Commercial Laboratory Guidance – Measles Molecular Testing

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Commercial laboratory testing for measles provides important advantages, including integration with standard specimen routing and providers' electronic medical record (EMR) systems.

At the same time, public health awareness of suspected measles cases, combined with molecular characterization by public health laboratories, is also essential to support case classification and outbreak response. To that end, timely genomic surveillance is critical to identifying transmission pathways, distinguishing importations from endemic transmission, and monitoring measles elimination in the United States.

To support these activities, commercial laboratories are strongly encouraged to do the following:

- **Specimen retention:** Commercial laboratories should retain all residuals from all primary specimens submitted for measles testing for 30 days until public health follow-up is complete.
  Upon identification of specimen(s) that test(s) positive for measles RNA, laboratories should:
    - Notify state health authorities according to state specific requirements.
    - If requested by the state public health laboratory (SPHL), expeditiously submit the original primary specimen (e.g., respiratory swab, urine), aliquot of the primary specimen (at least 250µL), and/or extracted nucleic acid (at least 50µL) through public health laboratory channels to the public health laboratory in the patient's state of residence for genotyping, whole genome sequencing or Measles Vaccine Assay (MeVA) testing. Information on when MeVA testing is needed is described here. A description of these tests is listed at the end of this document.
- **Shipping and storage conditions:** Commercial laboratories should store and ship original specimens for genotyping and MeVA testing to the designated receiving laboratory (in accordance with Centers for Disease Control and Prevention (CDC) and/or the Association of Public Health Laboratories Vaccine Preventable Diseases (APHL-VPD) Reference Centers (APHL-VPD) guidance. See test specific links or table below.
  Recommended storage practices include:
    - Storing upper respiratory specimens frozen (≤ -70°C) as soon as possible after receipt and limiting freeze-thaw cycles.
    - Unprocessed urine should be stored refrigerated and cannot be frozen.
    - Specimens that do not meet the storage requirements should still be forwarded to the appropriate public health laboratory, as they may remain suitable for additional surveillance testing.
- **Shipping notifications:** Commercial laboratories should notify the receiving public health laboratory prior to shipment and if possible, provide shipping and tracking information to provide awareness of the shipment and to help ensure timely receipt and processing.
- **Additional assistance:** For assistance in coordinating shipping of measles positive specimens, please reach out to state public health laboratories. CDC is also available to provide consultation and support as needed, please reach out to CDCMeaslesLab@cdc.gov.

Preferred Shipping, Storing and Testing Conditions of Measles Positive Specimens

Test	Original Specimen Type	Minimum Volume	Shipping Requirements
Measles Virus Sequencing **Measles Vaccine Virus Detection (MeVA)**	• Throat Swab in viral transport media • Nasopharyngeal (NP) swab in viral transport media • Cerebrospinal Fluid (CSF) • Acceptable at Minnesota VPDRC Only	250 µL	• Ship overnight • Store at -70°C, ship on dry ice
	• Urine	50 mL	• Ship overnight • Store at 2-8°C, ship on cold packs • Must be within seven (7) days of collection

Measles Virus Sequencing (Genotyping and Whole Genome Sequencing)

Molecular epidemiologic surveillance provides critical data that can support a link (or lack thereof) to cases or outbreaks to each other or to source countries. Genotyping, focusing on sequencing a short region within the N gene, is used to provide molecular information from circulating strains. This sequencing information is used to track transmission pathways and to support documentation of 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 a measles-containing vaccine. More recently, CDC is using whole genome sequencing to determine if there are any genomic features, beyond the short region used for genotyping, that can **rule out linkages among measles cases in the United States**. It is important that an aliquot of the original specimen is sent as soon as possible after the positive rRT-PCR result is reported to help 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.

Submission requirements: The specimen types and submission recommendations for the APHL-VPD Reference Centers can be found here; submission requirements for measles genotyping at CDC can be found here. Commercial laboratories should submit specimens to the receiving laboratory in accordance with the shipping and storage guidance provided by that laboratory and consistent with CDC and/or APHL recommendations. Specimens that do not meet the storage or shipping requirements should still be forwarded for genomic testing after consultation with the testing laboratory.

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 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 when an individual has both been recently exposed to wild-type measles and recently received a measles vaccine within 6-28 days before their rash onset. Commercial laboratories should establish processes for rapidly shipping the original specimen to the public health laboratory from the patient's state of residence for MeVA testing, when requests are made in accordance with MeVA testing guidance. MeVA testing may also be requested by the state epidemiologist.

Submission requirements: It is important that specimens are sent to the receiving laboratory 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.