



COMMITTEE DISCUSSION

**Impact of Rapid and Molecular Tests
for Infectious Disease Agents
on Public Health**



Workgroup Considerations

- Rapid and Molecular Testing: Now and in the Future
- Identifying Public Health Gaps and Challenges
- Assuring Quality and Maximizing Impact on Public Health



Rapid and Molecular Testing: Now and in the Future

- **What are the advantages and disadvantages of rapid and molecular tests for infectious disease?**
- **What is the current status and where is rapid testing for infectious disease agents heading in the future?**
 - What infectious agents are currently routinely identified using rapid or molecular tests?
 - What additional agents of PH significance are on the horizon?
 - Is there new technology that may be available soon that could drastically change laboratory testing?



Advantages of Rapid and Molecular Testing

- Reduced turnaround time in less traditional settings
- Lowered personnel qualifications needed for simple tests
- Rapid identification of an infectious agent improves patient care:
 - Sexually transmitted disease testing provides a rapid diagnosis while the patient is available for treatment
 - Rapid influenza tests may be useful because the physician can avoid prescribing antibiotics if the test is positive
- Rapid identification of an infectious agent can lead to more accurate reimbursement



Disadvantages of Rapid and Molecular Testing

- Lack of communication between physician office labs (POLs) and PH agencies:
 - ❑ Physicians are less inclined to report to PH if they do not get feedback
 - ❑ Costs associated with packing and shipping specimens to PH laboratories is a barrier
 - ❑ State-to-state variability in reporting requirements is confusing



Disadvantages of Rapid and Molecular Testing

- Rapid test site issues:
 - ❑ Performance specifications are not typically verified when introducing a waived test
 - ❑ Proficiency testing is not required for waived methods
 - ❑ There can be problems with proper specimen collection (e.g. using the appropriate specimen collection device or collecting an adequate specimen)
 - ❑ Decisions to purchase test kits may be influenced solely by marketing efforts
 - ❑ Minimal to no training and staff turnover



Disadvantages of Rapid and Molecular Testing

- Interpretation and use of rapid or molecular tests:
 - There may be a lack of understanding of the impact of disease prevalence, predictive values, sensitivity and specificity of test methods on test results
 - Physicians need to read the product insert to understand the sensitivity, specificity, and recommendations for confirmatory testing of positive or negative results
 - Understanding the intended use of a test (i.e. a screening, diagnostic, or confirmatory test) has important implications in patient care or PH actions
 - Screening asymptomatic vs. symptomatic patients can affect result interpretation



Considerations for Future Rapid and Molecular Technology

- FDA should consider the PH impact in the waiver decision process
- As technology is simplified, more tests are being waived and are moving from traditional laboratory settings (where there are requirements for specimen collection and personnel) to POLs and other sites with less stringent quality requirements (waived laboratories)
- Molecular tests have the potential to be considered for waived status



Considerations for Future Rapid and Molecular Technology

- New tests are being developed for avian influenza and other respiratory viruses, agents of viral encephalitis, HIV, parasites (including blood parasites)
- Molecular tests using multiplex and panel testing for biothreats and select agents are being developed
- Technologic development often advances before there is a practical understanding of how to use and interpret test results



Rapid and Molecular Testing: Now and in the Future

COMMITTEE DISCUSSION



Identifying Public Health Gaps and Challenges

- Facility requirements
- Personnel education and training
- Understanding test interpretation and results
- Multiplex testing for more than one agent
- Unclear/inconsistent testing algorithms
- Lack of specimen/isolate for additional PH activities
- Cost or reimbursement for specimen referral
- PH reporting
- PH communications
- Biosafety/waste disposal



Identifying Public Health Gaps and Challenges: Facility Requirements

- **What are the facility needs for conducting rapid and molecular tests for infectious disease agents, particularly molecular methods?**
 - The complexity of the test (waived vs. nonwaived method) and test platform (open vs. closed system) determine the resources needed
 - There is a trend to do all tests in a single location



Identifying Public Health Gaps and Challenges: Personnel Education and Training

- **What type of education and training do testing personnel receive and what training is essential, especially for those conducting CLIA-waived rapid tests?**
 - Waived tests are considered to be so simple that no one pays attention to the written instructions. Instructions may be passed on by word of mouth and inadvertently changed over time
 - Training is not required before performing waived tests, except for rapid HIV tests that are cleared with FDA sales restrictions
 - Because waived testing does not have Federal regulatory oversight, some minimal education should be required



Identifying Public Health Gaps and Challenges: Understanding Test Interpretation and Results

- **Where are there gaps with respect to understanding prevalence and predictive values associated with a test?**
 - Sensitivity and specificity are not enough to evaluate a test's usefulness
 - This information needs to be translated into non-laboratory language, with examples and solutions, to help educate people
 - Physician's perspective:
 - Physicians deal with the individual patient, not populations
 - PH needs to communicate with physicians
 - Physicians understand the probability of disease but diagnosis also depends on clinical presentations



Identifying Public Health Gaps and Challenges: Multiplex Testing

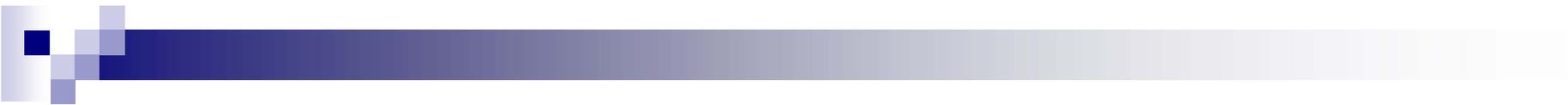
- **What are the challenges of multiplex testing for more than one agent?**
 - Physicians need guidelines for multiplex testing addressing:
 - Appropriate ordering
 - Clinical practice
 - Proper use of new test methods when clinical data are insufficient

 - Laboratory concerns are relevant in the case of:
 - Conflicting/multiple positive results
 - Positive results for tests not ordered
 - PH reporting of conflicting results



Identifying Public Health Gaps and Challenges: Multiplex Testing, cont.

- ❑ Reimbursement systems have not adapted to multiplex and reflex testing
- ❑ Tests may not be marketed in clinically appropriate combinations
- ❑ The sample for molecular methods may not be useful for reflex/confirmatory testing of an infectious disease agent
- ❑ Future tests may combine screening and confirmatory tests into the same test or multiplex product



Identifying Public Health Gaps and Challenges: Testing Algorithms

- **What challenges result from unclear or inconsistent testing algorithms?**
 - ❑ The efficacy of rapid molecular tests for some agents may be affected by demographic or epidemiologic limitations
 - ❑ Incorporating some tests into general panels could result in the inappropriate use of results and adversely affect patient care and overall test performance
 - ❑ The laboratory and the physician must understand the test result is only one piece of information used in making a diagnosis



Identifying Public Health Gaps and Challenges: Lack of Specimen/Isolate Availability

- **What challenges result from the lack of specimen or isolate availability for confirmatory testing, additional follow up tests (e.g., susceptibility testing), or epidemiological surveillance?**
 - Rapid or molecular tests may not require adequate specimen quantities for additional testing or may destroy the specimen, preventing its availability for other testing
 - Specimens need to be properly collected and transported rapidly to PH laboratories
 - Clinical isolates are essential to determine new circulating strains of viral influenza to aid in the selection of strains for future vaccine development



Identifying Public Health Gaps and Challenges: Lack of Specimen/Isolate Availability, cont.

- ❑ Epidemiologic outbreak investigations and subtyping for changes in serotype prevalence in populations may not be determined without isolates
- ❑ Laboratories may not be able to detect resistant organisms (i.e., MRSA, VISA, VRSA and *N. gonorrhoeae*) or identify emerging mechanisms of resistance
- ❑ It can be difficult or costly to maintain parallel cultures and perform molecular tests for PH purposes
- ❑ A waived laboratory cannot perform confirmatory cultures for waived rapid or molecular tests



Identifying Public Health Gaps and Challenges: Cost or Reimbursement for Specimen Referral

- **What is the impact of cost or reimbursement on specimen referral and PH reporting activities?**
 - Reimbursement often drives technology development and uptake by laboratories
 - Cost to POLs and clinical laboratories for referring specimens (packing, shipping, personnel training and certification) to PH laboratories is burdensome and is not reimbursed



Identifying Public Health Gaps and Challenges: PH Disease Reporting

- **What are the gaps and challenges of PH disease reporting?**
 - Requirements vary by state, adding to confusion
 - Adherence to PH reporting depends on who performs the test
 - Physicians expect the clinical laboratory to report diseases and may not be aware of their responsibility for PH disease reporting



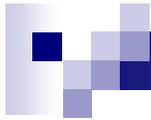
Identifying Public Health Gaps and Challenges: PH Communications

- **Where are there gaps in communicating with PH?**
 - Communication is needed between the physician, laboratory and PH
 - Finding the right person within the PH system can be challenging
 - Feedback to laboratories and physicians is inconsistent or minimal
 - PH lacks a standardized system for sharing electronic data and reports
 - PH laboratories may not be aware of the need for feedback to clinical laboratories and POC sites after these sites submit samples to PH



Identifying Public Health Gaps and Challenges: Biosafety and Waste Disposal

- **What are the biosafety and waste disposal concerns?**
 - As tests become simplified, biosafety and bloodborne pathogen awareness diminishes
 - Since physicians contact and treat patients, they may not always consider the potentially infectious nature of samples for testing
 - Infectious potential when using some POC tests is unclear or unknown



Identifying Public Health Gaps and Challenges

COMMITTEE DISCUSSION



Assuring Quality and Maximizing Impact on Public Health

- **What are some ways to address challenges or fill gaps in PH services?**
 - ❑ Personnel education and training
 - ❑ Correct interpretation and reporting of results
 - ❑ Unclear/inconsistent testing algorithms
 - ❑ Lack of specimen or isolate availability
 - ❑ Knowledge/awareness of PH disease reporting requirements
 - ❑ Improve communication using information technology
 - ❑ Manufacturers of test systems and specimen collection devices



Addressing Challenges or Filling Gaps: Personnel Education and Training

- Based on practice research, education is not the best way to improve quality
- Behavioral changes (forced functions) could be addressed using incentive-based, system changes and regulatory options
- The product insert should be an essential element in providing personnel training
- POC testing sites would benefit from learning about PH issues



Addressing Challenges or Filling Gaps: Correct Interpretation and Reporting of Results

- The PH system would benefit from a centralized web site listing appropriate codes for reportable diseases
- Guidelines should:
 - Define what is considered an “outbreak”
 - Be clear and readily accessible for primary care physicians
 - Include input from professional organizations that develop practice guidelines for physicians
 - Address pre- and post-analytic phases of test performance
 - Be updated when testing changes



Addressing Challenges or Filling Gaps: Correct Interpretation and Reporting, cont.

- Report information
 - Electronic reports are an opportunity to promote the appropriate use of a rapid/molecular test result
 - Electronic reports could incorporate educational links



Addressing Challenges or Filling Gaps: Clarification of Testing Algorithms

- Algorithms should be based on science rather than being defined by reimbursement
- Encourage physicians to change or comply with appropriate algorithms by demonstrating patient benefits



Addressing Challenges or Filling Gaps: Lack of Specimen or Isolate Availability for Additional Testing or Epidemiologic Surveillance

- Approaches to encourage collection of additional samples should be both incentive-based and compulsory (regulatory or certifying agency checklist questions/requirements)
- A mechanism for reimbursement of specimen transport to PH laboratories should be developed because clinical laboratories may be the first to receive outbreak specimens



Addressing Challenges or Filling Gaps: Knowledge and Awareness of PH Disease Reporting Requirements

- Use the product insert to promote reporting information
- Provide PH information (including MMWR reprints and Infectious Diseases Society of America guidelines) with rapid test kits for educational purposes
- PH outreach should form partnerships with manufacturers to reach varying types of test sites



Addressing Challenges or Filling Gaps: Knowledge and Awareness of PH Disease Reporting Requirements, cont.

- A centralized web site, such as the Council of State and Territorial Epidemiologists, should be developed to access information for each state:
 - Define what is reportable – confirmed vs. suspect cases
 - Case definitions could change with new methodologies
- Legislation is needed to fund the incentives for:
 - Specimen collection and requested data
 - Reporting mandated by states
 - Expanding sentinel laboratory networks at the national and state levels



Addressing Challenges or Filling Gaps: Improve Communication Using Information Technology

- Information needs to flow in all directions:
 - Laboratories and physicians need to provide information and specimens to the PH laboratories
 - PH laboratories need to provide feedback to the referring laboratories and physicians



Addressing Challenges or Filling Gaps: Improve Communication, cont.

- The PH system needs to take a pro-active approach to establish a nationwide, equal-state commitment to a system that includes:
 - Establishing contacts with POC sites
 - Minimum required information for reportable laboratory tests
 - Collaboration with all types of testing sites in electronic data reporting
 - Consistent data reporting (e.g. Laboratory Information Management System)
 - Guidance on facilities, biosafety and waste disposal
 - Extending the Laboratory Response Network (LRN) to include other infectious agents and reach more laboratories



Addressing Challenges or Filling Gaps: Improve Communication, cont.

- To reach and educate physicians, work through medical or other professional societies offering continuing education credits
- Seek assistance from clinical and reference laboratories. Large reference laboratories have unparalleled specimen transport and data exchange systems and need to be included in addressing PH issues
- PH laboratories should work with clinical laboratories to determine what is needed for a workable reporting system (The LRN is a successful model)



Addressing Challenges or Filling Gaps: Manufacturers' Contributions to PH Needs

- Manufacturers are willing to partner to produce safer, better tests
- When developing benchtop tests, take into consideration the relative risk of disease transmission
- As new tests are developed for use in non-traditional sites, include appropriate controls for all phases of the testing process



Addressing Challenges or Filling Gaps: Manufacturers' Contributions to PH Needs

- Consider a test design that incorporates a component for extra specimen collection for follow-up or referral testing
- Include information about submitting samples to PH laboratories in labeling
- Manufacturers and distributors have an opportunity to influence laboratory practices through information campaigns because of their access to a wide variety of testing sites
- Promote appropriate testing to the public



**Assuring Quality and Maximizing
Impact on Public Health:
Addressing Challenges or Filling Gaps in
Public Health Services**

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