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

Developed by the:

Texas Department of State Health Services Laboratory and Healthcare Safety Unit

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Introduction

Background

According to the Centers for Disease Control and Prevention's (CDC) 2019 Antibiotic Resistance (AR) Report in the United States, (U.S.) more than 2.8 million antibiotic resistant infections occur each year, resulting in more than 35,000 deaths[1]. CDC categorizes antimicrobial resistant threats based on three levels of concern to human health: urgent, serious, and concerning. Urgent threats include Carbapenem-resistant Enterobacterales (CRE), Carbapenem-resistant *Acinetobacter baumannii* (CRAB), and *Candida auris*. Serious threats include extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales and multidrug-resistant (MDR) Pseudomonas aeruginosa[1]. 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 can cause infections associated with high mortality, are highly transmissible, and have high potential for community spread. Treatment options against these organisms are limited, and it could be years before new compounds are available to treat them.

The Antimicrobial Resistance Laboratory Network (ARLN) was established by CDC in 2016 to expand AR testing capacity to detect and respond to emerging resistance in the U.S.[2] Prior to 2016, the CDC operated the only public health sentinel surveillance program for AR in the U.S.

The inception of the ARLN augmented the national public health laboratory infrastructure by connecting regional and local laboratories to better coordinate responses to the emerging resistance. The result has been an increase in testing capacity for all 50 states and five local jurisdictions[3]. The ARLN has provided faster detection of resistant organisms for a rapid and better coordinated public

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

[2] CDC's Antimicrobial Resistance (AR) Laboratory Networks https://www.cdc.gov/drugresistance/laboratories.html

[3] CDC ARLN's Connection with Local AR Capabilities https://www.cdc.gov/drugresistance/ar-lab-networks/domestic.html

response, as well as created communication channels to engage clinical laboratory partners nationwide.

The Texas AR Laboratory, within the Texas Department of State Health Services (DSHS) in Austin, TX, has served as both the Mountain Region AR Laboratory (from 2016 to 2019) and the ARLN state participating laboratory (from 2016 to present). The Laboratory has been performing AR testing and coordinating with Texas healthcare providers, other Mountain Region states, the City of Houston, and CDC programs since 2016. The Texas AR Laboratory has made significant contributions to the ARLN by expanding testing capacity and adopting new testing and reporting technologies. These contributions include 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. In 2018, the Laboratory established a process to identify *C. auris* in isolates and colonization swabs. In 2021 alone, the Laboratory received and tested 3990 C. *auris* colonization swabs by Polymerase Chain Reaction (PCR). The Texas AR Laboratory provides testing for organism identification, antimicrobial susceptibility, carbapenemase production, and mechanism 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).

In May 2017, the Texas AR Laboratory began testing isolates collected from Texas healthcare facilities. The Laboratory's initial recruitment drive involved mailing letters to healthcare facilities to encourage them to submit isolates for testing to laboratories statewide. This mailer was followed up with recruitment via word-of-mouth, by discussing the recruitment drive at in-person laboratory and infection prevention meetings across the state. Additionally, isolates were requested by Healthcare Associated Infection (HAI) epidemiologists who conducted investigations of reportable multidrug-resistant organisms (MDROs) in Texas when the isolates met the criteria for ARLN submission. Instructions for isolate submission were created by the Texas AR Laboratory and were shared by laboratory and epidemiology staff whenever a facility indicated an interest in submitting isolates.

In January 2023, the Texas AR Laboratory expanded testing to include colonization screening for carbapenemase-producing organisms (CPO) and antimicrobial susceptibility testing (AST) for *Neisseria gonorrhoeae* (GC). These

tools further improved the Texas AR Laboratory's potential for detection, containment, and treatment of AR organisms in local communities.

The overall goal of an HAI epidemiology response is to slow the spread of all MDROs, with a specific emphasis on the rapid containment of novel or rare MDROs or resistance mechanisms isolated from healthcare facilities. From August 2019 through December 2022, Texas public health departments were involved in 1140 public health responses due to ARLN alerts. The CDC's *Interim Guidance for a Public Health Response to Contain Novel or Targeted MDROs*[4] document was used by DSHS as guidance in developing containment steps for retrospective surveillance, point prevalence studies, on-site infection control assessments, and prospective surveillance.

Containment steps include systematic, aggressive responses to single cases of high-concern antimicrobial resistance, and a focus on stopping transmission. To aid Texas health departments, Texas HAI epidemiologists worked with the Texas AR Laboratory to develop the *Texas ARLN Response Plan and Epi Lab Work Plan*, which includes a statewide surveillance process for the detection of emerging resistance and a response process for ARLN alerts. The response plan also includes additional detailed steps not included in the CDC guidance document. Response activities have tiered approaches that are based on organism or mechanism attributes; responses may differ by geographic region. Texas HAI epidemiologists also collaborated with CDC and the Texas AR Laboratory to provide educational resources to facility staff and patients.

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: a coordinated work plan and an outreach plan. The work plan specifies the communication and information flow between the Texas AR Laboratory and the Healthcare Safety Unit (HSU). The purpose of the outreach plan is to coordinate connection between the Laboratory and HAI epidemiologists and clinical

[4] CDC's Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs): https://www.cdc.gov/hai/containment/guidelines.html

laboratories, and provide education and technical assistance to healthcare facilities, clinical laboratories, and other healthcare professionals to improve detection of targeted organisms across the state.

This Plan includes Texas response tiers for resistance mechanisms which include thresholds for conducting onsite infection-control assessments and colonization studies, as well as the events or results that would trigger ongoing follow-up visits. 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 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 the negative effect the Plan could have on public health capacity, the HAI epidemiologists established parameters to determine triggers for single or repeated colonization studies. These parameters are incorporated into the Plan and education on the parameters is provided to public health partners and healthcare facilities so rapid detection and containment can occur. The parameters facilitate a more efficient and effective implementation strategy for colonization screening until the spread of novel or high-concern MDROs is tracked and controlled.

Summary of Updates

The following sections have had notable adjustments made since the July 2022 publication of the Texas Response Plan.

1. Introduction
   a. Added details about GC AST and CPO colonization screening test additions in "Background".
   b. Updated data on public health responses from August 2019 to December 2022.
2. Roles and Responsibilities
   a. Antimicrobial Resistance / Antimicrobial Stewardship (AR/AS) Team is no longer combined. Antimicrobial Stewardship is now a separate team.
3. Laboratory Testing Capabilities
   a. CPO colonization screening details and capacity information added.
   b. Differentiated CRO vs CPO terminology.
4. Texas Response Tiers
   a. Major revisions to tier level definitions and the organisms in each tier.
5. Epidemiology Response
   a. Added subsection "Immediate Actions" containing details regarding coordination and education with infection preventionists.
   b. Added subsection "Implement a System to Ensure Adherence to Infection Control Measures".
   c. Added details to subsection "Whole Genome Sequencing (WGS)" about reflex testing and results.
6. Specimen Identification Guidelines
   a. Added flyer with graphics and examples of specimen ID errors and troubleshooting.
7. Appendix D
   a. Replaced with newest document version added from CDC published February 2023.
8. Appendix E
   a. New graphic added for containment tiers.
9. References
   a. Reference section in the appendix was deleted and footnotes were embedded throughout the document.

1. Roles and Responsibilities

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

AR Laboratory Expert/AR 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 Antimicrobial Resistance (AR) Team, consisting of epidemiologists, ensures requests for testing, test results, and any pertinent information are communicated between the laboratories, CDC, and local epidemiologists. These Texas DSHS 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 antimicrobial stewardship initiatives in Texas.

HAI Coordinator and HAI Epidemiologists

The HAI coordinator is responsible for the implementation of epidemiology responses per the Texas Response Plan and manages the HAI epidemiologists across the state. The HAI epidemiologists provide recommendations to health departments and healthcare facilities on control measures to take to prevent the spread of novel and targeted MDROs and communicable diseases. HAI epidemiologists also assist local health departments with obtaining supplies, implementing colonization screenings, and conducting onsite infection control assessments.

Regional Health Department Epidemiologists

The DSHS HAI epidemiologists work alongside DSHS Regional 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 local health department. They work directly with healthcare facilities and laboratories in their jurisdiction.

Local Health Department Epidemiologists

Local health department (LHD) epidemiologists are the primary epidemiology investigators for their jurisdiction. They work 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 a regular basis or due 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 as the SME on methods for preventing and controlling the spread of infectious disease.

Texas AR 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 Laboratory requests and secures funding and creates and submits required progress reports.

Regional Antimicrobial Resistance Laboratory Network Laboratory

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

AR 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, portal access, recruitment, and education.

AR Data Analyst

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

AR Laboratory Scientist

This laboratory scientist performs sample accessioning, testing, and results reporting.

2. Communication

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 (Antimicrobial Resistance Laboratory Network) Recruitment, ARLN Response Plan, and Epi-Lab Workplan workgroup meetings) are held to focus on specific activities, as needed. When urgent issues arise, the Texas AR Laboratory and the HSU communicate daily 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.

The Texas AR Laboratory and the HSU collaborate with the regional and local health departments 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. The AR Lab Liaison proactively initiates contact with healthcare facilities and laboratories to ensure testing and reporting are performed according to current CDC ARLN 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 face-to-face meetings. The Texas AR Laboratory and the HSU regularly update the DSHS Laboratory website with ARLN-related activities and guidance.

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 communicates with the Regional AR Laboratory regarding sample submissions that require further testing. The Texas AR Laboratory also contacts the Regional AR Laboratory for support with surge capacity.

The Texas AR Laboratory communicates regularly with the Houston Health Department (HHD) Lab, which is an independent ARLN laboratory, to compile statewide 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. More frequent communication occurs when necessary, such as during outbreak investigations. The HAI Investigation Team, AR Team, and AS Team

conduct frequent communication with CDC and Regional AR Laboratory during point-prevalence survey/colonization screening and outbreak investigations. More frequent notifications, email correspondences, meetings, and conference calls are required and scheduled to meet the requirement. 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 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, and bimonthly meetings that address new protocols, guidance, and ongoing outbreaks. The Texas AR Laboratory notifies the CDC when submitting samples requested by the agency, which follows CDC processing and reporting protocols. The Texas AR Laboratory plans to participate in projects conducted by the CDC and intends to report data as requested.

3. 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, doripenem, 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, or doripenem 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, ertapenem, meropenem, or doripenem by standard susceptibility testing methods.
- Confirmed or suspected *C. auris* or *C. haemulonii* isolates, unidentifiable yeast isolates and any Candida isolates that are not *C. albicans* are also accepted for testing.

Texas AR Laboratory performs the following tests on isolates:

- Organism species identification
- Carbapenemase production (CRE and CRPA only)
- Antimicrobial susceptibility testing (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 vs Carbapenemase Producing Organism

A carbapenem-resistant organism (CRO) resists the action of carbapenem antimicrobial 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 organism 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. The swabs and the FedEx airbill for shipping are provided by the Texas AR Laboratory free of charge. Submitting facilities can request swabs by coordinating the request with their regional HAI Epidemiologist. See section 5, 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. Report is sent out within one working day of completion of testing. The Texas AR Laboratory reports positive CRO 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. The testing capacity can accommodate up to 120 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: https://www.dshs.texas.gov/laboratory-services/programs-laboratories/antibiotic-resistance-lab-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 Mycology Team as soon as possible after receipt of the specimens.

If colonization specimens are positive for *C. auris* by PCR, the submitter and HAI epidemiologist are notified by email or telephone that same day. The Texas AR Laboratory reports *C. auris* identifications to CDC through REDCap within 24 hours.

Once the PCR testing is completed, a summary spreadsheet of the results is compiled by the Mycology Team and emailed to the HAI epidemiologist on that same day.

Additional Testing

The Texas AR Laboratory performs whole genome sequencing on all isolates that indicate novel resistance and isolates that test positive for *bla*NDM, *bla*IMP, *bla*VIM, *bla*OXA-48 like, *bla*OXA-23 like, *bla*OXA-24/40 like or *bla*OXA-58 like genes. Whole genome sequencing is also performed for CRPA and CRAB isolates that test positive for *bla*KPC. Submitting facilities can request whole genome sequencing on CRE isolates for *bla*KPC outbreak investigation by coordinating the request with their regional HAI Epidemiologist. Priority for sequencing is established based on CDC guidance.

4. Recruitment

Data Analysis

The ARLN Recruitment Workgroup reviewed the Texas ARLN data from 2018 to 2022. The types of healthcare facilities that submitted isolates directly to the Laboratory included ACHs, LTACHs, and reference laboratories. The reference laboratories submitted isolates from a variety of healthcare settings, most often acute care, but also long-term care and outpatient settings. ACHs were the healthcare facilities with the most isolate submissions, followed by LTACHs. SNFs were represented the least in past submissions. Data were also reviewed to understand the geographical locations where isolates with resistance mechanisms were collected and where AR positive patients reside.

Criteria for Targeting Facilities

For CRAB, CRE and CRPA isolates, the Texas AR Laboratory continues to recruit healthcare facilities in PHRs with historically low specimen submissions and laboratories serving high acuity settings such as LTACHs and SNFs. The Texas AR Laboratory will also target recruitment laboratories who previously submitted isolates but have not submitted isolates in one year.

Effective January 1, 2021, *C. auris* is a reportable condition in Texas and requires isolate submission to the Texas AR Laboratory. To establish a baseline for *C. auris* presence in Texas, the Texas AR Laboratory will focus recruitment activities on facilities that have historically submitted the most MDRO isolates. Recruitment activities will also focus on regions that have reported *C. auris* in the past, which are also the most populous regions in the state. HSU and the Texas AR Laboratory have also worked to establish relationships with other facilities, such as academic laboratories, that receive fungal isolates.

Methodology

The ARLN Recruitment Workgroup will continue to update the previous list of laboratories to target based on the criteria identified above. This list will be used to recruit laboratories in targeted PHRs and laboratories used by the targeted LTACHs and SNFs.

The ARLN Recruitment Workgroup will recruit laboratories located within healthcare facilities.

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 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, communicating via emails, and performing onsite visits such as Point Prevalence Surveys. 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.

5. Laboratory Submission Process

To submit specimens to the Texas AR Laboratory, submitters must adhere to the following steps (Also see 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 Laboratory Services Section 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 Submitter-ID-Request-Form-Sept--2017.pdf (texas.gov)

G-2E Specimen Submission Form

All samples sent to the Texas AR Laboratory 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.

FedEx Instructions

The Texas AR Laboratory has an account set up with FedEx to ship specimens (See Appendix B). Instructions for logging into the FedEx account may be obtained by emailing TexasARLN@dshs.texas.gov .

Specimen Collection and Shipment Instructions

All samples must be shipped following UN3373 shipping guidelines and be accompanied by a completed G-2E form. There must be two unique identifiers on the G-2E form that exactly match the identifiers on the specimen label (Appendix C lists acceptable unique patient identifiers). See Appendix B and https://www.dshs.texas.gov/laboratory-services/programs-laboratories/antibiotic-resistance-lab-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) the reader should take from the report.

6. Specimen Receiving and Processing

Specimens received by the Texas AR Laboratory are first processed by the Texas DSHS Specimen Acquisition Department. It is at this stage where specimens are reviewed for initial acceptance criteria and any issues with sample labeling, unique identifiers, and the G-2E Form. After this review, specimens are logged into the Laboratory Information Management System (LIMS), appropriate tests are ordered, and laboratory labels are printed and attached to the specimen and the attached G- 2E Form. The specimens are then delivered to the testing areas of the Texas AR Laboratory for the initiation of testing. Testing of isolates and rectal swabs for CRE, CRPA and CRAB are performed by the Molecular Microbiology Team. Whole genome sequencing of CRE, CRPA, and CRAB are performed by the Advanced Molecular Detection team. All *Candida* samples are tested by the Mycology Team.

7. Testing Process Workflow

Isolates for CRE, CRPA and CRAB

- **Day One** – CRE, CRPA and CRAB isolates are streaked on Trypticase Soy Agar (TSA) plates with 5% sheep's blood and incubated overnight.
- **Day Two** – Streaked plates are checked for purity. Organism ID is confirmed by MALDI-TOF. Antimicrobial susceptibility testing for CRE, CRPA and CRAB isolates is initiated with broth microdilution (BMD). 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 CDC PCR performed for *Klebsiella pneumoniae* Carbapenemase (*bla*KPC), New Delhi Metallo-beta-lactamase (*bla*NDM), Imipenemase (*bla*IMP), Verona Integron-Encoded Metallo-beta-lactamase (*bla*VIM), and Oxacillinase-48 (*bla*OXA- 48) like genes. CRAB isolates will also have CDC PCR performed for *bla*OXA23-like, *bla*OXA24/40 like and *bla*OXA58 like genes. If mCIM result is positive or indeterminate and PCR result is negative, mCIM and CDC PCR tests are repeated for confirmation. After data review and results release 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 priority set up by the CDC, isolates are whole genome sequenced. WGS ID and NCBI SRR ID are entered into REDCap alert.

Candida Isolates for Identification

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

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 ships identified Candida isolates to the Mountain Region AR Laboratory for susceptibility testing. The Mountain Region AR Laboratory sends results to the Texas AR Laboratory and the HSU. The Texas AR Laboratory notifies submitting laboratories of results received by attaching the Utah report to the final Texas report.

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 Positive and PCR Indeterminate swab solutions are inoculated into a Salt Sabouraud Dulcitol Broth enrichment culture medium with chloramphenicol and gentamicin. Cultures are incubated in a shaking 40°C incubator.
- **Day Three to Day Seven** – Incubated culture broths are inspected each day for growth. When there is growth, or at Day Seven 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.
- *C. auris* isolates are shipped to the Mountain Region AR Laboratory for susceptibility testing.

Colonization for Carbapenemase Producing Organisms

- **Day One** – Swabs are received in the lab, checked for compliance with CAP/CLIA regulations. Swabs should be processed the same day of receiving using the Cepheid Xpert Carba-R assay (an approved Real-time PCR assay) or stored overnight at refrigeration temperatures.
- **Day Two-Day Four** – Positive results are reported out within 48 hours of receipt of the specimens and 24 hours of resulting. PCR positive swabs are inoculated into Blood Agar Plates and MacConkey Agar Plates for isolation and further characterizations (species identification, antimicrobial susceptibility testing, carbapenemase production testing and mechanism testing).

8. Texas Response Tiers

CDC defines four tiers for epidemiology responses to novel or targeted MDROs. The definitions for each tier are outlined below. Based on results from an analysis of Texas data from 2017–2022, Texas established the following response tiers:

Tier 1

This category includes organisms or resistance mechanisms that have never (or very rarely) been 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
- Pan-not[5] susceptible *Candida auris (C. auris)*

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 organisms include:

- MDROs that 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.
- Organisms for 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).

[5] Pan-not susceptible is used to describe all organisms for which no current treatment exists. This includes organisms that were previously described as pan-non susceptible (Pan-NS) and pan-resistant (Pan-R).

- Pan-not[6] susceptible (CRAB, CRE, CRPA)
- *C. auris*
- CRAB (IMP, KPC, NDM (New Delhi Metallo), VIM (Verona Integron Mediated), 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 United States 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)

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[6] Pan-not susceptible is used to describe all organisms for which no current treatment exists. This includes organisms that were previously described as pan-non susceptible (Pan-NS) and pan-resistant (Pan-R).

9. Epidemiology Response

Notification and Confirmation of a Positive AR 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 lab report from DSHS CITRIX/Labware or DSHS Lab Online Portal and confirm results match the notification.
- If the lab 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 work day.

- If the CRAB, CRE, CRPA, or *C. auris* isolate is still available, 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 (state.tx.us).
- It 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 Section 5 above, provide facility the Submitter ID Request Form Submitter-ID-Request-Form-Sept--2017.pdf (texas.gov) and ask them to follow the instructions on the document.

Immediate Actions

The response strategies are described below for the local health department 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 this Plan.
- Notify the Infection Preventionist (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
    - 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 Measures for Carbapenem-resistant Enterobacterales (CRE)*.[10] These guidelines are applicable for novel or emerging multidrug-resistant organisms.
    - For *C. auris* cases, refer to the DSHS Emerging and Acute Infectious Disease Unit's Investigation Guidelines for control of *C. auris*[9] and use the guidance

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[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): https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html

[10] Texas Department of State Health Service Emerging and Acute Infectious Disease Guidelines: https://dshs.texas.gov/IDCU/investigation/Investigation- 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/fungal/candida-auris/c-auris-infection- control.html. See references for EPA List P[11], 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 antimicrobial resistance for the facility to educate staff and patient/visitors. If additional educational information is needed, recommend the IP contact the epidemiologist.
  - 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 to notify the IP of any additional lab positives with similar organisms or resistance and save the isolate for potential submission to the Texas AR Laboratory. IP should be asked to inform the epidemiologist of results within one workday.
- 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 resistant mechanism, cohort them accordingly. When possible, dedicate staff to care for positive patient(s) only.
  - Educate staff to complete duties for all other patients prior to caring for the patient(s) with an AR-relevant mechanism, when feasible (i.e., therapy staff, respiratory staff, housekeeping).
- Interfacility transfer communication:
  - If the patient is transferred to another healthcare facility, communicate MDRO history and isolation needs to the receiving facility.

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[11] Recommendations for Infection Prevention and Control for Candida auris: https://www.cdc.gov/fungal/candida-auris/c-auris-infection-control.html

[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

        - 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.
        - Collaborate with CDC as needed. During the investigation, the HAI epidemiologist may contact CDC for assistance or to collaborate on containment strategies, if needed or requested.

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, that 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 so, 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. Request assistance from the HAI epidemiologist if needed. This meeting may be via conference call or in person. 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

Either a remote or onsite Infection Control Assessment and Response (ICAR) should be conducted 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 infection prevention and control 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. The site visit 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 (Infection Control Assessment and Response) 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 site visit.
- Conduct a follow-up if additional cases occur after the initial visit.

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 mechanism was most likely acquired. The exception is *C. auris*, in which case healthcare exposures in the preceding three months should be investigated[13]. Contact an HAI epidemiologist for guidance.
- Facilities should be encouraged to update medical records, per their internal protocol, for flagging patients with multidrug-resistant organisms.
- 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, implementation of colonization screening should be considered.

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

Colonization Screening and Point-Prevalence Survey

Colonization screening is recommended for roommates and other close contacts of the index patient who are identified as high-risk contacts based on their level of interaction with the index patient in the one-month period prior to the identification of the mechanism or prior to the implementation of the appropriate control measures. 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)*[4] for screening recommendations according to the Response Tier of the organism. See Appendix E for a summary table of containment elements from the guidance document.

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

- 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 worker's 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.
  - Request the appropriate swabs be shipped for the specific pathogen or mechanism being tested. Coordinate with the HAI epidemiologist to obtain the appropriate swabs.
    - Once the specimen is collected on the swabs, they should be shipped within one day of collection. Note: Laboratory testing must be performed within four days of collection.
    - Resources for collection, packaging, and shipping can be provided by the HAI epidemiologist upon request.
    - If needed, a sample verbal consent script can be provided by the HAI epidemiologist.
  - Check with the HAI epidemiologist to verify the laboratory's testing capability for other resistance mechanisms or *C. auris*.
  - Coordinate with facility's IP to schedule a date for collecting swabs.
  - Coordinate with the HAI epidemiologist, who will ensure the collection date of the specimens correlates with the AR laboratory's schedule for receiving and setting up of specimens for testing. The swabs 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 swabs 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 swabs. Patient identifiers on both should match.
- If a colonization screening patient tests positive, a new round of contact tracing and testing will be done. To allow infection control measures to be implemented quickly, results will be sent to the local health department epidemiologist and healthcare facility by the HAI epidemiologist the same day they are received.

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

- Screening should continue until two rounds of no new positive results are obtained.
- Contact 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 new facility admitting the patient. Test results should be provided to both facilities.

Retrospective Review of Lab Results

- Clinical laboratories that perform culture isolations on specimens from healthcare facilities where the index patient received care in the previous 30 days should be targeted for retrospective surveillance to identify organisms with similar resistance profiles from other clinical cultures. Retrospective surveillance of results from such clinical laboratories should be performed to identify the presence of organisms with similar resistance patterns; the period under surveillance should extend 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 Texas AR Laboratory 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 Identification of Identification of Candida auris | Candida auris | Fungal Diseases | CDC[14] . 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 also 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.

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.

[14] Recommendations for Identification of Candida auris: https://www.cdc.gov/fungal/candida-auris/recommendations.html

- Ensure the sending laboratory receives information on how to submit specimens using their Texas AR Laboratory 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 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, Whole Genome Sequencing (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 isolates tested positive for *bla*NDM, *bla*IMP, *bla*VIM, *bla*OXA-48, *bla*OXA-23 like, *bla*OXA-24/40 like or *bla*OXA-58 like genes.
- 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.

10. Texas AR Laboratory Data

Lab Report Dissemination

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

If the result includes an alert value (See Appendix D), 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 are queried monthly from the LIMS and shared with the CDC through the APHL (Association of Public Health Laboratories) Informatics Messaging Services (AIMS) Portal (via CSV file upload). 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 lab 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 quarterly and graphs and organizes data to track trends. This information has been historically shared within DSHS and with public health epidemiologists and other stakeholders at local and state level meetings.

Data from Texas AR Laboratory, Mountain Region AR Laboratory, and Houston AR Laboratory from May 2017 through March 2021 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

A Data Workgroup was developed in August 2019. The workgroup consists 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 antimicrobial resistance 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, specifically CRE and multidrug resistant Acinetobacter (MDRA), DSHS identified facilities from areas reporting high MDRO burden and with no or limited isolate submission to target for recruitment. The addition of *C. auris* as a Texas reportable condition provides an opportunity to further characterize resistance mechanisms in Texas.

Texas counties that show high incidence rates of resistance mechanisms are targeted for educational initiatives, such as encouraging the adoption of the Texas Interfacility Transfer Form.

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
AS	Antimicrobial Stewardship
AST	Antimicrobial Sensitivity Testing
BAP	Blood Agar Plate
BMD	Broth Microdilution
C. auris	*Candida auris*
CDC	Centers for Disease Control and Prevention
CPO	Carbapenemase-Producing Organism
CRAB	Carbapenem-Resistant *Acinetobacter baumannii*
CRE	Carbapenem-Resistant Enterobacterales
CRO	Carbapenem-resistant organism
CRPA	Carbapenem-Resistant *Pseudomonas aeruginosa*
DSHS	Department of State Health Services
ESBL	Extended-Spectrum Beta-Lactamases
GC	*Neisseria gonorrhoeae*

Acronym	Full Name
HAI	Healthcare-Associated Infection
HCP	Healthcare Personnel
HSU	Healthcare Safety Unit
ICAR	Infection Control Assessment and Response
*bla*IMP	Imipenemase
IP	Infection Preventionist
*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
mCIM	Modified Carbapenem Inactivation Method
MCR	Mobilized Colistin Resistance
MDRA	Multidrug-Resistant Acinetobacter
MDRO	Multidrug-Resistant Organism
*bla*NDM	New Delhi Metallo-beta-lactamase
*bla*OXA	Oxacillinase
PCR	Polymerase Chain Reaction
PPS	Point Prevalence Survey
SNF	Skilled Nursing Facility

Acronym	Full Name
SNP	Single Nucleotide Polymorphism
TSA	Trypticase Soy Agar
*bla*VIM	Verona Integron-Encoded Metallo-beta-lactamase
WGS	Whole Genome Sequencing

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 Submitter-ID-Request-Form-Sept--2017.pdf (texas.gov) 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:

1. 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

2. The information provided on the specimen label **must exactly match the information provided on the G-2E specimen submission form**.
3. Master G-2E 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 packaged 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 the International Air Transport Association's (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"1. 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.

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 may be informal, consisting of a documented review of Category B biological substances shipping practices.
Please note: The DSHS Laboratory cannot take responsibility 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. 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:

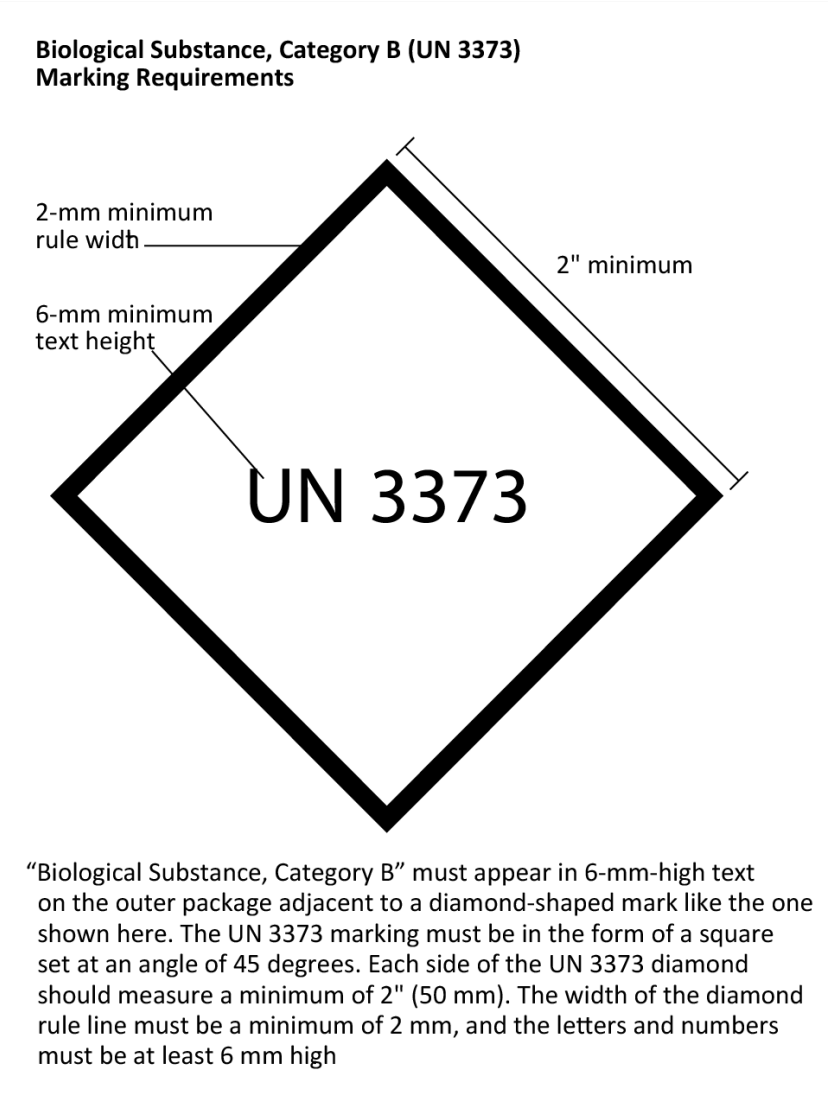


Figure 2. Biological substance, Category B dimensions and marking requirements.

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 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.

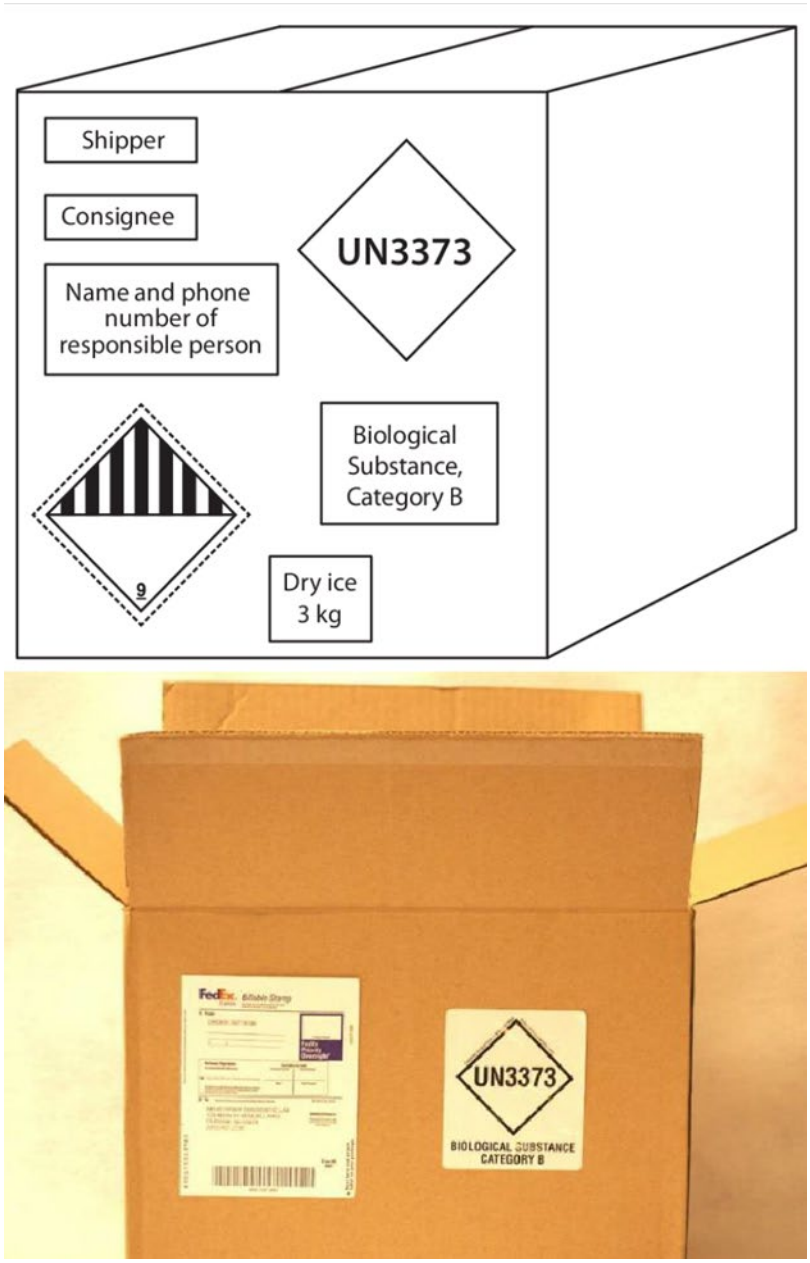


Figure 3. Above: A completely labeled outer mailer/package for a Category B biological substance specimen. When used, dry ice requires its own label, as seen in the bottom left corner. Below: A labeled outer mailer with a FedEx freight label.

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.

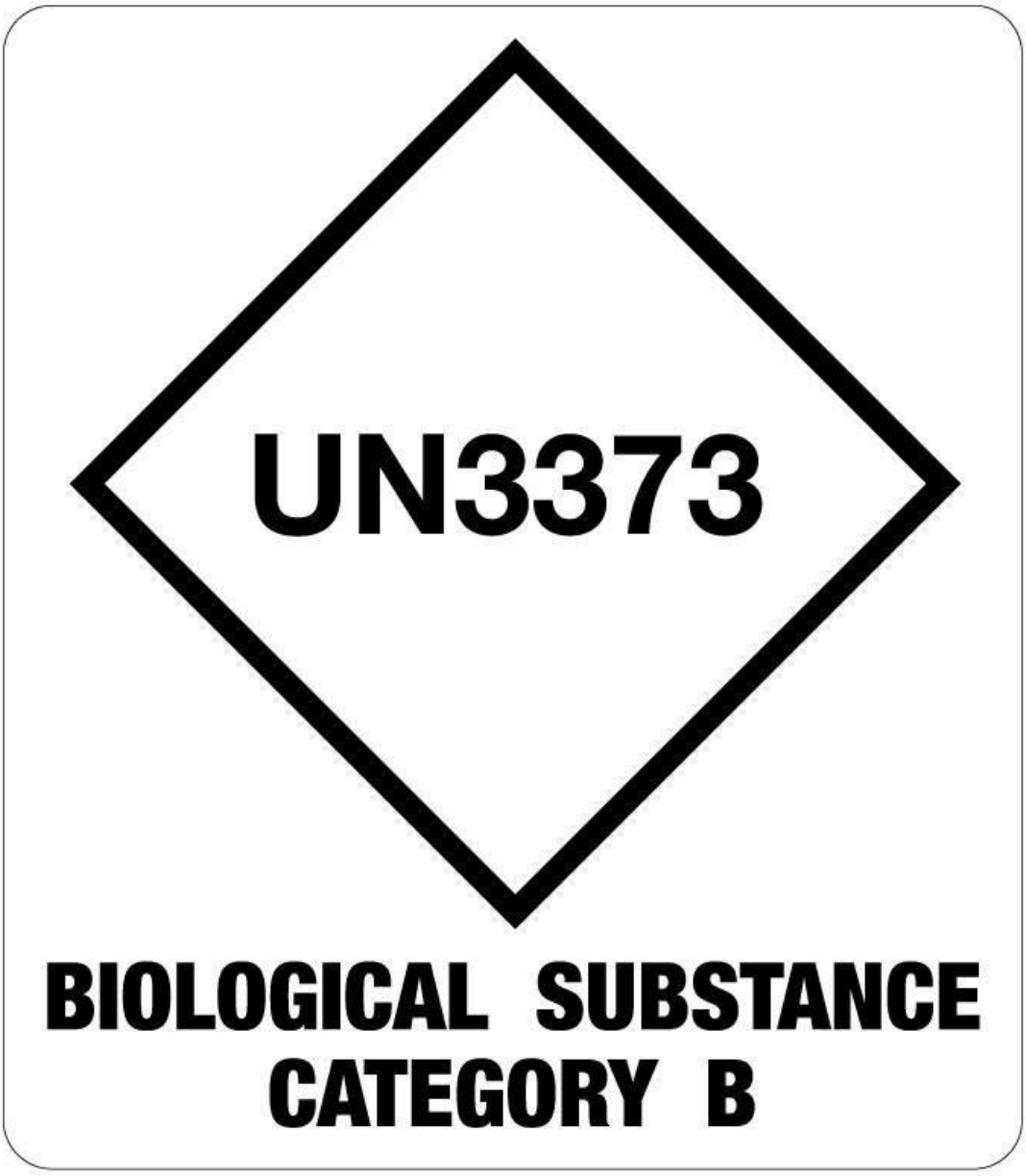


Figure 4. Biological substance, Category B label. Each side of the diamond must be a minimum of 2 inches (50 mm) long, with a border of at least 2 mm width. "Biological Substance Category B" and "UN3373" must be a minimum of 6 mm tall.

Appendix B. Guidance for Use of ARLN FedEx Account

March 22,2022

CDC AR LABORATORY NETWORK:

Guidance for Use of AR Lab Network FedEx Account

PURPOSE.

State, territory and large city public health labs (PHL) supported by the AR Solutions Initiative funding for antimicrobial resistance (AR) laboratory capacity will have access to a CDC funded 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 labs, state labs, regional labs and CDC.

GENERAL CONSIDERATIONS.

Each state, territory and large city PHL, supported by the AR Solutions Initiative 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 ARLN FedEx user agreement must be signed prior to using the FedEx account.

Additional Considerations:

- Submitting labs may batch shipments and include non-ARLN or FoodNet specimens in the shipment to the PHL.
- 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 labs 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 an invitation to create a FedEx website login (username and password) under that state/city/territory's unique Department ID for the ARLN account.
- The local administrator for the FedEx account may then provide the department's login information to clinical labs to ship isolates/samples to the local/state Public Health Lab, the ARLN Regional Lab, or to CDC. Alternatively, the local administrator may create shipping labels and send to clinical labs via email.
- This local administrator will be responsible for signing the ARLN FedEx user agreement
- Any suspected misuse of the account should be reported to CDC immediately (ARLN@cdc.gov), and the password for the account should be changed.

Shipping

- Labs that wish to ship samples for ARLN activities use login information (provided by PHL) to log on to FedEx.com and follow attached instructions for shipping
- PHLs may choose to provide labels to clinical labs rather than account information. This can be done
  using the "create return shipment" function.
  - This option is used to send a customer an email containing a link to retrieve their return label(s).
  - 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
- Domestic shipping only (except Puerto Rico, which is considered International)

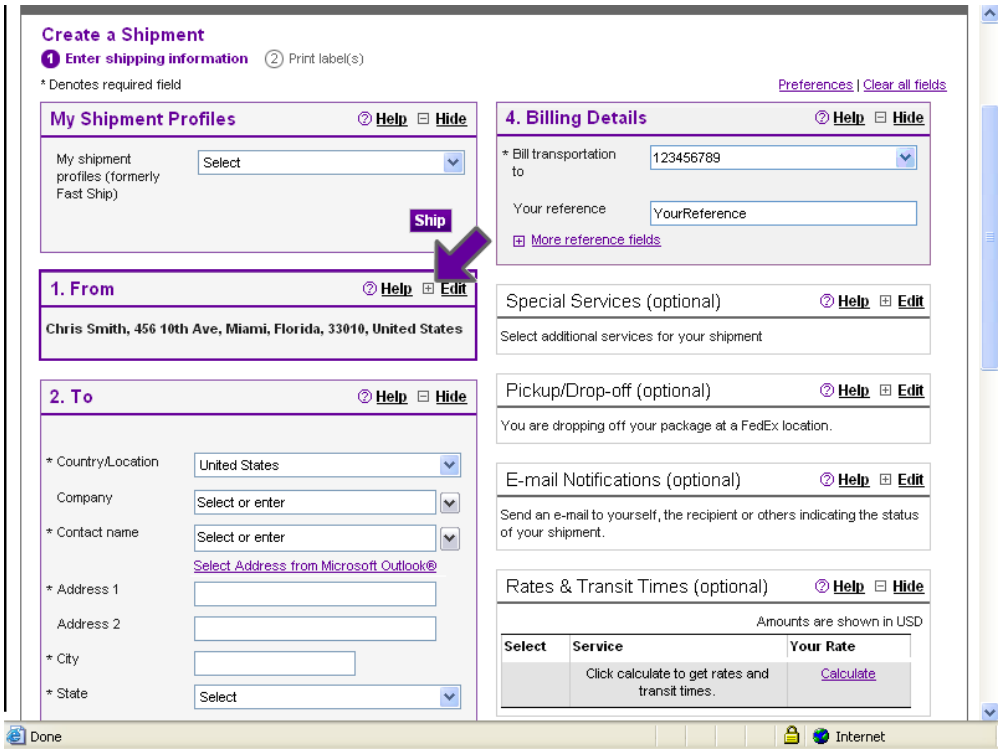
CONTACT INFORMATION.

For questions or further information, please contact CDC's ARLN Team at ARLN@cdc.gov.

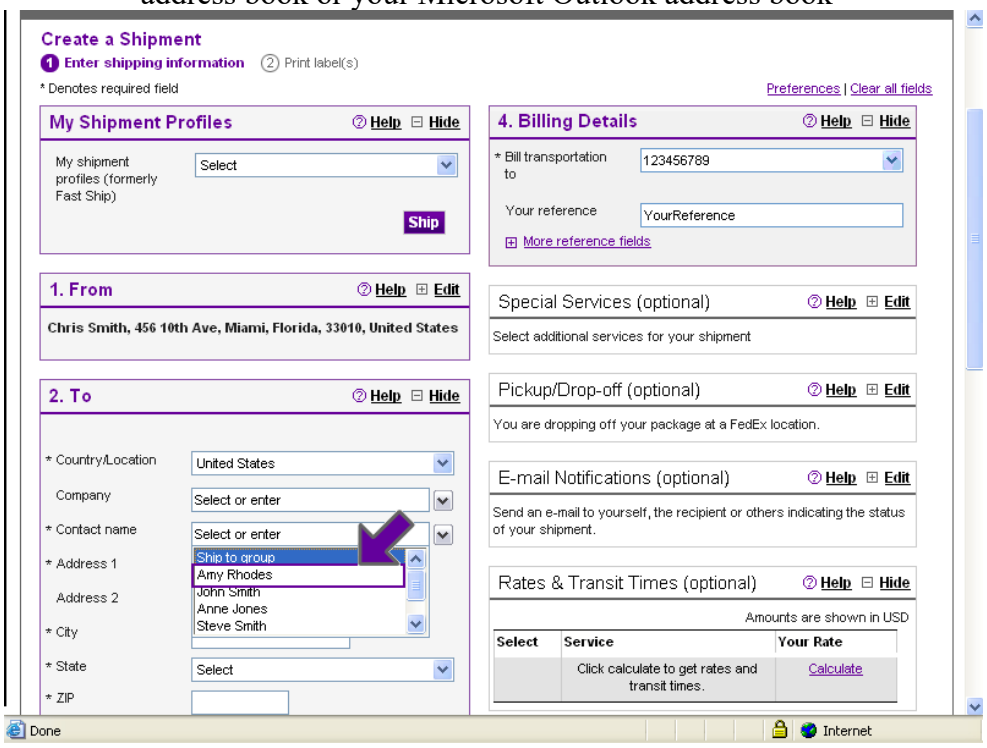
Domestic Shipping on fedex.com

➢ **Step by Step**

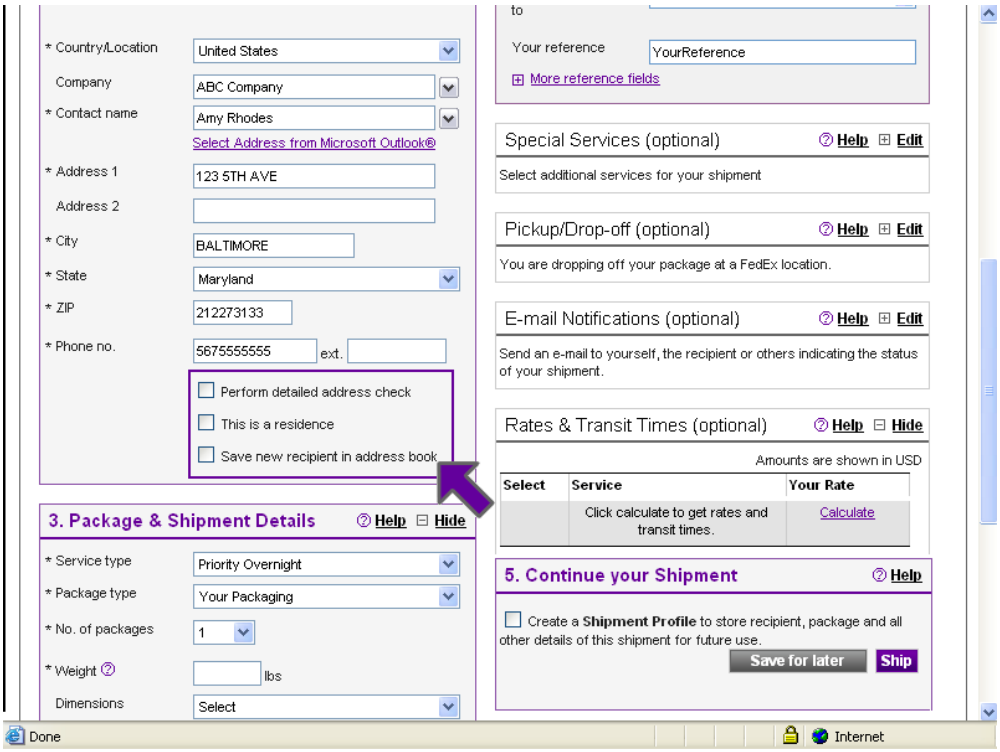
1. Verify the address you are shipping from or change it by clicking the *Edit* link.



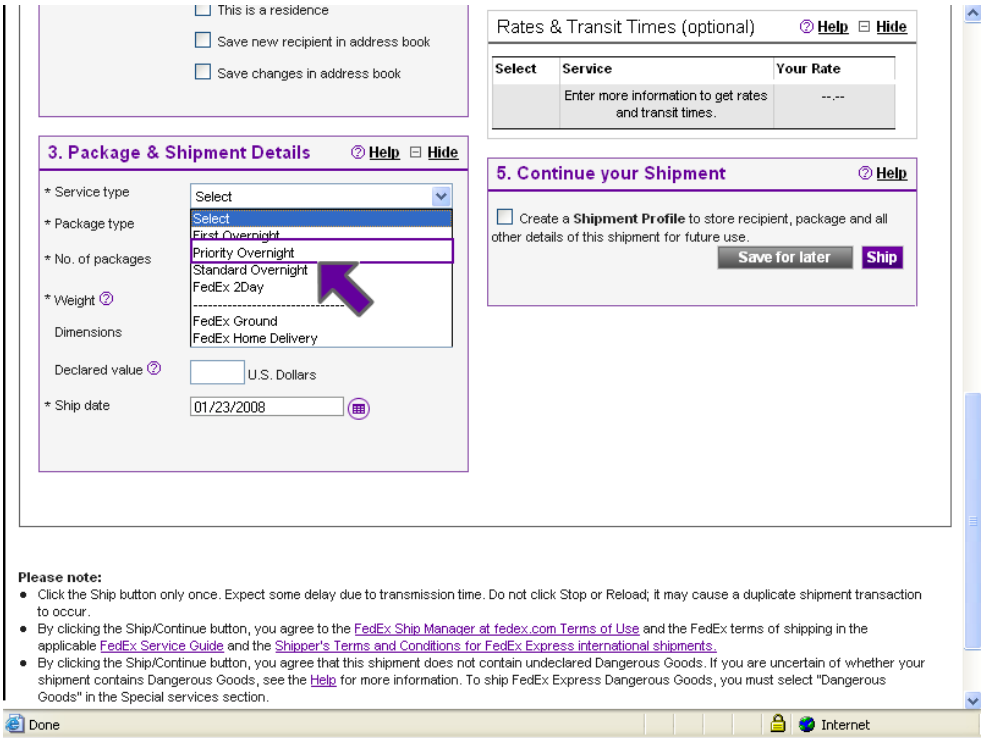
2. Enter the recipient's information or choose an address from your FedEx address book or your Microsoft Outlook address book



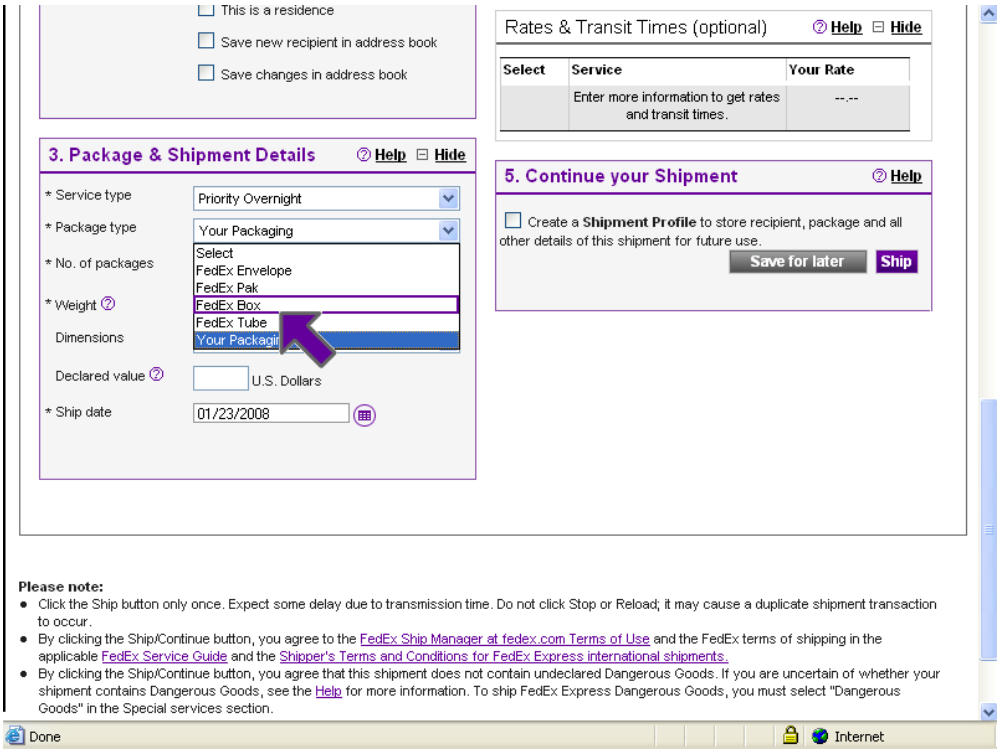
3. Choose any of the available options.



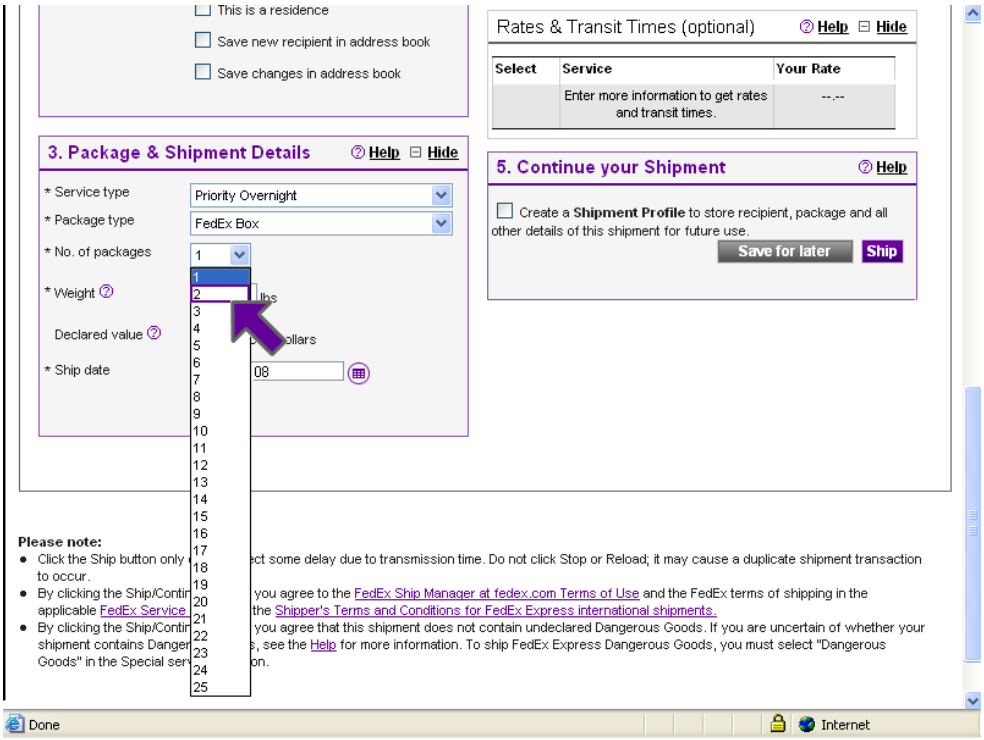
4. Priority Overnight is only available option for ARLN account



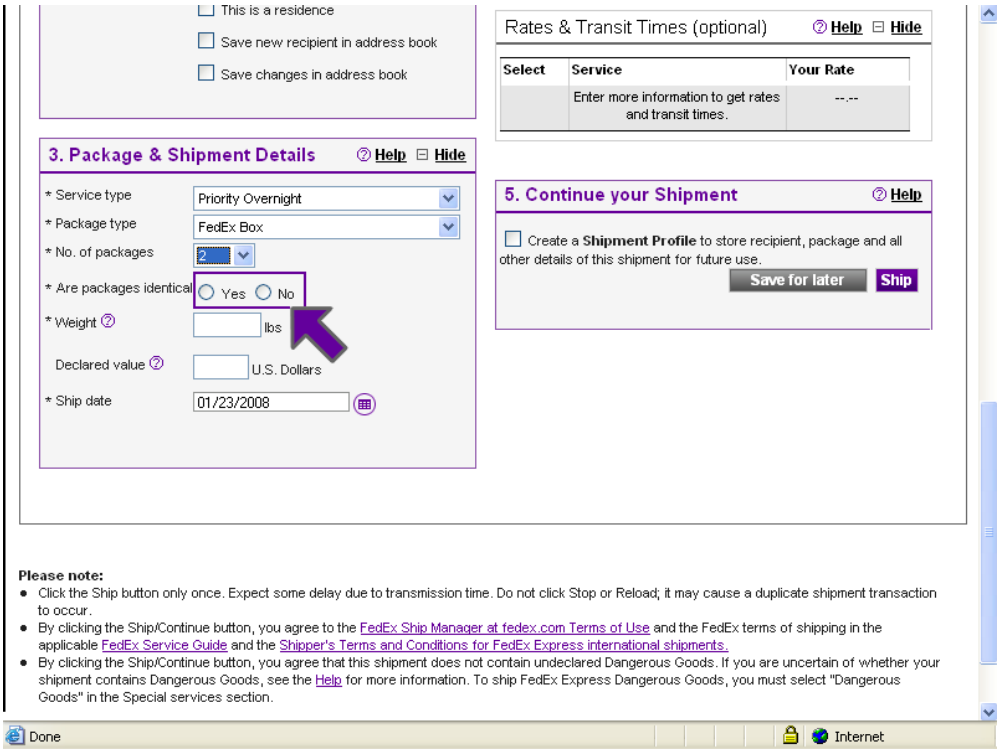
5. Indicate the package type.



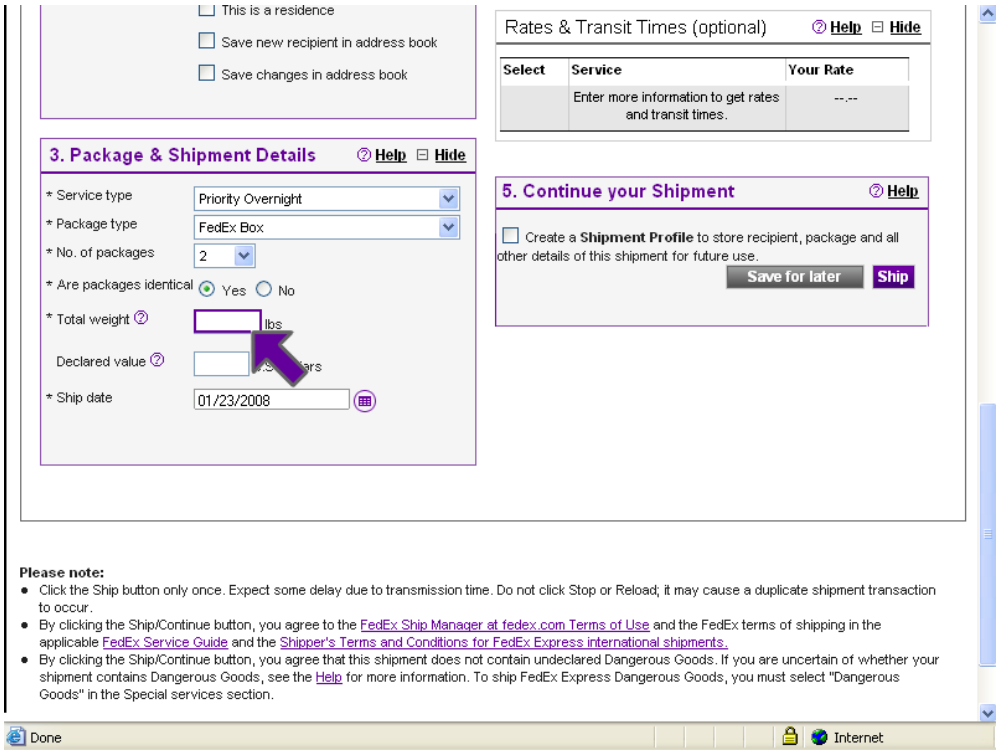
6. Enter the number of packages.



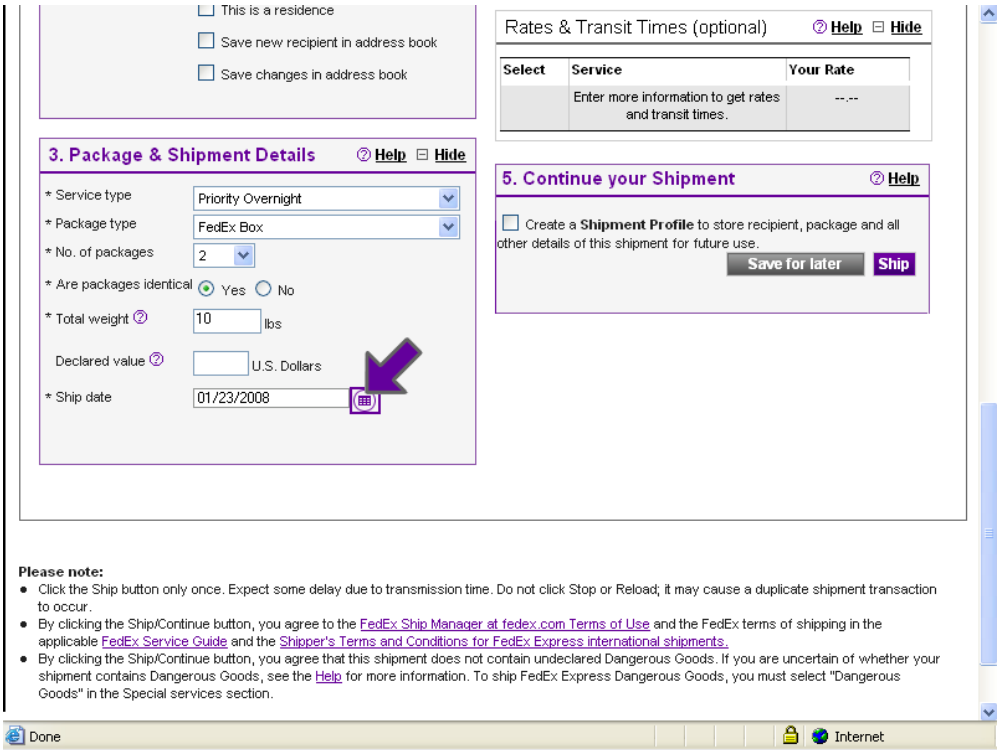
7. If more than one package, indicate whether the packages are identical or not.



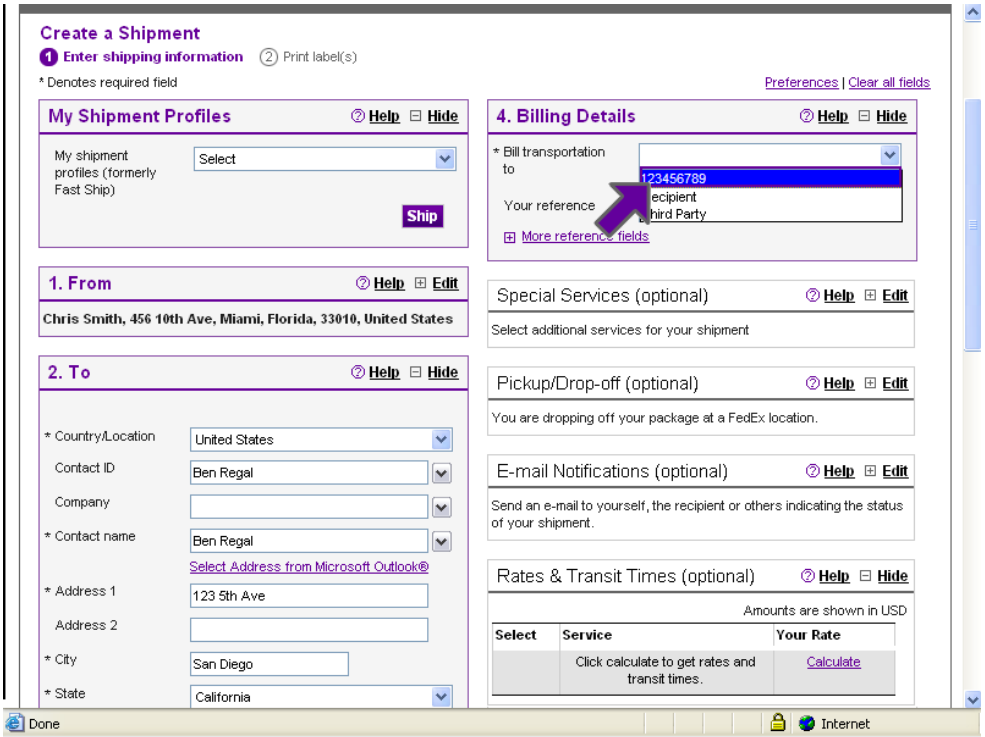
8. Enter the total weight.



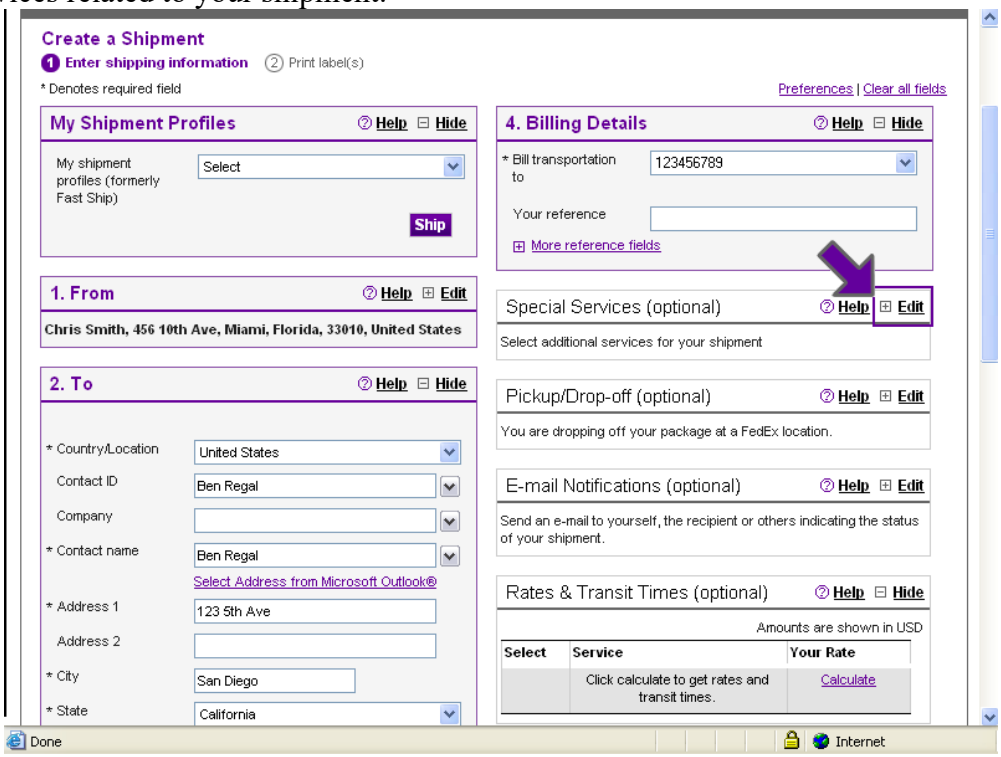
9. Verify the ship date or change it by clicking on the calendar icon.



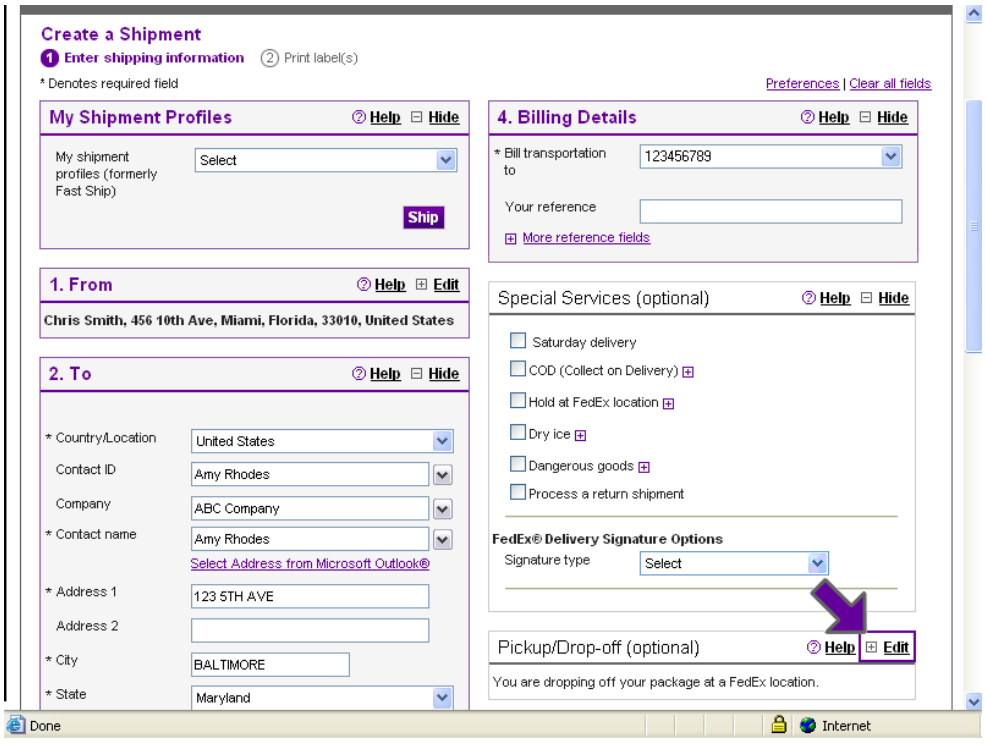
10. Verify the account number you would like to bill your transportation cost to.



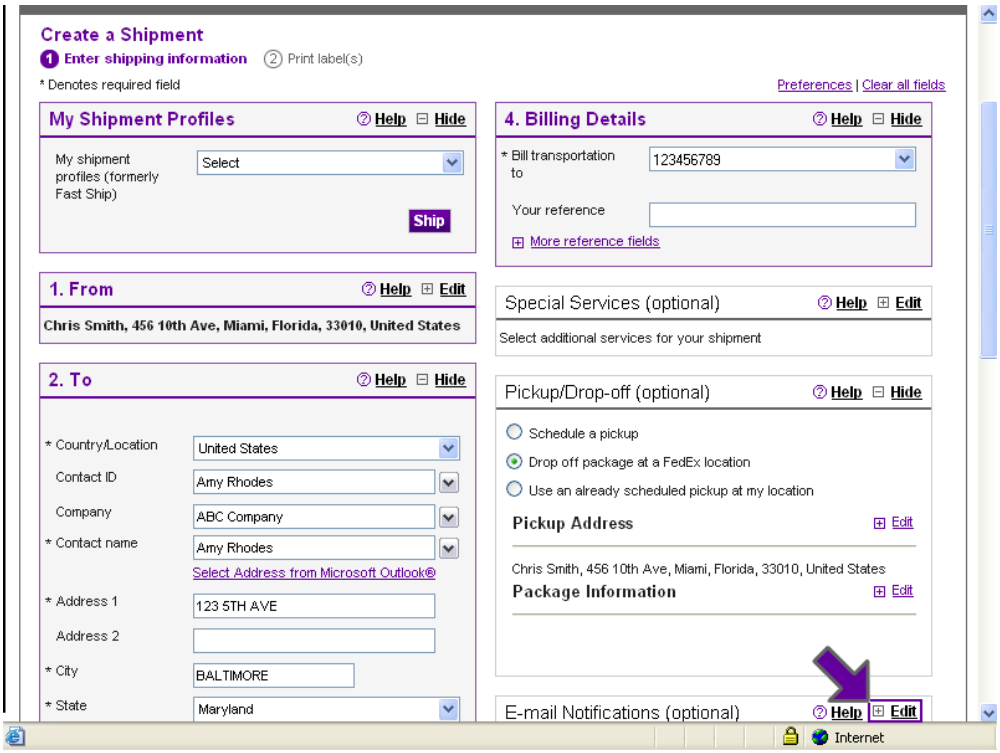
11. Click the ***Edit*** link in Special Services to view and/or choose any special services related to your shipment.



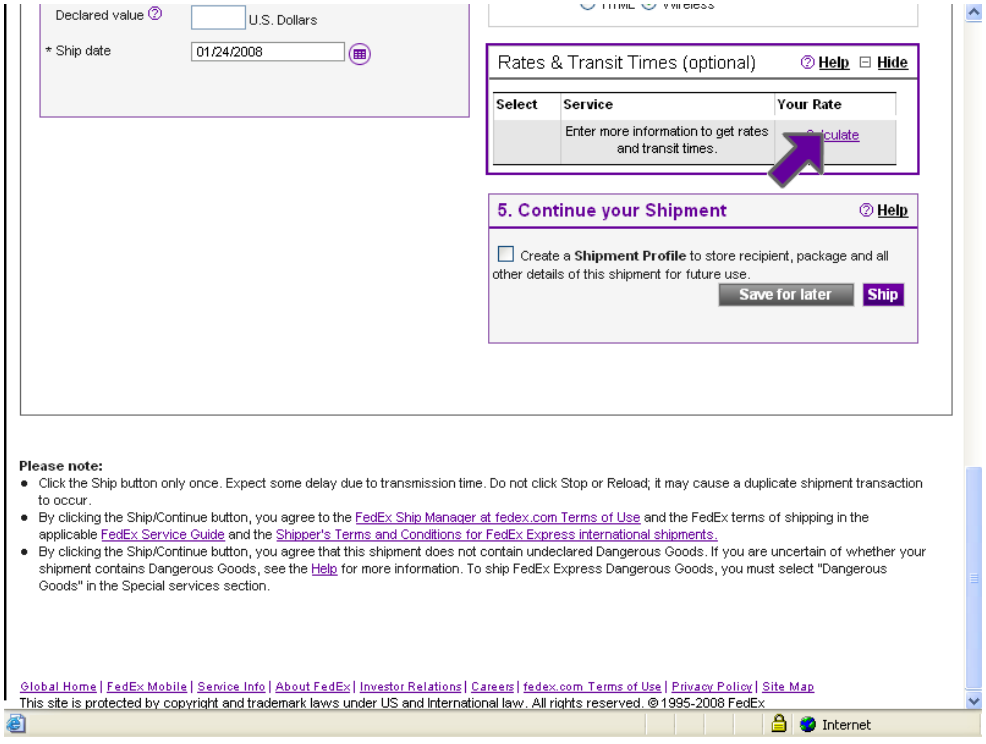
12. Click the ***Edit*** link in Schedule a Pickup/Drop-off to view your Pickup/Drop-off options.



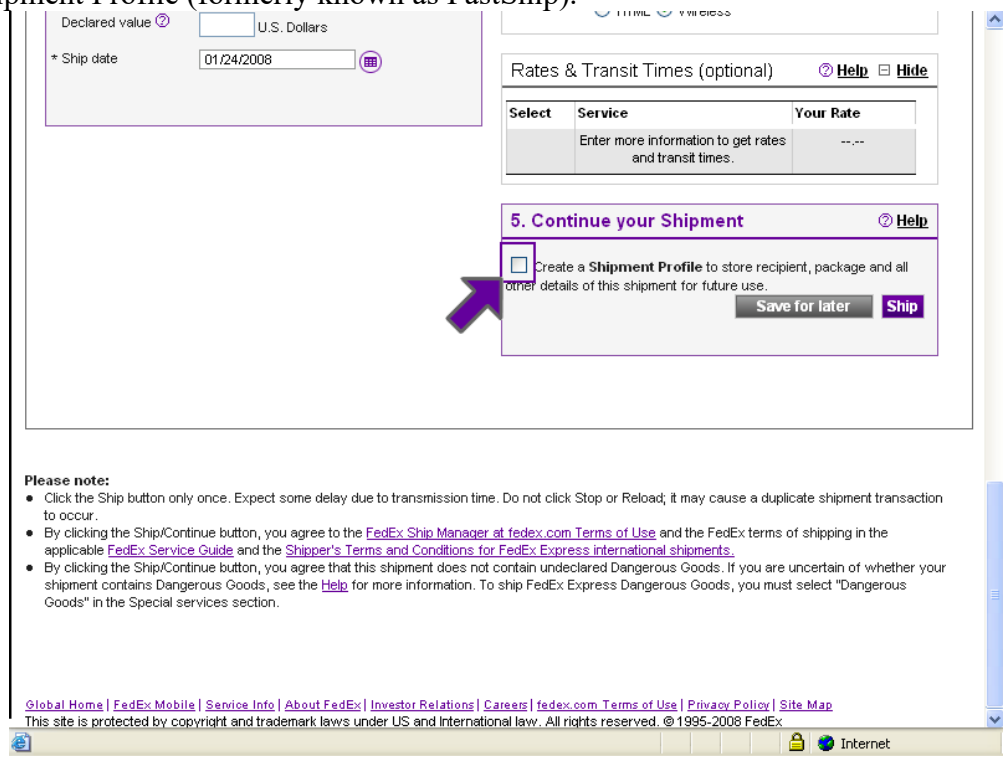
13. Click the ***Edit*** link in E-mail Notifications to send shipment, exception or delivery notifications to yourself, the recipient and two others.



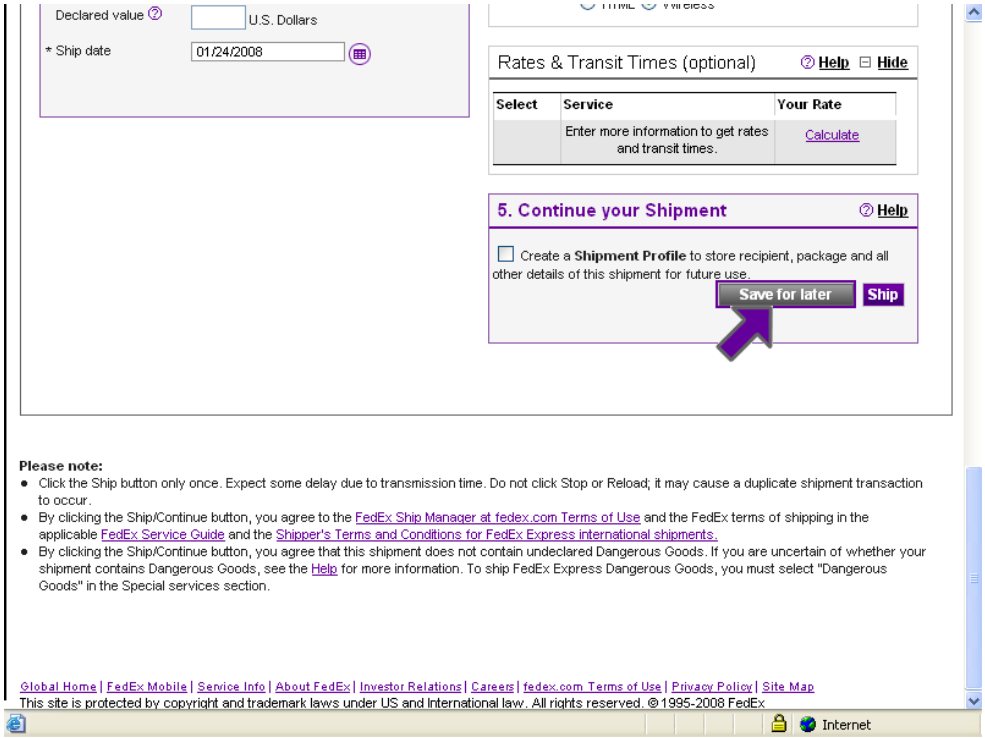
14. Click ***Calculate*** to view rates and transit times related to your shipment.



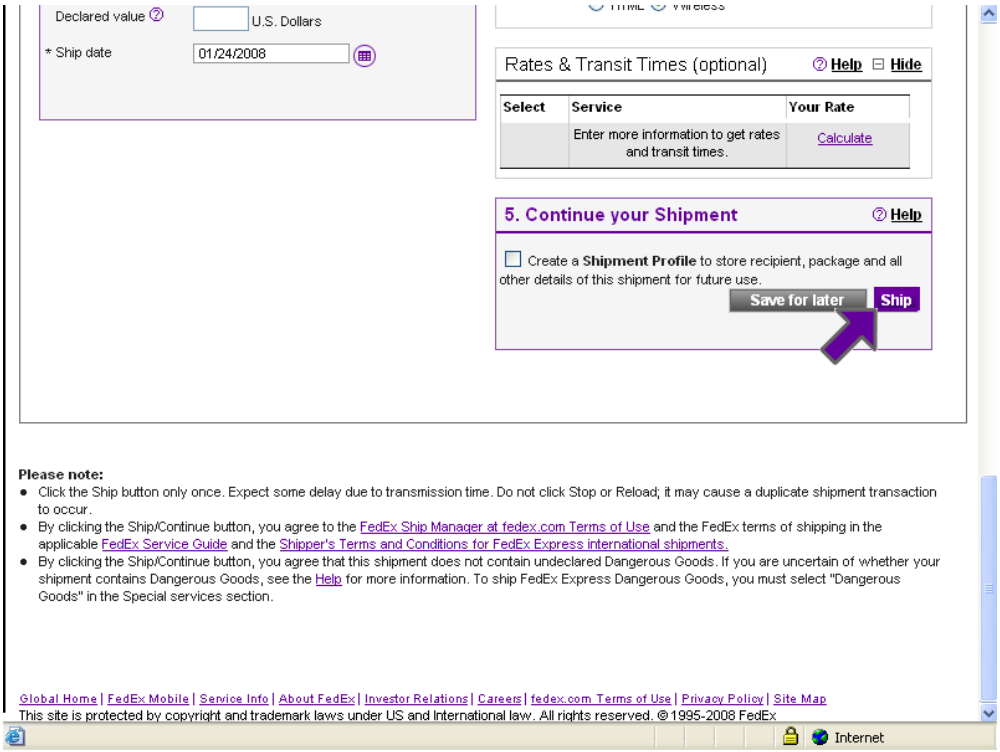
15. Indicate if you would like to save this shipment for future use as a Shipment Profile (formerly known as FastShip).



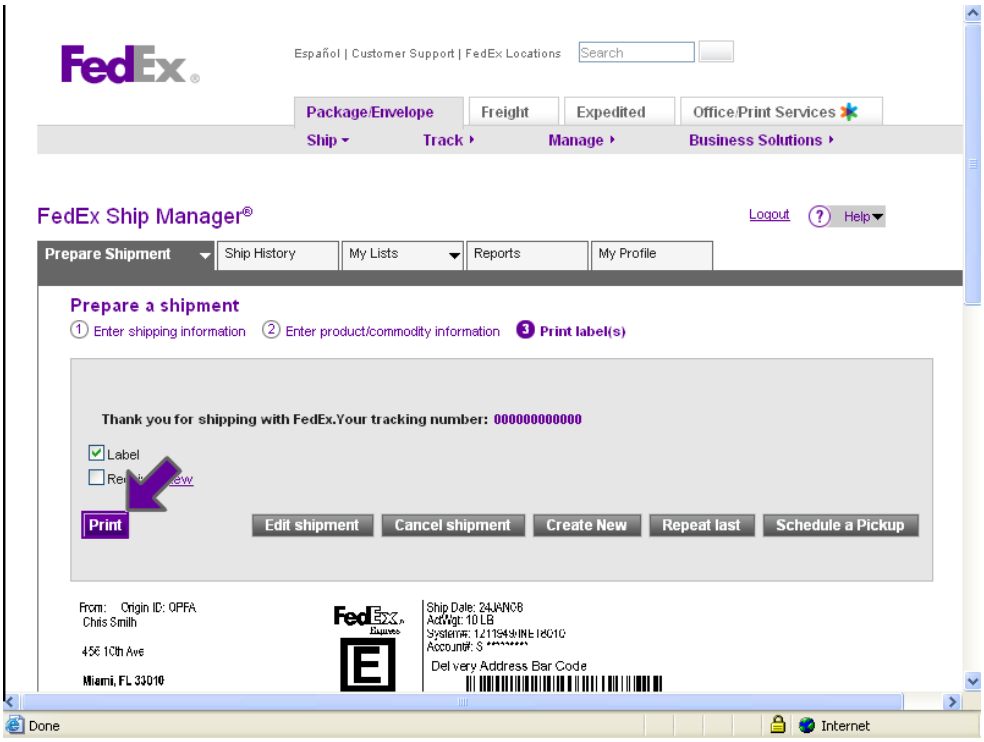
16. Or complete this shipment at a later time by clicking the ***Save for Later*** button.



17. Click the ***Ship*** button.



18. Print the label(s) displayed below, along with a receipt.



This information is provided to you and its use is subject to the FedEx Automation Agreement under which you obtained or have been authorized to use FedEx Ship Manager @ fedex.com. No warranties are extended and all warranties, including without limitation, THE IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS
FOR A PARTICULAR PURPOSE ARE DISCLAIMED, regarding this information. Any conflict between this information and the Automation Agreement, or transportation agreement between you and FedEx, or between this information and the FedEx Service Guide will be governed by the Automation Agreement, the transportation agreement and the FedEx Service Guide, in that order. Your use of this information constitutes your agreement to these term

Terms and Conditions for Use of Federal Express Shipping Administration Username and Password

The undersigned, by his/her signature on this document, certifies that he/she has read and understands the "terms and conditions for use of the Federal Express Shipping Administration Username and Password," and agrees to abide by the terms and the following conditions:

I understand that I am being provided with a user name and password for use with FedEx Shipping Administration exclusively for the purpose of supporting the Antibiotic Resistance Solutions Initiative.

I acknowledge and consent that I will use the assigned username and password exclusively for the shipment of isolates to authorized locations.

I understand and consent that shipments processed with my assigned username and password will be audited by the U.S government. Requests for audits will be complied with in a timely manner.

At any time, the U.S Government may collect, inspect and seize data affiliated with this username and password. Communications associated with my assigned username and password are not private, and are subject to routine monitoring, search, and may be disclosed or used for any U.S. Government authorized purpose.

I acknowledge and understand that I will be held responsible for misuse and/or negligence related to my assigned username and password.

Responsibility for assuring that shipments are authorized rest with the undersigned. In cases where doubt exists over the legitimacy of an authorized shipment, the undersigned is responsible for seeking advice from the account administrator.

Abuse and/or fraud associated with the username and password for this Federal Express Shipping Administration Account are violations of 18 United States Code Section 641, which prohibits misuse or theft of public funds and U.S. Attorney's Manual 1661 – Protection of Government Property. Violations are punishable by up to 10 years imprisonment and/or a fine equal to the amount taken, or double that amount.

I have read and understand this document and agree to accept responsibility on these terms.

_____

Organization

_____

Printed Name

_____

Signature

_____

Date

Appendix C. Specimen Identification Guidelines

Specimen Identification Guidelines

- A submission form is required for each specimen submitted.
- Each specimen must have **at least two patient-specific identifiers** attached to the primary specimen container at the time of collection.
- 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:

1. Patient's Name
2. Patient's Date of Birth
3. Patient's Medical Record Number
4. Specimen ID Number
5. CDC Number
6. Any Custom Unique Identification Number

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

Submission Forms must contain:

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

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

Guidelines for Proper Specimen Identification

All specimens submitted to DSHS for testing must be accurately labeled to ensure result integrity. Prior to shipment, please put at least two acceptable identifiers on the specimen container (tube, plate, etc.) that match the form exactly.

Specimens received with insufficient or mismatching identification will not be tested.

The specimen and form must have at least two acceptable identifiers that match exactly.

Acceptable Identifiers

- Full Patient Name
- Date of Birth
- Medical Record Number
- CDC / Medicare / Medicaid Number
- Unique Identification Number

Common Rejection Reasons

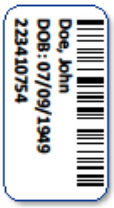
- Specimen container identifiers do not match form
- Lack of secondary identifier
- Unlabeled specimen
- Missing submission form
- *If applicable:* Missing previous lab reports *(such as prior antibiotic sensitivity tests)*

Rejected Specimen Example

Name is cut off and does not match form ✗

Unique ID # does not match form ✗

Acceptable Solutions



1. Rotate text to display full name and include ≥ 2 identifiers as backup.

2. Legible handwritten corrections on specimens are accepted

Example Form

Section 2 - PATIENT INFORMATION (REQUIRED)

NOTE: Patient name MUST match name on this form, Medicare/Medicaid card & specimen container. Specimen must have two (2) identifiers that match this form.

Doe | John

1100 W 49th St

Austin | TX | 78756

07/09/1949

12/14/2022

45322581

Comments/Notes

Accessioning Code: 223410754

3. Write unique ID# in comments section or MRN box

*Note: Address and date of collection are required form items, but they are not considered acceptable specimen identifiers

TEXAS Health and Human Services | Texas Department of State Health Services

For more information visit:
www.dshs.texas.gov/laboratory-services/
labinfo@dshs.texas.gov

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

Description of Activity	Tier 1 • Novel organisms and resistance mechanisms • Pan-not susceptible Candida auris	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)	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 during 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.

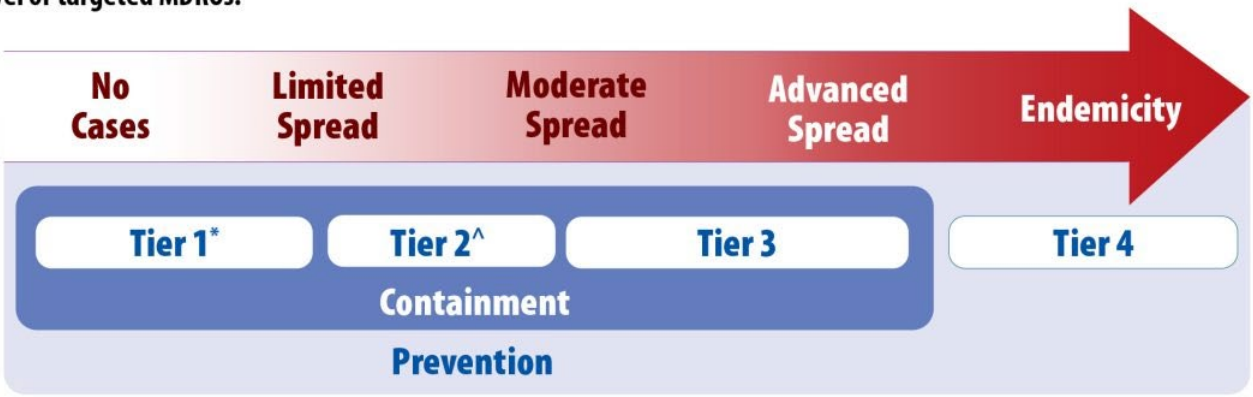
[3]If the index patient was not on Contact Precautions during their entire stay in a healthcare facility, then broader screening (beyond roommates) is recommended. Screening can initially be limited to the contacts at highest risk for acquisition, such as those still admitted who overlapped on the same 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 AR/HAI Alert Findings and Reporting for Public Health Laboratories

Title

ARLN AR/HAI Alert Findings and Reporting for Public Health Laboratories

Purpose

As part of the Antibiotic Resistance (AR) Regional Lab Network activities, state and local public health laboratories will conduct antimicrobial susceptibility testing and molecular assays for resistance mechanisms on a number of organisms recognized as important antibiotic resistance 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 [HAI COORDINATOR/DESIGNEE NAME] at [email address]
and
CDC AR/HAI staff using REDCap (https://rdcp.cdc.gov)

Please be prepared to include: state of specimen origin, state lab ID of isolate(s); specimen source; collection date; age of patient(s) (not DOB); 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 lab ID of the index isolate(s) that initiated the screening (though if point prevalence survey is not initiated in response to an index patient, write "not applicable").

Alert Type	State/Jurisdiction of Specimen Origin	Public Health Lab ID	Specimen Source	Patient Age (yrs)	Date of Isolate Collection (mm/dd/yyyy)	Description of Testing Completed and Results (including Organism ID)	*Colonization screening*	
							Detected During Colonization Screening (Y/N)?	Public Health Lab ID of Index Isolate

Alert Type	Findings	Organism	Follow Up Testing Actions	Send Alert To[1]
Pan-not susceptible CRE, CRPA or CRAB	CRE, CRPA or CRAB not-susceptible to all drugs tested by the submitting clinical laboratory and your public health laboratory[2]	Any	For pan-not susceptible CRE and pan-resistant CRAB or CRPA isolates detected: Forward isolate to regional lab if: • your public health laboratory performs AST using disk diffusion or gradient strips • your public health lab performs GNX2F or GN4F and your regional lab 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 lab uses GNX2F	CDC, HAI Coordinator
Pan-resistant CRE, CRPA or CRAB	CRE, CRPA or CRAB resistant to all drugs tested by the submitting clinical laboratory and your public health laboratory	Any		CDC, HAI Coordinator
Novel carbapenemase suspected[3]	Tests positive for carbapenemase production but RT-PCR-negative	Enterobacterales[4,5] *Pseudomonas aeruginosa*	Prioritize for sequencing or send to regional lab 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 lab for sequencing. Data should be uploaded to NCBI within 7-10 days of trigger result.	CDC, HAI Coordinator

KPC carbapenemase in Enterobacterales[6]	KPC carbapenemase in Enterobacterales	Enterobacterales	N/A	HAI Coordinator (*sending alert to CDC is not required*)
Carbapenemase-producing/-positive *Pseudomonas aeruginosa*	Tests positive for carbapenemase production (mCIM or CarbaNP) and/or bla_{KPC}, bla_{NDM}, bla_{VIM}, $bla_{OXA\text{-}48\text{-}like}$, or bla_{IMP} genes by PCR	*Pseudomonas aeruginosa*	Prioritize for sequencing or send to regional lab 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}, $bla_{OXA\text{-}48\text{-}like}$, or bla_{IMP} genes	*Acinetobacter baumannii*	Prioritize for sequencing or send to regional lab for sequencing. Data should be uploaded to NCBI within 7-10 days of trigger result.	CDC, HAI Coordinator
Carbapenemase-positive *Acinetobacter baumannii (other OXAs)*[8]	Tests positive by RT-PCR (Cepheid or other) for other bla_{OXA} genes, including $bla_{OXA\text{-}23\text{-}like}$, $bla_{OXA\text{-}24/40\text{-}like}$, or $bla_{OXA\text{-}58\text{-}like}$	*Acinetobacter baumannii*	N/A	CDC, HAI Coordinator
Carbapenemase detected from colonization screen	Tests positive for carbapenemase by RT-PCR[9]	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
Elevated aztreonam-avibactam MIC (Expanded Antimicrobial Susceptibility Testing for Hard-to-treat infections)[10]	Aztreonam-avibactam MIC ≥8/4 µg/mL.	Enterobacterales	CDC will enter alert into Alerts REDCap and isolate will be sent to CDC upon request.	CDC, HAI Coordinator
mcr-type resistance	Detection of any *mcr*- gene by PCR or WGS	Any[11]	N/A	CDC, HAI Coordinator
Suspected hypervirulence	Isolates carrying ≥1 targeted carbapenemase genes (bla_{KPC}, bla_{NDM}, bla_{VIM}, $bla_{OXA\text{-}48\text{-}like}$, or *bla*IMP) **AND** ≥1 of the following suspected genetic marker of hypervirulence :peg-344, $_{p}$rmpA, and $_{p}$rmpA2[12,13], *detected by*	*Klebsiella* spp. and *E. coli*	N/A	CDC (*These findings may require a public health response.* ***Please discuss with CDC before initiating a response***[14])

	analysis of WGS conducted for other priorities.			
Concerning resistance in Gram positive organisms	Plasmid mediated linezolid resistance (cfr, optrA and poxtA)	*Enterococcus*[15]	N/A	CDC, HAI Coordinator
	Elevated MICs to daptomycin MIC≥8 µg/mL and linezolid MIC≥8 µg/mL in vancomycin resistant *Enterococcus* (VRE)			
Other	Vancomycin resistant (MIC≥8 µg/mL) *Staphylococcus aureus* (VRSA)	*Staphylococcus aureus*	N/A	CDC, HAI Coordinator
	Other new or known but rare AR threats in HAI pathogens not covered above	Any		

[1] For any isolates that are being whole genome sequenced, please select the radio button beside "Is this isolate being sent for whole genome sequencing?" in the REDCap alert form and enter the HAI WGS ID and the NCBI HAI-Seq SRR ID associated with the isolate when sequencing is completed.

[2]Colistin susceptibility results will not be included in the definition for pan-not susceptible because of revised colistin breakpoints will only have intermediate and resistant interpretative categories. **This category excludes isolates that are resistant to all drugs tested (which should trigger a pan-r alert instead).**

[3]For confirmed novel carbapenemase alerts, please see additional guidance below regarding **immediate follow up actions**.

[4] 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*** 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).

[5] 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).

[6] Report all KPC-CRE to your HAI coordinator. Some jurisdictions, such as those where KPC is rarely identified, 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 response to specific cases should be sent to haioutbreak@cdc.gov.

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

[8] Jurisdictional public health labs should discuss reporting of *Acinetobacter baumannii* with *bla*$_{\text{OXA-23}}$, *bla*$_{\text{OXA-24/40}}$, *bla*$_{\text{OXA-58}}$ 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.

[9] For any organism isolated from a screening swab, please send a new alert for the isolate testing results.

[10] Alerts will be generated by testing regional lab, who will alert state/local jurisdictions when testing is performed and when an isolate with an alert value is detected.

[11]Detection of *mcr* genes has been de-escalated from AR Lab Network priorities, and therefore testing for *mcr* genes is no longer requested by DHQP. If labs prefer to continue testing, please still report positive findings to CDC for situational awareness. Note: *Proteus, Providencia, Serratia*, or *Morganella* have intrinsic resistance colistin and do not require *mcr* testing.

[12]Russo, T.A., et al. J Clin Microbiol, 2018. 56(9) https://jcm.asm.org/content/56/9/e00776-18.long.

[13]At this time, there is no set definition for hypervirulence markers or phenotype. Note that mucoviscosity of isolates is not a sufficient indicator of hypervirulence.

[14]Please contact CDC (haioutbreak@cdc.gov) to discuss implementation of containment responses related to the detection of suspected hypervirulence markers.

If you have confirmed the presence of a novel carbapenemase gene (excluding *bla*$_{\text{KPC}}$, *bla*$_{\text{NDM}}$, *bla*$_{\text{VIM}}$, *bla*$_{\text{IMP}}$, *bla*$_{\text{OXA-48-like}}$, *bla*$_{\text{IMI}}$, *bla*$_{\text{NMC}}$, *bla*$_{\text{SME}}$), please:

- Immediately notify CDC and your jurisdictional health department of any preliminary findings of novel carbapenemase genes.
- Select the radio button beside "*Is this isolate being sent for whole genome sequencing?*" in the REDCap alert form.
- If you have sequenced the isolate, return to the alert form in REDCap to enter the HAI WGS ID and the NCBI HAI-Seq SRR ID associated with the isolate when sequencing is completed.
- Note: Unless WGS activities are CLIA approved in your laboratory, we do not recommend reporting sequencing findings to submitting clinical laboratories.

[14]If you detect the presence of ≥1 targeted carbapenemase gene (*bla*$_{\text{KPC}}$, *bla*$_{\text{NDM}}$, *bla*$_{\text{VIM}}$, *bla*$_{\text{IMP}}$, *bla*$_{\text{OXA-48-like}}$) AND ≥1 suspected hypervirulence marker (peg-344, $_{p}$rmpA, and $_{p}$rmpA2) using WGS data please:

- Update your REDCap entry to specify the gene(s) detected.
- Implement appropriate containment responses for the carbapenemase gene(s) detected and contact CDC for appropriate guidance and recommendations related to suspected detection of hypervirulence marker(s).

[15] If you detect isolates with plasmid mediated linezolid resistance (cfr, optrA and poxtA), or there is a notable change in epidemiology (e.g. an increase in VRE bacteremia that might point to a concerning strain emerging), please contact CDC (haioutbreak@cdc.gov) to discuss implementation of containment responses.