Commercial laboratory guidance – measles molecular testing

Commercial laboratory testing for measles detection offers advantages including integration with standard specimen routing and integration with providers' electronic medical record systems. However, it is important that public health authorities are aware of suspect measles cases and that follow up testing by public health laboratories for genomic surveillance is performed. Genomic surveillance is used to help track transmission pathways and to monitor measles elimination in the US.

- Commercial laboratories should retain specimens sent for measles testing. Upon completion of testing, and working with state public health partners, laboratories should promptly send primary specimens that **test positive** for measles RNA to CDC or an APHL Vaccine Preventable Disease Reference Center (VPDRC) through routine channels for genotyping. If requested by the submitter, specimens should also be sent for Measles Vaccine Assay (MeVA) testing. A description of these tests is listed below.

- Commercial laboratories should store and ship original specimens for genotyping and MeVA testing according to the requirements described by CDC and/or the APHL-VPD Reference Centers, see test specific links or table below. Storing upper respiratory specimens frozen ≤ -70°C as soon possible after receipt and limiting freeze-thaw cycles is recommended. Unprocessed urine should be stored refrigerated and cannot be frozen.

- Commercial laboratories should inform the recipient laboratory before specimens are shipped and provide shipping information.

- For assistance in coordinating shipping of measles positive specimens please reach out to state public health laboratories or the CDC.

Measles Virus Sequencing (Genotyping)

Molecular epidemiologic surveillance provides critical data that can support a link (or lack thereof) of cases or outbreaks to each other or to source countries. Sequencing is used to track transmission pathways and to document the absence of endemic circulation of measles in the United States. Sequencing also can distinguish between wild type virus infection and a rash caused by a reaction to measles vaccine strain virus. Commercial laboratories should work with their state public health laboratories to routinely send any measles rRT-PCR positive specimens to APHL-VPD Reference Centers or CDC for sequencing. It is important that an aliquot of the original specimen (i.e. not nucleic acid) is sent as soon as possible after the positive rRT-PCR result is reported to ensure timely tracking of cases and outbreaks. Batching specimens is possible, but specimens should be sent at least on a weekly basis during periods when there are ongoing measles outbreaks. The specimen types and submission requirements for the APHL-VPD Reference Centers can be found here; submission requirements for measles genotyping at CDC can be found here.

Measles Vaccine (MeVA) Assay

Detection of measles RNA by rRT-PCR in clinical specimens confirms the diagnosis of measles, unless there has been recent vaccination. Approximately 5% of individuals vaccinated with a measles-containing vaccine develop fever and rash that can be clinically indistinguishable from measles infection. Rapid differentiation of vaccine reactions from infections with wild-type virus is critical for guiding the public health response to outbreaks. The Measles Vaccine (MeVA) Assay, available at the CDC the APHL-VPD Reference Centers, is able to rapidly determine if detected measles virus is vaccine-derived or wild-type virus, if necessary. The MeVA assay is a rRT-PCR assay that detects measles vaccine strains and is performed in conjunction with a standard rRT-PCR measles assay that detects all measles strains. Rapid identification of measles vaccine reactions may be needed in an outbreak setting where an individual was recently exposed (i.e., within 21 days of rash onset) to wild type-measles but also was recently vaccinated. Commercial laboratories should put processes into place for rapidly sending an aliquot of the original specimen (i.e. not nucleic acid extracts) to either the CDC and/or APHL-VPD Reference Centers for MeVA testing when requested by the submitter following the guidance for when MeVA testing is appropriate. It is important that specimens are sent as soon as possible, because MeVA test results have immediate clinical and public health follow-up actions and implications. The specimen types and submission requirements for the APHL-VPD Reference Centers can be found here; submission requirements for the CDC can be found here.

Shipping, Storing and Testing Requirements

<table>
<tr><th>Test</th><th>Laboratories</th><th>Original Specimen Type</th><th>Minimum Volume</th><th>Shipping Requirements</th></tr>
<tr><td rowspan="2">Measles Virus Sequencing (Genotyping)

Measles Vaccine Virus Detection (MeVA)</td><td rowspan="2">Vaccine Preventable Diseases Reference Centers

Centers for Disease Control and Prevention</td><td>◦Throat Swab in viral transport media

◦Nasopharyngeal (NP) swab in viral transport media

◦Cerebrospinal Fluid (CSF)
Acceptable at Minnesota VPDRC Only</td><td>250 µL</td><td>Ship overnight

Store at -70°C, ship on dry ice</td></tr>
<tr><td>◦Urine</td><td>50 mL</td><td>Ship overnight

Store at 2-8°C, ship on cold packs

Must be within 7 days of collection</td></tr>
</table>