DELAWARE HEALTH AND SOCIAL SERVICES

Division of Public Health

Laboratory

DELAWARE LABORATOR

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MMWR-EVALUATION OF RAPID INFLUENZA DIAGNOSTIC TESTS

KEY MESSAGES PREPARED BY:
CDC JOINT INFORMATION COMMITTEE
PUBLIC HEALTH WORKFORCE

SUMMARY

The August 6, 2009 *Morbidity and Mortality Weekly Report* article, "Evaluation of Rapid Influenza Diagnostic Tests (RIDT) for Detection of Novel Influenza A (H1N1) Virus—United States, 2009" evaluates three commercially available rapid influenza diagnostic tests (RIDTs) for their ability to detect novel influenza A (H1N1). RIDTs from three companies were reviewed and results indicate that these tests can detect novel influenza A (H1N1) in respiratory specimens, but the overall sensitivities range from 40-69% meaning that many influenza infections will be missed. Given the lower sensitivities found with RIDTs compared to rapid reverse transcriptase-polymerase chain reaction (rt-PCR), decisions regarding treatment and further testing among patients with negative results from RIDT testing should be based upon clinician suspicion, underlying medical conditions, severity of illness, and risk for complications in those persons suspected of having novel H1N1 virus infection. Early treatment with influenza antiviral medications of persons infected with influenza who are at increased risk of influenza complications and those people hospitalized with suspected influenza is important to maximize benefit of treatment and to lessen the severity of illness.

POINTS FOR CONSIDERATION

- Rapid Influenza Diagnostic tests (RIDTs) are tests that detect influenza A or B antigens and can provide results within 15 minutes.
- In this study, RIDTs from three companies were reviewed for their ability to detect influenza A viral antigens in selected original clinical samples submitted to CDC that tested positive for novel influenza A (H1N1), seasonal influenza A (H3N2), or seasonal influenza A (H1N1) viruses.
  - Sixty-five (65) original clinical samples were used for testing. Of those, 45 were positive for novel influenza A (H1N1), five samples were positive for seasonal influenza A (H1N1), and 15 samples were positive for seasonal influenza A (H3N2) by DC rRT-PCR.
  - The study found that commonly used RIDTs are capable of detecting novel influenza A (H1N1) from respiratory samples containing high virus titers, but sensitivities declined substantially as cycle threshold (Ct*) values increase.

*Cycle threshold (Ct) values are indicators of the amount of virus in a sample. Lower cycle threshold values indicate higher amounts of viral material in the specimen.

- The overall sensitivity of RIDTs to detect

Continued, page 2

Inside this issue:

SPECIAL POINTS OF INTEREST

FRONT PAGE ARTICLE:

MMWR EVALUATION OF RAPID INFLUENZA DIAGNOSTIC TESTS

FLU SEASON RESULTS

Page 3

SYNOPSIS OF THE LABORATORY PREPAREDNESS ADVISORY COMMITTEE MEETING

Page 5

Evaluation of Rapid Influenza Testing, continued

novel influenza A (H1N1) was less than 70% among all samples tested, with a range from 40-69%.

- The overall sensitivity was determined by the percentage of test positive samples versus all clinical materials positive for this virus by rRT-PCR.
- Overall sensitivity to detect novel influenza A (H1N1) was 69% for QuickVue A+B; 49% for Directigen EZ; and 40% for BinaxNOW.

- All RIDTs performed well compared to rRT-PCR for samples with cycle threshold (Ct)* values less than 20 with 89-100% sensitivity.
  - Sensitivities of the RIDTs was highest among specimens with Ct values of <20.
  - Among samples with Ct values of 20 or greater, the sensitivity declined substantially.
- Given the lower sensitivity of RIDTs compared to other assays, such as rRT-PCR, clinicians should understand that a negative result by RIDT does not exclude influenza virus infection.
- Decisions regarding treatment and further testing among patients with negative results from RIDT testing should be based upon clinician suspicion, underlying medical condition, severity of illness, and risk for complications in those persons suspected of having novel H1N1 virus infection.
- The findings from this study are similar with other recent studies, which reported that the sensitivity of some RIDTs to detect novel influenza A (H1N1) in clinical specimens ranged from 10-51% compared with rRT-PCR.
- CDC's guidance on interpretation of RIDTs for testing of patients with suspected novel H1n1 virus infection is available at http://www.cdc.gov/h1n1flu/guidance/rapid_testing.htm

BACKGROUND ON RIDTs

- RIDTs may be referred to as "point-of-care" tests because they provide results quickly enough to inform clinical decisions during a patient's office visit.
  - A positive test means that influenza infection is likely and can inform influenza treatment decisions by providing influenza type (A vs. B).
- RIDTs vary in their capacities to detect influenza. For instance some can detect and distinguish between influenza A and B, others can detect but not distinguish between influenza A and B, and some can only detect influenza A.
- RIDTs do not distinguish between influenza A subtypes and cannot provide information about antiviral drug susceptibility.
- The sensitivities of RIDTs depend on multiple factors including virus type (A or B), subtype of influenza A, quality of specimen collection and handling, type of specimen collected, age of the patient, and time from illness onset to specimen collection.
- Due to the limited sensitivities of RIDTs to detect influenza, interpretation of the test results should be done with care as false negative results are common.

QUESTIONS & ANSWERS

What RIDTs were used for this study?

This study used the Inverness Medical BinaxNOW® Influenza A&B (Binax, Inc. Scarborough, Maine), Becton Dickinson Directigen™ EZ Flu A+B test (Becton, Dickinson and Company, Sparks, Maryland) and Quidel QuickVue® Influenza A+B (Quidel Corporation, San Diego, California).

How were the RIDTs chosen for this study?

The RIDTs used in the study were chosen as they are the three most widely used FDA-approved RIDTs in the United States at this time. Other RIDTs are currently being evaluated using the same methodology.

Are there plans to conduct further testing with more RIDTs and more specimens?

There are plans to test more novel H1N1 flu, seasonal H3N2 flu and seasonal H1N1 flu samples and negative samples. All three RIDTs tested for this study will be a part of the continuing evaluation. Additional FDA-approved RIDTs will also be included in this study.

What do the results of this study mean for clinicians using RIDTs to detect novel influenza A (H1N1)?

RIDTs can provide useful information that might impact patient care; however the tests have limitations. While the findings from this study indicate that RIDTs can detect novel influenza A (H1N1) in respiratory specimens, given the overall sensitivities found, many infections will be missed and false negatives may occur.

For instance, a negative RIDT result does not necessarily exclude influenza virus infection. For those patients that test negative by RIDT a diagnosis of influenza should still be considered if they have influenza-like symptoms. Decisions regarding treatment and further testing among patients with negative results from RIDT testing should be based upon clinician suspicion, underlying medical conditions, severity of illness, and risk for complications in those persons suspected of having novel H1N1 virus infection. Early treatment with influenza antiviral medications of persons infected with influenza who are at increased risk of complications and those people hospitalized with suspected influenza is important to maximize benefit of treatment and to lessen the severity of illness.

Flu Results from October 4 - November 30, 2009	
Total Number of sample tested	1,575
Results include the following:	
Equivocal due to low viral load	46
Equivocal; Sent to CDC for confirmation	11
Invalid results due to suboptimal specimen collection or specimen type	7
Nucleic Acid Detected; Positive for Influenza A and Influenza B	1
Nucleic Acid Detected; Positive for Influenza A:H1N1/swine-like	1,504
Nucleic Acid Detected; Positive for Influenza A; not swine-like; no further subtyping performed	5
Nucleic Acid Detected; Positive for Influenza B	1
Total	1,575

WHAT I DID FOR MY ENVIRONMENTAL LEADERSHIP ACADEMY PROJECT … OR THE LABORATORY CHEMICAL MANAGEMENT SYSTEM

TARA M. LYDICK, ANALYTICAL CHEMIST IV, B.S. CHEMISTRY, NR-EMT-B, NBFSPQ FIREFIGHTER II, FIRE OFFICER II, FIRE INSTRUCTOR II, DSFS FIELD INSTRUCTOR, DE BLS FIELD TRAINING OFFICER

During the summer and fall of 2009, the Department of Natural Resources & Environmental Control (DNREC) sponsored the inaugural class of the Environmental Leadership Academy (ELA). This ten-session program took thirty participants selected from DNREC and four from the Division of Public Health and utilized leadership training techniques developed and presented by the Dale Carnegie Training Institute. With homework assignments increasing in complexity, on the spot verbal reports, and the challenge of stepping outside your comfort zone, participants developed processes and people skills needed for every level of leadership. The academy culminated with each participant presenting/selling an implementation project designed to increase efficiency and provide a cost savings to the organization. The participants presented their projects to the leadership of DNREC and public health for evaluation and consideration. During February 2010, the class will reassemble to provide an update on the progress of each individual's implementation project.

Most of the projects were focused on very specific processes or areas. I initially struggled with what type of implementation project would be of most benefit to public health and the laboratory. I decided to build on the work begun in 2008 with the APHL-sponsored Delaware Laboratory System Assessment -- how could the state laboratory *system* become more than just an idea on paper? There are currently six separately functioning state laboratories: Delaware Public Health Laboratory, DNREC Division of Laboratory Sciences, Office of the Chief Medical Examiner (OCME) Forensic Sciences Laboratory, Delaware Department of Agriculture Laboratory groups, Delaware State Police Criminal Laboratory, and the Delaware Department of Transportation Materials & Research Laboratory. With the recent initiatives from the Governor's office and the involvement of each of the laboratories' leadership, a goal readily materialized: develop a system that could be interlinked between all six laboratories and their diverse services to reduce redundancy and increase personnel efficiency. I concentrated on a particular area of need across all laboratories: chemical management and safety.

Part of the implementation process and the Dale Carnegie leadership principles is developing customer buy-in by making a process that belongs to them. In this case, the customers are not just the leadership of the laboratories, but the staff working at the laboratory bench. These are the individuals who are faced with the day-to-day operational impact. Members of five of the six laboratories participated in multiple conference calls that defined the main areas of need for a consistent laboratory based chemical management system across the facilities. The group identified two main needs: 1) a physical asset management system for

Continued, page 4

Environmental Leadership Academy, con't

tracking chemical waste, managing Material Safety Data Sheets, tracking materials (inventory and ordering); and 2) a chemical training and collaboration program to provide a unified safety training program and encourage cross-laboratory coordination and cooperation. Using the green-light thinking model, the group sought solutions to the two needs utilizing the Dale Carnegie 10 step planning process. We distilled the three best solutions for the two needs, the advantages and disadvantages for each solution, and the resources needed for implementation (including a cost benefit analysis). The final product of this work was a 5-minute PowerPoint presentation to the leadership of DNREC and public health including the DNREC Cabinet Secretary and Director of Public Health.

Work on this project continued after the ending of the class. In a joint effort, Margaret Zimmerman (DNREC Analytical Chemist III) and I hosted the first Laboratory Technical Working Group for technical staff performing bench level analyses within the state laboratory system on October 11, 2009. Building on the framework from the implementation project, the meeting clarified three areas to begin laboratory cooperation (ColLABoration) and efficiency improvement. The group will continue expanding this work meeting again in the January – February 2010 timeframe and quarterly thereafter.

While a very demanding and challenging experience, I would heartily recommend the DNREC Environmental Leadership Academy and Dale Carnegie Training Institute to anyone involved with or desiring to participate in any type of leadership or supervisory role. But be prepared -- where else can you expect to dance like a flamingo, remember over 30 participants' names, perform tag-team interviewing and career discussion, and develop an implementation project potentially affecting the current laboratory view within the state?

MY SUMMER AT THE DELAWARE PUBLIC HEALTH LABORATORY

Sarah Beabout, University of Delaware-DPHL Summer 2009 Fellow

My summer at the Delaware Public Health Laboratory (DPHL) was a very enjoyable and worthwhile experience. I gained a lot of knowledge working with the employees at DHPL. Through the fellowship program between DPHL and the University of Delaware, I gained experience in another career option in the scientific field – working in the public health lab. I value the fact that I experienced a completely different career option. I observed and performed procedures in the microbiology department that as a medical technology student, I would never have experienced. These included pulse field gel electrophoresis, Chlamydia and Gonorrhea testing and working with bioterrorism organisms such as *Yersinia pestis* and *Bacillus anthracis*. I really enjoyed learning about pulse field gel electrophoresis and the numerous steps involved in running a gel to identify strains of Salmonella, Shigella and E.coli through their DNA bands. I found quantiferon fun to observe because I learned about enzyme-linked immunosorbent assays in school but never had the chance to perform the procedure. It was interesting to see another way to test for M. tuberculosis other than the PPD shot. High pressure liquid chromatography was also interesting because I had never been exposed to such a procedure involving mycolic acids. The graphs produced by the instrumentation were something I had never seen before.

I will take the experience and knowledge I gained from DPHL and pass it on to my fellow classmates and future students, so they too can appreciate all that is done at DPHL and consider the public health laboratory as a career path.

HAPPY NEW YEAR!!!

THE LABORATORY PREPAREDNESS ADVISORY COMMITTEE

MARION T. FOWLER, MT (ASCP)

The Laboratory Preparedness Advisory Committee (LPAC) met on September 10, 2009 at the Delaware Public Health Laboratory (DPHL). The meeting took place almost two months earlier than its regularly scheduled time to prepare for the upcoming flu season. Delaware Public Health officials and employees, DPH epidemiologists, sentinel laboratorians and other interested parties met to organize and coordinate the collection, courier pickup routes, testing and resulting of flu specimens. Review of last year's procedures yielded many helpful suggestions for improving communication between all laboratories, doctors and state personnel.

Cases of flu are usually in decline by spring; however, at the end of April 2009 testing for Influenza A, Swine A, Swine H1 and RNP (an indicator of the quality of the collection) continued with a large number of positive tests throughout the summer months.

Paula Eggers and Susan Shore, DPH epidemiologists, discussed the Division of Public Health policy for testing Delaware's citizens for seasonal flu, which now includes Novel H1N1. The policy states: "The Bureau of Epidemiology follows guidance from the Centers for Disease Control and Prevention (CDC) when making recommendations for influenza diagnostic testing. Most patients with uncomplicated influenza illness do not require testing for clinical management once influenza activity has been documented in the area. The patients who should be considered for testing are 1) hospitalized patients with suspected influenza and 2) patients for whom a diagnosis of influenza will help with decisions regarding clinical care, infection control, or management of close contacts. This includes persons who are at high risk for complications related to influenza. If testing is indicated, the Bureau of Epidemiology encourages physicians to send the testing to commercial laboratories. The only providers who may send samples to DPHL are those participating in the sentinel provider network surveillance program in cooperation with the Division of Public Health. An exception to this policy is possible if clusters of influenza illnesses are apparent in long term care facilities, schools, etc., If this were to occur, Epidemiology will coordinate with DPHL to have testing performed at the DPH laboratory."

Collection of flu specimens from patients not included in the above recommendations can be performed by physicians, walk-in medical units, etc., and the specimen sent out or referred to private reference laboratories for testing. FDA-approved flu testing is now offered by Quest (Focus) and several other commercial laboratories.

The World Health Organization (WHO) designated the first full week of October 2009 as the official start of this year's flu season at which time DPHL changed to a test algorithm that detects Influenza A, Novel H1N1 and Influenza B. The algorithm used over the spring and summer did not detect influenza B. The test algorithm is subject to change when new information is received from CDC and WHO.

Other issues discussed at the LPAC meeting included the Agents of Bioterrorism: Annual Sentinel Lab Update Workshop. The workshop will be a full day and will includes lectures and slideshows in the morning with emphasis on American Society of Microbiology (ASM) guidelines for the rule out or referral of a possible bioterrorism agent. The afternoon session will be a wet workshop utilizing attenuated and/or vaccine strains of bioterrorism agents. Tentative dates for this training are scheduled for April 29 and 30, 2010. New Delaware sentinel laboratory employees working in microbiology or other microbiologists who wish to review and update their knowledge of procedures, safety and use of the ASM guidelines are invited to attend.

The lab received the College of American Pathologists Laboratory Preparedness Exercise (CAP LPX) in June 2009. All of Delaware's sentinel laboratories participated in the exercise, followed the CAP directions properly and reported their results of "unable to rule out a bioterrorism agent" to DPHL. Once the sentinel laboratory notified DPHL of their results, they were directed to package and ship a simulated specimen according to the IATA guidelines.

www.dhss.delware.gov/dhss/dph/lab/labs.html

NEW!!

- *Information about Nasopharyngeal Sample Collection that includes videos and FAQs*
- *Laboratory Preparation for the 2009-2010 Influenza Season including algorithm and specimen collection kit instructions*
- *Evaluation of Rapid Influenza Diagnostic Tests*

EMPLOYEE NEWS

Tiffany Santoro joined the molecular virology lab at DPHL in the middle of the swine flu outbreak on October 26th. She came from the Hospital of the University of Pennsylvania where she worked for a number of years in the microbiology lab. A Pennsylvania native, this is not her first time living in Delaware. She received her Bachelors degree in Medical Technology at the University of Delaware. Some of her training was spent at Christiana and Kent General hospitals. Tiffany worked for several years as a medical technologist. In 2006 she obtained a double Masters degree in Biotechnology and Business from Macquarie University in Australia. She spent a year and a half in this country and was fortunate enough to travel all over that part of the world.

DPHL bids a fond farewell to Yvette Jackson who retired October 1, 2009 after over 30 years of service. Yvette provided excellent and much needed support services in the washroom and media preparation while serving as an analyst in water bacteriological testing and lending a helping hand whenever needed. While working at DPHL, she earned her Associates Degree in Human Services with a concentration in gerontology. Keeping busy during retirement, Yvette's goals are to continue working with seniors, others, devoting her time to her family and friends…and cheering for her Philadelphia Eagles. We'll miss you!

DELAWARE'S DIVISION OF PUBLIC HEALTH LABORATORY

Delaware Public Health Laboratory
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Built: 1990

Business Hours: 8 a.m. – 4:30 p.m.

Purpose: The Division of Public Health Laboratory currently offers consultation and laboratory services to state agencies, Delaware Health and Social Services and Division of Public Health programs including:

- HIV surveillance and prevention
- Immunization
- Lead
- Epidemiology
- Newborn Screening
- STD prevention
- TB Elimination
- Drinking water
- Preparedness

Karyl Rattay, MD, MS, FAAP, FACPM
Director, Delaware's Division of Public Health

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Christina Pleasanton, MS, Deputy Director, Delaware Public Health Laboratory

If you have questions regarding these articles or would like to receive a hard copy of this newsletter, contact the Delaware Public Health Laboratory at 302.223.1520.

To receive this newsletter by email, contact liz.moore@state.de.us.

"To Protect and Enhance the Health of the People of Delaware"

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