Texas Antimicrobial Resistance Laboratory Network (ARLN) Response Plan and Epi-Lab Work Plan

Texas Department of State Health Services Public Health Laboratory Division and Healthcare Safety Unit

May 2026

TEXAS
Health and Human Services

Texas Department of State Health Services

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List of Acronyms

Acronym	Full Name
ACH	Acute Care Hospital
AIMS	Association of Public Health Laboratories Informatics Messaging Services
APHL	Association of Public Health Laboratories
AR	Antimicrobial Resistance
ARLN	Antimicrobial Resistance Laboratory Network
ARX	Antimicrobial Resistance Coordination and Strategy Unit (CDC Unit)
AS	Antimicrobial Stewardship
AST	Antimicrobial Susceptibility Testing
BAP	Blood Agar Plate
BMD	Broth Microdilution
BP	Budget Period
C. auris	*Candida auris*
CDC	Centers for Disease Control and Prevention
CEMB	Clinical and Environmental Microbiology Branch (CDC Branch within DHQP)
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CPO	Carbapenemase-Producing Organism
CRAB	Carbapenem-Resistant *Acinetobacter baumannii*
CRE	Carbapenem-Resistant Enterobacterales
CRO	Carbapenem-Resistant Organism
CRPA	Carbapenem-Resistant *Pseudomonas aeruginosa*
DHQP	Division of Healthcare Quality Prevention (CDC Division)
DSHS	Department of State Health Services
ESBL	Extended-Spectrum Beta-Lactamases
GAS	Group A Streptococcus
GBS	Group B Streptococcus
GC	*Neisseria gonorrhoeae*
HAI	Healthcare-associated Infection
HCP	Healthcare Personnel
HHD	Houston Health Department
HSU	Healthcare Safety Unit
IATA	International Air Transport Association

Acronym	Full Name
ICAR	Infection Control Assessment and Response
*bla*IMP	Imipenemase
IP	Infection Preventionist
IPC	Infection Prevention Control
*bla*KPC	*Klebsiella pneumoniae* Carbapenemase
LHD	Local Health Department
LIMS	Laboratory Information Management System
LTACH	Long-Term Acute Care Hospital
MAC	MacConkey Agar Plate
MALDI-TOF	Matrix Assisted Laser Desorption/Ionization-Time of Flight
MDB	Mycotics Diseases Branch (CDC Branch)
mCIM	Modified Carbapenem Inactivation Method
MCR	Mobilized Colistin Resistance
MDRA	Multidrug-Resistant Acinetobacter
MDRO	Multidrug-Resistant Organism
NCBI	National Center for Biotechnology Information
NEDSS	National Electronic Disease Surveillance System
*bla*NDM	New Delhi Metallo-beta-lactamase
*bla*OXA	Oxacillinase
PCR	Polymerase Chain Reaction
PHL	Public Health Laboratory
PHMSA	Pipeline and Hazardous Materials Safety Administration
PHR	Public Health Region
POC	Point of Contact
PPS	Point Prevalence Survey
PRB	Prevention and Response Branch (CDC Branch)
SME	Subject Matter Expert
SNF	Skilled Nursing Facility
SNP	Single Nucleotide Polymorphism
TSA	Trypticase Soy Agar
U.S.	United States
*bla*VIM	Verona Integron-Encoded Metallo-beta-lactamase
WGS	Whole Genome Sequencing

Introduction

Background

History

According to the Centers for Disease Control and Prevention's (CDC) 2019 publication Antibiotic Resistance Threats in the United States, more than 2.8 million antimicrobial resistant (AR) infections occur in the United States (U.S.) each year, resulting in more than 35,000 deaths.[1] CDC categorizes AR organism threats based on three levels of concern to human health: urgent, serious, and concerning.

- **Urgent threats** require urgent and aggressive action. Urgent threats include Carbapenem-resistant Enterobacterales (CRE), Carbapenem-resistant *Acinetobacter baumannii* (CRAB), *Candida auris (*also known as *Candidozyma auris* or *C. auris)*, and drug-resistant *Neisseria gonorrhoheae*[1].
- **Serious threats** require prompt and sustained action. Serious threats include extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales, methicillin-resistant *Staphylococcus aureus* (MRSA), and multidrug-resistant (MDR) *Pseudomonas aeruginosa*.[1]
- **Concerning threats** require careful monitoring and prevention action. Concerning threats include Erythromycin-resistant group A *Streptococcus* (GAS), and Clindamycin-resistant group B *Streptococcus* (GBS).[1]

These organisms each represent emerging threats to public health because they are highly transmissible, have high potential for community spread, and can cause infections associated with high mortality. Treatment options against these organisms can be limited, and it could be years before new compounds are available to treat them.[1]

The CDC has outlined a five-pillar strategy to swiftly respond to these emerging AR threats: 1) rapid detection of targeted pathogens and their resistance mechanisms, 2) on-site infection control assessments by trained experts to identify gaps in infection prevention, 3) screening of exposed contacts to identify asymptomatic colonization, 4) coordination of the response among facilities, and 5) continuing

[1] Antibiotic Resistance Threats in the United States 2019 https://www.cdc.gov/antimicrobial-resistance/media/pdfs/2019-ar-threats-report-508.pdf

these interventions until transmission is controlled.[2]

In support of their 5-pillar strategy, the CDC established the Antimicrobial Resistance Laboratory Network (ARLN or "AR Lab Network") in 2016 to enhance testing capacity and respond to emerging resistance within the U.S. With congressional support and resources, the CDC made transformative investments in national infrastructure, linking laboratories and healthcare facilities across all 50 states, Puerto Rico, six major cities, and seven regional laboratories.

Healthcare facilities, clinical laboratories, state public health labs, and regional public health labs each face unique challenges and gaps in AR testing and identification. The ARLN infrastructure addresses these challenges to ensure that no single entity must combat an AR threat alone. Network participants support each other with knowledge and testing resources.[3]

Local and regional laboratories within the network provide healthcare facilities with confirmatory isolate testing for resistant organisms and colonization testing to uncover hidden reservoirs of disease. Select laboratories sequence confirmed isolates and alert the CDC, contributing valuable data to understand overall threats and identify potential variants. Nationally, the CDC offers training to regional staff on susceptibility and colonization techniques, ensuring consistent and accurate testing practices nationwide. AR isolates are deposited into the CDC's AR Isolate Bank, which serves both CDC and ARLN labs for validating testing methods.[4]

As new AR threats continue to emerge, the AR Lab Network's agile infrastructure ensures that partners nationwide are well-trained and equipped to effectively address future threats.

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[2] Vital Signs: Containment of Novel Multidrug-Resistant Organisms and Resistance Mechanisms – United States, 2006-2017
https://www.cdc.gov/mmwr/volumes/67/wr/mm6713e1.htm
[3] Antimicrobial Resistance Laboratory Network
https://www.cdc.gov/antimicrobial-resistance-laboratory-networks/php/about/domestic.html
[4] New CDC Network Established as Fungal Threat Emerges
https://archive.cdc.gov/www_cdc_gov/drugresistance/solutions-initiative/stories/ar-lab-network-early-success.html

Texas Antimicrobial Resistance Laboratory

Antimicrobial Resistance Laboratory Network Participation

The Texas AR Laboratory, within the Texas Department of State Health Services (DSHS) Public Health Laboratory in Austin, TX, has been an ARLN participating state laboratory (from 2016 to present) and previously served as the Mountain Region AR Laboratory (from 2016 to 2019). Since joining the network in 2016, the Laboratory has been performing AR testing and coordinating with Texas healthcare providers, the City of Houston, Utah Public Health Laboratory (current Mountain Region AR Laboratory), other Mountain Region states, and CDC programs.

Antimicrobial Resistance Testing and Contributions

Texas AR Laboratory provides testing for organism identification, antimicrobial susceptibility, carbapenemase production, and mechanisms of resistance. In conducting these tests, it uses conventional and molecular methods, but also state-of-the-art technology, such as Matrix Assisted Laser Desorption/Ionization-Time of Flight (MALDI-TOF) and Whole Genome Sequencing (WGS). By offering these tests, the Texas AR Laboratory has made significant contributions to ARLN including testing thousands of specimens of CRE, CRAB, ESBL-producing Enterobacterales, Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), *Neisseria gonorrhea*, and performing colonization screening of CRE, CRPA and CRAB.

Expansion of Testing Capabilities

The Texas AR Laboratory continues to increase testing capabilities to better support state-wide surveillance activities since joining ARLN in 2016. In 2018, the Texas AR Laboratory established a process to identify *C. auris* in isolates and colonization swabs. As a result of these processes, in 2024 the Texas AR Laboratory received and tested 5,043 *C. auris* colonization swabs by Polymerase Chain Reaction (PCR) demonstrating both the laboratory's capacity and the demand from our submitter community for this testing. In March 2024, the Texas AR Laboratory further enhanced our services by offering whole genome sequencing (WGS) testing of *C. auris* samples.

Texas Antimicrobial Resistance Epidemiology

The overall goal of a healthcare-associated infections (HAI) epidemiology response is to slow the spread of all multidrug-resistant organisms (MDROs), with a specific emphasis on the rapid containment of novel or rare MDROs, or resistance mechanisms isolated from healthcare facilities. Since 2017, Texas public health

departments have been implementing HAI epidemiology responses due to ARLN alerts. The CDC's *Interim Guidance for a Public Health Response to Contain Novel or Targeted MDROs*[5] document is used by DSHS as guidance for containment steps such as retrospective surveillance, point prevalence studies, onsite infection control assessments (i.e., ICARs), and prospective surveillance.

Containment steps include systematic, aggressive responses to single cases of high-concern AR, and a focus on stopping transmission. To aid Texas public health departments, DSHS HAI epidemiologists worked with the Texas AR Laboratory, the CDC Division of Healthcare Quality Promotion Program, and CDC Mycotic Diseases Branch to develop this plan, which includes a statewide surveillance process for the detection of emerging resistance and a response process for ARLN alerts.

Purpose

The Texas ARLN Response Plan and Epi-Lab Work Plan (hereafter referred to as "the Texas Response Plan," or "the Plan") is used to solidify Texas' strategies for identification and containment of MDROs and to increase the state's capacity to respond to AR threats. The Texas Response Plan includes two components: 1) a coordinated work plan, 2) an outreach plan.

- The work plan specifies the communication and information flow between the Texas AR Laboratory and the Healthcare Safety Unit's (HSU) HAI epidemiologists.
- The outreach plan outlines the coordination of information between the Texas AR Laboratory, the HSU's HAI epidemiologists, and clinical laboratories. Outreach activities include providing education and technical assistance to healthcare facilities, clinical laboratories, and other healthcare professionals to improve detection of targeted organisms across the state. Additionally, outreach activities are performed for recruitment of isolate submissions and raising awareness of ARLN.

The Plan includes Texas response tiers for resistance mechanisms which include thresholds for conducting onsite ICARs and colonization screenings, as well as the events or results that would trigger ongoing follow-up assessments. Feedback is solicited from internal and external partners annually to modify or update the Plan. This annual review supports an informed and effective public health and infection prevention team to rapidly detect, report, and respond to individual cases and

[5] CDC's Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs): https://www.cdc.gov/healthcare-associated-infections/php/preventing-mdros/mdro-containment-strategy.html

outbreaks of novel or high-concern MDROs.

To ensure response investigations are conducted thoroughly and rapidly to identify and contain organisms with novel and high-concern resistance, Texas HAI epidemiologists align the Plan with the CDC Containment Strategy. To help limit potential negative effects the Plan could have on public health resources and testing capacity, the HAI epidemiologists established parameters to determine triggers for single or repeated colonization studies. These parameters, designed to balance CDC guidance in a way that is not overwhelming to public health partners, are incorporated into the Plan. Education on the parameters is provided to public health partners and healthcare facilities so rapid detection and containment can occur. These parameters facilitate a more efficient and effective implementation strategy for colonization screening until the spread of novel or high-concern MDROs is controlled.

Summary of Updates

The following sections had notable adjustments made since the July 2024 publication of the Texas Response Plan.

1. Cover Sheet
    a. Updated text to distinguish April 2026 publication from the July 2024 publication.
2. Acronyms
    a. Updated with acronyms found in the newly added Appendix G.
3. Background
    a. Added *Candidozyma auris* to align with nomenclature on CDC website.
    b. Updated numbers related to C. auris PCR testing for 2024.
    c. Added clarification that the Antimicrobial Resistance Laboratory Network can be referred to as either "ARLN" or "AR Lab Network" which aligns with CDC branding efforts.
4. Communication
    a. Updated sections to further detail communications at the Mountain Region and CDC level.
5. Laboratory Testing Capabilities
    a. Updated isolate testing section to remove doripenem from the criteria to align with CDC state isolate testing guidance from May 2024. CDC's reason for removal was due to doripenem no longer being clinically available in the US.
    b. Specified considerations for CPO colonization screenings based on test limitations such as patient age and detectable genes.
6. Recruitment
    a. Updated sections to reflect the past year's recruitment efforts and goals for this year.
7. Laboratory Submission Process
    a. Differentiated which test requests are submitted on the G-2E submission form compared to the G-2B submission form.
8. Testing Process Workflow

a. Added details regarding duplicate isolate submissions for CROs and *Candida*.

b. Updated triggers for colonization swabs of CPOs and *Candida* that would reflex to culture and WGS.

c. Specified that WGS is completed by TX Laboratory's in-house Armadillo pipeline based on the CDC's PHOeNIX pipeline.

9. Texas Response Tiers

   a. Removed "Pan-Not Susceptible *Candida auris*" and "Echinocandin-Resistant (Ech-R) *Candida auris*" from Tier 1 organisms.

   b. Edited *C. auris* in Tier 2 organisms to include "Pan-Not Susceptible *Candida auris*" and "Echinocandin-Resistant (Ech-R) *Candida auris*"

10. Epidemiology Response

    a. Updated wording throughout the section for clarity.

    b. Updated link to CDC's *C*. *auris* Infection Control Webpage.

    c. Updated colonization screening recommendations for high-risk contacts based on organism, mechanism, and positive specimen collection.

    d. Clarified process for the retrospective review of lab results.

11. Texas Antimicrobial Resistance Laboratory Data

    a. In the data summary reports section, CRPA, CRE, and CRAB results are now transmitted to CDC in real time through HL7 messaging.

    b. Updated the Using Data For Action section to specify that this year's efforts will be focused on virtual education and conferences.

12. Appendix A

    a. Updated references to the G-2E submission form to also include the G-2B submission form.

13. Appendix B

    a. Updated to align with September 2025 version of CDC document.

    b. Clinical laboratories and healthcare facilities are no longer able to access the AR Lab Network FedEx account directly to create shipping labels. Instead, they must reach out to the state public health laboratory or a local health department. These entities can create labels and send to clinical laboratories and healthcare providers.

c. Local Health Departments may request access to the FedEx account by signing an agreement and emailing it to TexasARLN@dshs.texas.gov.

d. Removed the text and screenshots in the step-by-step section to reflect the changes in obtaining FedEx shipping labels.

e. Removed text and screenshots related to last year's transition of FedEx tools.

14. Appendix D

a. Removed "Pan-Not Susceptible *Candida auris*" and "Echinocandin-Resistant (Ech-R) *Candida auris*" from Tier 1 organisms.

Roles and Responsibilities

This section includes a list of the roles and responsibilities of the team members involved in the implementation of the Plan.

Antimicrobial Resistance Laboratory Expert/Antimicrobial Resistance Laboratory Manager

The manager serves as the subject matter expert (SME) on the laboratory testing workflow, capability, and capacity and is the point of contact (POC) for all technical questions.

Antimicrobial Resistance Team

The AR Team, consisting of DSHS HAI epidemiologists, ensures requests for testing, test results, and any pertinent information are communicated between the laboratories, CDC, and HAI epidemiologists. These epidemiologists have a primary responsibility to communicate AR results from the Texas AR Laboratory to the regional and local health departments.

Antimicrobial Stewardship Team

The Antimicrobial Stewardship (AS) Expert oversees and implements all activities related to AS initiatives in Texas.

Healthcare-Associated Infections/Antimicrobial Resistance Coordinator and Healthcare-Associated Infections Epidemiologists

The HAI/AR Coordinator is responsible for recommending the implementation of epidemiology responses per the Plan and manages the DSHS HAI epidemiologists across the state. The HAI epidemiologists provide recommendations to health departments and healthcare facilities on control measures to implement to prevent the spread of novel and targeted MDROs and communicable diseases. DSHS HAI epidemiologists also assist local health departments (LHD) with obtaining supplies, implementing colonization screenings, and conducting onsite ICARs.

Antimicrobial Resistance Data Analyst

The AR Data Analyst collects, manages, and compiles data on specimen volume, results statistics, turnaround time, and other quality indicators.

Antimicrobial Resistance Laboratory Scientist

The AR Laboratory Scientist performs sample accessioning, testing, and results reporting.

Regional Health Department Epidemiologists

The DSHS HAI epidemiologists work alongside DSHS Regional Health Department epidemiologists who serve as the primary epidemiology contacts for all counties in their Public Health Region (PHR). DSHS HAI epidemiologists and regional epidemiologists are also the primary epidemiology investigators for counties that do not have a LHD, working directly with healthcare facilities and laboratories in their jurisdiction.

A map of public health coverage jurisdictions across Texas counties and PHRs can be found on the Local Health Department and DSHS Public Health Region Coverage Map

Local Health Department Epidemiologists

LHD epidemiologists are the primary epidemiology investigators for their jurisdiction, working directly with healthcare facilities and laboratories in their jurisdiction.

Submitting Facilities

Submitting facilities include any healthcare facility or laboratory that submits isolates or surveillance samples to the ARLN. Submissions may occur on an ongoing, regular basis or in response to a public health investigation.

- Examples of submitting facilities include acute care hospitals (ACHs), long-term acute care hospitals (LTACHs), skilled nursing facilities (SNFs), outpatient clinics, or reference laboratories. These facilities send isolates collected at their own facility or those collected at another healthcare facility, in accordance with the Texas AR Laboratory submission guidance.

Infection Preventionist

The healthcare facility designates an Infection Preventionist (IP) as the SME on methods for preventing and controlling the spread of infectious disease.

Texas Antimicrobial Resistance Laboratory

The Texas AR Laboratory is housed within the Texas DSHS Laboratory, which is the State Public Health Laboratory of Texas. The Texas AR Laboratory is responsible for receiving and testing samples to meet Clinical Laboratory Improvement Amendments (CLIA) requirements, forwarding specimens or isolates as appropriate to the Regional Laboratory or the CDC, issuing CLIA-compliant reports, and ensuring the submitter receives reports. The Texas AR Laboratory communicates regularly with the Regional AR Laboratory so that testing and reporting are performed according to current CDC ARLN guidance. It also serves as a resource for proper collection, shipping, and storage of specimens. In addition, the Texas AR Laboratory requests and secures funding, and creates and submits required progress reports.

Regional Antimicrobial Resistance Laboratory

The Regional AR laboratory of the larger ARLN provides support to the Texas AR Laboratory and to public health department laboratories by providing additional testing capabilities and gathering data to detect existing and emerging AR, changes in resistance, and/or outbreaks in the greater region. Currently, the Utah Public Health Laboratory serves as the Regional Laboratory for the Mountain Region ARLN.

Antimicrobial Resistance Lab Liaison

The AR Lab Liaison facilitates communication between the Texas AR Laboratory, epidemiologists, healthcare facilities and laboratories, and the Regional AR Laboratory to coordinate specimen receipt, result reporting, submitter setup, recruitment, and education.

Communication

Internal Processes

The Texas AR Laboratory and the HSU communicate on a regular basis to coordinate functions. The HSU is responsible for leading and ensuring coordination and communication between the two groups. This is achieved by scheduling regular monthly meetings to discuss topics that include, but are not limited to, laboratory capacity, capability, timeline for colonization surveys, specimen submission criteria, specimen shipping and handling, turnaround time, result reporting, notable investigations/outbreaks, and improvement opportunities. Topic-specific meetings (e.g., ARLN Recruitment, ARLN Response Plan, and Epi-Lab Workplan workgroup meetings) are held to focus on those activities, as needed. When urgent issues arise, the Texas AR Laboratory and the HSU communicate through emails or phone calls. To facilitate collaboration, past and current processes, shared activities, and communications are documented and archived electronically in a shared folder between the groups.

External Processes

The Texas AR Laboratory and the HSU collaborate with the regional and LHDs to recruit and educate facilities to submit isolates to the Texas AR Laboratory for testing. The HAI epidemiologists provide infection control recommendations to health departments and healthcare facilities to prevent the spread of novel and emerging MDROs and *Candida auris*. The AR Lab Liaison proactively initiates contact with healthcare facilities and laboratories to ensure testing and reporting are performed according to current CDC AR Lab Network guidance, and to identify and address other issues that may arise. The Texas AR laboratory and the HSU update submitting facilities with new information and any changes in sample submission processes through ListServ notices, emails, and meetings. The Texas AR Laboratory and the HSU regularly update the DSHS Laboratory website with AR Lab Network related activities and guidance.

Mountain Region

The Texas AR Laboratory, as a member of the Mountain Region ARLN, participates in all conference calls, meetings, and trainings organized by the Regional AR Laboratory. The Texas AR Laboratory and HSU communicate with the Regional AR Laboratory regarding sample submissions that require further testing. The Texas AR Laboratory participates in quarterly state calls with the Regional AR Laboratory and

contacts them for support with surge capacity. HSU participates in the bi-monthly Mountain Region Epidemiology Subcommittee meetings.

Houston Health Department

The Texas AR Laboratory communicates regularly with the HHD Lab, which is an independent ARLN laboratory, to compile statewide HAI statistics. The HHD reports test results to the DSHS HSU and collaborates with DSHS on outbreak investigations. The Texas AR Laboratory and HHD hold regular monthly meetings to ensure collaboration. In addition to the regular monthly meetings, a process improvement workgroup was established in April 2024 to better communicate significant results and facilitate the submission of samples from HHD to DSHS. More frequent communication occurs when necessary, such as during outbreak investigations.

Centers for Disease Control and Prevention

The HAI Investigations Team and AR Team frequently communicate with CDC and Regional AR Laboratory during point-prevalence surveys (PPS)/colonization screenings and outbreak investigations. As needed, more frequent notifications, email correspondences, meetings, and conference calls are required and scheduled to meet the requirement of the specific investigation or response activities. The response activities include communication about specimen submission and reporting and coordination with different teams.

The Texas AR Laboratory maintains regular communication with the CDC about ARLN activities. Representatives of the Texas AR Laboratory attend all meetings held by the CDC, including the meetings held at the beginning of each fiscal year to address expectations over the coming year, bimonthly meetings that address new protocols, guidance, ongoing outbreaks, and one-on-one subject matter expert (SME) meetings. The Texas AR Laboratory notifies the CDC when submitting samples requested by the agency, which follows CDC processing and reporting protocols, such as HL7. The Texas AR Laboratory participates in projects conducted by the CDC and reports data as requested.

Laboratory Testing Capabilities

Tests Conducted on Isolates

Texas AR Laboratory tests isolates for the following organisms:

- Carbapenem-resistant Enterobacterales (CRE) such as *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, and *Enterobacter* spp. that are resistant to imipenem, meropenem, or ertapenem by standard susceptibility testing methods. Also accepted for testing are less-common genera of CRE, such as *Providencia*, *Proteus*, *Morganella*, *Citrobacter*, and *Serratia* that are resistant to carbapenems other than imipenem since many of these organisms are intrinsically resistant to imipenem.
- Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) resistant to imipenem, meropenem, and non-susceptible (intermediate or resistant) to cefepime or ceftazidime by standard susceptibility testing methods; only non-mucoid isolates are accepted for testing. CRPA isolates that are non-susceptible to all antimicrobials tested should be submitted routinely to the Texas AR Laboratory.
- Carbapenem-resistant *Acinetobacter baumannii* (CRAB) that are resistant to imipenem, or meropenem by standard susceptibility testing methods.
- All *Candida* isolates except *C. albicans* are acceptable for testing.
- Difficult to treat or suspected resistant *Neisseria Gonorrhea* isolates and clinical samples.

Texas AR Laboratory performs the following tests on isolates:

- Organism species identification.
- Phenotypic carbapenemase production (CRE and CRPA only).
- AST on bacterial isolates.
- Mechanism testing for carbapenemase genes.

At the Texas AR Laboratory, isolates identified as *C. auris* are forwarded to the Mountain Region AR Laboratory for susceptibility testing.

Colonization Testing Conducted

Carbapenem Resistant Organism versus Carbapenemase Producing Organism

A Carbapenem Resistant Organism (CRO) may resist the action of carbapenem antimicrobials by several different mechanisms. Some CROs use a specific resistance mechanism involving production of carbapenemase enzyme. This enzyme directly breaks apart carbapenem antibiotics, making them ineffective. These organisms are called carbapenemase-producing organisms (CPO).

Carbapenemase-Producing Organisms Colonization Screening

The Texas AR Laboratory performs CPO colonization testing using a real-time PCR method on rectal swabs. Texas AR Laboratory has a testing capacity of up to 120 swabs per day with advanced coordination. The Copan Cepheid sterile transport dual swab collection and transport kits should be used for specimen collection.

When considering the use of this screening test, it is important to note that it has not been FDA cleared for pediatric patients (defined as individuals younger than 22 years old, excluding those on their 22nd birthday). Additionally, the test only detects five resistance genes: KPC, NDM, IMP, VIM, and OXA-48. A negative result would indicate that none of these specific genes were detected. However, this would not rule out carbapenem resistance due to other mechanisms or the presence of other resistance genes, such as OXA-23, that are not detected by the assay.

The swabs and the FedEx shipping costs are provided by the Texas AR Laboratory free of charge. Submitting facilities can request swabs by coordinating the request with their regional HAI Epidemiologist by emailing HAIOutbreak@dshs.texas.gov. See section "Laboratory Submission Process" for information on specimen collection and shipping.

If colonization specimens test positive for any resistance mechanism, HAI epidemiologists are notified by an alert email within one working day. The test report is sent out within one working day of completion of testing to the submitter. The Texas AR Laboratory reports positive CPO colonization results to the CDC through REDCap within one day of test completion.

Candida auris Colonization Testing

The Texas AR Laboratory performs *Candida* colonization testing using a real-time PCR method on ESwabs sampled from body sites such as axilla and groin. The Texas AR Laboratory provides swabs for testing. Submitting facilities can request swabs by coordinating the request with their regional HAI Epidemiologist by emailing HAIOutbreak@dshs.texas.gov. The testing capacity can accommodate up to 100 swabs per day with advance coordination. The Copan Transystem swab designed for CPO colonization testing cannot be used for PCR testing. Additional guidance on specimen collection and shipping can be found here: Texas Antimicrobial Resistance (AR) Laboratory Network.

If a colonization specimen is unsatisfactory for testing, or the total specimen count received does not match the line listing of swabs collected by a facility, the HAI epidemiologist is notified by the DSHS Laboratory Mycology Team as soon as possible after receipt of the specimens.

If the colonization specimens are positive for *C. auris* by PCR, the submitter and HAI epidemiologist are notified by email or telephone within 24 hours. The Texas AR Laboratory reports *C. auris* identifications to CDC through REDCap, a secure web application for building and managing databases, within 24 hours.

Once the PCR testing is completed, a summary spreadsheet of the results is compiled by the DSHS Lab Mycology Team and emailed to the HAI epidemiologist within 24 hours.

Additional testing

The Texas AR Laboratory performs WGS on all CPOs excluding *bla*KPC producing CREs. Submitters may request outbreak investigation, including WGS, by coordinating with their regional HAI Epidemiologist. Requests are dependent on current capacity and capabilities. Priority for sequencing is established based on CDC guidance described in Appendix G of this document.

Recruitment

Data Analysis

The ARLN Recruitment Workgroup reviews data related to isolates submitted to the TX AR Laboratory. The types of healthcare facilities that submit isolates directly to the DSHS Laboratory include ACHs, LTACHs, and reference laboratories. The reference laboratories submit isolates from a variety of healthcare settings including acute care, long-term care, and outpatient settings. Data are reviewed to understand the geographical locations where isolates with resistance mechanisms are collected and where AR-positive patients reside.

In the Spring of 2024, the HSU and DSHS Laboratory developed a survey and distributed it to AR laboratories statewide to assess barriers to isolate submission. The data was analyzed to identify respondents' barriers to isolate submission in Texas. The results will be used by the DSHS Laboratory and HSU to modify the recruitment process and materials accordingly to increase isolate submission.

Criteria for Targeting Facilities

To increase the submission of CRAB, CRE, CRPA, and *C. auris* isolates, the Texas AR Laboratory continues to recruit laboratories serving Texas healthcare facilities, which includes clinical laboratories and reference laboratories. Healthcare facilities in PHRs with historically low specimen submissions and laboratories serving high acuity settings such as LTACHs and SNFs are targeted for isolate submissions. The Texas AR Laboratory will also target laboratories which previously submitted isolates but have not submitted isolates in one year. Additionally, HSU will recruit laboratories serving areas in Texas with the highest MDRO burden who are not submitting isolates to the AR Laboratory Network.

Recruitment activities will also focus on regions that have reported *C. auris* in the past. HSU and the Texas AR Laboratory will continue to establish relationships with other facilities, such as academic laboratories, which receive fungal isolates.

Methodology

Initial recruitment efforts involved mailing recruitment letters to laboratories statewide. This mailer was followed up with recruitment via word-of-mouth and by discussing AR Lab Network activities at in-person laboratory and infection prevention meetings across the state. In August of 2024, the Texas AR Laboratory distributed a clinical engagement letter that summarized the isolates tested at the lab and how they align with national AR trends. Additionally, while HAI

epidemiologists conducted investigations of reportable MDROs, isolates that met submission criteria were requested to be submitted for additional testing. Instructions for isolate submission were shared by laboratory and epidemiology staff whenever a facility indicated an interest in submitting isolates. Additionally, the DSHS Laboratory continues to update the DSHS ARLN website to provide facilities with up-to-date information on AR specimen submission criteria, submission steps, shipping guidance, and how to obtain specimen collection kits.

The ARLN Recruitment Workgroup will continue to update the list of laboratories to target based on the criteria identified above, to recruit laboratories in PHRs used by the targeted LTACHs and SNFs. Additionally, the Texas AR Laboratory will utilize a list of clinical laboratories from which to recruit submissions. This list is compiled from information gathered by the ARLN Recruitment Workgroup, targeted LTACH and SNF reference labs, and Laboratory Information Management System (LIMS) queries of prior AR sample submitters. The HSU and Texas AR Laboratory will develop materials to utilize in these recruitment efforts for consistency of methodology and information. Examples of the Texas approach include sending ListServ notices, making telephone calls, surveying laboratories, conducting webinars or in-person meetings and communicating via emails. In addition, recruitment letters and flyers developed by the HSU and Texas AR Laboratory will be emailed to healthcare laboratories and posted on the DSHS Laboratory website.

MDRO burden will be assessed by extracting notifiable CRE and *C. auris* case data from the National Electronic Disease Surveillance System | CDC. The data will be reviewed to identify the top three PHRs with the highest number of cases by organism. A list of facilities that reported CRE and *C. auris* in these PHRs (based on patient's county of residence) will be created and compared to the current DSHS Laboratory submitter list to identify the laboratories used by facilities not currently submitting isolates to DSHS.

Collectively, these tools and collaborative efforts have further improved the Texas AR Laboratory's potential for detection, containment, and treatment of AR organisms in Texas communities.

Technical Support

The DSHS Laboratory and HSU will continue to provide technical and epidemiologic consultations, which includes providing instructions on isolate submission criteria, collection of colonization screening specimens, completion of the laboratory's specimen submission form, labeling of each specimen, and packaging and shipping specimens. Virtual education opportunities will offer a proactive approach to preventing common issues for technical support.

For epidemiological consultation and collection of colonization screening specimens the HSU can be contacted by emailing HAIOutbreak@dshs.texas.gov. The Texas AR Laboratory can provide technical assistance and support for sample submission issues by emailing TexasARLN@dshs.texas.gov.

Laboratory Submission Process

To submit specimens to the Texas AR Laboratory, submitters must adhere to the following steps (Appendix A):

Create a Submitter ID Account

Submitters of colonization swabs and/or isolates to the Texas AR Laboratory must have a Submitter ID Account with Texas DSHS Public Health Laboratory Division in Austin prior to submitting samples. New submitters (or current submitters needing to update previous account information) must complete a Submitter ID Request Form, which is located at www.dshs.texas.gov/lab/MRS_forms.shtm#Microbiological

G-2E Specimen Submission Form

Specimens sent to the Texas AR Laboratory for the following tests must be accompanied by a G-2E Submission Form. Specimen submission forms prepopulated with facility specific identification may be requested by emailing LabInfo@dshs.texas.gov or by calling (512) 776-7578.

- CPO Colonization Screenings
- CRO Isolates
- Candida Screenings
- Candida Isolates
- Candida WGS

G-2B Specimen Submission Form

Specimens sent to the Texas AR Laboratory for the following tests must be accompanied by a G-2B Submission Form. Specimen submission forms prepopulated with facility specific identification may be requested by emailing LabInfo@dshs.texas.gov or by calling (512) 776-7578.

- HAI WGS of Bacteria
- Isolates and identification testing uses G-2E above
- GC AST Testing

FedEx Shipping Labels

FedEx shipping label available upon request through the ARLN Shipping Label Request Form.

Specimen Collection and Shipment Instructions

All samples must be shipped following UN3373 shipping guidelines and be accompanied by a completed G-2E or G-2B form. There must be two unique identifiers on the form that exactly match the identifiers on the specimen label (Appendix C lists acceptable unique patient identifiers). All CRO isolate submissions must include culture reports indicating carbapenem resistance as indicated in the Laboratory Testing Capabilities section on page 30. See Appendix A and Texas Antimicrobial Resistance (AR) Laboratory Network for more information on specimen collection and shipping.

Technical Support

The Texas AR Laboratory provides technical assistance and support for sample submission issues. Technical support may be obtained by emailing TexasARLN@dshs.texas.gov a brief statement regarding the key point(s) of the inquiry.

Specimen Receiving and Processing

Specimens received by the Texas AR Laboratory are first processed by the Texas DSHS Specimen Acquisition Branch. The specimen check-in process is typically swift, usually taking less than half a day. However, if specimens fail to meet accessioning criteria or arrive later in the workday, they may take longer to reach the testing area. Submitters should be mindful of their organism's testing window and consider the duration of time between sample collection and arrival at the laboratory.

- Upon delivery, specimens are transported to the designated receiving area. Here, they undergo inspection to ensure they were transported at the correct temperature, adhering to the laboratory's requirements. The specimen container's condition is also examined for appropriate sample volume and any visible signs of damage or leakage.
- Simultaneously, accompanying paperwork (specimen submission forms) is meticulously reviewed for completeness and accuracy. Each specimen is cross-referenced with the submission form to verify proper labeling, including two matching unique patient identifiers, as well as the date and time of collection.
- Specimens that meet all shipping, documentation, and accessioning criteria are logged into the LIMS and receive a DSHS barcode. Conversely, specimens that fall short of the testing criteria are temporarily held at check-in while the submitter is contacted.
    - The submitter will be notified if the issues are eligible to be resolved over the phone, by email, or via fax. Timely resolution is crucial to expedite sample testing.
    - In cases where issues cannot be resolved, either due to the nature of the issue or expiration of the testing window, the specimen is declared unsatisfactory for testing and the test order is cancelled. Submitters will receive a test report for cancelled samples including a note describing the reason for cancellation. If desired, submitters have the option to submit a new specimen for testing.
- From the laboratory check-in area, the specimens are sent to the relevant testing areas. Testing of isolates and rectal swabs for CRE, CRPA, and CRAB are performed by the Bacteriology Branch. Whole genome sequencing of CRE, CRPA, CRAB, and Candida are performed by the Advanced Molecular

Detection (AMD) team. All Candida samples are tested by the DSHS Laboratory Mycology Team.

Testing Process Workflow

Isolates for Carbapenem-Resistant Enterobacterales, Carbapenem-Resistant *Pseudomonas aeruginosa*, and Carbapenem-Resistant *Acinetobacter baumannii*

- **Day One** – CRE, CRPA, and CRAB isolates are struck to Trypticase Soy Agar (TSA) plates with 5% sheep's blood and incubated overnight.
- **Day Two** – Streaked plates are checked for purity and adequate growth for testing. Organism ID is confirmed by MALDI-TOF. Antimicrobial susceptibility testing by broth microdilution is initiated for CRE, CRPA, and CRAB. The Modified Carbapenem Inactivation Method (mCIM) is initiated for CRE and CRPA only.
- **Day Three** – BMD and mCIM results are interpreted. CRE and CRPA mCIM positive isolates as well as all CRAB isolates will have real time PCR performed for *bla*KPC, *bla*NDM, *bla*IMP, *bla*VIM, and *bla*OXA- 48 like genes. CRAB isolates will also have CDC PCR performed for *bla*OXA-23-like, *bla*OXA-24/40-like and *bla*OXA-58-like genes.
    - After data review and results are released in LIMS, PCR results are sent to the HAI epidemiologists. Specimen results that meet CDC alert guidance are entered into the REDCap alerts website. Using the sequencing priorities set up by the CDC, certain isolates are whole genome sequenced. WGS ID and NCBI SRR ID[6] are entered into REDCap alert.
- Duplicate Isolates:
    - Duplicate submissions consume additional time and resources, leading to slower results and redundant data. To reduce the number of duplicate isolates tested, the AR Laboratory checks internal databases for recently received results from that organism and patient.

[6] When samples are uploaded to a sequence read archive (SRA) database, they are given a unique accession code with a three-letter prefix. The prefix SRR indicates that this sample was uploaded to the NCBI database, and the data represented is a run.

- Criteria: If an AR isolate has already been submitted within the past 6 months from the same patient, same collection source, and same organism.
- If duplicate isolate(s) arrive with different specimen sources, the more invasive collection source is prioritized, ex: blood> sputum > wound.
- Isolates identified as duplicates will be canceled and the submitter will be notified.

Exceptions: If there is a significant change in AST profile, if there is suspicion of carbapenemase gene acquisition, or specific epidemiological request, the AR laboratory will test an isolates again.

Candida Isolates for Identification

- **Day One or Day Two** – *Candida* isolate is received in the lab and subcultured within three days to fresh culture medium.
- **Day Two to Day Three** – Identification of *Candida* isolate is performed from fresh subculture by MALDI-TOF.

Duplicate Isolates:

- Duplicate submissions consume additional time and resources, leading to slower results and redundant data. To reduce the number of duplicate isolates tested, the AR Laboratory checks internal databases if the lab has recently received results for that organism and patient.
  - Criteria: If an AR isolate has already been submitted within the past 6 months from the same patient, same collection source, and same organism.
  - If duplicate isolate(s) arrive with different specimen sources, the more invasive collection source is prioritized, ex: blood> sputum > wound.

Exceptions:

- Because *C. auris* is reportable, identification will be performed on all isolates received. Duplicate specimens may be ruled out for AFST and WGS depending on the situation. If there is specific epidemiological request, the AR laboratory will test an isolate again.
- If identification is *Candida auris*, the submitter and HAI epidemiologist are notified by email or telephone that same day. The Texas AR Laboratory reports *C. auris* identifications to the CDC through REDCap within 24 hours.

Candida Isolates for Antifungal Susceptibility Testing

The Texas AR Laboratory performs susceptibility testing on identified *Candida* isolates that meet the CDC screening criteria.

. Colonization for *Candida auris*

- **Day One** – Swabs are received in the lab, checked for compliance with CAP/CLIA regulations and stored overnight at refrigeration temperatures.
- **Day Two** – DNA is extracted from the swab transport solution and PCR for *C. auris* is performed. Note: if necessary, extracted DNA may be stored for PCR to be performed at a later date.
- **Day Two** – PCR Indeterminate swab solutions are inoculated into a Salt Sabouraud Dulcitol Broth enrichment culture medium with chloramphenicol and gentamicin. Cultures are incubated in a 40°C incubator.
- **Day Three to Day Seven** – Incubated culture broths are inspected each day for growth. When there is growth, or at Day Five if no growth is detected, cultures are inoculated to CHROMagar plates and incubated for two additional days. Yeast colonies on CHROMagar are identified by MALDI-TOF. Note: a weekend may extend the timeline by two days.

Colonization for Carbapenemase-Producing Organisms

- **Day One** – Swabs are received in the laboratory, checked for compliance with CAP/CLIA regulations. Swabs should be processed the same day of receiving using the Cepheid Xpert Carba-R assay (an FDA approved real-time PCR assay) or stored overnight at refrigeration temperatures.
- **Day Two-Day Four** – Positive results are reported within 24 hours of testing. PCR positive swabs are inoculated into Blood Agar Plates and MacConkey Agar Plates to attempt isolation of the CPO. Note that a positive PCR result does not indicate organism viability and CPO isolation may not be possible.
- **Day Five and beyond** – Any positive colonization swabs will be cultured. If the CPO is successfully isolated from the swab, the AR Laboratory will

perform the full panel of testing (described above for isolates) including WGS.

Isolates and Clinical Samples of *Neisseria gonorrhea* for Antibiotic Susceptibility Testing

Disclaimer: this testing is not coordinated with the regional HAI Epidemiologists. Coordination of testing is done through the Public Health Laboratory Division.

Isolate Testing of *Neisseria gonorrhea*

- **Day One** – Neisseria gonorrhea isolates are streaked on chocolate agar plates and modified Thayer martin and incubated overnight.
- **Day Two** – Streaked isolates are checked for purity. Organism ID is confirmed by MALDI-TOF. Antimicrobial susceptibility testing for Neisseria gonorrhea isolates is initiated with Etest.
- **Day Three** – Etest results are interpreted. Neisseria gonorrhea positive isolates resistant for cefixime or ceftriaxone will have WGS performed.
    - After data review and results release in LIMS, AST specimen results that meet CDC alert guidance are sent to the HIV/STD epidemiologists and entered into REDCap within 24 hours. Using the priority set up by the CDC, isolates are whole genome sequenced. WGS ID and NCBI SRR ID are entered into REDCap alert.

Clinical Sample Testing of *Neisseria gonorrhea*

- **Day One** – *Neisseria gonorrhea* clinical samples are streaked on chocolate agar plates and modified Thayer martin and incubated overnight.
- **Day Two to Day Three** – If *Neisseria gonorrhea* colonies are present, the lab will re-streak and attempt to isolate pure colonies. The isolation process may take an additional three to five days.
- **Day Four and beyond** – Pure isolates of *Neisseria gonorrhea* have their Organism ID confirmed by MALDI-TOF. Antimicrobial susceptibility testing for *Neisseria gonorrhea* isolates is initiated with Etest. Once completed, the Etest results are interpreted.
    - After data review and results release in LIMS, AST specimen results that meet CDC alert guidance are sent to the HIV/STD epidemiologists and entered into REDCap within 24 hours. Using the priority set up by the

CDC, isolates are whole genome sequenced. WGS ID and NCBI SRR ID are entered into REDCap alert.

Whole Genome Sequencing and Cluster Analysis

The beginning of the WGS process depends on if the specimen is already in the laboratory and whether it has already completed laboratory processes, such as DNA extraction. Once DNA extraction is completed, the Advanced Molecular Detection (AMD) team, within the DSHS Laboratory's Genetic Sequencing Branch, commences their workflow from day one, by selecting the highest priority organisms to sequence. Once sequencing is completed, the bioinformaticians perform cluster analysis of sequenced organisms.

- **Pre-WGS (One - Three Days)** - Relevant teams perform specimen check-in, isolation, and applicable tests (MALDI, E-test, qPCR) prior to DNA extraction. Note that weekends may extend this timeline by two or more days.
- **Day One to Day Two** – The AMD team performs library preparation and sequencing using the Illumina MiSeq or NextSeq. Raw sequence FastQ files are stored locally. Priority level of sequencing requests are determined using the CDC guidance in Appendix G of this document.
- **Day Three to Day Four (AMD)** – Samples are running on the instrument (MiSeq/NextSeq).
- **Day Five to Day Six (AMD)** – Amazon Web Services (AWS) upload is conducted for analysis using the in-house Armadillo pipeline (based on the CDC's PHOeNIX pipeline). Quality metrics of sequencing data are assessed, and AMR genes and hypervirulence genes, if present, are identified. Data are submitted to NCBI, and the SRR ID is retrieved. WGS results are entered, reviewed, and released in LabWare. Alerts are recorded in REDCap.
- **Day Seven to Day Eight (Bioinformaticians)** - The Bioinformatics team, upon request and with epidemiologist approval, conducts cluster analyses. Metadata files containing demographic data, multilocus sequence type (MLST) characterization, and relatedness trees are shared exclusively with the epidemiologist. This analysis serves as an additional tool for the epidemiologist's interpretation of potential relatedness, considering the specimen history and facility of origin. It is important to note that the laboratory's cluster analysis should not be used for diagnostic or treatment purposes.

Texas Response Tiers

CDC defines four tiers for epidemiologic response to novel or targeted MDROs. The definitions for each tier are outlined below. Based on results from an analysis of Texas data from 2022–2025, Texas established the following response tiers:

Tier 1

This category includes organisms or resistance mechanisms that have never (or very rarely) identified in the U.S. and for which experience is extremely limited. The objective of Tier 1 organism investigations is to identify all cases and prevent further transmission. Tier 1 organisms in U.S. healthcare settings require more extensive evaluation to define the risk for transmission and the extent of spread.

Tier 1 organisms include:

- Novel organisms and resistance mechanisms.

Tier 2

For Tier 2 organisms, information is available from U.S. or comparable settings about how transmission of these organisms occurs and the groups primarily at risk. Tier 2 MDROs are primarily associated with healthcare settings and are not commonly identified in the region. Generally, these have either not been previously identified in the region or have been limited to sporadic cases or small outbreaks (i.e., correspond to "not detected" or "limited to moderate spread" epidemiologic stages). However, these MDROs might be found more commonly in other areas of the U.S. or even in other regions or patient sharing networks within the same jurisdiction. Tier 2 Organisms include organisms which no current treatment options exist (pan-not susceptible) and that have the potential to spread more widely within a region (e.g., have plasmid-mediated resistance mechanisms), even if more susceptible isolates of the same organism and mechanism are more commonly identified (i.e., Tier 3 or endemic).

Tier 2 organisms include:

- Pan-not susceptible[7] (CRAB, CRE, CRPA)
- CRE, CRAB, or CRPA with dual mechanisms identified (e.g., NDM and OXA-48).
- *C. auris*, including Pan-not susceptible[7] and Echinocandin-resistant (Ech-R)
- CRAB (IMP, KPC, NDM, VIM, uncommon plasmid-mediated OXA)

- CRE (IMP, VIM)
- CRPA (IMP, KPC, NDM, OXA-48)

Tier 3

For Tier 3 organisms, information is available from U.S. about how transmission of these organisms occurs and the groups primarily at risk. These are MDROs targeted by the facility or region for their clinical significance and potential to spread rapidly (e.g., to other regions where they are less common). Tier 3 MDROs have been identified more frequently across a region than Tier 2 MDROs and are typically in stages of advanced spread but are not considered to be endemic. These organisms might be endemic in other areas of the U.S. but are not endemic in this region.

Tier 3 organisms include:

- CRE (NDM, OXA-48)
- CRPA (VIM)
- mCIM+/PCR-

Tier 4

Endemic (Tier 4) organisms are endemic in a region, but can be less common in other areas of the U.S. These are MDROs that have been targeted by public health for their clinical significance and potential to spread rapidly (e.g., to other regions where they are less common). Information is available from the U.S. about how transmission of these organisms occurs and the groups primarily at risk

Tier 4 organisms include:

- CRE (KPC, mcr)
- CRAB (OXA-23, OXA-24/40, OXA-58)

Epidemiology Response

Notification and Confirmation of a Positive Antimicrobial Resistance Lab Network Result

If the report comes from the Texas AR Laboratory, Houston AR Laboratory, or Mountain Region AR Laboratory, the HSU will perform the following within one workday:

- Retrieve laboratory report from DSHS CITRIX/LabWare or DSHS Lab Online Portal and confirm results match the notification.
- If the laboratory report cannot be retrieved in DSHS CITRIX/LabWare or DSHS Lab Online Portal, request a copy from the Texas AR Laboratory (TexasARLN@dshs.texas.gov) or Houston AR Laboratory (HoustonARLN@houstontx.gov).
- Forward the confirmed result to the health department in the jurisdiction of the facility where the specimen was collected.

If the report comes from a facility or reference laboratory, the epidemiologist conducting the investigation will obtain the laboratory report to confirm the reported result within one workday.

- If the CRAB, CRE, CRPA, or *C. auris* isolate is still available and meets ARLN submission criteria, the epidemiologist will request that it be sent to the Texas AR Laboratory for additional testing as needed.
- Submission of *C. auris* isolates is mandatory pursuant to Title 25, Part 1, Chapter 97.3 of the Texas Administrative Code https://texreg.sos.state.tx.us/public/readtac$ext.TacPage?sl=R&app=9&p_dir=&p_rloc=&p_tloc=&p_ploc=&pg=1&p_tac=&ti=25&pt=1&ch=97&rl=3It is highly recommended to send pan-not susceptible isolates to the Texas AR Laboratory.
- If the laboratory has not submitted to the Texas AR Laboratory previously, they will need to create an account. The HAI epidemiologist will follow the steps listed in the section "Laboratory Submission Process," provide facility the Submitter ID Request Form www.dshs.texas.gov/lab/MRS_forms.shtm#Microbiological and ask them to follow the instructions on the document.

Immediate Actions

The response strategies are described below for the LHD epidemiologist (also referred to as the "investigating" epidemiologist) with jurisdiction over the healthcare facility. These strategies may occur concurrently or in a different sequence from the numbered strategies in the guidance. The order of the strategies does not reflect their relative importance.

- Determine response tier by utilizing the response tier definitions in the Plan.
- Notify the IP.
  - It is important that the IP at the patient's current facility be notified of the result. The epidemiologist should provide education to the IP on the organism and resistance mechanism.
  - Prioritize the facility where the index patient is currently admitted for a rapid infection control assessment to identify and address any potential gaps in infection prevention and control (IPC).
  - If the MDRO was present on admission, notify the transferring facility so appropriate investigation can occur at that facility.
- Implement control measures at current facility.
  - Ensure contact precautions[7,8] or enhanced barrier precautions[9] are initiated, if not already implemented. Discuss the need for strict adherence to precautions. Removal of the patient from precautions is discussed further below.
  - Refer to the *DSHS Emerging and Acute Infectious Disease Unit's Investigation Guidelines* for control of *Carbapenem-resistant Enterobacterales* (CRE).[10] These guidelines are applicable for novel or emerging multidrug-resistant organisms.
  - Refer to the DSHS Emerging and Acute Infectious Disease Unit's

[7] Management of Multidrug-Resistant Organisms in Healthcare Settings, 2006: http://www.cdc.gov/hicpac/pdf/MDRO/MDROGuideline2006.pdf.
[8] CDC's Guidelines for Isolation Precautions, 2007: http://www.cdc.gov/hicpac/2007ip/2007isolationprecautions.html.
[9] CDC Implementation of Personal Protective Equipment (PPE) in Nursing Homes to Prevent Spread of Novel or Targeted Multidrug-resistant Organisms (MDROs): Implementation of Personal Protective Equipment (PPE) Use in Nursing Homes to Prevent Spread of Multidrug-resistant Organisms (MDROs) | LTCFs | CDC
[10] Texas Department of State Health Service Emerging and Acute Infectious Disease Guidelines: https://dshs.texas.gov/IDCU/investigation/Investigation- Guidance/

Investigation Guidelines for control of *C. auris*[10] and use the guidance from CDC[11] and Environmental Protection Agency (EPA)[12] as listed on the CDC's *C. auris* Infection Control webpage, found at: https://www.cdc.gov/candida-auris/hcp/infection-control/index.html. See references for EPA List P[12], the current list of EPA-approved products for *C. auris* disinfection.

- Recommend the following minimum education be provided to the facility:
  - ◊ Since the resistance mechanism may be new to staff, provide information on AR for the facility to educate staff and patient/visitors. If additional education is needed, the IP should contact the epidemiologist.
  - ◊ The IP should re-educate staff on appropriate moments and methods for hand hygiene, proper personal protective equipment (PPE) usage, and environmental cleaning and disinfection.
  - ◊ Request the facility or reference laboratory notify the IP of any additional laboratory reports identifying similar organisms or resistance and save the isolate(s) for potential submission to the Texas AR Laboratory. The IP should inform the epidemiologist of results within one working day.
- Staffing and patient placement:
  - ◊ Place the patient in a private room. If a private room is not available and there are multiple patients with the same organism and resistance mechanism, cohort them accordingly. When possible, dedicate staff to care for positive patient(s) only.
  - ◊ Educate staff (i.e., therapy staff, respiratory staff, housekeeping) to complete duties for all other patients prior to caring for the patient(s) with an AR organism or mechanism, when feasible.
- Interfacility transfer communication:
  - ◊ If the patient is transferred to another healthcare facility, communicate MDRO history and the need for transmission-based precautions to the receiving facility via the DSHS Inter-Facility Infection Prevention Transfer Form, found at

[11] Recommendations for Infection Prevention and Control for Candida auris: Infection Control Guidance: Candida auris | Candida auris (C. auris) | CDC

[12] EPA List P: Antimicrobial Products Registered with EPA for Claims Against Candida Auris :https://www.epa.gov/pesticide-registration/list-p-antimicrobial-products-registered-epa-claims-against-candida-auris.

https://www.dshs.texas.gov/sites/default/files/IDCU/health/Healthcare-Safety/Interfacility-Transfer-Form-final-Revised-AM-111221.pdf .

- ◊ If the patient has been transferred to their current facility from another healthcare facility, please follow recommendations in the "Previous Facilities" section of this document.

- Notify the patient about the results and infection control measures being implemented.
- Notify leadership.
  - ◊ Follow the health department jurisdiction's protocols for notifying leadership of ARLN alerts and investigations.
  - ◊ During the investigation, the HAI epidemiologist may contact the CDC for assistance or to collaborate on containment strategies.

Obtain Patient History

Obtain the patient's healthcare history, as outlined below. Use the DSHS Line List Template provided by the HAI epidemiologist to record and update obtained information.

Request medical records (or electronically review records) to identify possible risk factors for the infection. Historical information should be obtained from the facility where the specimen was collected, the current facility, and/or the transfer facility. Below are the items to be requested:

- History and physical (H&P)
- Discharge summary
- Reason for testing, and affiliated infectious disease/physician notes
- Control measures, including contact precautions, which have been implemented, including date(s) initiated and date(s) discontinued.
- Bed/Room assignments (including roommates)
- Medical History:
  - Existing conditions
  - Positive cultures for the last month
  - Ongoing procedures/treatments such as hemodialysis, wound care, etc.
  - Existing indwelling devices or drains at the time of culture.
- Hospitalization status

- Healthcare Exposures:
  - In the 30 days prior to the collection date and in the time after the positive collection date, inquire if the patient had any other healthcare admissions, outpatient visits, or medical procedures.
    - ◊ List facility names and location, the reason for the visit, and admission dates, discharge dates, and procedure dates.
    - ◊ If the patient had roommates during these recent healthcare admissions, obtain the same information noted above for each roommate.
  - Follow recommendations in the "Previous Facilities" section of this document.
  - Notify the HAI epidemiologist of facilities identified outside of the LHD jurisdiction.
- Travel History:
  - Inquire about any trips, hospitalizations, or surgeries outside the U.S. in the previous 12 months.
    - ◊ If travel is identified, obtain travel dates and locations.
    - ◊ List healthcare visit information that occurred while traveling (including delineating outpatient versus overnight stay). If able, obtain the names of the healthcare facilities and the dates of care.

Meet with Current Facility

Meet with the patient's current facility via conference call or in-person and request assistance from the HAI epidemiologist, if needed. The purpose of the meeting is to explain the organism and resistance mechanism, transmission methods, the importance of appropriate infection control measures, and to address questions from administration and staff. The facility press officer should be invited, as needed.

Conduct Infection Control Assessments

Conduct either a remote or onsite ICAR at the patient's current facility, facilities where the patient has been admitted since the positive collection date, and facilities the patient was admitted to in the 30 days prior to the positive collection date. The ICAR aims to ensure that appropriate IPC measures are in place to prevent MDRO transmission. A remote ICAR can be conducted prior to the onsite ICAR, and findings may prompt an onsite ICAR.

An onsite ICAR is warranted if the patient was not on contact precautions, or the facility reports non-compliance or unknown compliance in the areas of hand hygiene, PPE usage, or environmental cleaning and disinfection. An onsite ICAR is also an excellent opportunity to have a face-to-face meeting with facility administration, infection control practitioners, and laboratory management to provide education and address questions and concerns.

General guidelines for conducting ICARs include:

- Use of an appropriate CDC ICAR tool for the specific type of healthcare facility. Consult with an HAI epidemiologist for the most appropriate tool for the setting.
- Observations of the following:
  - Proper isolation precautions signage.
  - Hand hygiene.
  - PPE selection.
  - Donning/doffing of PPE.
  - Appropriate use of disinfectants.
  - Cleaning/disinfection processes for the equipment (dedicated and shared equipment).
  - Cleaning/disinfection processes for the environment that are conducted by all staff (Environmental Services, nursing, etc.).
  - Processes for waste disposal (linen, trash, biohazard waste).
  - Proper handling of medical devices (central lines, urinary catheters, respiratory support, etc.).
  - Interfacility communication processes for MDROs.
- Review of documentation of staff education (i.e., sign-in sheets, presentation, handouts).
- Assessment of staff knowledge and processes.
- Discussion of an action plan that will address any gaps identified at the conclusion of each ICAR.
- Conduct a follow-up meeting if additional cases occur after the initial ICAR.

Previous Facilities

- In general, healthcare exposures that occurred in the month prior to the positive specimen collection should be investigated unless the information is available about the time the AR organism or mechanism was most likely acquired[13]. Contact an HAI epidemiologist for guidance.
- Facilities should be encouraged to update medical records, per their internal protocol, for flagging patients with MDROs.
- Conduct an onsite ICAR if the patient was not on contact precautions, or if the facility reports non-compliance or unknown compliance in the areas of hand hygiene, PPE usage, or environmental cleaning and disinfection.
- Depending on the infection control measures implemented at these healthcare facilities, colonization screening may be recommended.

Prospective and retrospective surveillance should be implemented per the guidance in this document.

Colonization Screening and Point-Prevalence Survey

Colonization screening is recommended for high-risk contacts (i.e. roommates, patients who shared a bathroom). High risk contacts are identified based on their level of interaction with the index patient in the month prior to the positive specimen collection of the AR organism or mechanism. Screening should occur even if the index patient was being managed with Contact Precautions or Enhanced Barrier Precautions. If indicated, the epidemiologist will:

- Identify high-risk contacts at patient's current and previous facilities.
  - High-risk contacts are defined as patients or residents at the highest risk for acquisition.
  - Refer to the CDC's Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs)[14] for screening recommendations according to the Response Tier of the

[13] CDC Screening for *C. auris* colonization https://www.cdc.gov/candida-auris/screening/index.html

[14] CDC's Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs): https://www.cdc.gov/healthcare-associated-infections/php/preventing-mdros/mdro-containment-strategy.html

organism. See Appendix D for a summary table of containment elements from the guidance document.

- For Tier 1, family members may be considered for testing, depending on the patient's and family members' medical history. Consult with the HAI epidemiologist.
- Screening may be necessary for high-risk contacts who have been discharged from the facility prior to the implementation of control measures. This should be implemented in consultation with the HAI epidemiologist.
- Screening healthcare workers is generally not recommended. For Tier 1, healthcare workers may be considered for testing, depending on the epidemiology factors identified in the investigation. The epidemiology is usually more consistent with transmission occurring through contamination of healthcare workers' hands and clothes, shared medical equipment, or the environment, rather than through a colonized healthcare worker.

- Obtain specimens
  - The HAI epidemiologist will provide the investigating epidemiologist with the appropriate laboratory submission form to be used for each specimen collected.
  - Coordinate with the HAI epidemiologist to obtain the appropriate swabs for the specific organism or mechanism being tested
  - After the specimen is collected, the specimen should be shipped within one day of collection. Laboratory testing must be performed within four days of specimen collection.
  - Educational resources for collection, packaging, and shipping are available from the HAI epidemiologist upon request.
  - A sample verbal consent script can be provided by the HAI epidemiologist upon request.
  - Check with the HAI epidemiologist to verify the laboratory's testing capability for resistance mechanisms or *C. auris*.
  - Coordinate with the HAI epidemiologist and the facility's IP to schedule a date for collecting specimens. The HAI epidemiologist will confirm testing capacity with the AR laboratory. The specimens should be shipped within one day.

    - The Texas AR Laboratory does not receive shipments on the weekend, holidays, or DSHS holidays. Do not ship specimens to the Texas AR Laboratory on Thursdays, Fridays, or Saturdays.
    - Ensure that employees tasked with packaging and shipping swabs are properly trained to ship infectious substances. If they are not trained, request assistance from public health partners for training.
    - Complete the DSHS Colonization Screening Line List, which will be provided by the HAI epidemiologist. Email the completed list to the HAI epidemiologist on the day the specimens are collected.
    - Once shipped, obtain the FedEx tracking number and email it to the HAI epidemiologist.
    - Two patient identifiers are required for submission on both the submission form and the specimen tube. Patient identifiers on both must match.
- To allow infection control measures to be implemented quickly, results will be sent to the LHD epidemiologist and/or healthcare facility by the HAI epidemiologist the same day they are received. If a colonization screening patient tests positive, a new round of contact tracing and testing will be done.

A PPS should be implemented if there is evidence or suspicion of ongoing transmission in a facility. In a PPS, every patient on a given unit or floor where transmission is suspected should be screened. Consider doing a PPS even if all known cases have been discharged.

- Periodic (e.g., every two weeks) response-driven PPS should be conducted until transmission is controlled, defined as two consecutive PPS with no new cases identified or, in facilities with high colonization pressure, substantially decreased transmission.
    - If high levels of transmission persist across multiple point prevalence surveys in long term care settings, consider increasing the interval between surveys (e.g., performing every 4-6 weeks) or temporarily pausing them while reassessing infection control and implementing interventions.
- Contact Precautions or Enhanced Barrier Precautions should be initiated for patients who are waiting for screening results and for all positive patients. If a patient with pending results is transferred to another facility, the pending result status should be communicated to the facility admitting the patient. Test results should be provided to both facilities.

Retrospective Review of Laboratory Results

- Engage clinical laboratories that serve healthcare facilities where the index patient received care in the previous 30 days for prospective and retrospective surveillance to identify organisms with similar resistance profiles from clinical cultures. Perform retrospective surveillance of results from these laboratories to identify organisms with similar resistance patterns, extending six months prior to identification of the index case. If available, these retrospective isolates should be sent to Texas AR Laboratory for testing.
  - Coordinate with the HAI epidemiologist to ensure the Texas AR Laboratory or the Mountain Region AR Laboratory has the capacity to test the specimens.
  - Ensure the sending laboratory receives information from the Texas AR Laboratory on how to submit specimens using their Submitter ID Account. If the laboratory has not submitted to the Texas AR Laboratory previously, the submitter can send an email to LabInfo@dshs.texas.gov for account setup assistance.
  - The HAI epidemiologist can download final Texas AR Laboratory results from the DSHS Lab Portal.
- *C. auris* can be misidentified depending on the identification method used by the laboratory. To identify which organisms to include in the retrospective review, refer to the CDC's webpage on Identification of *C. auris*[15]. Consider submitting *C. auris* isolates, *C. haemulonii* isolates, and yeast isolates to Texas AR Laboratory when unable to identify their species after identification has been attempted. Consider submitting *Candida* isolates that cannot be identified and were isolated from invasive infections in normally sterile body sites.
- Depending on patient history, consider requesting historical data at the patient's other healthcare facilities to identify patients with similar diagnoses for potential case findings.

[15] Recommendations for Identification of Candida auris: https://www.cdc.gov/candida-auris/hcp/laboratories/identification-of-c-auris.html

Prospective Surveillance

- Prospective surveillance involves testing isolates from clinical laboratories that performed cultures from the healthcare facilities where the index patient received care in the 30 days before the positive specimen collection and after the positive specimen collection. The purpose of this testing is to identify organisms with similar resistance patterns from clinical cultures. This surveillance will continue for three months after the last positive specimen.
  - Coordinate with the HAI epidemiologist to ensure the Texas AR Laboratory or the Mountain Region AR Laboratory has the capacity to test the specimens.
  - Ensure the sending laboratory receives information on how to submit specimens using their Submitter ID Account. If the laboratory has not submitted to the Texas AR Laboratory previously, the submitter can send an email to LabInfo@dshs.texas.gov for account setup assistance.
  - Ensure the IP at the facility is aware of new suspect cases.
  - The HAI epidemiologist can download final Texas AR Laboratory results from DSHS Lab Portal.

Implement a System to Ensure Adherence to Infection Control Measures

- Educate and inform the healthcare personnel (HCP) and visitors for the index patient about the organism and precautions indicated to prevent transmission. Ensure that adequate supplies are available to implement Transmission-Based or Enhanced Barrier Precautions. Conduct ongoing adherence monitoring of infection control practices and provide feedback to HCP. Flag affected patients' medical records to initiate appropriate infection control precautions upon readmission.
- Make plans for how receiving facilities will be notified of affected patients' MDRO status, if the patient is transferred, including whether to notify the health department prior to transfer.

Outbreak Considerations

If an outbreak is suspected, additional measures may need to be taken beyond what is listed for the specific Response Tier.

Whole Genome Sequencing

- If there is more than one case of the same organism and mechanism at the facility or in the geographical area, WGS may be helpful in determining the presence of transmission and relatedness to positive results in other areas of the state or country. Use of WGS is dependent on the facility and community history and may not be necessary for all investigations.
- WGS is a reflex test for all phenotypically positive CRO isolates excluding blaKPC-producing CRE.

The WGS results, including Single Nucleotide Polymorphism (SNPs) counts and a phylogenetic tree, will be sent to the HAI epidemiologist, who will forward the information to the investigating epidemiologist.

Removal of Patient from Contact Precautions

There is currently not enough information for CDC to make a general recommendation on when isolation may be discontinued for patients colonized or infected with CRE, CRAB, CRPA, or *C. auris*. In general, screening individuals with a history of colonization or infection with a targeted MDRO with the aim of discontinuing transmission-based precautions is not recommended. With HAI epidemiologist and CDC guidance, a process for removing a patient from contact precautions will be established on a case-by-case basis.

Texas Antimicrobial Resistance Laboratory Data

Laboratory Report Dissemination

When testing is complete for a specimen, the final report is sent back to the submitting laboratory via mail, fax, or web portal within two business days.

If the result includes an alert value (Appendix E), a notification is sent to CDC and the HAI epidemiologist.

- All alerts are sent to the CDC through REDCap within one business day.
- All alerts are sent to the MDRO Inbox for public health action through an email within one business day.

Data Storage

All test results for samples received by the Texas AR Laboratory are stored in LIMS. Along with test results, patient demographic information and submitters of the samples are logged to facilitate the generation of laboratory reports and data files.

Shared network space has been created so that both the laboratory and epidemiology staff can easily store, share, and retrieve data as needed.

Data Management

When Texas AR Laboratory data are requested by the laboratory, the HSU epidemiologists, or the CDC, the data are queried from the LIMS and reformatted in Microsoft Access or Microsoft Excel to meet the needs of the requestor.

The Mountain Region AR Laboratory provides data to the Texas AR Laboratory and the MDRO Inbox, upon request.

Data Summary Reports

- CDC: CRPA, CRE, and CRAB results are transmitted to the CDC in real time through HL7 messaging. Candida identification data are sent to the CDC through REDCap and shared by epidemiologists through monthly spreadsheets/Excel files.
- Texas AR Laboratory: Monthly turnaround time reports are queried from the LIMS and used for internal purposes. These reports are put on the shared drive and a summary is shared during epidemiology-laboratory meetings.

- HSU epidemiologists: Data from the Texas AR Laboratory are saved to the shared laboratory and epi folder for the HSU epidemiologists each month. HSU epidemiologists review and analyze the data for trends and produce data summary reports, as needed.

Data Analysis

The HSU analyzes Texas AR Laboratory data annually and graphs and organizes data to track trends.

Data from Texas AR Laboratory, Mountain Region AR Laboratory, and Houston AR Laboratory from January 2022 through October 2025 were analyzed to determine the MDRO response tiers for Texas. Alongside this analysis, these data were also used to create maps of Texas that show the distribution of resistance mechanisms by county. Data will be reviewed annually to determine if a change in the response tiers is necessary.

Using Data for Action

In 2019, a Data Workgroup was developed, consisting of representatives from the laboratory and epidemiology teams. Meetings occur as needed to discuss various data needs and requirements, with an emphasis on data governance, stewardship, and quality.

ARLN testing has led to the characterization of AR mechanisms across Texas. One limitation of the ARLN data in Texas is that except for *C. auris*, isolate submission is voluntary. By comparing ARLN data to reportable MDRO data, DSHS can identify facilities from areas reporting high MDRO burden and with limited or no isolate submission to target for recruitment. The Data Workgroup collaborates with the laboratory's Informatics Team and testing areas to develop specialized queries. These queries are instrumental in identifying targeted facilities in areas with high occurrences of CRE and *C. auris* but limited isolate submission for recruitment into the ARLN. This collaborative effort not only addresses data needs but also supports the strategic expansion of isolate submissions.

Furthermore, the Data Workgroup characterizes AR mechanisms across Texas and examines currently submitting laboratories that exhibit high sample submission error rates. By focusing on these metrics, the Data Workgroup ensures the reliability and accuracy of the data being collected and contributes to the overall enhancement of data quality.

To extend the impact of these efforts, targeted facilities with high incidence rates of resistance mechanisms and submission error rates become the focal point for education initiatives. The AR Liaison will offer virtual education to these submitters,

providing essential resources and troubleshooting assistance. Additionally, the AR Liaison will collaborate with infection preventionists by presenting and/or having an informational booth at conferences. This proactive approach not only strengthens the relationship between DSHS and local healthcare facilities and laboratories, but also facilitates a more robust response to emerging antimicrobial resistance challenges.

Appendix A. General Shipping Guidance

Labeling Requirements

All Submitters MUST Have a Submitter ID Number with DSHS. If you do not already have an account or submitter ID number or you need to update information already on file, please download a Submitter ID Number Request Form www.dshs.texas.gov/lab/MRS_forms.shtm#Microbiological and fill it out. Complete all applicable fields and email the completed form to LabInfo@dshs.texas.gov, or fax it to (512) 776-7533. Once a facility's information is verified, a submitter ID account is created.

Specimens must be clearly labeled with:

- A minimum of two unique patient identifiers. Acceptable identifiers include:
  - Patient's Full Name
  - Patient's Date of Birth
  - Custom Unique Identification Number such as:
    - Medical Record Number
    - CDC ID
    - Accessioning Number
    - Specimen ID number

The information provided on the specimen label must exactly match the information provided on the G-2E or G-2B specimen submission form.

Master specimen submission forms may be obtained by contacting LabInfo@dshs.texas.gov.

Biological Substance, Category B, UN3373 Shipping Requirements

Submitters are responsible for shipping specimens in accordance with all safety and labeling regulations. Per federal law, submitters follow the federal regulatory standards for the transport of biological specimens, such as those of the International Air Transport Association (IATA), the U.S. Department of Transport (DOT), and the U.S. Pipeline and Hazardous Materials Safety Administration (PHMSA). 49 CFR (Code of Federal Regulations) parts 171 through 179 shipping and packing regulations are available online at the PHMSA's website at http://hazmat.dot.gov/.

Biological substances must be triple packed (primary receptacle, secondary receptacle, sturdy outer container) for shipping.

Required Packaging: Primary Receptacle

- Primary receptacles must be leakproof and must be able to maintain their shape during shipping. Swab collection/transport tubes qualify as a primary receptacle.
- The screw cap of swab collection containers must be sealed tightly to avoid leakage.
- Container caps may also be wrapped in laboratory film to prevent leaks.

Required Packaging: Secondary Receptacle

- Secondary receptacles must be sealable, watertight, and leak-proof.
- Sealable plastic bags are acceptable as secondary receptacles.
- Multiple collection tubes may be placed in the same secondary receptacle.
- To minimize cross-contamination of specimens, individually bag each collection tube before combining into one large secondary container.
- Do not overfill the secondary receptacle as it MUST be securely closed.
- Secondary container should be placed within strong, outer mailer before shipping.

Required Packaging: Absorbent Material

- Enough absorbent material (e.g., cellulose wadding, paper towels, or cotton balls) to soak up the entire contents of the primary receptacle(s) must be placed around the primary container(s) in the secondary container, in case of leakage.

Required Packaging: Sturdy Outer Container/Outer Mailer

- Once swabs/isolates are secured in a sealed secondary receptacle such as a sealable plastic bag, place the secondary receptacle into a sturdy outer container.
- FedEx shipping requires the outer container be made of a sturdy material such as corrugated fiberboard or wood, (Figure 1).

- Foam boxes, paper bags, and envelopes are not acceptable as an outer package for FedEx shipping of these specimen types as they are too easily damaged.

  The box should be an appropriate size to completely enclose the sealed bag of swabs/isolates (secondary receptacle); not too big and not too small.

Acceptable Outer Container Types

Figure 1. Outer packaging/mailers for shipping Category B Biological Substances must be able to withstand being dropped from a height of 1.2 meters (4 feet) without breaking.

Unacceptable Outer Container Types

Shipping and Transport

The guidelines below are specific to FedEx requirements under IATA for the shipping of "Biological Substances, Category B." A Category B biological substance is defined as "an infectious substance not in a form generally capable of causing permanent disability or life-threatening or fatal disease in otherwise healthy humans or animals when exposure to it occurs".[15] The IATA guidelines require Category B biological substances to be triple contained for shipping, which is identified in these guidelines. Please note, however, that shipping guidelines may vary among transport/courier services.

[15] International Air Transport Association Classification https://www.iata.org/contentassets/b08040a138dc4442a4f066e6fb99fe2a/dgr-64-en-3.6.2.pdf

A special permit/certification is not required to ship Category B biological substances; however, to ensure proper packaging of shipments and to reduce risks of exposure during transportation, federal regulations require training for all personnel who handle and ship Category B specimens. Training can be provided by the hazardous materials employer (specimen submitter) or by other public or private sources. However, the employer must certify compliance with hazardous materials training requirements and retain records of the training.

Please note: The DSHS Laboratory is not responsible for improperly shipped specimens.

General Considerations for Shipping

- Employers/leadership must ensure that employees tasked with packing and/or shipping specimen are properly trained on how to handle them.
- **Cold packs should be considered if shipping temperatures are expected to exceed 28°C/82°F. It is best to use an insulated box with an inner polystyrene liner to prevent ice from melting.**
- **Shipment must include a line list/manifest of specimens being shipped when shipping swabs.**
- Multiple secondary containers/bags of swabs/isolates can be placed in one box, but the weight should not exceed 4Kg.
- Specimen Submission Form(s) must be placed between the secondary receptacle and the outer package, in a sealable plastic bag to prevent it/them from getting wet.
- **All identifying information on a specimen must match the identifying information on its accompanying specimen submission form.**
- Packages containing Category A or Category B biological specimens should NEVER be dropped off at a FedEx Express® Drop Box.
- The outer mailer must have at least one surface with a minimum area of 3.9 inches by 3.9 inches (100 mm by 100 mm) for the required labeling. The surface of the outer container should be clearly and durably marked/labeled with UN 3373 label (See below the specification of UN 3373 label)
    - Label Specs: At least 6-mm-tall text stating "Biological Substance, Category B" that is adjacent to the diamond-shaped label UN 3373. All required label dimensions are shown below in Figure 2:

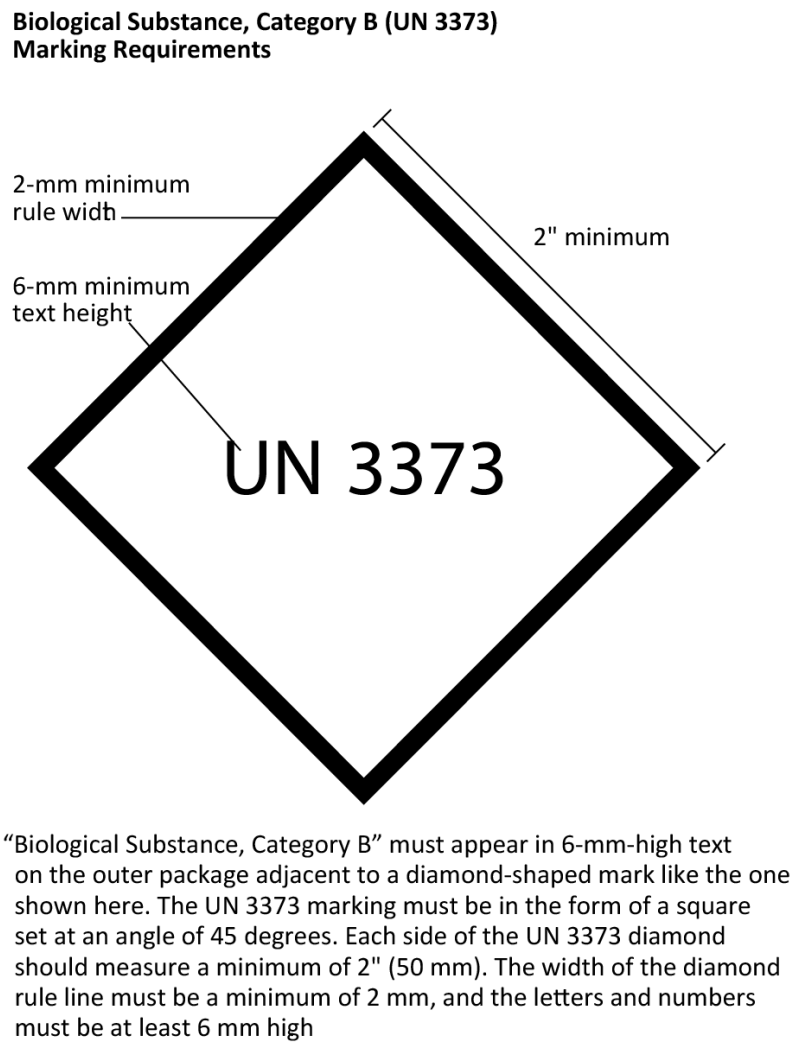


Figure 2. Biological substance, Category B dimensions and marking requirements.

Sourcing a UN 3373 Label Labels may be purchased from Fisher Scientific, catalog numbers 22- 130-067 or 22-130-069. Alternatively, the UN3373 label shown in Figure 4 below may be sized to the required specification, printed, and affixed to the outer mailer with clear packing tape.

The shipper's and recipient's names, addresses, and telephone numbers must be displayed clearly on the box, as shown in Figure 3 below.

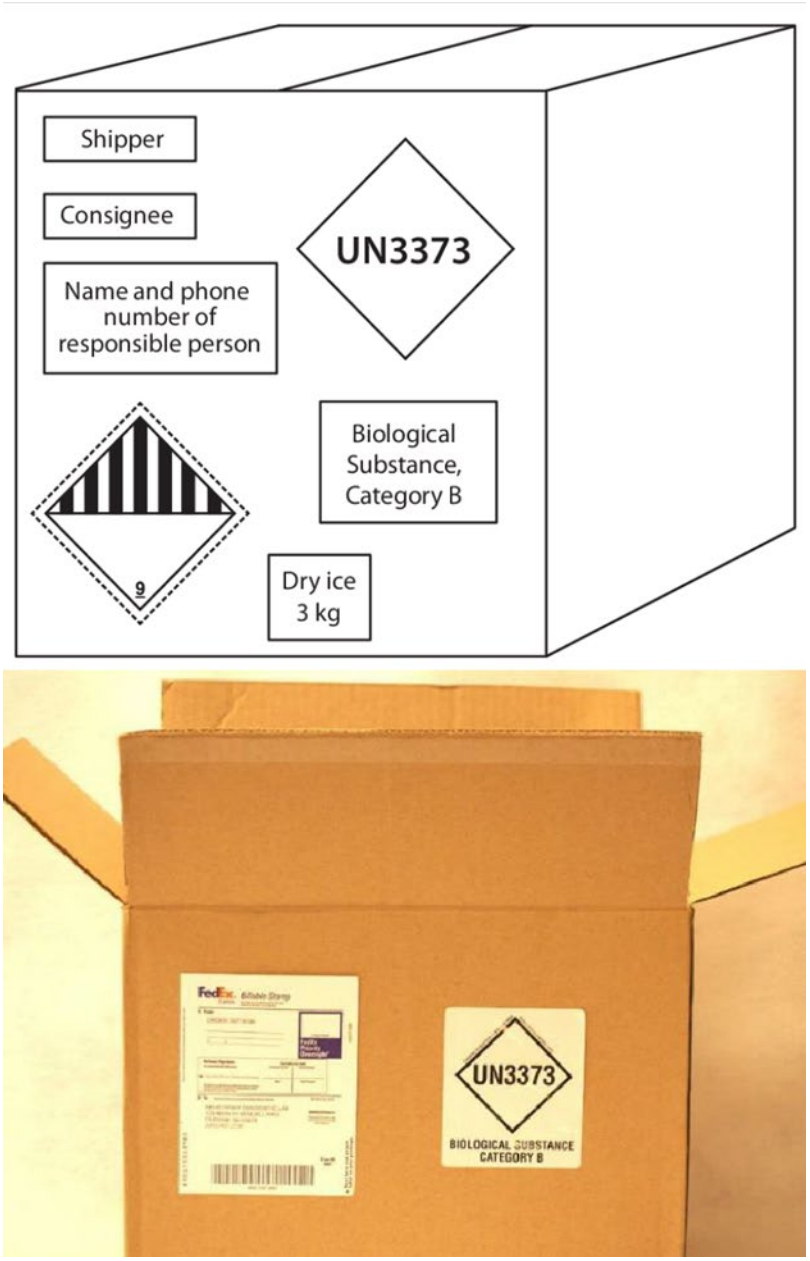


Figure 3. Above: A completely labeled outer mailer/package for a Category B biological substance specimen. When used, dry ice requires its own label, as seen in the bottom left corner. Below: A labeled outer mailer with a FedEx freight label.

Blackline Image Source: J.M. Miller et al. (2012) Guidelines for safe work practices in human and animal medical diagnostic laboratories. Recommendations of a CDC-convened, Biosafety Blue Ribbon Panel, MMWR. CDC surveillance summaries: Morbidity and mortality weekly report. CDC surveillance summaries / Centers for Disease Control 61 Supply (1):1-102.

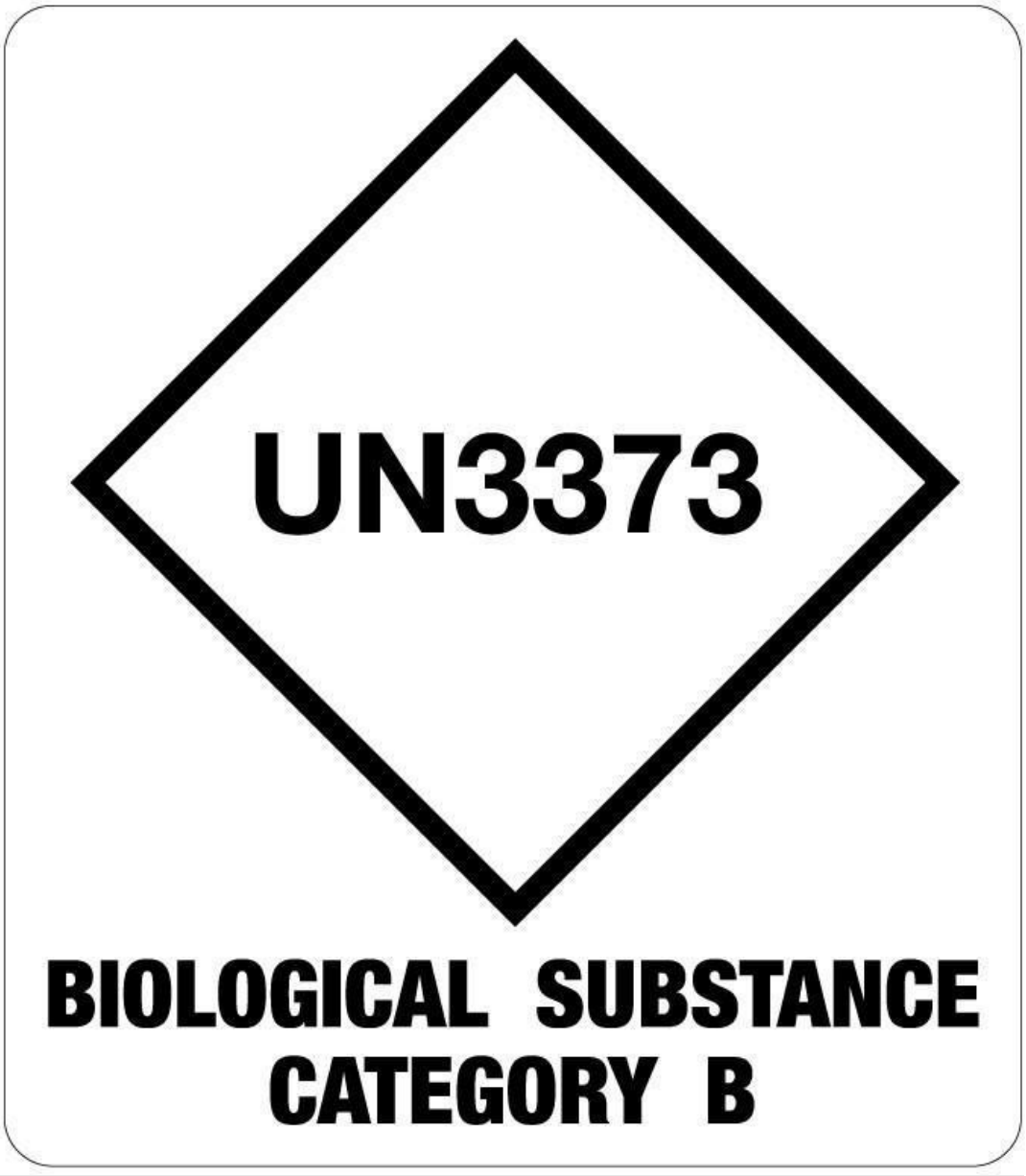


Figure 4. Biological substance, Category B label. Each side of the diamond must be a minimum of 2 inches (50 mm) long, with a border of at least 2 mm width. "Biological Substance Category B" and "UN3373" must be a minimum of 6 mm tall.

Appendix B. Guidance for Use of Antimicrobial Resistance Laboratory Network FedEx Account

Note: This Appendix was adapted from the September 2025 document of the same name published by CDC to align with details specific to the TX AR Laboratory and Health and Human Services (HHS) accessibility guidelines. The original CDC document may be requested by reaching out to TexasARLN@dshs.texas.gov.

Purpose

State, territory, and large city public health laboratories (PHL) supported by funding for AR laboratory capacity will have access to an APHL managed AR Lab Network FedEx account. This includes the AR Lab Network and Foodborne Diseases Active Surveillance Network (FoodNet). This account may be used for shipping and includes the shipping of isolates and samples between clinical laboratories, state laboratories, regional laboratories, and CDC.

General Considerations

Each state, territory, and large city PHL, funded under ELC or other Cooperative Agreement, will be provided access to the ARLN FedEx account under a unique Department ID and will be responsible for complying with the Terms and Conditions for the use of the account. An AR Lab Network FedEx user agreement must be signed prior to using the FedEx account and emailed to TexasARLN@dshs.texas.gov.

Additional Considerations

- Submitting laboratories may batch ARLN or FoodNet specimens in regular shipments to the PHL. However, shipments made using the APHL managed FedEx account should be limited to those included in the guidance (i.e. organisms covered under Project I).
- PHLs are not required to use this method of shipping for ARLN and FoodNet specimens; however, additional funding for shipping using other methods (such as couriers) may not be provided.
- There may be differences between jurisdictions regarding shipping procedures and this may impact work with large commercial laboratories that

perform multi-state testing. Please feel free to contact CDC regarding any concerns or unexpected issues related to multi-state testing and shipping.

Please note that Internet Explorer is not a supported browser for FedEx. Microsoft Edge is recommended to avoid login issues.

FedEx Shipping

Administration

- A point of contact (local administrator) from each funded PHL will receive communication from ARLN@cdc.gov to create a FedEx website login (username and password) under that state/city/territory's unique Department ID for the AR Lab Network account.
- The local administrator may create shipping labels and send to clinical laboratories to ship isolates/samples to the local/state Public Health Laboratory, the AR Lab Network Regional Lab, or to CDC.
- This local administrator will be responsible for signing the ARLN FedEx user agreement.
- Any suspected misuse of the account should be reported to APHL immediately (infectious.diseases@aphl.org), and the password for the account should be changed.

Shipping

- ARLN Laboratories that wish to ship samples for ARLN activities use login information (provided by APHL) to log on to FedEx.com and follow attached instructions for shipping.
  - PHLs may choose to provide labels to clinical laboratories. This can be done by using the "create return shipment" function. The customer prints the label, applies it to the package, and ships the package.
  - Up to 10 labels can be created and emailed to a customer at once and there is no limit to the total amount of return labels that can be created.
- The shipper also has the ability to select the date range (up to two years) for which labels are accessible.
- Shipping services are limited to FedEx Priority Overnight. Priority overnight is not delivered on the weekends so any shipments are encouraged to be sent Monday through Thursday only.

- Domestic shipping only (except Puerto Rico, which is considered International).

Contact Information

For questions or further information, please contact APHL at infectious.diseases@aphl.org.

Appendix C. Specimen Identification Guidelines

1. A submission form is required for each specimen submitted.
2. Each specimen must have at least two patient-specific identifiers attached to the primary specimen container at the time of collection.
    - Three patient specific identifiers are recommended in case one identifier is unusable due to error or illegibility.
3. Patient-specific identifiers on specimen and submission form must match.

Note: The primary specimen container is the innermost container that holds the original specimen before processing and testing (e.g., specimen collection tube, swab, or cup).

Acceptable specimen identifiers include but are not limited to the:

- Patient's Name
- Patient's Date of Birth
- Patient's Medical Record Number
- Specimen ID Number
- CDC Number

Any Custom Unique Identification Number

Note: Location-based identifiers such as hospital room number or street address are NOT acceptable.

Submission Forms must contain:

- At least two patient-specific identifiers
- The Submitter Number or Texas Provider Identifier (TPI)
- The Date of Collection
- The Specimen Source/Type
- The Test(s) Requested
- The Ordering Physician's (when applicable), Name and National Provider Identifier (NPI) number

When sending isolates, please submit a copy of your laboratory's antimicrobial susceptibility report along with the sample.

Appendix D. Summary of Response Recommendations for Multi-Drug Resistant Organisms Containment by Tier

Description of Activity	Tier 1 Novel organisms and resistance mechanisms	Tier 2 •Pan-not susceptible (CRAB, CRE,CRPA) •*C. auris* •CRAB (IMP, KPC, NDM, VIM, uncommon plasmid-mediated OXA) •CRE (IMP, VIM) •CRPA (IMP, KPC, NDM, OXA-48) •CRE, CRAB, or CRPA with dual mechanisms	Tier 3 •CRE (NDM, OXA-48) •CRPA (VIM) •mCIM+/PCR-
Healthcare Investigation[1]			
Review the patient's healthcare exposures prior to and after the positive culture	Always	Always	Always
Contact Investigation[2]			
Screening of healthcare roommates	Always	Always	Usually
Broader screening of healthcare contacts[3]	Always	Sometimes	Sometimes
Prospective lab surveillance[4]	Always	Always	Always
Retrospective lab surveillance[5]	Always	Always	Rarely
Household Contact Screening	Usually	Rarely	Rarely
Environmental Sampling	Sometimes	Rarely	Rarely
Healthcare Personnel Screening	Usually	Rarely	Rarely
Evaluate potential spread to Healthcare Facilities that regularly share patients with the index healthcare facility[6]	Sometimes	Sometimes	Rarely
Infection Control Measures			
Prompt notification of healthcare providers and patient and implementation of appropriate transmission-based precautions	Always	Always	Always
Clear communication of patient status with transferring facilities	Always	Always	Always
Onsite Infection Control Assessment with observations of practice, such as Epidemiology and Laboratory Capacity (ELC) Infection Control Assessment and Response (ICAR)	Always	Always	Sometimes

[1]For **Tier 1 and 2** organisms/mechanisms, healthcare exposures and healthcare contacts over the preceding 30 days should be investigated unless information is available about the time the organism was most likely acquired. This includes any healthcare facility where the patient had an overnight stay d uring that time period. In some investigations, outpatient facilities and emergency departments might also be included.
For **Tier 3** organisms, investigation of healthcare exposures and healthcare contacts is generally limited to the current and sometimes prior admission.
Tier 4 organisms are not included in this containment chart because these organisms generally do not warrant a containment response. The primary focus of Tier 4 is prevention of these organisms and mechanisms. See Figure 1 below for the relationship between response tiers, containment response, and prevention activities. See Section 7, Page 16 of this document for a description and list of Tier 4 organisms.

[2]This may include targeted screening of contacts at highest risk for acquisition and/or unit point prevalence surveys (PPS). Periodic (e.g., every two weeks) response-driven PPS should be conducted until transmission is controlled, defined as two consecutive PPS with no new cases identified or, in facilities with high colonization pressure, substantially decreased transmission. If high levels of transmission persist across multiple point prevalence surveys in long term care settings, consider increasing the interval between surveys (e.g., performing every 4-6 weeks) or temporarily pausing them while reassessing infection control and implementing interventions.

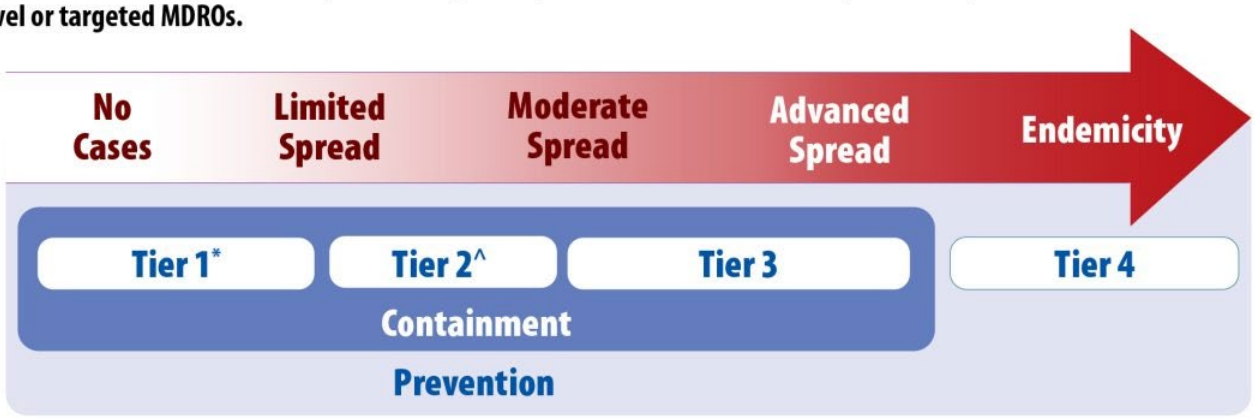
[3]If the index patient was not on Contact Precautions during their entire stay in a healthcare facility, then broader screening (beyond roommates) is recommended. Screening can initially be limited to the contacts at highest risk for acquisition, such as those still admitted who overlapped on the same ward as the index patient and who have a risk factor for MDRO acquisition (e.g., bedbound, high levels of care, receipt of antibiotics, or mechanical ventilation). Alternatively, facilities may choose to screen entire units using point prevalence surveys.

[4]Prospective surveillance of clinical cultures should be conducted for 3 months after the last identified case.

[5]Conduct a laboratory lookback covering at least 6 months prior to identification of index case.

[6]A public health investigation should also be initiated at healthcare facilities known to regularly share patients with healthcare facilities where transmission has occurred, such as post-acute care facilities. At a minimum, this should include notification of the facility and a request to retrospectively and prospectively evaluate clinical cultures for the phenotype of interest. This could also include admission screening of patients at the facility (e.g., transfers from the index facility) and/or point prevalence surveys of high-risk patients or units.

Figure 1. Relationship between epidemic stages, response tiers, containment response, and prevention activities for novel or targeted MDROs.



Organism or resistant mechanism that have

*Never (or very rarely) been identified **in the United States** and for which experience is extremely limited are Tier 1.

^Never (or very rarely) been identified **in a public health jurisdiction but are more common in other parts of the U.S.** are Tier 2.

Source: Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs): Updated December 2022 (cdc.gov).

Appendix E. AR Lab Network Antimicrobial Resistance/Healthcare-Associated Infections Alert Findings and Reporting for Public Health Laboratories

Note: This Appendix was adapted to align with HHS accessibility guidelines from the March 2024 document of the same name published by CDC.

Purpose

As part of the AR Regional Lab Network activities, state and local public health laboratories will conduct antimicrobial susceptibility testing and molecular assays for resistance mechanisms on several organisms recognized as important AR threats. For some findings, state and local HAI coordinators and CDC should be notified immediately so that appropriate infection control measures may be implemented. The table below summarizes the findings that should trigger these alerts.

Contact Information

Alerts should be sent to:

Your jurisdictional HAI epi program at HAIOutbreak@dshs.texas.gov and CDC AR/HAI staff using REDCap (https://rdcp.cdc.gov)

Please be prepared to include state of specimen origin, state laboratory ID of isolate(s), specimen source, collection date, age of patient(s) (not date of birth), and description of testing completed and results of those tests. If the result is part of colonization screenings, please also include that information along with the state laboratory ID of the index isolate(s) that initiated the screening (though if PPS is not initiated in response to an index patient, write "not applicable").

Contact Information Alert Template

Alert Type	State/Jurisdiction of specimen Origin	Public Health Lab ID	Specimen Source	Patient Age (years)	Date of Isolate Collection (mm/dd/yyyy)	Description of Testing Completed and Results (Including organism ID)	Colonization screening: Detected during colonization screening (Y/N)?	Colonization Screening: Public Health Lab ID of Index Isolate

Healthcare-Associated Infections Alert Guidance

Alert Type	Findings	Organism	Follow Up Testing Actions	**Send Alert To**
Pan-not susceptible CRE; Pan-resistant CRE, CRPA, or CRAB	CRE not susceptible or resistant to all drugs tested by the submitting clinical *and* your public health laboratories. CRPA or CRAB resistant to all drugs tested by the submitting clinical laboratory *and* your public health laboratory	Any	For pan-not susceptible CRE and pan-resistant CRE, CRAB, or CRPA isolates detected: Forward to regional laboratory if: •Your public health laboratory performs AST using disk diffusion or gradient strips. •Your public health laboratory performs GNX2F or GN4F and your regional laboratory uses GN7F. **OR** Forward isolate to CDC if: •Your public health laboratory performs GN7F, GNX2F, or a custom BMD panel with newer drugs/drug combinations and your regional laboratory uses GNX2F	CDC, HAI Coordinator

Alert Type	Findings	Organism	Follow Up Testing Actions	**Send Alert To**
Novel carbapenemase suspected	Tests positive for carbapenemase production but RT-PCR-negative	Enterobacterales[17,18] *Pseudomonas aeruginosa*	Prioritize for sequencing or send to regional laboratory for sequencing for detection of novel or other rare carbapenemases (including *bla*$_{IMP}$ variants not detected by Cepheid). Data should be uploaded to NCBI within 7-10 days of trigger result.	CDC, HAI Coordinator
Non-KPC carbapenemase in Enterobacterales	Non-KPC carbapenemase in Enterobacterales	Enterobacterales	Prioritize for sequencing or send to regional laboratory for sequencing. Data should be uploaded to NCBI within 7-10 days of trigger result.	CDC, HAI Coordinator
KPC carbapenemase in Enterobacterales[19]	KPC carbapenemase in Enterobacterales	Enterobacterales	N/A	HAI Coordinator (sending alert to CDC is not required)

[17] Please **exclude** *Serratia* spp. resistant to carbapenems and susceptible to 3rd generation cephalosporins. This resistance profile indicates an SME gene, not novel resistance. Please also **exclude *Enterobacter*** spp. isolates that are cefotaxime, ceftriaxone, and ceftazidime resistant but cefepime susceptible. This AST profile is consistent with false positive mCIM+ results, likely because of high levels of AmpC beta-lactamase(s).

[18] Please **include** isolates that are resistant to carbapenem(s) but susceptible to cefotaxime, ceftriaxone, and ceftazidime. This AST profile is indicative of a possible IMI or NMC gene (both class A carbapenemases).

[19] Report all KPC-CRE to your HAI coordinator. Some jurisdictions, such as those where KPC is rarely defined, might choose to report KPC-CRE to CDC; this is acceptable but not required. Note that in most of the United States, KPC meets criteria for a Tier 2 (not regularly found in the region) or Tier 3 (identified before in the region but not endemic) organism for which each identification requires a public health response, as outlined in the Interim Guidance for a Health Response to Contain Novel or Targeted multidrug-resistant Organisms (MDROs). Your local epidemiology should inform your response activities. Note that the containment response guidance is not intended to be applied to endemic MDROs. Questions about strategies for KPC response or responses to specific cases should be sent to haioutbreak@cdc.gov.

Alert Type	Findings	Organism	Follow Up Testing Actions	**Send Alert To**
Carbapenemase-producing / carbapenemase-positive *Pseudomonas aeruginosa*	Tests positive for carbapenemase production (mCIM or CarbaNP) and/or *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{OXA-48-like}$[20] , or *bla*$_{IMP}$ genes by PCR	*Pseudomonas aeruginosa*	Prioritize for sequencing or send to regional laboratory for sequencing. Data should be uploaded to NCBI within 7-10 days of trigger result.	CDC, HAI Coordinator
Carbapenemase-positive *Acinetobacter baumannii* (Big 5)	Tests positive by RT-PCR (Cepheid or other) for *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{OXA-48-like}$, or *bla*$_{IMP}$ genes	*Acinetobacter baumannii*	Prioritize for sequencing or send to regional laboratory for sequencing. Data should be uploaded to NCBI within 7-10 days of trigger result.	CDC, HAI Coordinator
Carbapenemase-positive Acinetobacter baumannii (other OXAs)[21]	Tests positive by RT-PCR (Cepheid or other) for *bla*$_{OXA}$ genes, including *bla*$_{OXA-23-like}$, *bla*$_{OXA-24/40-like}$, or *bla*$_{OXA-58-like}$	Acinetobacter baumannii	N/A	CDC, HAI Coordinator

[20] *bla*$_{OXA-48-like}$ has not been identified in *Pseudomonas aeruginosa* therefore routine testing for *bla*$_{OXA-48-like}$ is not recommended. However, if *bla*$_{OXA-48-like}$ is identified in this organism, an alert should be sent.

[21] Jurisdictional public health labs should discuss reporting of *Acinetobacter baumannii* with *bla*$_{OXA-23}$, *bla*$_{OXA-24/40}$, *bla*$_{OXA-58}$ to their HAI coordinator. If these organisms are not endemic or routinely identified in the region, an alert should be sent to the HAI coordinator and to CDC. For regions where these organisms are endemic or routinely identified, an alert does not need to be sent to CDC.

Alert Type	Findings	Organism	Follow Up Testing Actions	**Send Alert To**
Carbapenemase detected from colonization screen	Tests positive for carbapenemase by RT-PCR	Enterobacterales; *Pseudomonas aeruginosa; Acinetobacter*	All positive swabs should be cultured to recover and characterize the organism(s) (ID, AST, RT-PCR, all gene targets) carrying carbapenemase identified	CDC, HAI Coordinator
Concerning resistance in Gram positive organisms	• Plasmid mediated linezolid resistance (cfr, optrA and poxtA) • Elevated MICs to daptomycin MIC ≥8µg/mL and linezolid MIC ≥8µg/mL in vancomycin resistant Enterococcus (VRE)	*Enterococcus*	N/A	CDC, HAI Coordinator
Other	• Vancomycin resistant (MIC ≥8µg/mL) *Staphylococcus aureus* (VRSA) • Other new or known but rare AR threats in HAI pathogens not covered above	• *Staphylococcus aureus* • Any	N/A	CDC, HAI Coordinator

Appendix F. Guidance on Antimicrobial Resistance Lab Network *Candida auris* Alerts

Note: This Appendix was adapted to better align with HHS accessibility guidelines from the March 2023 document of the same name published by CDC. The original document can be requested by reaching out to TexasARLN@dshs.texas.gov.

This document is a supplement to the Alert Guidance for Laboratory Actions in Appendix E and describes criteria for *C. auris* specimens of interest that should generate an alert.*

Criteria as of March 2023*:

- All isolates (screening or clinical) with concerning resistance (micafungin/anidulafungin MIC ≥ 4 or amphotericin MIC ≥ 4), which matches CDC's guidance for C. auris REDCap alerts.
- All specimens (screening or clinical) with unique epidemiology based on input from LHDs or CDC†.
  - Examples include (but are not limited to): previous healthcare from another state/country, from a facility with recent echinocandin-resistant cases, pediatric, patients with no or atypical healthcare exposures (e.g., outpatient), or unusual laboratory findings.
  - For these, please comment in the alert what unique aspect of the case or specimen triggered the alert (e.g., "Patient had prior healthcare in Antarctica").
- All other isolates (screening or clinical) from non-high burden areas (defined as tier 2 in the CDC containment strategy guidance).
  - Exclude isolates (screening or clinical) from higher burden areas (defined as tier 3 or tier 4‡ in the containment strategy guidance) unless submission is indicated for another reason listed above.

* For laboratories that are not yet fully onboarded to both antifungal susceptibility testing and WGS (including testing and reporting to CDC and NCBI) with corresponding approvals from CDC, all isolates triggering these alerts should be shipped to CDC or to your corresponding regional laboratory, as appropriate.

† These criteria apply to *Candida auris* only, not other Candida species.

‡ Tier 4 is endemic

Appendix G. General Guidance for Whole Genome Sequencing of Healthcare-Associated Infections/Antimicrobial Resistance Pathogens

Note: This Appendix was adapted to better align with HHS accessibility guidelines from the September 2022 document of the same name published by CDC. Only the relevant sections for the Plan were included in this Appendix. A full copy of the original document can be requested by reaching out to TexasARLN@dshs.texas.gov.

1.0 Sequencing Priorities

Overview: The intent of these sequencing priorities for the ARLN is to support improved detection and containment of novel and emerging resistance threats in HAI pathogens in the United States and beyond. Data generated from these efforts will inform a general understanding of the biology and epidemiology of novel and emerging HAI/AR threats, thereby helping to shape the containment and prevention strategies used to help stop their spread and improve patient safety. Sequencing will help to identify sequence types, gene variants, plasmid types, virulence factors, geographic hotspots of specific clones, and other key aspects related to circulating strains. Although not referred to directly in this guidance, isolates collected from HAI outbreak response investigations will often fall under one or more of the below priority areas, as well as other emerging HAI/AR threats identified more recently by Division of Healthcare Quality Prevention (DHQP). Isolates selected for sequencing should align with the priorities detailed below, listed in the order they should be addressed by public health laboratories. To further aid in the selection of isolates in accordance with this guidance, see the decision trees in Appendix H.

Please note the required turnaround times for each priority. There are two types of acceptable turnaround time periods based on the importance of the sequencing priority: data sharing within 7-10 days of trigger result (HIGH PRIORITY; Priority 1), and data sharing within 7-10 days of sequencing completion (Priorities 2-6).

- **Carbapenemase-producing/PCR-negative CRE/CRPA isolates**. These are isolates that are positive for carbapenemase production by phenotypic methods (e.g., mCIM-positive, or CarbaNP-positive) AND negative for the "Big 5" carbapenemase genes by PCR, including blaKPC, blaNDM, blaOXA-48-like, blaVIM, and blaIMP (when tested for expanded IMP assay variant

targets; see below box). This profile could suggest the presence of a novel carbapenemase gene, for which a validated assay may not exist.

Required turnaround time (HIGH PRIORITY): Isolates should be sequenced and WGS data shared to NCBI CDC HAI-Seq Umbrella Project Gram Negative Bacteria BioProject PRJNA288601 within 7-10 business days of trigger result. Given the implications of a potential novel carbapenemase gene on assay development, if sequencing and data sharing within 7-10 business days from trigger finding is not feasible, please contact your regional laboratory or Clinical and Environmental Microbiology Branch (CEMB) (HAISeq@cdc.gov) for assistance so data sharing can occur in the appropriate time frame.

- **NOTES**:
  - ◊ Genes detectable by Cepheid GeneXpert Carba-R include blaKPC, blaNDM, blaOXA-48-like, blaVIM, and blaIMP. However, Cepheid GeneXpert Carba-R does not detect all blaIMP variants currently circulating in the United States. Refer to current Cepheid package insert for an up-to-date list of all variants detectable and not detectable in vitro. Please ensure that extended blaIMP variants are tested using an appropriate assay (e.g., CDC IMP assay) before suspecting a novel carbapenemase. If you are unable to complete such testing, please reach out to your regional laboratory or CEMB for assistance.
  - ◊ Please exclude isolates with antibiotic susceptibility profiles that explain positive phenotypic results for carbapenemase production. For example:
    - o mCIM+/PCR- Enterobacter intermediate/resistant to cefotaxime, ceftriaxone, and ceftazidime, but susceptible to cefepime suggests false-positive mCIM results, likely because of high levels of AmpC beta-lactamase(s) (encoded by the blaAmpC gene).
    - o mCIM+/PCR- Serratia spp. resistant to carbapenems, but susceptible to third generation cephalosporins suggests the presence of the blaSME gene (encodes a class A carbapenemase), not novel resistance.

- **CRAB carrying Class A, Class B, or blaOXA-48-like carbapenemase genes.** These are CRAB isolates that have targeted Class A and/or Class B carbapenemase genes detected by PCR, including blaKPC, blaNDM, blaVIM, and blaIMP. If capacity allows, laboratories may test for additional blaOXA variants by PCR as warranted by local epidemiology; if blaOXA-48-like is

detected by PCR, those isolates may be sequenced under this priority. CEMB requests that WGS for CRAB be conducted after PCR results are available, not in place of PCR.

Required turnaround time: WGS data should be uploaded to NCBI CDC HAI-Seq Umbrella Project Gram Negative Bacteria BioProject PRJNA288601 7-10 business days from sequencing completion.

- **NOTES:** Besides blaOXA-48-like genes, all other CRAB carrying Class D carbapenemase genes should be sequenced under Priority 5 (see below).

- **Carbapenemase-producing/carbapenemase-gene positive CRPA.** These are P. aeruginosa isolates that are positive for carbapenemase production by phenotypic methods (e.g., mCIM-positive or CarbaNP-positive) and positive for carbapenemase genes by PCR, including blaKPC, blaNDM, blaIMP, blaVIM and blaOXA48-like. Required turnaround time: WGS data should be uploaded to NCBI CDC HAI-Seq Umbrella Project Gram Negative Bacteria BioProject PRJNA288601 7-10 business days from sequencing completion.
- **Carbapenemase-producing/carbapenemase-gene positive CRE.** These are Enterobacterales isolates that are positive for carbapenemase production by phenotypic methods (e.g., mCIM-positive or CarbaNP-positive) and positive for carbapenemase genes by PCR, including blaNDM, blaVIM, blaOXA-48-like, and blaIMP.

  Required turnaround time: WGS data should be uploaded to NCBI CDC HAI-Seq Umbrella Project Gram Negative Bacteria BioProject PRJNA288601 7-10 business days from sequencing completion.

  - Note: To avoid overwhelming current sequencing capacity, CEMB does not recommend sequencing blaKPC in CRE isolates under this priority.
- **Other CRAB with clinically or epidemiologically significant profiles.**
  - Generally, the order of precedence are isolates:
    - ◊ Resistant to all beta-lactams tested.
    - ◊ Resistant to all carbapenems, but not all beta-lactams tested.
    - ◊ Positive for other Class D carbapenemase genes (e.g., blaOXA-23-like, blaOXA-24/40-like, blaOXA-58-like) that are NOT common in the submitting jurisdiction.

- Required turnaround time: WGS data should be uploaded to NCBI CDC HAI-Seq Umbrella Project Gram Negative Bacteria BioProject PRJNA288601 7-10 business days from sequencing completion.

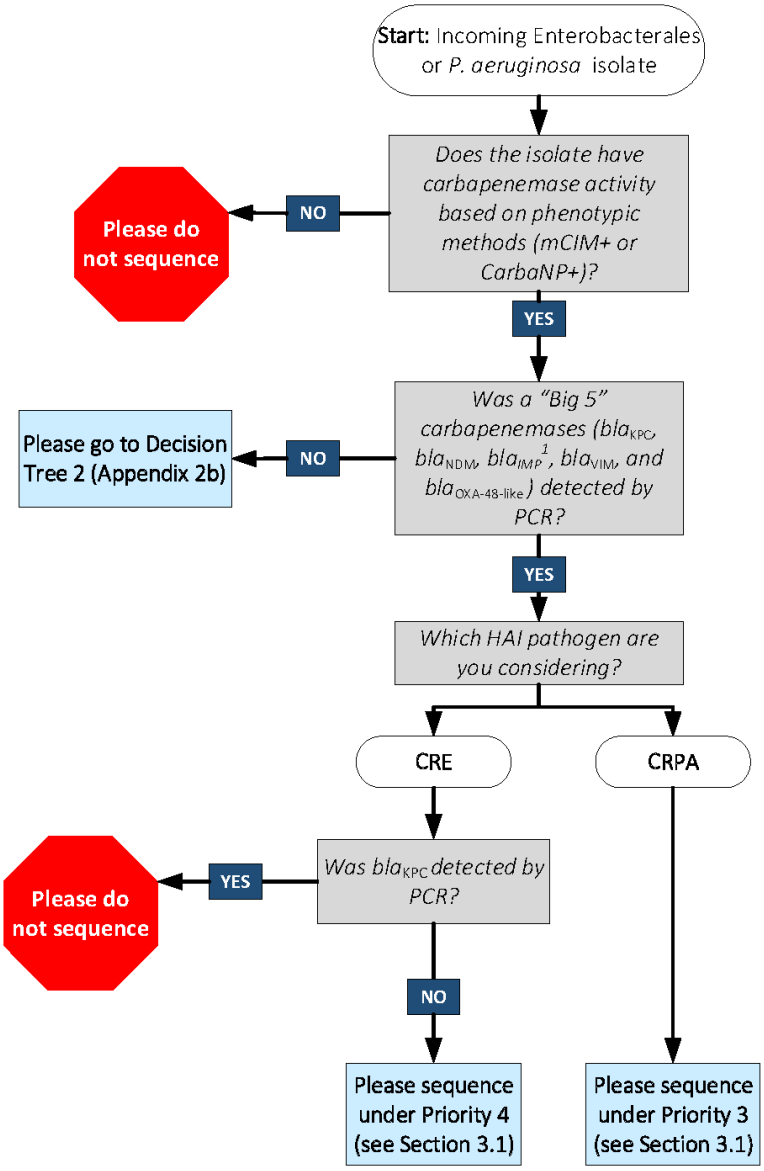
- **If funding remains, WGS may be directed to support other epidemiological investigation priorities, particularly**:
  - CRE/CRPA. Although many of the top WGS priorities listed above include CRE/CRPA that are the focus of many epidemiological investigations, there are additional situations that may be supported, including:
    - ongoing investigations with newly associated locations within a facility, new CRE species (carbapenemases in less common Enterobacterales, organisms not frequently identified in that jurisdiction, etc.), new strains, or newly discovered epidemiology exposures (e.g., large proportion of case-patients have received care from the same healthcare worker, or a history of exposure to the same medical device).
    - continued problems or suspected transmission at a facility after the initial infection control assessment and interventions have been implemented.
  - CRAB. The following situations increase the value of WGS for CRAB investigations:
    - inform a regional response.
    - ii. Initial interventions in a facility are not successful.
    - iii. Define local epidemiology if this has not been done recently or ever (e.g., test a subset periodically).
  - Required turnaround time: WGS data should be uploaded to NCBI CDC HAI-Seq Umbrella Project Gram Negative Bacteria BioProject PRJNA288601 7-10 business days from sequencing completion.

Summary: Collecting WGS data on the above prioritized isolates is an important step in understanding the overall landscape of emerging resistance in the U.S. and is used in tandem with **AST** and other data to better inform efforts to tailor sequencing priorities and prevention recommendations.

Appendix H Priorities Decision Trees

1: Decision Tree 1

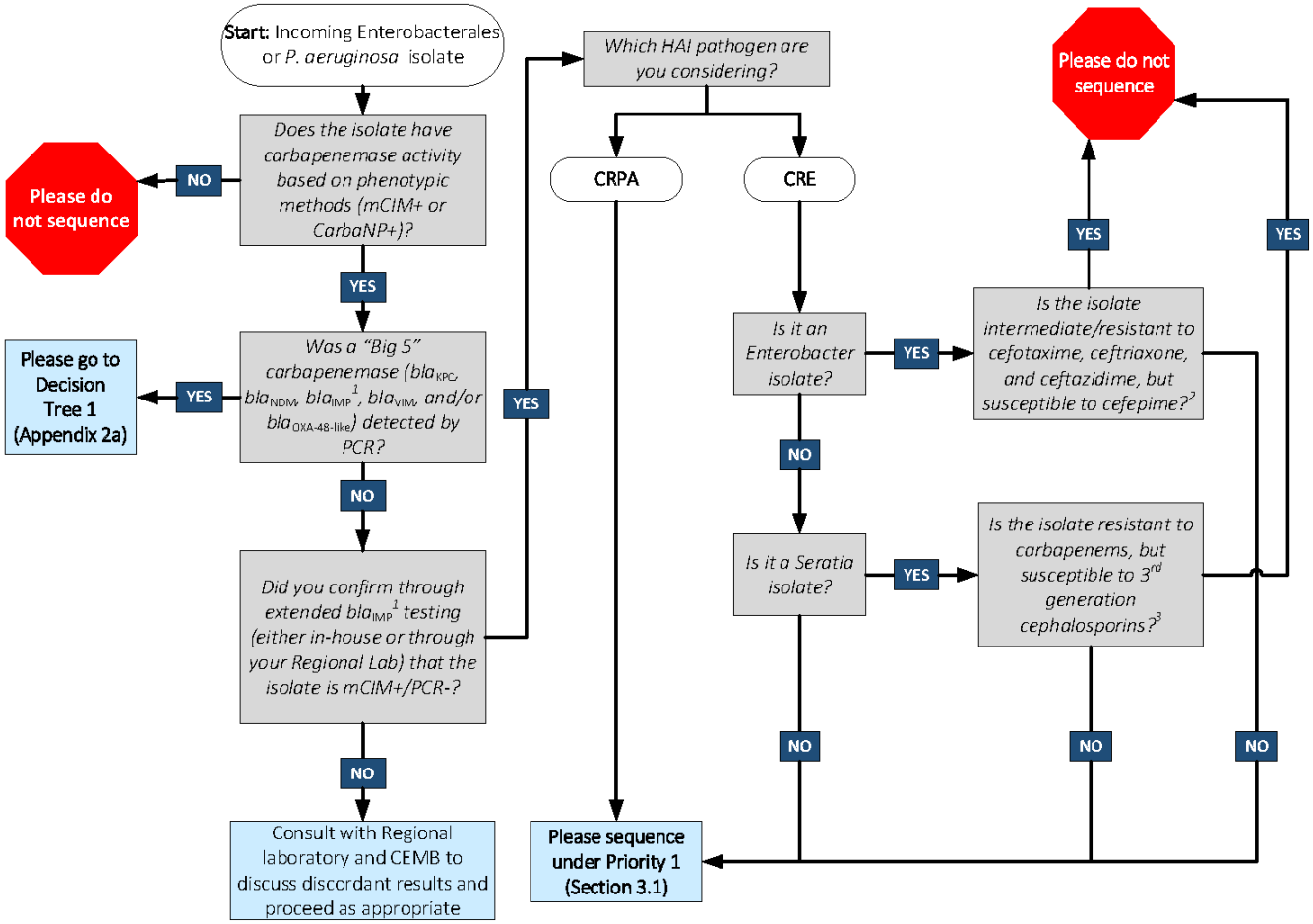
Sequencing Decision Tree for Carbapenemase-positive/PCR-positive CRE and CRPA Isolates



[1]Extended *bla*$_{IMP}$ testing for additional IMP variants should be completed before suspecting a novel carbapenemase. This may be performed using the CDC IMP Assay or a comparable in-house assay.

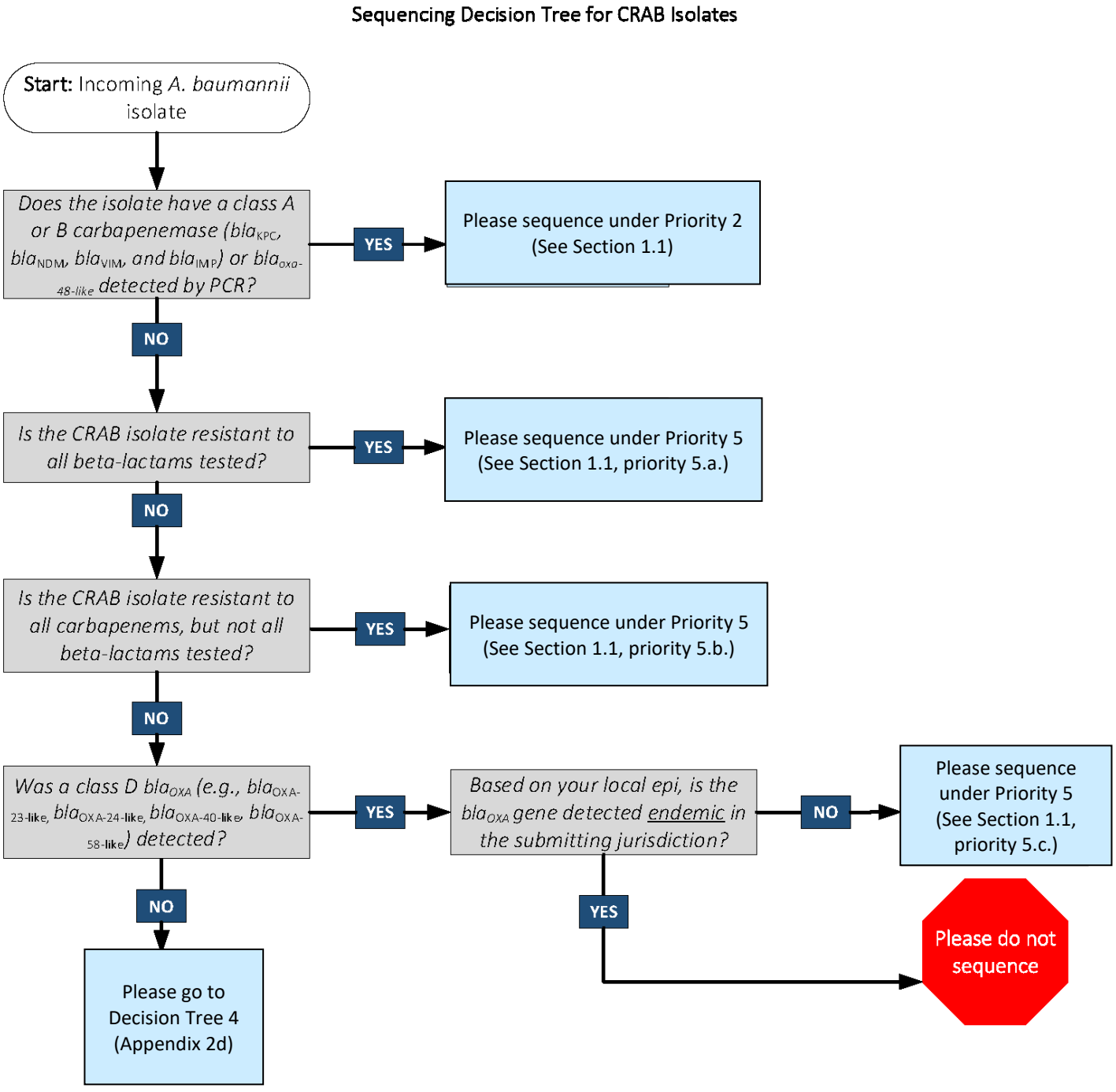
2: Decision Tree 2

Sequencing Decision Tree for Carbapenemase-positive/PCR-negative CRE and CRPA Isolates



[1]Extended *bla*$_{IMP}$ testing for additional IMP variants should be completed before suspecting a novel carbapenemase. This may be performed using the CDC IMP Assay or a comparable in-house assay.
[2]This profile suggests high levels of AmpC beta-lactamase, not novel resistance.
[3]This profile suggests the presence of the blaSME gene, not novel resistance.

3: Decision Tree 3



4: Decision Tree 4