



# **CLIAC Workgroup Report**

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

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## Workgroup Members

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# Background

- **February 2006 CLIA discussed**
  - Increased use of rapid, direct testing in physician offices and other point-of-care sites
  - Expanded use of molecular testing in a variety of laboratories
  - Assuring quality of rapid and molecular testing
  
- **Concerns emerged about the impact on public health (PH)**
  - Users may not be aware that
    - Some rapid tests are screening tests and require confirmatory testing
    - PH disease reporting is required
  - Specimens or isolates may not be available for submission to PH



# CLIAC – February 2006

## Recommendations

- Form a Workgroup to include key stakeholders – CLIAC, clinical and PH laboratories, epidemiologists, industry and government
- Workgroup should address issues related to the impact of rapid testing technology on clinical laboratories, PH laboratories and epidemiology
- Present Workgroup findings at the February 2007 CLIAC meeting for Committee deliberations



# CLIAC Workgroup

## “Impact of Rapid and Molecular Tests for Infectious Disease Agents on Public Health”

### Workgroup charge:

- Surface key issues related to the impact of rapid and molecular technologies for infectious disease agents on PH and consider ways to maximize this impact by assuring:
  - Quality of testing when using these methodologies
  - Specimens are collected and maintained for confirmatory testing or epidemiologic surveillance
  - Required PH disease reporting is carried out



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

## Discussion Topics:

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

NOTE: The Workgroup defined **rapid tests** as waived or nonwaived point-of-care (POC) tests that can be performed in one hour or less.



## **Rapid and Molecular Testing: Now and in the Future**

- **What are the advantages and disadvantages of rapid and molecular tests for infectious diseases?**
- **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?



## Rapid and Molecular Testing: Now and in the Future

**Advantages** of rapid and molecular tests for infectious disease agents:

- 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



## Rapid and Molecular Testing: Now and in the Future, cont.

**Disadvantages** of rapid and molecular tests for infectious disease agents:

- 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



## Rapid and Molecular Testing: Now and in the Future, cont.

### Disadvantages, cont.

- 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



## Rapid and Molecular Testing: Now and in the Future, cont.

### Disadvantages, cont.

- 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



## **Rapid and Molecular Testing: Now and in the Future, cont.**

### **Considerations for future 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



## Rapid and Molecular Testing: Now and in the Future, cont.

### **Considerations for future technology, cont.:**

- 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



# Identifying Public Health Gaps and Challenges

## **Discussion topics**

- Facility requirements
- 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

- **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, cont.

- **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, cont.

- **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 the doctors
    - Physicians understand the probability of disease but diagnosis also depends on clinical presentations



## Identifying Public Health Gaps and Challenges, cont.

- **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, cont.

- **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, cont.

- **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, cont.

- **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 the destroy 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 and to aid in the selection of strains for future vaccine development



## Identifying Public Health Gaps and Challenges, cont..

- **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, cont.

### ■ Lack of specimen, 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
- Waived laboratories cannot perform confirmatory cultures for waived rapid or molecular tests



## Identifying Public Health Gaps and Challenges, cont.

- **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



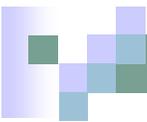
## Identifying Public Health Gaps and Challenges, cont.

- **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 laboratories may not be aware of the need for feedback to clinical laboratories and POC sites after these sites submit samples to PH
  - PH lacks a standardized system for sharing electronic data and reports



## Identifying Public Health Gaps and Challenges, cont.

- **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



## Assuring Quality and Maximizing Impact on Public Health

- **What are some ways to address challenges or fill gaps in PH services with respect to the following?**
  - 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
  - Facilities, biosafety and waste disposal
  - Improve communications using information technology
  - Manufacturers of test systems and specimen collection devices



## Addressing Challenges or Filling Gaps in Public Health Services

### ■ 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 in Public Health Services, cont.

- **Correct interpretation and reporting of results in different settings and test configurations**
  - The PH system would benefit from a centralized web site listing appropriate codes for reportable diseases
  
  - 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 in Public Health Services, cont.

- **Correct interpretation and reporting, cont.**
  - 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 in Public Health Services, cont.

- **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 in Public Health Services, cont.

- **Lack of specimen or isolate availability for additional testing or epidemiological surveillance**
  - Approaches to encourage collection of additional samples should be both incentive-based and compulsory (regulatory or certifying agency checklist questions/requirements)
  - A mechanism 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 in Public Health Services, cont.

- **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



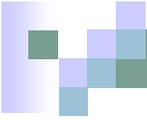
## Addressing Challenges or Filling Gaps in Public Health Services, cont.

- **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 in Public Health Services, cont.

- **What are some ways to improve communications among POC sites, clinical laboratories and PH laboratories, particularly considering 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 in Public Health Services, cont.

- **Improving 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
    - 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
    - Collaboration with all types of testing sites in electronic data reporting



## Addressing Challenges or Filling Gaps in Public Health Services, cont.

### ■ Improving 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 in Public Health Services, cont.

- **What are some ways test system or specimen collection manufacturers could contribute to meeting 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 in Public Health Services, cont.

- **Ways manufacturers can contribute, cont.**
  - 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