert Panel meeting and report was supported under Cooperative Agreement #U66/CCU303019 between the Centers for Disease Control and Prevention and the Association of Public Health Laboratories.
Introduction

The role of the laboratory in the management of tuberculosis (TB) has been greatly underestimated in the past and is still not fully appreciated in the medical community (1). Following a resurgence of TB and the emergence of drug-resistant TB in the United States (US) in the early 1990s, investments in public health TB laboratory services resulted in more rapid detection of new cases and drug resistance. These efforts contributed to an overall decline in the incidence of TB in the US and the decrease in drug-resistant TB. However, these successes are threatened by a 14-year spell of reduced and stagnant federal funding for public health TB laboratories, resulting in a substantial decline in both real and inflation-adjusted dollars (2).

The World Health Organization (WHO) estimates 9.2 million new TB cases in 2006--7.4 million occurring in Asia and sub-Saharan Africa. A total of 1.2 million people died of TB, including 200,000 patients infected with HIV (3). Although the incidence of TB in the US remains low (approximately 13,300 cases in 2007), foreign-born persons and racial/ethnic minority populations are disproportionately affected. In 2006, the TB rate among foreign-born persons in the US was 9.5 times that of U.S.-born persons (4). Worldwide, drug resistance surveys and ongoing surveillance efforts reveal that drug-resistant TB is geographically widespread (3). However, the true number of drug-resistant TB patients is likely underestimated in many settings due to insufficient laboratory capacity and policies to accurately and promptly detect drug-resistant TB patients.

Multidrug-resistant TB (MDR TB) has become a serious threat to global TB control as a result of the difficulties in diagnosis and treatment and the associated high cost to TB control programs. Documented transmission of MDR TB to vulnerable populations and in high-burden HIV settings compounds the problem. The emergence of extensively drug-resistant TB (XDR TB)—with its poor treatment outcomes, extraordinarily high mortality in HIV-infected patients and potential to spread widely—has alarmed public health officials. XDR TB is a potentially untreatable epidemic that could derail recent advances in global TB control.

In May 2007, an international traveler was reported to have drug-resistant tuberculosis based on laboratory testing performed at the Centers for Disease Control and Prevention (CDC). This resulted in an international health scare and massive public health response. CDC’s laboratory found the TB bacteria to be resistant to both first-line and two important second-line TB medications, meeting the definition of XDR TB. On June 28, CDC was notified by physicians at National Jewish Hospital that drug-susceptibility tests performed in their laboratory on the TB bacteria obtained from the patient confirmed resistance to first-line TB medications, meeting the definition of MDR TB, but not resistant to the specific second-line TB medications, the resistance that defines XDR TB. Although the public health response for a traveler infected with MDR TB and XDR TB would be the same, this event raised many questions about the quality and validity of TB drug-susceptibility testing results performed in different laboratories.

It is well-documented that TB drug-susceptibility testing (DST) is one of the most difficult procedures to standardize in the mycobacteriology laboratory (5). The laboratory methods are complex and require significant technical proficiency to produce reliable, accurate results. In the course of evaluating a patient, specimens and isolates may be referred to multiple laboratories for
TB identification, first- and second-line DST, resulting in delays and occasional discrepant results. Discrepant results occur for many reasons, even in the most competent laboratories. In response to concerns about the validity and utility of TB DST, CDC and the Association of Public Health Laboratories (APHL) convened a two-day meeting of TB experts to discuss inherent challenges and propose solutions. The expert panel included representatives from clinical, national reference and public health laboratories, TB clinicians, APHL, the National TB Controllers Association, the American Society for Microbiology, Clinical and Laboratory Standards Institute (CLSI), WHO, and CDC.

Meeting Goals:

• Provide recommendations to update CLSI’s 2003 M24 standard on susceptibility testing for mycobacteria with an emphasis on second-line drug-susceptibility testing (SL-DST) practices.
• Develop national strategies to ensure rapid, comprehensive SL-DST in selected referral laboratories
• Review DST quality standards and proficiency testing programs and provide guidance on laboratory and program level practices to assure the accuracy of testing at all levels.
• Provide guidance on priorities for operational research to improve current practices and promote implementation of methods and algorithms for the rapid detection of drug resistance.

Highlights of the Panel’s Recommendations

• Develop a limited number of “centers of excellence” to provide comprehensive, rapid and accurate services. Offer fast track molecular detection of MDR TB from specimens of high risk patients at these sites.
• Incorporate the expert panel’s recommended revisions of the first- and second-line drug-susceptibility panels and algorithms into an updated CLSI standard.
• Encourage the numerous low volume laboratories (processing fewer than 50 isolates/year) to refer specimens or cultures to laboratories with demonstrated DST proficiency.
• Provide resources for collaborative multi-center research to establish reliable testing standards for second-line drugs, especially those prioritized for MDR TB treatment trials.
• Develop reproducible testing and clinical trial standards to acquire the data needed to create guidelines on the potential use of fluoroquinolones in first-line drug regimens.
• Develop standard guidelines for quality assurance, and establish appropriate proficiency testing panels for detecting MDR and XDR TB.
• Align US guidelines, where appropriate, with WHO DST recommendations, recognizing that many US DST recommendations are not applicable in resource poor settings.


Current Practices

Reliable laboratory TB DST enables clinicians to design effective multi-drug treatment regimens. Currently the American Thoracic Society recommends that DST with the primary (first-line) drugs isoniazid (INH), rifampin (RIF), ethambutol (EMB) and pyrazinamide (PZA) be performed on the initial isolate from all patients. All rifampin-resistant organisms—or organisms resistant to any two first-line drugs—are tested for susceptibility to secondary drugs including fluoroquinolones, amikacin, kanamycin and capreomycin. A complete second-line drug panel should be tested for all MDR-TB isolates (6).

A certain proportion of drug resistant bacteria exists in all populations of drug susceptible Mtb. Current methods for susceptibility testing of M. tuberculosis complex (MTBC) are based on proportion methods, which rely on a bacteriologic definition of drug resistance that was developed in recognition of the difficulties in defining clinical resistance for mycobacteria. These methods provide qualitative results of “susceptible” or “resistant,” defining resistance as growth of greater than 1% of an inoculum of bacterial cells in the presence of a “critical” concentration of the drug. The critical concentrations of drugs were established on an empiric basis and adopted by international convention. The critical concentration represents the lowest concentration of drug that inhibit 95% of “wild strains” of Mycobacterium tuberculosis (Mtb), and not inhibiting strains of Mtb isolated from patients unresponsive to therapy and considered resistant.

In the US, first-line DST (FL-DST) is generally performed using commercial broth systems, which provide more rapid results than the traditional agar proportion method. Some of these systems have FDA-cleared DST assays for isoniazid, rifampin, ethambutol, streptomycin and pyrazinamide (6). Second-line DST is generally performed using agar proportion. There are no FDA-cleared rapid broth methods for SL-DST. However, some laboratories do perform SL-DST with commercial broth systems following in-house verification of equivalency to agar proportion. Although CLSI has published some guidelines for standardizing the test procedure and selecting the panel of drugs to be tested, the technical challenges inherent in the testing methodology—such as mixed population of organisms with different rates of growth—contribute to variations in test results.

US Labs that perform TB testing

- Hospital and medical center laboratories (mycobacteriology is generally part of microbiology)
- Governmental public health laboratories
- Commercial and reference laboratories

Problems and concerns with the current practices

- **One Patient, Multiple Labs:** Most testing algorithms are based on referrals of specimens or isolates to reference level laboratories. Problems that can arise:
  - Mycobacteriology laboratory services are often piecemeal, dispersed among different facilities: smear, or smear and culture, may be performed in a hospital laboratory; positive samples are then transferred to a reference laboratory for
identification and DST. SL-DST, if needed, may be performed in another laboratory.

- Communication among laboratories may be inefficient.
- Communication with care-giver/TB program can be limited, especially as the testing moves further away from the original lab.

- **Inefficient use of rapid methods:** A laboratory may wait for the TB isolate to grow on solid media rather than perform DST directly from broth isolate.

- **Discordant results are not uncommon:** Although expected, the discordant results in DST testing contribute to a lack of confidence in test results.

- **Lack of confidence in test results contributes to delays:** Laboratorians are reluctant to report resistance prior to confirmation. CDC reports that 50% of the samples it receives for supplemental testing are more than 90 days old. The delay is often due to re-testing in the clinical or public health laboratory. Repeat testing may be necessary to confirm resistance to primary drugs; however, this should not delay the reflex to second-line testing.

- **Comprehensive External Quality Assessment (EQA) is lacking:** Currently CLIA-compliant proficiency testing panels are provided by the College of American Pathologists and voluntary quality assessment panels are available through the CDC Model Performance Evaluation Program. Both programs include only pan-susceptible or first-line mono-resistant organisms. No EQA is available for MDR TB or second-line drug resistance.

- **Expense is significant:** The total costs for performing DST are not well-defined or adequately funded.

- **Training and workforce shortages:** As with other esoteric, high-complexity laboratory testing, workforce shortages and the limited availability of hands-on training programs are problematic.

**Discordant results**

There are inherent limitations in the TB DST methods that can result in differences in inter- and intra-lab results. Factors contributing to the reproducibility challenges include:

- Bacterial population (isolate vs. subculture)
  - Re-testing may result in a false susceptible result if the isolate is repeatedly subcultured, as the slower-growing resistant population may be lost.

- Differential growth kinetics in the bacterial population

- Different inoculation methods (size, clumps)

- Different methods or media

- Methodology not standardized

- Cross-contamination

- Transcription or labeling errors

- Problem strains: some isolates are more difficult to grow

- Problem drugs

- Minimal Inhibitory Concentration (MIC) of drug for some isolates is close to the critical concentration
DST Recommendations
The expert panel developed recommendations for technical DST procedures, drug panels, proficiency standards, referral patterns and operational policy, as well as research needs. These recommendations will need further review in the larger TB diagnostic community prior to implementation.

Proficiency
• **Encouraging Experience:** Laboratories performing FL-DST should test a minimum of 50 patient isolates per year to maintain technical proficiency and also have a documented ability to detect drug-resistant strains. If a laboratory performing fewer than 50 patient tests per year chooses to perform DST, additional quality control or proficiency testing is necessary to ensure reliable results. Studies that evaluate the minimum test volumes required to maintain proficiency are needed to support testing recommendations.

• **Consolidating Specialized Testing:** CDC should establish national Centers of Excellence (Centers) to perform SL-DST. Due to the low prevalence of MDR/XDR TB in the US, this practice will ensure that laboratories are proficient in detecting resistance to second-line drugs, and will provide faster turn-around time for comprehensive DST testing.
  o **Selection Criteria:** The selection criteria for a laboratory to become a Center need to be established. Technical proficiency with DST and molecular assays, as well as national geographic distribution, should be considered.
  o **Outreach Capability:** A Center should have access to clinicians with TB expertise to help communicate the interpretation of results and any need for supplemental testing. A Center would have the opportunity to collaborate with the TB Regional Training and Medical Consultation Centers to educate clinicians and public health officials in the appropriate use and interpretation of DST.
  o **Financial Resources:** Establishing these centers will require sufficient financial resources to ensure that all national testing needs are met. These improvements cannot be accomplished by redirecting the currently limited federal support provided to public health laboratories. A study to determine the true costs of establishing and maintaining these Centers must be conducted. Adequate resources must then be identified prior to implementation.
  o **Research:** These Centers could evaluate and validate new tools (such as molecular methods) for detecting resistance markers, as well as refine existing practices.
  o **International Role:** Potentially, a Center could provide international technical assistance or serve as a Supranational Reference Laboratory.

• **Improving Oversight:** Existing External Quality Assessment (EQA) and quality control programs need enhancement. Effective EQA, especially for MDR or second-line drug resistance, is not available; yet, ensuring accurate and prompt testing is vital.
  o CDC should help define criteria for FL- and SL-DST proficiency panels. Second-line drug mono-resistant strains may need to be developed to avoid the biosafety risks associated with MDR and XDR strains. Laboratories performing DST must accept MDR strains for proficiency testing.
  o Currently a pan-susceptible strain of Mtb is recommended for routine quality control. This may be inadequate in monitoring ability to detect drug resistance.
CDC should develop a library of well-characterized susceptible and resistant Mtb strains (with known molecular mutations, where possible) that can be used to test the proficiency of laboratories performing DST and to evaluate and validate new methods.

Referral Patterns

- **Assess Current Practices**: Both APHL and CDC have recommended that a comprehensive assessment of available TB laboratory services in each state be conducted to identify current practices and measure the capabilities and capacities of jurisdictional laboratory networks (2,7). This assessment should identify all public and private laboratories performing DST and all algorithms used for specimen and isolate testing and referral. CDC should provide funding for this assessment.

- **Proper Notification Needed**: Clinical laboratories should notify public health laboratories when specimens and/or isolates are being referred to other laboratories (including Centers of Excellence or CDC) to ensure proper tracking and appropriate reporting to clinicians and public health-TB Control authorities.

Testing Algorithms

- **Reflex to Simultaneous Testing**: Some experts recommended that any TB resistance to a first-line drug should automatically reflex to simultaneous confirmatory testing and SL-DST. This may be controversial, and additional research is needed to evaluate clinical utility and impact on laboratories.

- **Report Resistance Promptly**: First-line resistance should be promptly reported to clinicians even if confirmatory or repeat testing is being performed. The initial results would be labeled: “Preliminary Report. A reference laboratory will confirm results –or- Repeat testing is being performed. Due to the complex nature of TB DST, discordant results may occur.”

- **Fast-track High Risk Patients**: Some experts recommended that specimens from patients at risk of drug-resistant Mtb or in high-risk settings be “fast-tracked” to a laboratory capable of conducting the full spectrum of TB identification, as well as FL- and SL-DST, to avoid delays. Fast-track testing should include any available molecular tests for resistance markers. Criteria for fast-tracking should be incorporated in the new testing guidelines and should include persons with a history of previous TB treatment, foreign-borne patient, or contact with an MDR/XDR-TB case, as well as patients from high risk-settings (such as a school teacher or ICU nurse).

- **Refer Specimens**: Some experts recommended that all smear positive specimens be referred to a full service mycobacteriology laboratory for molecular testing to identify TB and for rapid access to DST.

- **Monitor Treatment Outcome**: Repeat testing—a currently recommended if a patient remains culture positive at 3 months—may be needed at 2 months or sooner if drug therapy appears to fail. Laboratorians should work with clinicians to provide supplemental testing sooner if needed to guide treatment decisions.

- **Train Routinely**: Training and education for DST laboratories and clinicians interpreting test results need to be available on a recurring basis.
Panels

- The **first-line panel** should always include: INH (low level), RIF, EMB and PZA.
  - It is increasingly difficult to predict PZA resistance based on historical data and geographic location, so this drug should be included in the standard FL-DST panel. Note that including PZA to the standard first-line panel for all patients doubles the cost of FL-DST.
  - Based on jurisdictional needs, high level INH may be tested in the first-line panel, or as part of a second-line drug panel if INH low level resistance is detected in FL-DST.

- The **second-line panel** should include ALL recommended second-line drugs, following CLSI method and drug concentration recommendations.
  - Cycloserine testing is not recommended due to reproducibility issues.
  - Fluoroquinolones hold promise as possible first-line regimens in the near future, but currently there is scarce data and lack of agreement on testing standards and reproducibility. Further research is needed to establish standardized, reproducible methods and drug concentrations for detecting fluoroquinolone resistance in Mtb.

Methods

- **Resolve Known Problems**: Becton-Dickenson should be required to resolve MGIT broth to broth DST inoculation problems and update the FDA-cleared product insert with new technical procedures.

- **Improve Technical Guidance**: More detailed technical guidance for SL-DST agar proportion and broth methods should be developed and made available to laboratories. Guidelines should address proper use of solvents in preparing drug solutions and standardized, model CLIA-compliant verification criteria for SL-DST in commercial broth systems. Where possible, the guideline should be included in updates to the CLSI M24 document.

- **Study MIC Benefits**: Currently, testing of multiple concentrations of drugs to determine the minimum inhibitory concentration (MIC) is not recommended for Mtb due to a lack of standardized procedures and clinical correlation. Some laboratories do perform MIC testing to provide supplemental information to physicians, especially for patients unresponsive to therapy. Further studies are needed to determine the clinical utility of MIC testing, and to establish standardized procedures and interpretive criteria for the laboratory, clinicians and public health-TB Control.

- **Improve Drug Information**: The stability of second-line drug stock solutions and media is not well understood. Additional research is necessary.

- **Align Internationally**: To the extent possible, technical guidance for SL-DST should align with the WHO technical guidelines currently in development.

Resolving Discrepancies

- **Guidelines for Discordant Result Interpretation**: CDC and its partners should explain testing discordance challenges to clinicians and laboratorians through the development of guidelines. This information would help laboratories evaluate whether discordant results came from inherent method variability or quality issues; and physicians understand the limitations of the test methods and select appropriate treatment regimens.
Discordant Strain Collection: CDC should develop a program to collect discordant strains to support a systematic evaluation of the scope of problems that contribute to discrepant results, and develop solutions where possible. Research is needed to evaluate the variability among methods and among laboratories, as well as to identify the advantages and challenges of broth-based or molecular methods.

Costs

Lab Capacity, Capability Assessment: As previously described, CDC should provide the resources to support a comprehensive assessment of available TB laboratory services to fill gaps in our knowledge about the capabilities and capacities of laboratories and networks in every jurisdiction.

Cost Assessment: Both APHL and CDC have recommended that an assessment of the true costs of TB laboratory services in the US be performed (2,7). This assessment should consider all payment sources (federal, state and private) to justify a base level of funding necessary to support these services. CDC should provide the resources to support this assessment.

Establishing Centers of Excellence: A study should be conducted to determine the true costs of establishing and maintaining the Centers of Excellence for SL-DST. Adequate resources must be then identified prior to implementation.

Packaging, Shipping: To encourage effective referral patterns, costs for packaging and shipping specimens and isolates in compliance with federal and international hazardous materials shipping regulations must be considered and properly funded.

Improved Services: Implementing all new testing guidelines will require additional resources for laboratories. For example, including PZA in the standard first-line panel for all patients doubles the cost of FL-DST. Federal funding for public health laboratories and standards for the reimbursement of clinical laboratories/hospitals from third-party payers are needed.

Training

To enhance the impact of laboratory testing on TB case detection and control, standardized training programs should be established to inform:

- clinicians and public health officials of the TB systems approach, optimal specimen referral patterns, testing algorithms, interpretation of results, and reasons for discrepant results among and within laboratories, and
- laboratorians of the TB systems approach, optimal specimen referral patterns, standardized testing methods and algorithms, quality assurance procedures, interpretation of results and reasons for discrepant results among and within laboratories.

Research

Research is needed to improve the quality, reproducibility and clinical utility of TB DST.

Technical Research Opportunities

- Development and evaluation of methods for rapid detection of resistance markers.
- Role of molecular methods to detect primary resistance and in treatment failures.
• Testing standards for the higher ethambutol hydrochloride (higher concentration) to address correlation with clinical efficacy, develop interpretative guidance, and establish the role of MIC testing.

Operational Research Opportunities
• Correlation of the laboratory’s proficiency at detecting resistance with the number of tests performed
• Assessment of current laboratory practices and referral strategies to develop optimal strategies to improve TB detection and DST turn-around times.

Clinical Research Opportunities
• Clinical correlation of in-vitro DST results with treatment outcomes
• Clinical utility of testing two concentrations of INH
• Standardized, reproducible methods and drug concentrations for detecting fluoroquinolone resistance in Mtb.
• Utility of monitoring serum drug levels in patient management
• Clinical utility of MIC testing; establishment of standardized procedures and interpretive criteria for laboratory and clinicians.
References:


Appendices

Appendix 1: Agenda
Appendix 2: Participant List
Day 1: Wednesday, December 12

8:30-9:00 am     Breakfast

9:00-9:30 am     Welcome and Introductions
   - CDC Welcome (Terence Chorba, Associate Director for Science-NCHHSTP; John Ridderhof, Associate Director for Laboratory Science-NCPTDCID)
   - Renewed Interest in Drug Susceptibility Testing (DST)
   - Purpose of this Meeting
   - Meeting Objectives
   - Expectations for Meeting and Product Goals

9:30-10:30 am    Domestic TB DST Overview
   - Current US Practices (Ridderhof)
     - MPEP data
   - Drug Susceptibility Testing Methodology (Metchock)
     - Current Practices
     - In the Pipeline
   - Q & A for Clarification of Information

10:30-10:45 am   Break

10:45-11:45 am   Clinical Laboratory Standards Institute (CLSI) Update (Woods)
   - Highlights of CLSI M24 standards
   - Future Plans for Document
   - Impact of Standards on Public Health Practice
   - Q & A for Clarification of Information

11:45 am-12:30 pm Lunch (Working lunch to continue discussions)

12:30-1:30 pm    Global TB DST Overview (Weyer)
   - Overview of WHO Policy Guidance on DST of Second-Line Drugs
   - International Drug Susceptibility Testing Methodology
     - Current Practices
     - In the Pipeline
   - The Future of Drug Susceptibility Testing
   - Stop TB Partnership Goals
   - Q & A for Clarification of Information
1:30-2:00 pm  Identifying Technical Issues Related to DST (Group Brainstorm)
   o  Examples include:
      ▪  Methodology – Broth vs. Agar Proportion
      ▪  Reporting of Results
      ▪  Variability of Results
      ▪  Use of Rapid Methods (i.e. molecular)
      ▪  Research Gaps
      ▪  Panels for First- and Second-Line Drugs
      ▪  Other Areas

2:00-3:00 pm  Addressing Technical Issues within Scope of Meeting
   o  Clarifying Role of Scope of This Expert Panel
      ▪  Identifying Knowledge Gaps
      ▪  Identifying Recommended Actions
   o  Selection of Priority Areas

3:00-3:15pm  Break

3:15-4:30 pm  Addressing Technical Issues within Scope of Meeting (continued)

4:30-5:00 pm  Technical (Day 1) Wrap-up
Day 2: Thursday, December 13

8:30-9:00 am  Breakfast

9:00-9:15 am  Opening Remarks
  o Framing Technical Discussions
  o Purpose of Day 2
    ▪ Discussion of Programmatic Issues

9:15-10:15 am  Specimen Flow from TB ID to DST Result to Reporting
  9:15-9:45 am  Ideal DST Algorithms (Group Brainstorm)
  9:45-10:15 am  Reality Check – What is possible?

10:15-10:30 am  Break

10:30am-1:15pm  Building the Right Systems

10:30-11:15 am  Who Should be Performing DST?
  o First-Line DST
  o Second-Line DST
  o Knowledge Gaps and Research Needs

11:15am-Noon  Operational Issues with Referral of Specimens
  o To and From Clinical, Commercial, and Public Health Laboratories, and CDC
  o Impact on Turnaround Times
  o Knowledge Gaps and Research Needs

Noon-12:30 pm  Lunch

12:30-1:15 pm  Assessing Proficiency/Quality Systems
  o Susceptibility and Reporting Issues
  o Knowledge Gaps and Research Needs

1:15-2:45 pm  Next Steps
  o Prioritizing Research Needs to Fill Knowledge Gaps
    ▪ Technical
    ▪ Programmatic
  o Guidelines Requirements
    ▪ Technical
    ▪ Programmatic
  o Action Steps Required Moving Forward

2:45-3:00 pm  Closing Remarks
John Bernardo, MD
Boston University School of Medicine

Henry M. Blumberg, MD
Emory University School of Medicine

Kenneth Castro, MD
Centers for Disease Control

Terence Chorba, MD, MA, MPH, MPA, FACP
Centers for Disease Control and Prevention

Edward P. Desmond, PhD
Microbial Diseases Laboratory
California Dept. of Public Health

Frances P. Downes, DrPH
Michigan Public Health Laboratory

Lauren Grosso, MSPH
Association of Public Health Laboratories

Bruce A. Hanna, PhD
NYU School of Medicine

Leonid Heifets, MD, PhD
National Jewish Medical Research Center

Rosemary Humes, MS, MT(ASCP)SM
Association of Public Health Laboratories

Kenneth Jost Jr., MT(ASCP)
Laboratory Services Section
Texas Dept. of State Health Services

Philip LoBue, MD, FACP, FCCP
Centers for Disease Control and Prevention

Beverly Metchock, DrPH
Centers for Disease Control and Prevention

Bonnie Plikaytis, MS
Centers for Disease Control and Prevention

John Ridderhof, DrPH
Centers for Disease Control and Prevention

Barbara Seaworth, MD
Heartland National TB Center

Susan E. Sharp, PhD
American Society for Microbiology

Angela M. Starks, PhD
Centers for Disease Control and Prevention

Stephen Suffin, MD
Quest Diagnostics

Anthony Tran, MPH, MT(ASCP)
Association of Public Health Laboratories

Karin Weyer, DSc
World Health Organization

Gail Woods, MD
University of Arkansas Medical Sciences