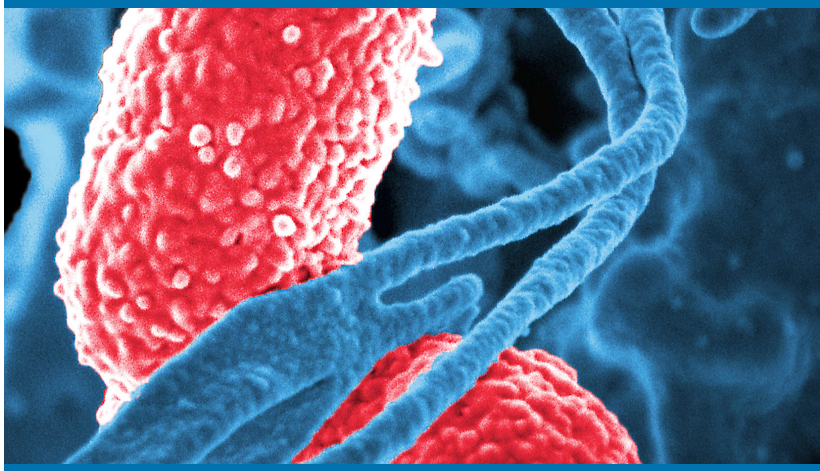
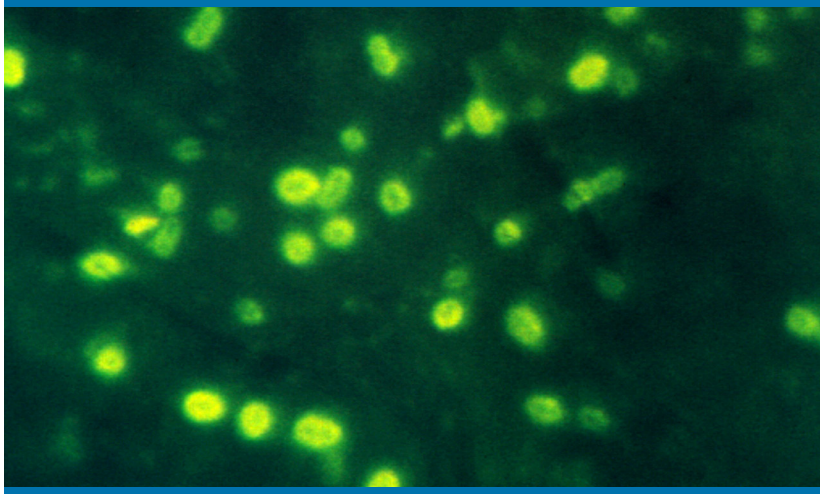
APHL/CDC Vaccine Preventable Disease Reference Centers

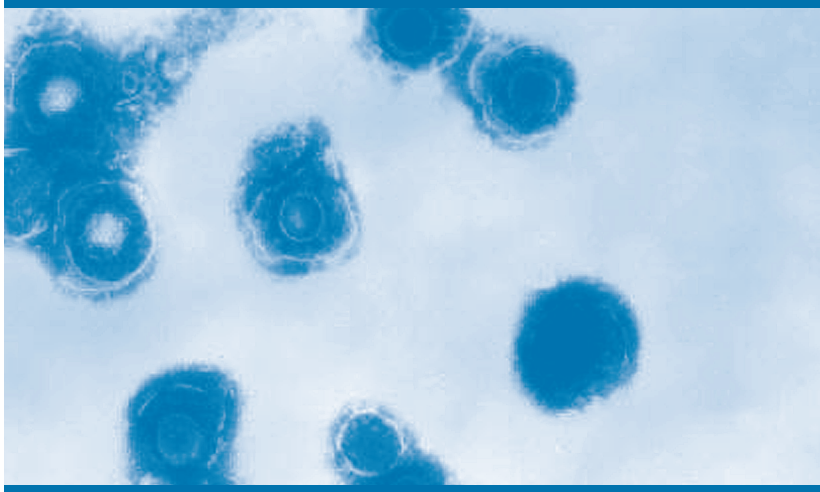
A Year in Review

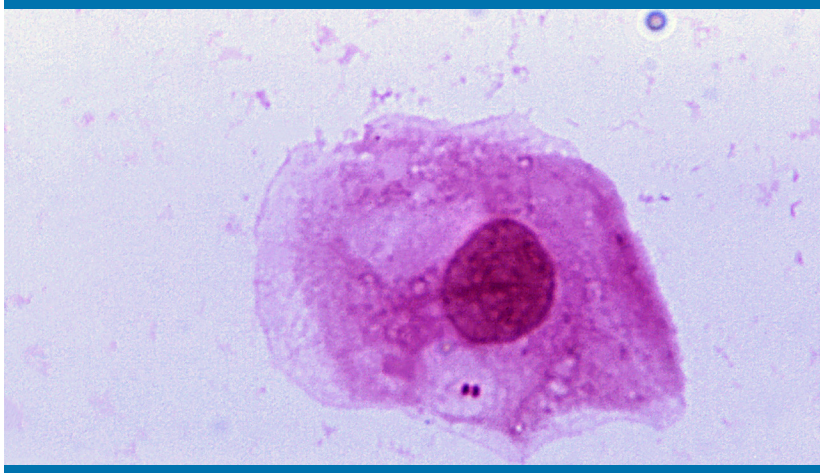
April 2013–June 2014

APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES®









Cover photos, from top:

A digitally-colorized scanning electron micrograph (SEM) depicts a blue-colored, human white blood cell interacting with two pink-colored, rod-shaped, multidrug-resistant (MDR) Klebsiella pneumoniae bacteria. Credit: David Dorward; PhD; National Institute of Allergy and Infectious Diseases (NIAID)

Photomicrograph of Haemophilus influenzae using immunofluorescence. Credit: CDC

Transmission electron micrograph of varicella-zoster virions from vesicle fluid of patient with chickenpox. Credit: CDC/Dr. Erskine Palmer

A photomicrograph of *Neisseria meningitidis* recovered from the urethra of an asymptomatic male; Magnified 1125X. Credit: CDC/James Volk

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National Center for Immunization and Respiratory Diseases (IP)
Office of Surveillance, Epidemiology and Laboratory Services (OSELS)
National Center for HIV, Viral Hepatitis, STDs and TB Prevention (PS)
National Center for Zoonotic, Vector-borne, and Enteric Diseases (CK)
National Center for Environmental Health (NCEH)
Coordinating Office for Terrorism Preparedness and Emergency Response (CTPER)

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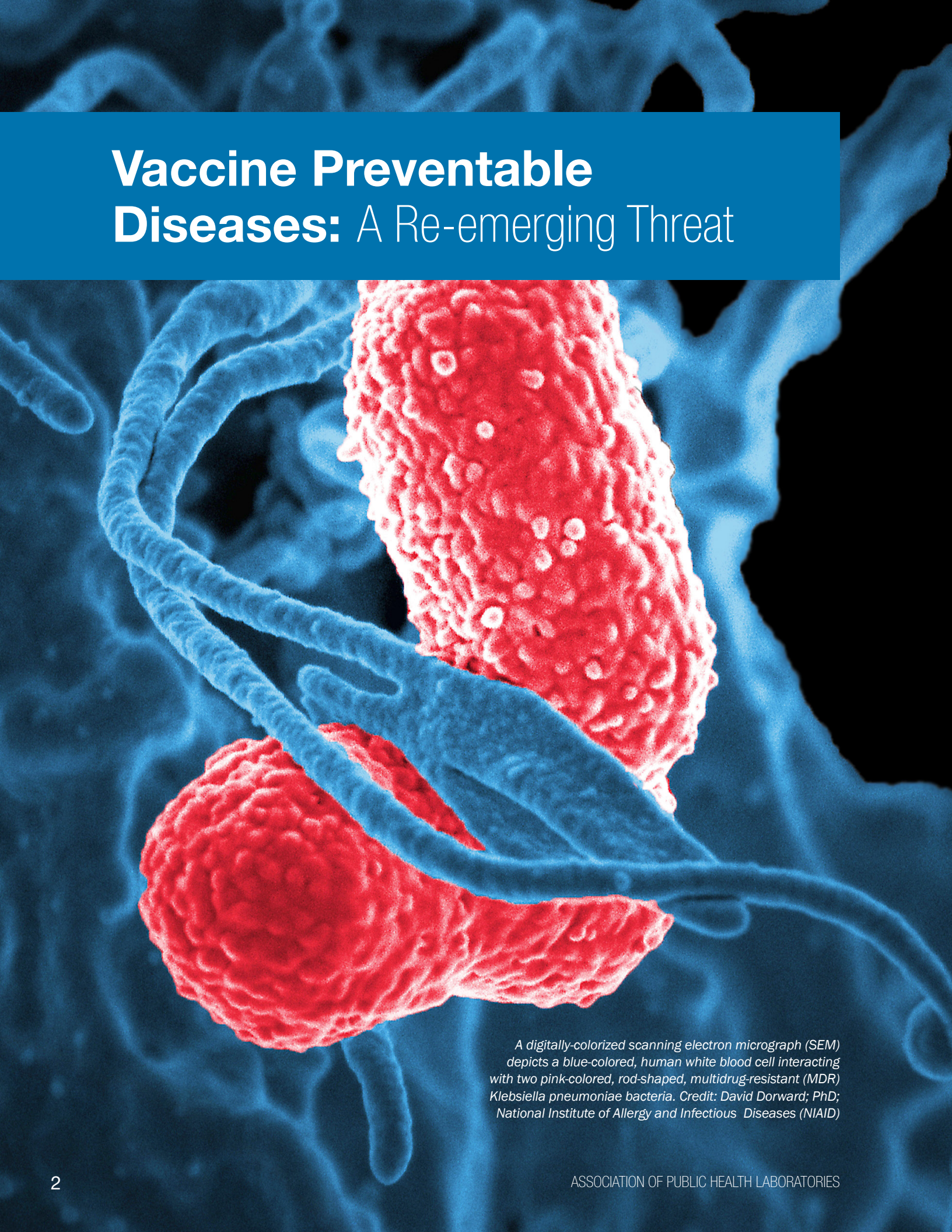
Vaccine Preventable Diseases: A Re-emerging Threat



A digitally-colorized scanning electron micrograph (SEM) depicts a blue-colored, human white blood cell interacting with two pink-colored, rod-shaped, multidrug-resistant (MDR) Klebsiella pneumoniae bacteria. Credit: David Dorward; PhD; National Institute of Allergy and Infectious Diseases (NIAID)

Vaccines are one of the most effective public health interventions that has ever been employed. Routine use of vaccines has significantly reduced or eliminated many previously common childhood vaccine preventable diseases (VPDs) in the US. However, increased globalization and a reluctance to follow the recommended vaccination schedule in certain populations, has led to more common outbreaks of VPDs that had once been rare, such as measles or whooping cough. The years 2013 and 2014 saw outbreaks of increased frequency and size.

Measles

In 2013, there were 11 measles[1] outbreaks and 503 cases,[2] while the Centers for Disease Control and Prevention (CDC) reported nearly 300 confirmed cases of measles in the first half of 2014 alone.[3] Outbreaks in 2013 and the beginning of 2014 occurred in many states including North Carolina, Texas, Massachusetts, California, Ohio and Washington. The outbreak sizes ranged from small outbreaks of three cases to large outbreaks of over 100 cases.[3,4]

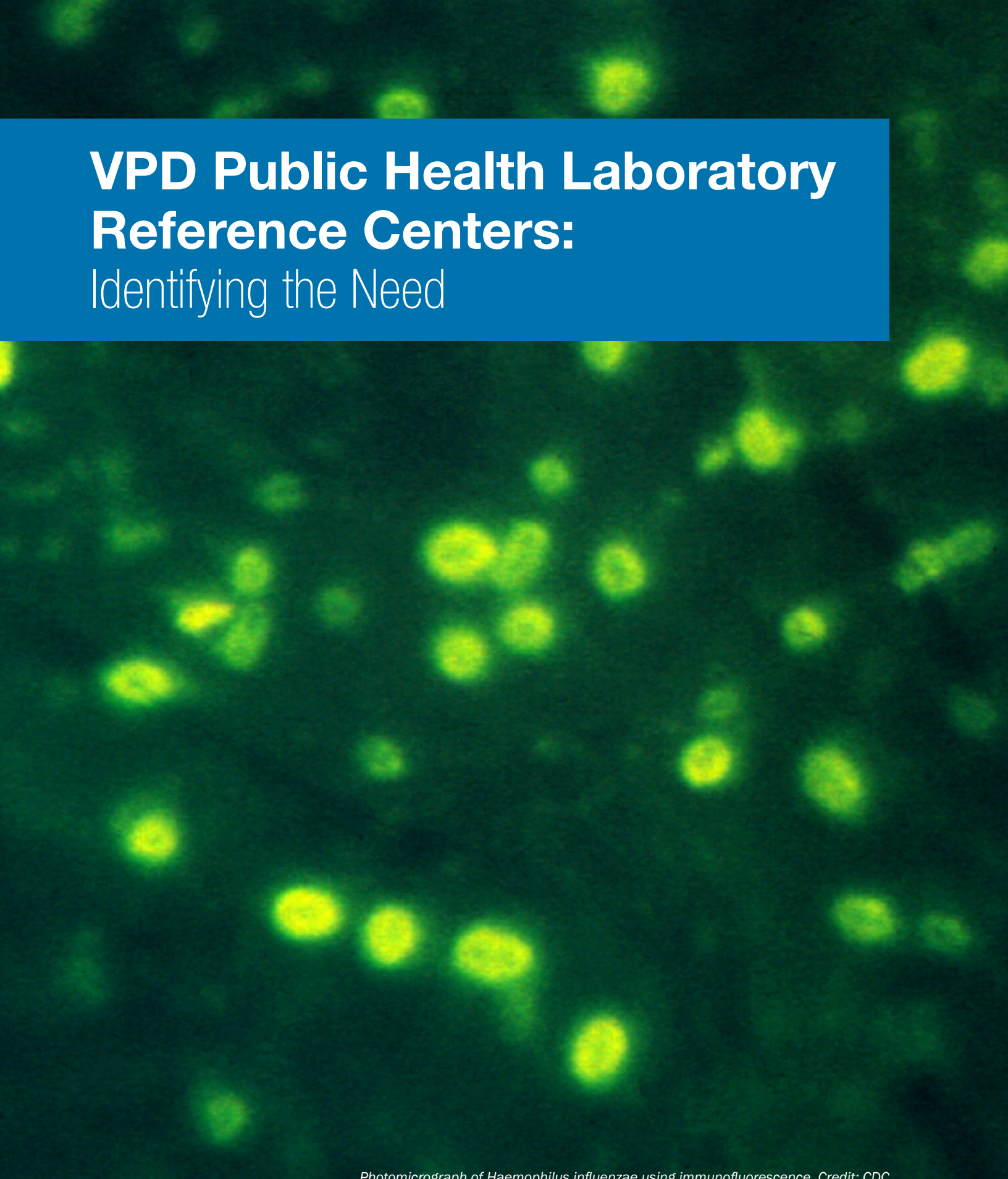
Mumps

In 2013, CDC received reports of 438 cases of mumps from 39 states. The first half of 2014 has seen 871 cases, more than double the number of mumps cases reported to CDC in 2013.[5,6] These cases involved four large outbreaks originating on four different university campuses, including those in Ohio, Wisconsin and New York City.[5,6] Outbreaks ranged from three cases to over 300 cases[5] in 2013 and the first half of 2014.

Bordetella pertussis

While rates of *B. pertussis* in the United States decreased from 2012–2013, 13 states reported an increase in cases in 2013 and large outbreaks have occurred in California, Ohio, Texas, Washington, Wisconsin and Minnesota.[7,8] There has been a 30% increase of *B. pertussis* cases reported to CDC in the first half of 2014 compared to the same time period of 2013.[9] Additionally, in the first half of 2014, 27 states reported an increase in cases compared to the same time period in 2013.[10]

VPD Public Health Laboratory Reference Centers:
Identifying the Need



Photomicrograph of Haemophilus influenzae using immunofluorescence. Credit: CDC

Although re-emerging in many cases, outbreaks of most VPDs are uncommon and routine laboratory testing for VPDs is not practical. This makes it difficult for every public health laboratory (PHL) to identify resources necessary to implement and sustain capacity for state of the art testing services for a broad range of VPDs. This is particularly true of molecular testing methods, which allow for more reliable identification of VPDs in the earlier days of infection. Recognizing this challenge, CDC and APHL established a partnership in 2010 to begin to examine gaps in VPD testing capabilities and identify potential solutions.

A series of surveys, key informant interviews and stakeholder meetings led to the concept of establishing PHL reference centers that would serve a variety of functions: diagnostic testing, testing for surge capacity, surveillance testing, confirmatory testing, serotyping/serogrouping, sequencing, proficiency testing and access to subject matter experts. In 2012, APHL and CDC selected and established four VPD Reference Centers (Figure 1): California Department of Public Health Laboratory, Minnesota Public Health Laboratory Division, New York State Department of Health: Wadsworth Center and Wisconsin State Laboratory of Hygiene (WSLH). Laboratory staff were trained on CDC protocols and validated them in their own laboratories.

The Reference Centers have been providing enhanced capacity for molecular and serologic testing for eight VPDs in a shared service model since 2013 (Table 1). Other public health laboratories enroll in the program voluntarily and receive the testing services at no cost to their laboratories or VPD programs. The WSLH also provides proficiency testing panels for public health laboratories choosing to offer select VPD services and serves as a specimen repository for VPD specimens that can be used for evaluation and validation of new testing methods.

"The addition of the VZV SNP PCR assay has revolutionized the way in which we are able to provide more precise data regarding VZV suspect patients. We can now provide results on whether a case is vaccine-related or is from a wild-type strain. This has proved useful to testing specimens submitted from VPD project labs as well as our local laboratories."

~ Jill Hacker, PhD, MPH, California Department of Public Health, Viral and Rickettsial Disease Laboratory

VPD Reference Centers

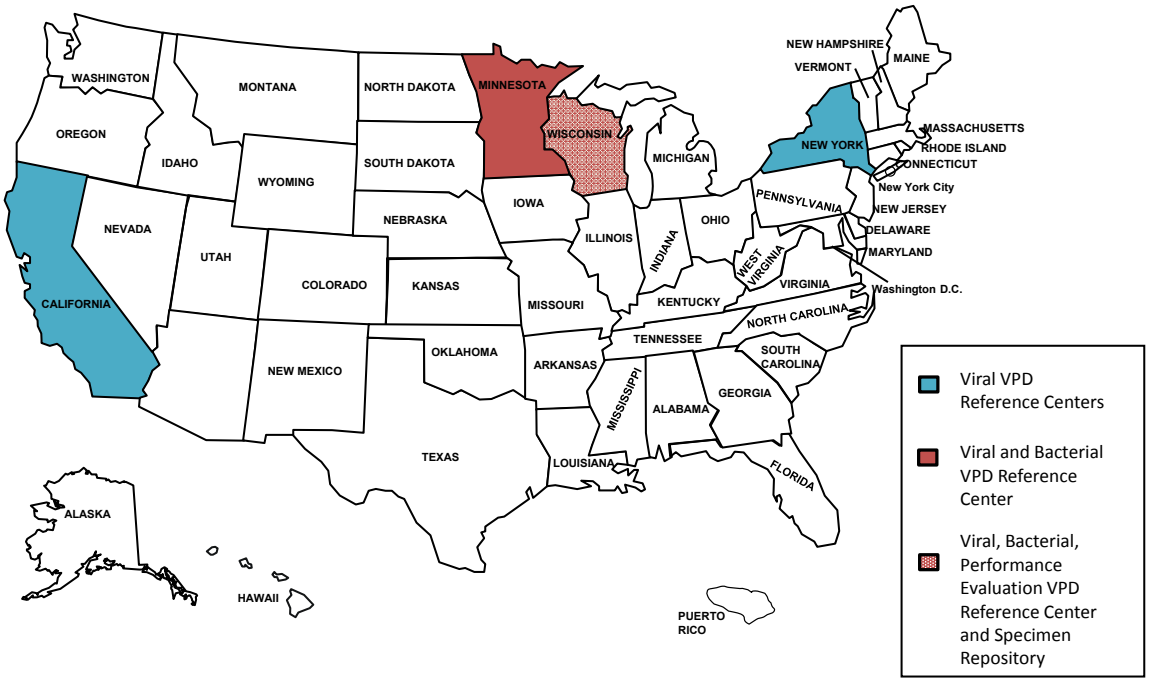


Figure 1: *VPD Reference Centers: California and New York provide viral VPD testing services to their assigned submitting laboratories. Minnesota provides bacterial and viral VPD testing services to their submitting laboratories. Wisconsin provides bacterial and viral VPD testing services and serves as a Performance Evaluation Center and holds a VPD specimen repository.*

Viral Diseases	Real Time RT-PCR	Serology	Genotyping	Maximum Turn Around Times
Measles	✓		✓	PCR: 2 days Genotyping: 10 Days
Mumps	✓		✓	
Rubella	✓		✓	
Varicella-zoster	✓		✓	
Bacterial Diseases	**Real Time PCR**	**Serology**	**Serotyping/ Grouping**	**Maximum Turn Around Times**
B. pertussis	✓	✓		PCR: 2 Days Serology: 5 Days Serotyping/grouping: 5 Days
S. pneumoniae	✓		✓	
N. meningitidis	✓		✓	
H. influenzae	✓		✓	

Table 1: *Vaccine Preventable Disease Reference Center Test Menu*
Genotyping: *Genotyping will be performed on all PCR positive specimens unless otherwise indicated as a part of a larger outbreak.*
***S. pneumoniae:** At this time the Bacterial VPD Reference Centers will only accept S. pneumoniae specimens or isolates from children ≤5 years old with history of vaccination (PCV13 or PPSV23)*

The First Year of Testing: 2013–14

From April 22, 2013 to June 30, 2014, the VPD Reference Centers received 567 specimens from enrolled submitting laboratories and performed over 800 VPD tests. A total of 46 PHLs (Figure 2), 36 state PHLs and 10 local PHLs, were enrolled as submitting sites as of June 30, 2014. The VPD Reference Centers have assisted in testing for six VPD outbreaks in the first year. Results are routinely reported to the submitting site within 24 hours of specimen receipt for PCR requests and within 3-5 days for further characterization. In addition to reporting the results to the submitter, the Reference Centers also report results for specimens tested to CDC via electronic HL7 messaging or a secure FTP site (Figure 3). This messaging of results to CDC does not replace state notifications to CDC through the Nationally Notifiable Diseases Surveillance System.

This report further describes the testing performed at the Reference Centers during the 15 months and includes accounts of success stories from Reference Centers and their submitters.

VPD Enrolled Submitting Sites

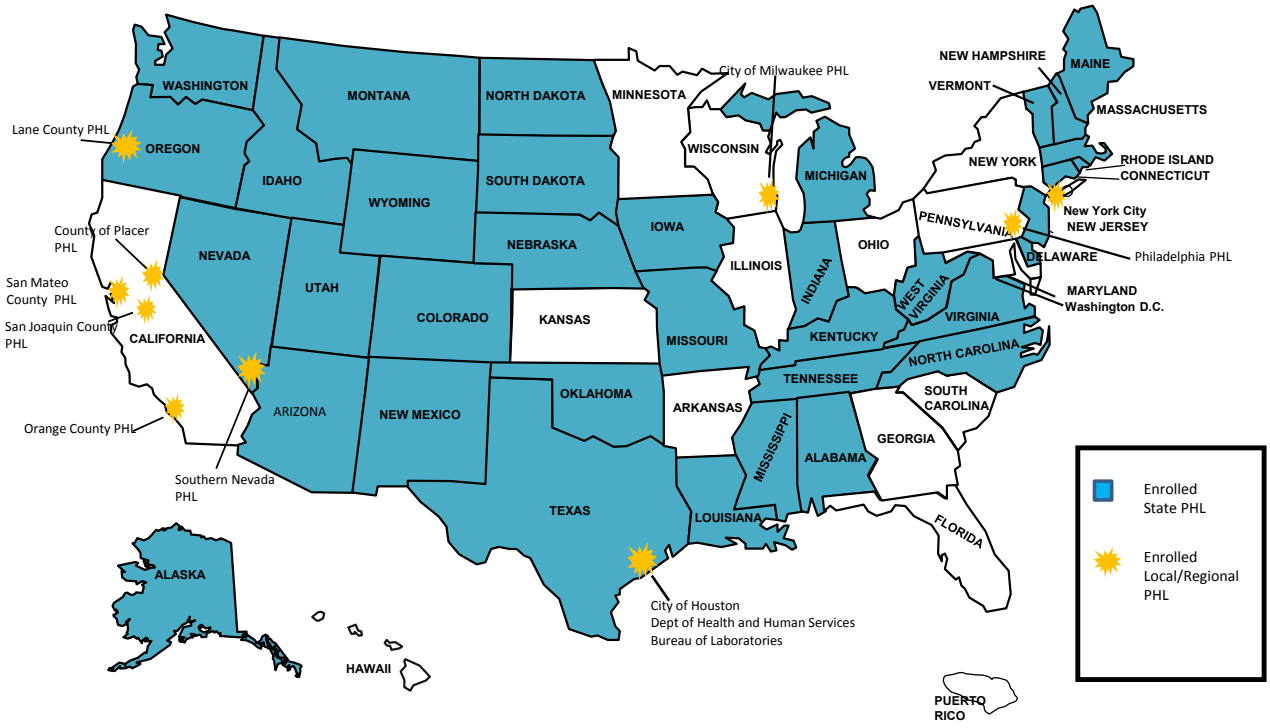


Figure 2: *As of June 30, 2014, 46 (36 state and 10 local) public health laboratories were enrolled as VPD Submitting Sites.*

FLOW DIAGRAM

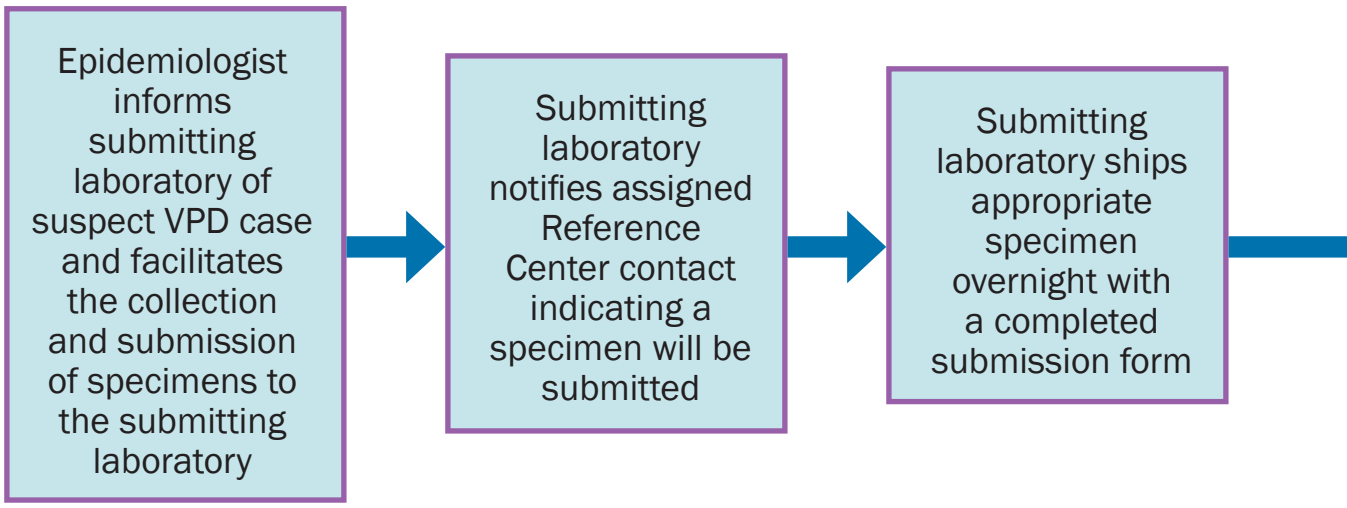
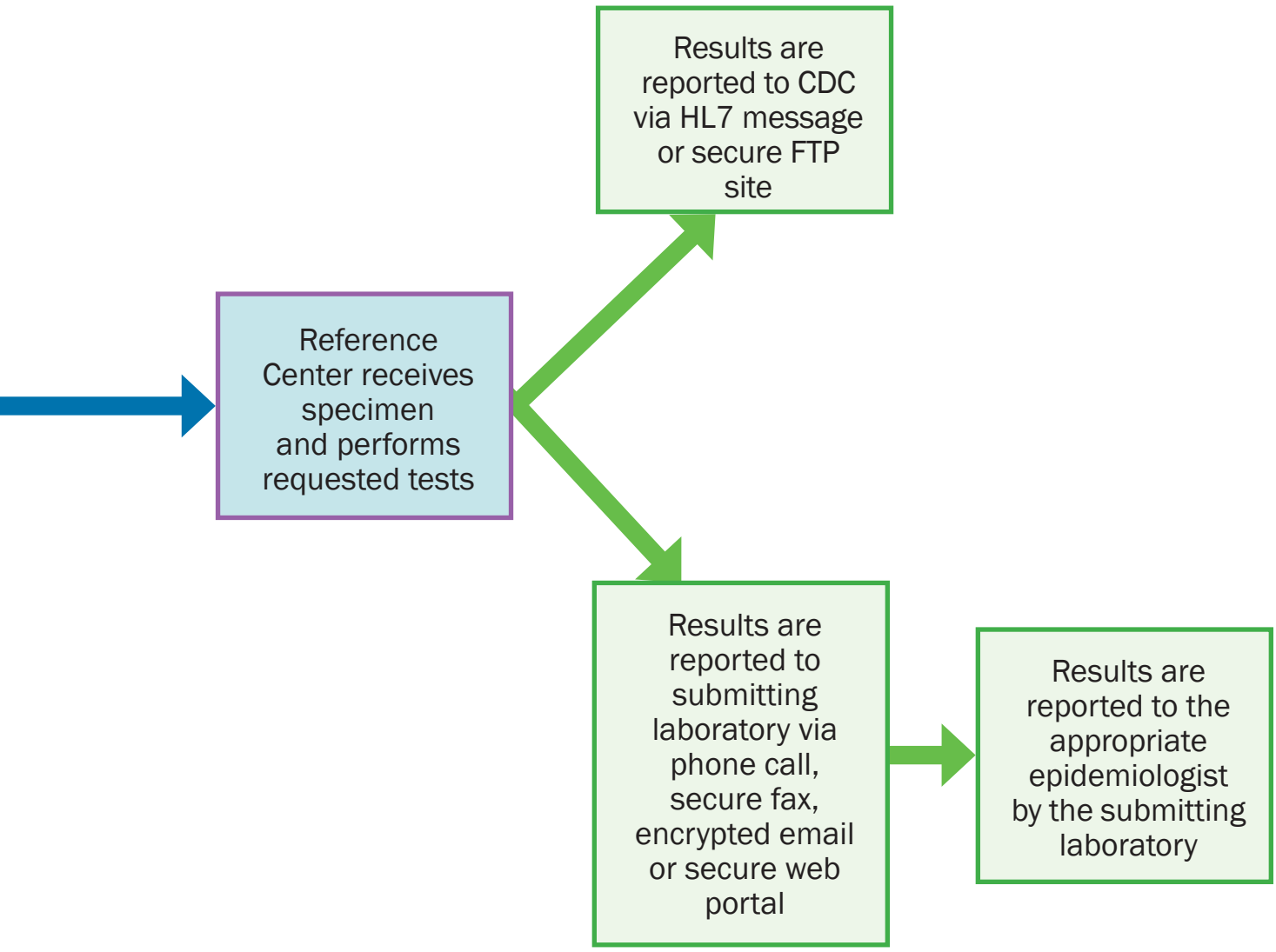


Figure 3: *Flow Diagram of the Specimen Submission Process: Once notified of a potential VPD case, appropriate specimens are collected by clinicians and sent to the enrolled submitting site. The submitting site then contacts their assigned Reference Center and prepares the specimen for shipping with the appropriate requisition form. When the specimen is received by the Reference Center, it is tested and results are promptly reported back to the submitting site. Viral RT-PCR results are routinely reported within 24 hours of specimen receipt.*

Specimen Submission Process



Experiences of the VPD Reference Centers

California Department of Public Health, Public Health Laboratories in Richmond, CA

California Department of Public Health Viral and Rickettsial Disease Laboratory

Rubella was declared eliminated in the US in 2002, yet cases continue to occur due to importation. Far fewer cases of rubella are reported annually, with a national range of 3-10 cases per year (0 to 2 in California) from 2009-2013. Because the clinical presentation of measles and rubella can be similar, the Reference Centers reflex all PCR-negative suspect measles cases for rubella testing. At CDPH VRDL, specimens submitted for measles PCR are tested simultaneously for both viruses.

Using the concurrent testing approach, rubella was identified in two cases reported as suspect measles. In May, real-time PCR identified rubella in an adult male traveler from India. One month later, the same approach detected rubella in an adult female traveler from Afghanistan. The female case was not pregnant and neither case had known contact with pregnant women. These were the first cases of rubella in California since 2012. Both cases were genotype 2B, and no additional rubella cases were identified. These cases highlight the utility and benefit of concurrent measles and rubella PCR testing.

The CDPH VRDL 2014 experience with measles and rubella has highlighted the important role of swift laboratory confirmation in the investigation of both of these diseases. With a disease as highly infectious as measles, rapid availability of laboratory data permits epidemiologists to focus their investigative efforts on known cases and their contacts, particularly high risk contacts who may urgently need post-exposure prophylaxis.

Similarly, detection of a case of rubella facilitates the identification of exposed pregnant women whose infants may be at risk for congenital rubella syndrome. With the established standardized genotyping methods, the VPD Reference Centers provide molecular epidemiological data that have proved invaluable in responding to cases and outbreaks and generate useful genotyping data for future strain comparisons.

"Over the course of the last 12 months, ASVL has submitted 27 samples to our designated APHL/CDC Vaccine Preventable Disease Reference Lab in Richmond, California. Communication and TAT's have been superior."

~ Bonnie Bond, Virology Manager, Alaska Division of Public Health Laboratory

CDPH VRDL VPD Team: Back row (from left): Chris Preas, Ashraf Fadol, Chris Anderson, Oliver Oyler, Anthony Moore. Seated: Alex Espinosa, Regina Chase, Jill Hacker, Dongxiang Xia, Abiy Tadesse, Carlos Gonzalez. Not shown: Giorgio Cosentino, Natasha Espinosa

Ashraf Fadol testing a VPD specimen

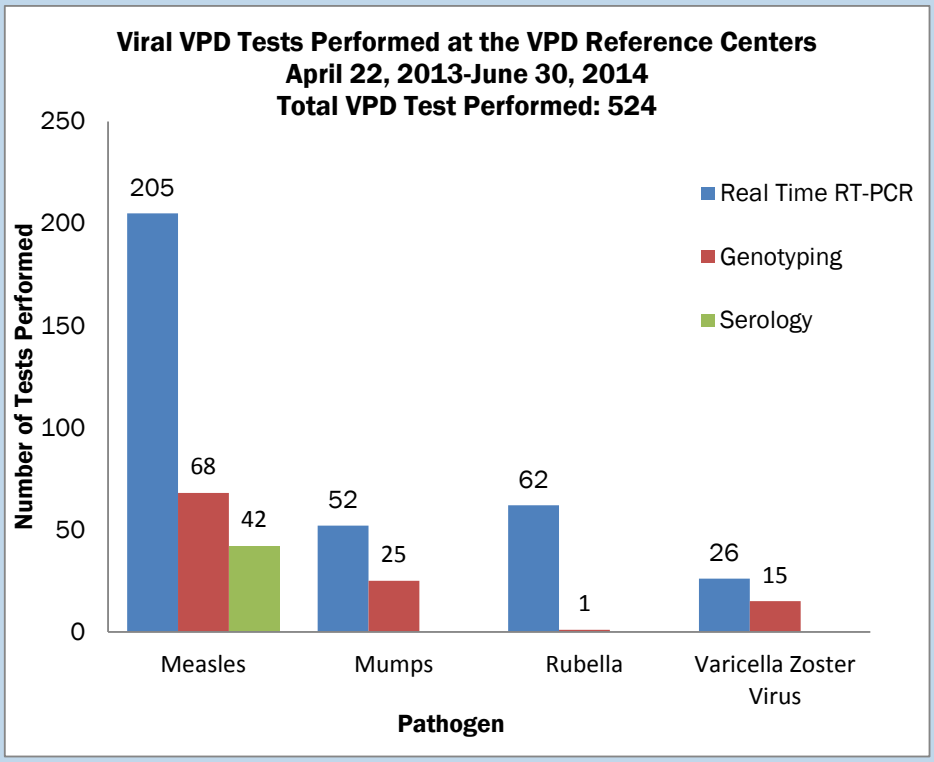


Figure 4: *Viral Testing by the Numbers: Viral VPD tests performed at the VPD Reference Centers April 22, 2013-June 30, 2014. The graph above depicts the testing performed at the four viral VPD Reference Centers: the California Department of Public Health, New York State: Wadsworth Center, the Minnesota State Department of Health and the Wisconsin State Laboratory of Hygiene. The data includes only submissions from enrolled submitting sites.*

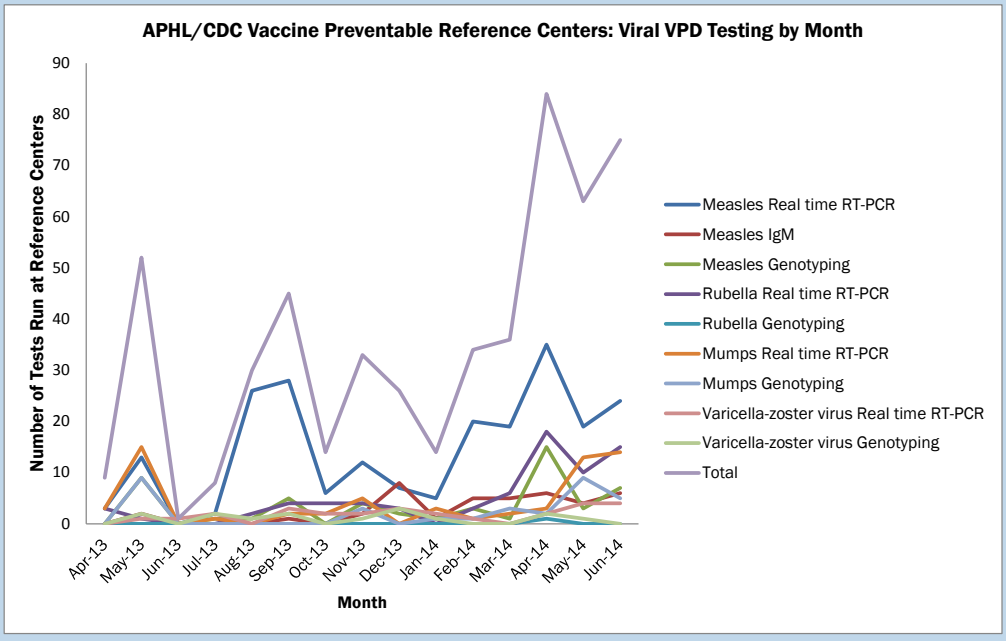


Figure 5: *Viral VPD Testing Performed by Month: The graph above depicts the testing performed at the four viral VPD Reference Centers: the California Department of Public Health, New York State: Wadsworth Center, the Minnesota State Department of Health and the Wisconsin State Laboratory of Hygiene. The Reference Centers began accepting specimens on April 22, 2013. The data includes only submissions from enrolled submitting sites. Spikes in the testing numbers correlate with several outbreaks.*

Patrick Bryant, PhD from the New York Department of Health: Wadsworth Center

New York State Department of Health, Wadsworth Center

Wadsworth Center Congenital Rubella Case

In December of 2013, the Wadsworth Center Virology Laboratory received specimens collected from a newborn in Erie County with suspected congenital rubella syndrome (CRS). At this time, the newborn was being kept in isolation in the NICU in Erie County with symptoms consistent with CRS. The patient's mother also had travel history to Yemen and an undetermined vaccination history.

Fortunately, the Wadsworth Center had recently begun a new collaboration with the CDC and APHL as a reference center for APHL's Vaccine Preventable Disease Project. The Wadsworth Center Virology Laboratory, with the assistance of CDC, recently established CDC's Rubella real-time RT-PCR assay and conventional RT-PCR typing assays for the detection and genotyping of rubella in the laboratory. As a result, the Virology Laboratory was able to perform testing on a throat swab, NPS and Urine from the newborn, all of which were positive by real-time RT-PCR. Genotyping by sequencing determined the genotype to be 1E, which has a large global distribution and is often associated with CRS.

A further detailed phylogenetic analysis performed by CDC determined that the rubella sequence generated by the Virology Laboratory was most closely related to two rubella specimens that had been isolated in Yemen in 2008. The infant was placed in isolation in the family home and continues to be monitored for viral shedding by the Virology Laboratory. As of May 14, 2014, samples collected from the infant were still testing positive for rubella, however, on July 11, 2014 an NPS sample collected on the child was negative.

"Kentucky DLS has been sending specimens to the New York State Department of Health in conjunction with APHL/CDC's Vaccine Preventable Disease Research Center Project. Since enrolling in the program, we have sent close to 10 specimens for measles or mumps PCR testing and have received reports within 3 days. Obviously, a much better turnaround time than what we could accomplish with culture testing. I have gained access to their LIS test ordering and result retrieval portal which enhances their ability to assist us. Overall, this program has been very useful and the testing has been rapid, which has aided disease diagnosis for the citizens of the Commonwealth of Kentucky. We greatly appreciate the help!"

~ Mathew Johnson, Virology Supervisor, Kentucky Department of Public Health, Public Health Laboratory

Minnesota Department of Health, Public Health Laboratory

Minnesota Department of Health Public Health Laboratory

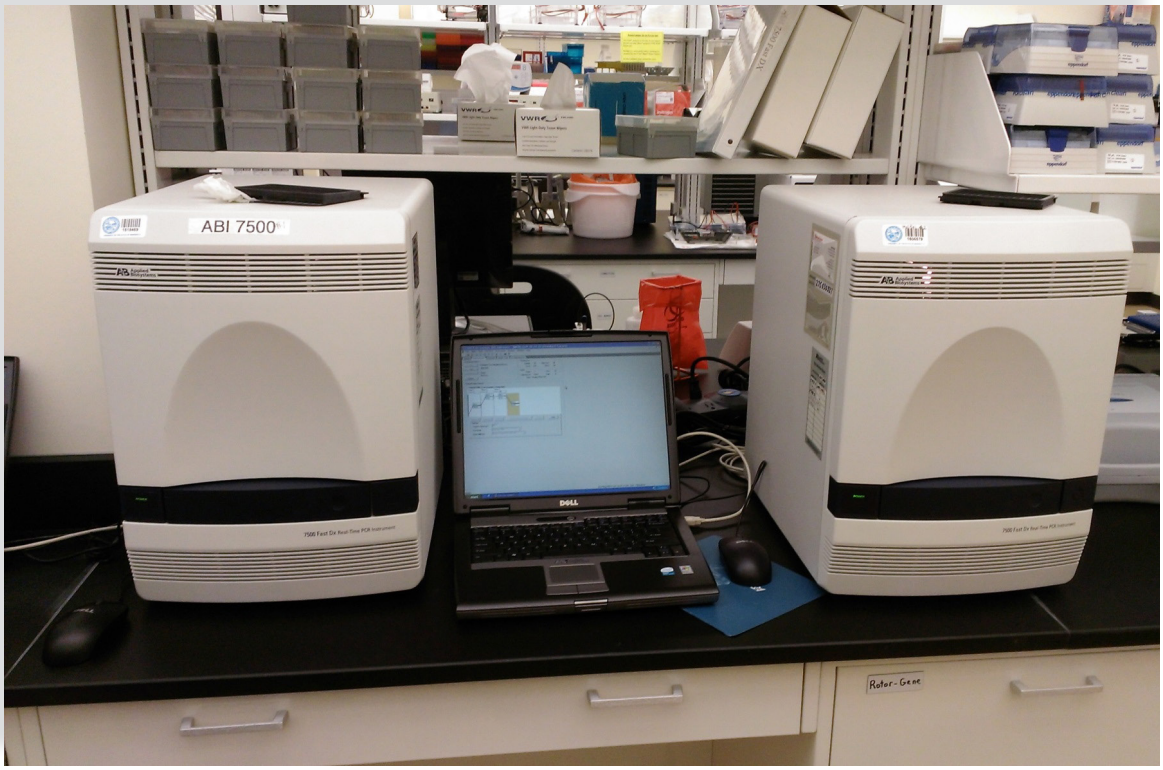
In September 2013, the Minnesota Department of Health (MDH) received a request from APHL that MDH add the Texas Department of Health as a laboratory that submits specimens to MDH for VPD testing. Within hours of the request, MDH was communicating with Texas. Texas had a suspect measles case that needed testing as soon as possible. MDH received the specimen the following day by overnight delivery and immediately tested the sample. By the end of the day, testing revealed that the specimen was positive for measles virus. MDH immediately notified the Texas Department of Health so they could begin conducting their investigation.

The measles virus is extremely easy to pass from an infected person to a susceptible person. During the investigation of the case, the Texas Department of Health determined that the case spent time at a large Texas-based church that had a lot of unvaccinated members. The affected church's leadership communicated with members to strongly encourage unvaccinated individuals to get vaccinated.

Rapid testing and communication of results was critical for identification of a case and prevention of future illness. Over the course of this outbreak investigation, MDH tested 45 samples, nine of which were positive for measles by RT-PCR.

"Texas began using the APHL/CDC VPD Reference Centers in 2013 in the middle of a measles outbreak. Our reference center, Minnesota, was able to provide for all of our PCR testing needs during the outbreak and has continued to meet our needs ever since. Minnesota almost always provides measles PCR results the same day as specimen receipt, which is critical when trying to decide whether to mount a vaccination clinic or not! Our contact at Minnesota (Dave) has also been extremely helpful (and nice!) in answering our questions about specimen submission, testing, and results, not just for measles but for all VPDs. We're extremely grateful to have the laboratory support of Minnesota and the Reference Center project."

~ Rachel Wiseman, MPH, Epidemiologist, Texas Division of State Health Services



Applied Biosystems® ABI 7500 Real-Time PCR System used to test viral and bacterial VPD specimens at the Minnesota Department of Health, Public Health Laboratory

The VPD Reference Centers have been successful in their primary goal of increasing access to quality molecular testing for eight VPDs.

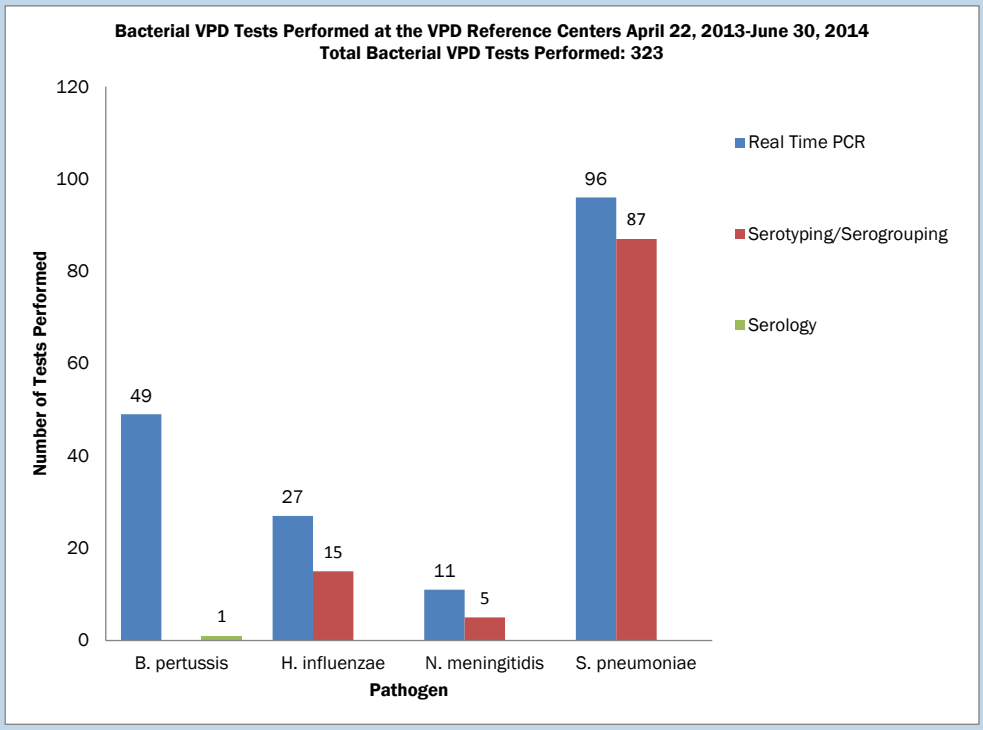


Figure 6: *Bacterial Testing by the Numbers: The above graph depicts the testing performed at the Minnesota Department of Health and the Wisconsin State Laboratory of Hygiene April 22, 2013-June 30, 2014. The data includes only submissions from enrolled submitting sites.*

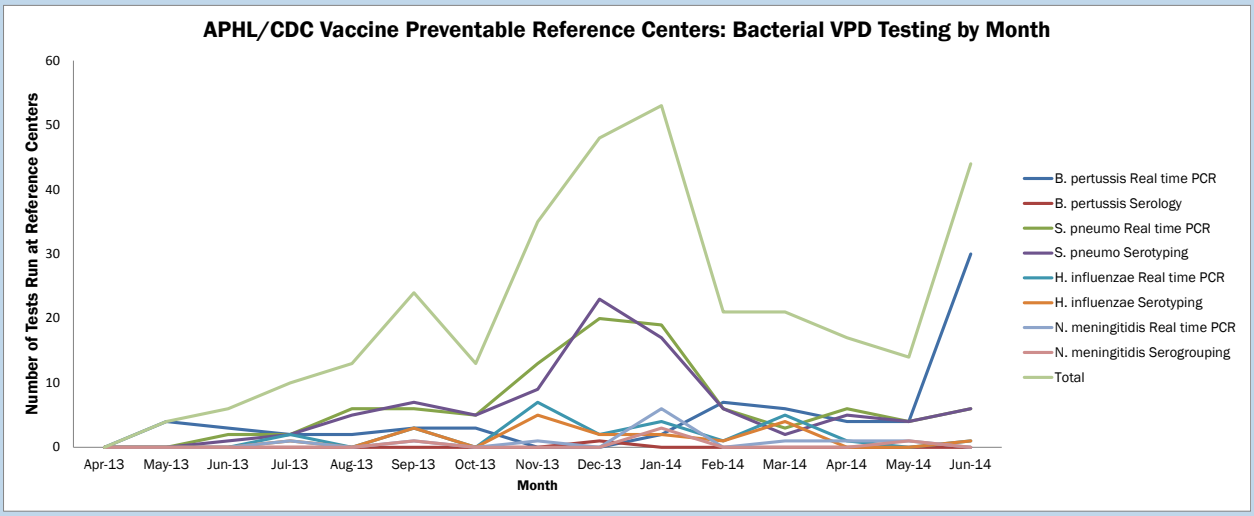


Figure 7: *Bacterial VPD Testing Performed by Month: The above graph depicts the testing performed at the Minnesota Department of Health and the Wisconsin State Laboratory of Hygiene by month. The data includes only submissions from enrolled submitting sites. In January 2014, APHL/CDC placed criteria on S. pneumoniae specimen submissions due to the influx of submissions in December 2013.*

WSLH Advanced Microbiologist Jim Powell pipetting in preparation for vaccine-preventable disease testing. VPDs such as measles, mumps and rubella are reportable conditions in Wisconsin

Wisconsin State Laboratory of Hygiene

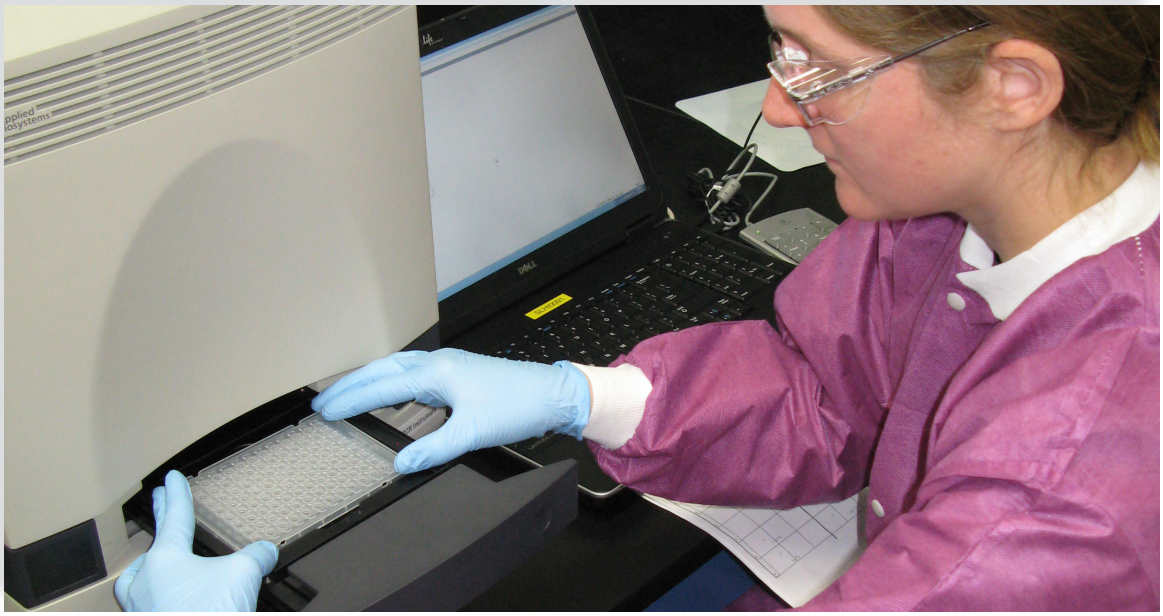
An epidemiologist at the Alabama State Health Department sits at her computer reviewing the reportable disease reports from earlier in the day when a case of pneumococcal meningitis in a four-year-old catches her attention. She immediately wonders if this is a case of vaccine failure or a more virulent serotype that may be circulating in the population. Last week, she had another case of pneumococcal meningitis in a three-year-old.

Epidemiologists in Alabama, an enrolled VPD submitting site, now have the capability to investigate these cases because they can take advantage of the services of their assigned VPD Reference Center, the Wisconsin State Laboratory of Hygiene, which can serotype *Streptococcus pneumoniae* isolates using molecular methods. Because many states only have a small number of isolates that need testing each year, it's not feasible for their state public health laboratory to offer this testing because of the complexity and expense of the testing. If the isolates from these patients are vaccine strains, the epidemiologist will investigate if there is a possible problem with the vaccine such as improper storage of at the vaccination center and they will also offer pneumococcal vaccine to household members as appropriate. The serotyping results can also tell epidemiologists if there is a specific serotype that is circulating that may be causing more severe disease.

Prior to establishment of the VPD program a little over a year ago, many jurisdictions could not perform this important timely follow up. Alabama now sends all *S. pneumoniae* isolates from vaccinated children under five years of age with severe pneumococcal disease to the Wisconsin State Laboratory of Hygiene for serotyping. At this time, epidemiologists in Alabama have not seen any cases of possible vaccine failure, but they are pleased that they now have the capability to detect one.

"The VPD Reference Center at the Wisconsin State Laboratory of Hygiene is phenomenal! They are easy to work with and provide immediate response when needed. Dave Warshauer and his team provide excellent service and a very quick turn-around-time with results. They accept Saturday deliveries which has helped us out with those last minute specimens. The system is great and has given us the opportunity to utilize these services that we cannot ourselves provide to our citizens. We hope the VPD Reference Centers stay around for a long time."

~ Christi Clark, Microbiology Section Supervisor, West Virginia Department of Health and Human Resources, Office of Laboratory Services



Microbiologist Tonya Danz putting a tray into the PCR

Proficiency Testing Services

Although many PHLs do not have the capacity to maintain testing for all VPDs, many maintain services for VPDs important to their jurisdictional public health goals. In order to ensure proper testing and adhere to various laboratory accrediting bodies, periodic checks of performance by means of proficiency or performance evaluation panels are required. Because VPDs are diseases of low incidence, few proficiency programs exist in the United States.

In order to address this gap, the WSLH provides performance evaluation panels for select VPDs at no cost to PHLs who enroll in the programs. In the first 15 months of the project, WSLH provided four performance evaluation panels including a bacterial meningitis panel and measles and mumps panel. The measles and mumps panel yielded the greatest participation as a total of 47 PHLs participated in the fall 2013 event. In the coming years and as funding allows, WSLH will offer a measles and mumps panel in both the fall and spring.

Messaging of VPD Test Results

One of the other goals in establishing the VPD Reference Centers, was to develop the capability for real-time reporting of laboratory results to CDC to aid CDC in their ability to monitor VPD cases and rapidly identify outbreaks. The four VPD Reference Centers have used the standardized Health Level Seven International (HL7) Electronic Laboratory Reporting (ELR) as described in the ELR Guide 2.5.1 message guide to send standardized VPD results and applicable genotype data to CDC laboratories.

The APHL Technical Assistance Team works with each laboratory to map local Laboratory Information Management System (LIMS) codes to standardized codes and to build the technical architecture needed for the electronic laboratory surveillance message (ELSM) data exchange with CDC. When a VPD result is finalized, the data is automatically made available in the LIMS, and if necessary, is transformed in an integration engine and used to generate the HL7 message that is sent automatically to CDC (Figure 2).

Currently, the reference laboratories are sending ELSM for seven of the eight VPD conditions. Since April 2013, the Reference Centers have been submitting real-time data to CDC via secure FTP site. In September 2013, they started submitting HL7 ELR 2.5.1 ELSM to CDC for measles, mumps, rubella and pertussis. Capability to message Varicella-zoster Virus, *Streptococcus pneumoniae* and *Haemophilus influenzae* results was added in June 2014. The Bacterial VPD Reference Centers are currently working on building the capacity to message *Niesseria meningitidis* results to CDC. It is anticipated that this will be complete by June 2015. Figure 8 illustrates the route of the results message from the Reference Center to CDC and submitter.

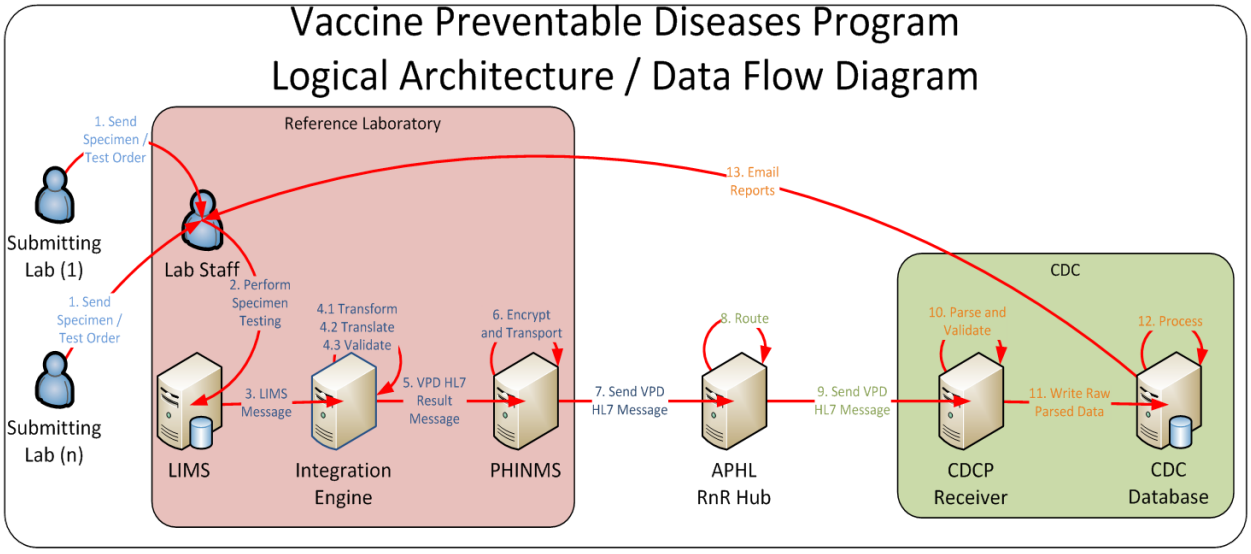
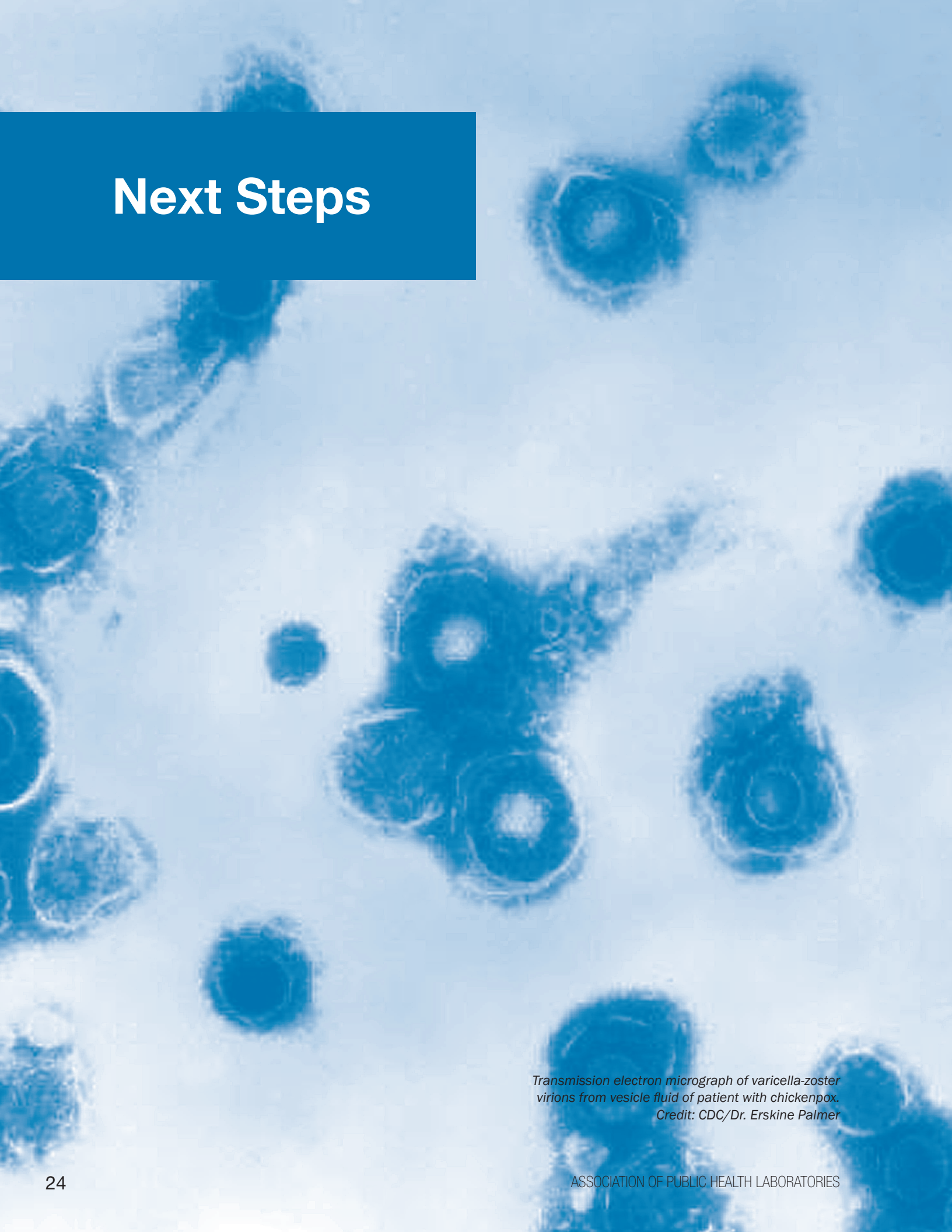


Figure 8: *Schematic of VPD results to CDC via HL7 2.5.1 Messaging*

Next Steps



Transmission electron micrograph of varicella-zoster virions from vesicle fluid of patient with chickenpox. Credit: CDC/Dr. Erskine Palmer

The VPD Reference Centers have been successful in their primary goal of increasing access to quality molecular testing for eight VPDs and have proven to be of great utility in meeting the needs of diagnostic surge capacity and increased access to performance evaluation panels. In the coming year, the Reference Centers plan not only to maintain capacity for molecular testing, but also make continuous improvements and enhancements to existing services.

- In 2015, CDC and APHL plan to work with the Reference Centers to collect data on the performance of existing serological and molecular tests for measles and mumps in order to improve recommendations on which tests should be used in laboratories and ordered by clinicians.
- A routine schedule for performance evaluation panels will be established and publicized allowing laboratories utilizing this service to better plan their quality assurance activities.
- In the spirit of continuous quality improvement, APHL fielded a customer satisfaction survey to VPD Submitting Sites and Epidemiologists in December 2014. APHL and CDC will work together to address any areas for possible improvement or any gaps in services.
- By June 2015, results for all eight VPDs tested for at the Reference Centers will be electronically transmitted to CDC. APHL will explore improvements to results messaging and enrollment services including establishing online enrollment and investigating the feasibility of instituting electronic results reporting to submitters.

For more information, see the APHL VPD Information Sheet in Appendix A for more details on the project and accepted specimen types.

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Patrick Bryant, PhD, Research Scientist II, New York State Department of Health: Wadsworth Center

Christi Clark, Microbiology Section Supervisor, West Virginia Department of Health and Human Resources, Office of Laboratory Services

Linda Cohen, MPH, PMP, Manager, Informatics Programs, APHL

Jill Hacker, PhD, MPH, Viral and Rickettsial Disease Laboratory, California Department of Public Health

Mathew Johnson, Virology Supervisor, Kentucky Department of Public Health, Public Health Laboratory

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Appendix A

APHL/CDC Vaccine Preventable Disease (VPD) Reference Centers

Who are the VPD Reference Centers?

The VPD Reference Centers are four public health laboratories that were selected through a competitive process to perform testing for eight VPDs using standardized methods developed by the Centers for Disease Control and Prevention (CDC). The Reference Centers work closely with APHL and CDC to provide quality testing to other public health laboratories and public health departments free of charge. The Reference Centers include:

- California Department of Public Health Laboratory provides measles, mumps, rubella, and varicella-zoster virus real time RT-PCR and genotyping
- Minnesota Public Health Laboratory Division provides measles, mumps, rubella, and varicella-zoster virus real time RT-PCR and genotyping as well as *B. pertussis*, *S. pneumoniae*, *H. influenzae*, *N. meningitidis* detection PCR and molecular serotyping/serogrouping
- New York State Department of Health: Wadsworth Center provides measles, mumps, rubella, and varicella-zoster virus real time RT-PCR and genotyping
- Wisconsin State Laboratory of Hygiene provides measles, mumps, rubella, and varicella-zoster virus real time RT-PCR and genotyping as well as *B. pertussis*, *S. pneumoniae*, *H. influenzae*, *N. meningitidis* detection PCR and molecular serotyping/serogrouping

Submitting sites are assigned to one or two of the VPD Reference Centers depending on the services requested. If you forget the Reference Center(s) to which you are assigned, please contact Laura Kovach (laura.iwig@aphl.org).

What testing is available at the VPD Reference Centers?

Table 1: Vaccine Preventable Diseases Reference Center Test Menu

Viral Diseases	real time RT-PCR	Serology	Genotyping	Maximum Turn Around Times
Measles	✓		✓	PCR: 2 days Genotyping: 10 Days
Mumps	✓		✓	
Rubella	✓		✓	
Varicella-zoster	✓		✓	
Bacterial Diseases	**real time PCR**	**Serology**	**Serotyping/Grouping**	**Maximum Turn Around Times**
B. pertussis	✓	✓		PCR: 2 Days Serology: 5 Days Serotyping/grouping:5 Days
S. pneumoniae	✓		✓	
N. meningitidis	✓		✓	
H. influenzae	✓		✓	

Genotyping: Genotyping will be performed on all PCR positive specimens unless otherwise indicated as a part of a larger outbreak. ***S. pneumoniae***: At this time the Bacterial VPD Reference Centers will only accept *S. pneumoniae* specimens or isolates from children ≤5 years old with history of vaccination (PCV13 or PPSV23).

How are VPD Reference Center results reported?

The VPD Reference Centers should not alter the communication channels between the submitting laboratory and their jurisdictional epidemiologists. The VPD Reference Centers will receive specimens and perform the appropriate tests, with anticipated turn-around-times as listed in Table 1. Results will be reported, with patient identifiers, by the Reference Laboratory to the submitting site through secure web portal, encrypted email, secure fax or over the phone. Results for all specimens tested will be reported to CDC by the Reference Laboratory via electronic HL7 messaging or a secure FTP site; however, these data will not replace state notifications to CDC through the Nationally Notifiable Diseases Surveillance System (NNDSS), which should be submitted per the usual protocol.

For more information visit: www.aphl.org/aphlprograms/infectious/emerging/Pages/re-emergence.aspx or contact Laura Kovach, senior specialist, infectious disease programs, 240.485.3831 or laura.iwig@aphl.org.

Table 2: Vaccine Preventable Diseases Reference Center Specimen and Shipping Recommendations

Viral Disease Assay	Specimen Type	Min. Specimen Volume	Specimen Storage	Shipping Recommendations
Measles real time RT-PCR	• Throat Swab in VTM • Nasopharyngeal Swab in VTM • Combined Throat/ Nasopharyngeal Swab in VTM • Urine	250µl	Place swabs in 2mL standard viral transport media. Store at 4°C and ship within 24 hours. If shipping is delayed, store at -70°C.	Ship on cold packs if shipping within 24 hours otherwise ship frozen.
Mumps real time RT-PCR	• Buccal Swab in VTM • Nasopharyngeal Swab in VTM • Throat Swab in VTM			
Rubella real time RT-PCR	• Throat Swab in VTM • Nasopharyngeal Swab in VTM			
Varicella-zoster virus real time RT-PCR	• Skin Lesion Swab • Scab	N/A	Store at room temperature	Ship scabs and lesion swabs at ambient temperature

***Swabs must be synthetic. Do NOT use cotton swabs for viral specimen collection**

Bacterial Disease Assays	Specimen Type	Min. Specimen Volume	Specimen Storage	Shipping Recommendations
***B. pertussis* Real time PCR**	• Nasopharyngeal swab or isolate	600µl	Swabs should be refrigerated at 4°C as soon as possible. Isolates should be stored refrigerated in Regan-Lowe transport medium or frozen on cryobeads	Refrigerated specimens should be shipped on cold packs. Frozen specimens should be shipped on dry ice.
***B. pertussis* serology**	• Serum	500µl	Serum should be separated and refrigerated at 4°C within 24 hours of collection and can be stored for up to 7 days. If stored for longer than 7 days, serum should be frozen at -20°C	Refrigerated specimens should be shipped on cold packs. Frozen specimens should be shipped frozen on dry ice.
***S. pneumoniae* Real time PCR or serotyping**	• CSF; or • Isolate	250µl	Primary specimen should be frozen. Isolates should be transported on chocolate agar slants or frozen stock and stored at ambient temperature.	Isolates can be shipped at ambient temperature. Frozen primary specimens or isolates should be shipped on dry ice.
***N. meningitidis* PCR and Serogrouping**	• CSF; or • Isolate	500µl		
H. influenzae	• CSF; or • Isolate	500µl		

End Notes

1. Centers for Disease Control and Prevention. (2014, September). Measles Cases and Outbreaks. Retrieved from http://www.cdc.gov/measles/cases-outbreaks.html
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9. Centers for Disease Control and Prevention (2014, August). Pertussis Outbreak Trends. Retrieved from http://www.cdc.gov/pertussis/outbreaks/trends.html
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More information on the VPD Reference Centers is available at aphl.org.

Association of Public Health Laboratories

The Association of Public Health Laboratories (APHL) is a national nonprofit 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 residents and to prevent and control disease globally.

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