



CDC AR LABORATORY NETWORK: Guidance for CPO Colonization Testing

PURPOSE.

At the direction of state or local HAI epidemiologists or CDC's Division of Healthcare Quality Promotion, AR Lab Network Regional Laboratories will conduct screening for carbapenemase producing organisms (CPOs) as part of a public health response to the detection of epidemiologically important MDROs. This Guidance document identifies options for CPO colonization testing and details recommended procedures for isolate storage, handling, and reporting.

GENERAL CONSIDERATIONS.

- This Guidance outlines recommended options for laboratory testing methods. Methods used by laboratories are not limited to these options, but other testing methods may require in-house validation prior to use with clinical samples.
- All testing should be implemented in compliance with Clinical Laboratory Improvement Amendments (CLIA) regulations.
- Regional Laboratories should maintain databases of test results and retain these results for a minimum of 7 years.
- Regional Laboratories should report results back to submitting healthcare facilities and jurisdictional state/local Department of Health (DOH) within 1 working day of results.
- Regional Laboratories should store colonizing CPO isolates recovered from culture for a minimum of 2 years.

COLONIZATION SCREENING RATIONALE.

As described in the 2015 Update to the CDC CRE Toolkit (<http://www.cdc.gov/hai/pdfs/cre/CRE-guidance-508.pdf>) and the Interim Guidance for a Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs) (<https://www.cdc.gov/hai/pdfs/containment/Health-Response-Contain-MDRO-H.pdf>) if a culture from a patient not previously known to be CPO colonized grows epidemiologically- important CPOs (e.g., carbapenemase-producing CRE [CP-CRE], carbapenemase-producing CRPA [CP-CRPA], and carbapenemase-producing CRAB [CP-CRAB]), facilities should consider screening patient contacts to identify transmission. Patients considered contacts might vary from setting to setting; however, at minimum should include any roommates of the index patient for the duration of their stay.

For patients with long stays prior to their positive culture, during which they might have had undetected CPO colonization, or if CPO transmission is documented, consideration should be given to screening a broader group of patients to identify ongoing transmission. Facilities could perform one or multiple point prevalence surveys during which all the patients on a particular unit or ward are screened. If transmission is documented on a point prevalence survey, follow-up surveys should be conducted to document that transmission is halted. Generally,



transmission is considered halted when at least two point prevalence surveys conducted at least one week apart do not identify new patients that are colonized or infected with the strain of concern.

Specimens should only be submitted to a Regional Laboratory for colonization testing if a state epidemiologist (i.e., from the jurisdictional state of the affected healthcare facility) and the Regional laboratory approve the testing request.

In accordance with the MDRO guidance, we recommend priorities for screening based on a tiered approach. Facilities may initiate request for colonization screening due to suspected local transmission or positive result. Facilities must coordinate with public health department and receive approval before regional lab will approve the request.

If the testing is approved, the state or local health department will request the collection of rectal swab samples among patient contacts. These samples will be sent to Regional Laboratories for testing. Testing should be done in a timely manner (initiated upon receipt of samples; results reported within two days of sample receipt). Results will be simultaneously reported to the submitting healthcare facility and the jurisdictional state or local DOH (including designated contacts from state public health laboratory and hospital-associated infections program). A monthly compilation of testing results will be reporting to CDC.

LABORATORY TESTING.

Methods

This guidance recommends and discusses laboratory testing for CPO colonization.

- **Cepheid Xpert Carba-R**
 - Cepheid Xpert Carba-R is the only FDA-approved, commercially available CPO detection assay. This methodology requires the use of the Cepheid Gene Xpert system, Carba-R analysis software, and proprietary kit reagents. This molecular assay has a turn-around time of ≤ 1 day.
 - This molecular assay uses real-time PCR technology to detect genes for the most common carbapenem resistance mechanisms: KPC, NDM, VIM, OXA-48-like, and IMP (group 1 only).
 - **Limitation**
 - Detection of resistance mechanisms is restricted to the target capacity of the assay's primer and probes. For example, Cepheid does not detect all IMP variants that are circulating in the US. If the index case isolate is not Cepheid detectable, the use of Cepheid for screening is not recommended.
 - For any Cepheid swab that tests positive, specimens should be cultured to recover and characterize the organism (organism ID, AST, and PCR for all gene targets).
- **Non-Cepheid Screening**
 - Culture-based methods, such as broth enrichment or direct mac, should be used for non-Cepheid targets: mcr, pan-ns, non-group 1 IMP, or OXA 23, -24/40 -58 variants (protocols can be found on Sharefile).
 - All colony types identified should be worked up to detect all CPOs present, not just the target organism.
 - Organisms isolated should be characterized using the full workflow (organism ID, AST, and PCR for all gene targets).



SAMPLE COLLECTION AND TRANSPORT

Sample Collection

- **Swabbing, labeling, packing, and shipping guidance will be provided by your coordinating regional AR Lab Network laboratory.**
 - Briefly, rectal swabs collected using the Cepheid dual-swab collection kit should be inserted in the tube's universal transport media and shipped at room temperature (15-28°C) to the Regional Laboratory within 1 day of collection.
 - If climate or weather will put the specimens at risk of high temperatures, please discuss ice packs with your coordinating regional lab
- **Use of Cepheid dual swab collection kit (Cepheid catalog #900-0370) is encouraged.** This is the manufacturer-recommended sample collection device for use with the Cepheid GeneXpert Carba-R assay.
 - Cepheid dual swab collection kits will be provided to healthcare facilities or coordinating public health departments upon initiation of colonization screening.
 - If stool specimens are collected, a swab sample must be prepared from the stool once received in the laboratory, prior to testing.
- **If IMP is identified in index case using CDC PCR protocol, index case isolate should be forwarded to the regional lab for preliminary testing** on Cepheid to confirm sensitivity for the type of IMP detected before testing swabs are sent for colonization screenings (Cepheid detects IMP-1 group only).
 - Coordinate with jurisdictional health department and laboratory to forward the index case isolate.
 - Swabs collected for colonization screening should be processed after confirming Cepheid detects IMP in index isolate.
- Colonization screening methods for other AR threats (e.g. pan-r, mcr, non-group 1 IMP, etc.) and using other specimen types (i.e. tracheal, wound, sputum) have been or are being validated (depending on lab). Protocols will be made available.

REQUIRED REPORTING.

- **Regional Laboratories will simultaneously report testing results back to the submitting healthcare facility and the coordinating jurisdictional HAI epidemiologist via secure communications** (i.e., established protocols that may include utilization of standardized data exchange platforms and systems such as ETOR, secure fax, or encrypted e-mail). Some regional labs will also report to jurisdictional lab.
- **Results from colonization testing (primary assay) should be reported within 1 working day of results**
- **Regional laboratories will provide a monthly report to CDC summarizing colonization screening activities by the 10th of each month for the previous months testing.** This report will be submitted through the APHL AIMS portal. In the meantime, monthly summaries may be submitted using the monthly reporting form for colonization screening (available on the ShareFile site).
- **Labs should report any specimens with ARLN Alert values to their state HAI coordinator and CDC within 1 day via by emailing the jurisdictional HAI coordinator and CDC (using REDCap).**

STORAGE AND SUBMISSION OF CERTAIN ISOLATES.

- **Isolate storage:** CPO-positive isolates obtained from culturing positive swabs should be stored in the -70°C for a minimum of 2 years.



- **Submission of Isolates to CDC:**
 - CDC may request bacterial isolates from a single patient of interest, or a group of associated patient contacts, for further characterization or banking. An aliquot of these isolates should be sent on slants within 1 week of request.
 - If a Regional Laboratory is seeking additional confirmatory testing by CDC, email ARLN_DHQP@cdc.gov and ship the aliquot of the indicated isolate on a slant to CDC.

LABORATORY TRAINING AND ASSAY VALIDATION

- **Laboratory Training:** CDC will provide training to regional laboratory staff on all testing, shipping, and reporting protocols.
- **Assay validation:** CDC can assist in the Laboratory's validation of a selected testing method by providing an isolate panel from the AR Bank or by providing expertise in methods and/or results interpretation.

CONTACT INFORMATION.

For questions or further information, please contact Dr. Sarah Malik (vgg9@cdc.gov) or the CDC AR Lab Network inbox at ARLN@cdc.gov.

