Technical Appendix

Antibiotic Resistance Laboratory Network Data on Healthcare-Associated Resistance Threats in the Antibiotic Resistance & Patient Safety Portal

Infrastructure

In 2016, CDC established the Antibiotic Resistance Laboratory Network (AR Lab Network) to address gaps in national laboratory testing capacity. The AR Lab Network can rapidly detect antibiotic resistance in samples or isolates from healthcare, food, and the community, and inform local responses to prevent spread and protect people. In healthcare settings, the AR Lab Network works in conjunction with CDC's Containment Strategy to rapidly identify unusual resistance and help contain its spread. In 2017, the public health laboratories of all 50 states, five large cities, and Puerto Rico began testing and characterizing clinical isolates of carbapenem-resistant Enterobacterales (CRE) and *Pseudomonas aeruginosa* (CRPA). Seven state public health laboratories serve as regional laboratories and support all jurisdictions within their region by testing colonization screening swabs for carbapenemase-producingorganisms (CPOs) and characterizing isolates of carbapenem-resistant *Acinetobacter baumannii* (CRA).

Isolate Recruitment

Each public health laboratory has worked to establish or collaborate with a network of clinical laboratories to submit isolates to the AR Lab Network for phenotypic and molecular testing. For Enterobacterales, testing is focused on isolates submitted by clinical laboratories that are resistant to ertapenem, imipenem, meropenem, or doripenem using standard antimicrobial susceptibility testing definitions (minimum inhibitory concentrations of ≥4 µg/ml for imipenem, meropenem, and doripenem or ≥2 µg/ml for ertapenem). The AR Lab Network has prioritized testing of *Klebsiella oxytoca, Klebsiella pneumoniae,Escherichia coli,* and *Enterobacter* species but encourages testing of additional genera of Enterobacterales where local capacity and capabilities allow.

For *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, isolates resistant to imipenem, meropenem, or doripenem at clinical laboratories, using standard antimicrobial susceptibility testing (minimum inhibitory concentrations of ≥8 µg/ml) are targeted. *Acinetobacter baumannii* testing is done through sentinel surveillance conducted by the seven regional laboratories and includes isolates recruited from at leastone clinical laboratory in each AR Lab Network jurisdiction within each region.

The size and coverage of isolate submission networks in each jurisdiction varies. Some states have near or fully comprehensive coverage because of reporting rules that require isolate submission. For those states without isolate submission requirements, CDC recommends that isolate submission be focused on populations, specific healthcare facilities, or healthcare facility types with higher rates or likelihood of resistant infections.

Note: The AR Lab Network was not designed to be a traditional surveillance system. Isolates tested are a convenience sample and include clinical, surveillance, and outbreak specimens. Within each state, isolate submissions and testing are determined by state priorities and reporting regulations.

Isolate Testing

Data include clinical, surveillance, and outbreak isolates and specimens. Some isolates may not have confirmed as carbapenem-resistant when retested at participating state and local public health laboratories. State and local public healthlabs use a variety of methods to test for organism identification, carbapenemase production, and mechanism testing.

Organism identification

Organism identification platforms include, but are not limited to, Vitek 2, Microscan, Phoenix, API20E, andMALDI-TOF (matrix-assisted laser desorption/ionization-time of flight) mass spectrometry.

Carbapenemase production

Laboratories use either the modified carbapenem inactivation method (mCIM) or CarbaNP as phenotypic tests to determine whether an organism is carbapenemase-producing.

Mechanism testing

Isolates are tested for the presence of bla_{KPC}, bla_{NDM}, bla_{VIM}, bla_{OXA-48}, and bla_{IMP} carbapenemase genes using real-time PCR assays, Streck ARM-D kits, or FDA-approved diagnostics (i.e., Cepheid Gene Xpert Carba-R, or Nanosphere Verigene).

The AR Lab Network does not routinely test for other mobile oxacillinase (OXA) genes known to be common in CRA, such as blaOXA-23-like, blaOXA-24/40-like, and blaOXA-58-like. Additional information about carbapenemase genes tested for, and detected among, CRA can be found in the Featured Item: **[Carbapenem-resistant *Acinetobacter baumannii* (CRA): An update for healthcare epidemiologists and infection preventionists regarding an urgent public health threat](#)**

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing (AST) is performed using disk diffusion, commercially available broth microdilution panels, and/or gradient diffusion strips. Testing is against a range of drugs, including at least two carbapenems. Minimum inhibitory concentrations (MICs) or zone diameters are evaluated using the CLSI M100-Ed31 breakpoints for interpretation where available.

Tiered testing structure

The testing in the AR Lab Network is tiered. Most isolate characterization occurs in the state and local public health laboratories. Regional laboratories provide surge capacity and confirmatory testing for isolates or mechanisms not characterized at their state and local public health laboratories. CDC provides surge capacity and confirmatory testing for any specimens or molecular targets not characterized or CLIA validated by state, local, or regional public health laboratories.

Colonization Screening

In accordance with manufacturer's instructions for use, public health laboratories use the Gene Xpert Carba-R assay (Cepheid, Sunnyvale, CA) to detect the presence of bla_{KPC}, bla_{NDM}, bla_{VIM}, $bla_{OXA-48-like}$, and bla_{IMP-1} carbapenemase genes in rectal swab specimens. Cepheid's Gene Xpert Carba-R is currently unable to detect most variants ofbla_{IMP} known to be circulating in the United States. CDC provides surge capacity for regional labs duringperiods of validation.

Reporting

Laboratories in the AR Lab Network report data to CDC at least monthly. During 2017, most labs transmitted their data via email using an Excel file that had specified fields. By the end of 2018, 40 states could upload standardized CSV formatted files directly from their Laboratory Information Management Systems (LIMS) using a secure online portal. Starting in January 2021, participating public health laboratories began transitioning to Health Level 7 (HL7) messaging of data daily.

Data Processing

At CDC, data have been compiled using SAS 9.4, standardized, and stored as a SAS dataset. All isolates identified as carbapenem-resistant and submitted from clinical laboratories to public health laboratories were defined as carbapenem-resistant, even carbapenem resistance was not confirmed at the public health laboratory. Data are cleaned, standardized, and stored as a SAS Dataset on a monthly basis. *Klebsiella aerogenes* isolates are classified as *Enterobacter aerogenes*. At the end of each calendar year, data are reconciled in partnership with all reporting labs to verify the number of isolates and the data associated. Each isolate is counted once; testing results from state, local, and regional laboratories are consolidated into one record.

Note: The AR&PSP includes AR Laboratory Network closed out data available as of July 2021.

Dictionary of Terms

- **AR:** Antimicrobial/Antibiotic Resistance
- **AR Lab Network:** Antibiotic Resistance Laboratory Network
- **AST:** Antimicrobial susceptibility testing
- **Carbapenemase:** Group of beta-lactamase enzymes active that hydrolyze carbapenems
- **CP:** Carbapenemase gene-positive
- **CPO:** Carbapenemase-producing organism
- **CRE:** Carbapenem-resistant Enterobacterales
- **CRPA:** Carbapenem-resistant *Pseudomonas aeruginosa*
- **CSV:** Comma separated value
- **FDA:** U.S. Food and Drug Administration
- **HAI:** Healthcare-associated infection
- **IMP:** Imipenemase Metallo-beta-lactamase
- **KPC:** *Klebsiella pneumoniae* Carbapenemase
- **LIMS:** Laboratory Information Management System
- **MALDI-TOF:** Matrix-assisted laser desorption/ionization-time of flight
- **MBL:** Metallo-beta-lactamase
- **mCIM:** Modified Carbapenem Inactivation Method
- **MIC:** Minimum inhibitory concentration
- **NDM:** New Delhi Metallo-beta-lactamase
- **OXA-48:** Oxacillinase-48-like beta-lactamase
- **PCR:** Polymerase chain reaction

- **PHL:** Public Health Laboratory
- **VIM:** Verona Integron-encoded Metallo-beta-lactamase
- **SAS:** Statistical Analysis Software