

# Multi-Drug Resistant Organism (MDRO) Guidance for Long-Term Acute Care Hospitals (LTACHs)

The purpose of this document is to serve as a reference guide for Los Angeles County LTACHs on core MDRO prevention activities, including infection control measures and cohorting patients. It synthesizes guidance provided by the Centers for Disease Control and Prevention (CDC) and the California Department of Health (CDPH) and supplements it with best practices compiled by the Los Angeles County Department of Public Health (LACDPH).

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# Introduction, background, and definitions

**Multi-drug resistant organisms (MDROs)** are microorganisms (bacteria, fungi) that are resistant to one or more classes of antimicrobial agents. MDROs are a growing public health concern because of their resistance to available treatment options and their ability to spread easily across healthcare settings. Proper MDRO management at healthcare facilities is crucial to patients' health and safety.

MDRO transmission in LTACHs is common. More than 50% of LTACH patients may be **colonized** with an MDRO, meaning that they carry the organism in or on their body but are not symptomatic nor ill compared to an **infected** patient who displays symptoms or illness caused by the organism. Colonized patients can be carriers for life and can pass the organism on to others when infection control measures are not in place.

MDRO surveillance within a facility is necessary to identify organisms and their transmission source, and to monitor the prevalence and transmission rates among patients. As part of these efforts, it is important for facilities to maintain a list of infected and colonized patients. The surveillance of patients' clinical microbiology results and the performance of point prevalence screenings (PPS) are all important activities to determine if there is spread within a facility. If a patient tests positive for an MDRO infection or colonization, a PPS may be conducted to determine if there are other positive patients and to determine the extent of the spread in the facility.

Carbapenem-resistant organisms (CROs) include gram-negative bacteria which are resistant to Carbapenems, one of the last line of antibiotics used to treat infections. A subset of these organisms called carbapenemase producing organisms (CPOs) are of even greater concern because of their ability to produce enzymes capable of making carbapenems ineffective and additionally can be easily passed to other bacterial species. CROs and CPOs can result in serious infections and death in a small number of susceptible patients who become infected, though most MDRO carriers will never develop an infection.

Laboratory tests are used for MDRO identification to the species level and inform clinical decisions.

- Antimicrobial Susceptibility Testing (AST)- test to check if an organism is susceptible (S), resistant (R), or intermediate (I) to antibiotics of varying concentrations.
- Phenotypic test- identifies if organism produces carbapenemase (e.g., modified carbapenem inactivation method (mCIM), ).
- Genotypic test- identifies if organism has a gene for carbapenemase (e.g., polymerase chain reaction (PCR)).

**Novel MDROs** and **Targeted MDROs** refer to MDROs that are considered epidemiologically and clinically concerning in LA County. Novel MDROs are organisms with a resistance pattern or mechanism that has never or very rarely been identified in the LA County and the wider U.S. These are usually classified as MDRO Containment Tier 1 organisms. Targeted MDROs often are organisms that are resistant to most or all available antimicrobials and with the potential to spread widely. See Table 1 for a list of these organisms.

Table 1: LAC Novel and Targeted MDROs

MDRO	Organism(s) included	Description
Carbapenemase- Producing Organism (CPO)	IMP-, VIM-, and OXA-like- Producing Carbapenem- Resistant Enterobacterales (CRE)	<ul> <li>Order of gram-negative bacteria commonly found in the body's normal flora, includes organism like <i>Escherichia coli</i> and <i>Klebsiella pneumoniae</i>.</li> <li>Can cause serious infection if introduced to sterile site.</li> <li>Can spread rapidly in healthcare settings.</li> </ul>
	NDM-, IMP-, VIM-, and KPC- producing carbapenem- resistant <i>Acinetobacter</i> baumannii (CRAB)	<ul> <li>Bacterium commonly found in soil and water.</li> <li>Frequently associated with large outbreaks in healthcare settings.</li> <li>Resistant to common antibiotics.</li> </ul>
Pan-Resistant Organisms	Enterobacterales Pseudomonas aeruginosa Acinetobacter baumannii	<ul> <li>Resistant (R) to all drugs tested at public health laboratories (including the CDC).</li> </ul>
Concerning Candida auris (C. auris)	C. auris that is echinocandinor pan-resistant	<ul> <li>Yeast that can spread easily and cause outbreaks in healthcare settings.</li> <li>Can colonize the skin and it is difficult to eliminate from the patient environment with common healthcare disinfectant.</li> <li>Strain currently circulating in LA County and Southern California is susceptible to most antifungals. However, more resistant strains are concerning.</li> </ul>
Novel organisms	n/a	Newly identified MDRO as defined by the CDC.

Each of these organisms are categorized into MDRO Containment Tiers as defined by <u>CDC</u>. These tiers dictate the level of response activities and infection control recommendations based on the level of epidemiological and clinical concern for each organism. Assignment of MDROs into these tiers changes over time as their specific epidemiology evolves.

For the most updated list of how LACDPH assigns MDROs into containment tiers, please see here: <a href="http://publichealth.lacounty.gov/acd/docs/LACDPH MDRO Tiers ExternalGuidance.pdf">http://publichealth.lacounty.gov/acd/docs/LACDPH MDRO Tiers ExternalGuidance.pdf</a>

Novel and targeted MDROs are listed as Tier 1 and Tier 2 organisms in this guidance.

For the most up-to-date information on MDROs in LA County, please see our Annual MDRO Report and Targeted MDRO dashboard on our MDRO website: <a href="mailto:publichealth.lacounty.gov/acd/Diseases/NMDRO.htm">publichealth.lacounty.gov/acd/Diseases/NMDRO.htm</a>

# How to identify these MDROs

# Example of concerning C. auris lab report

Identification			Candida auris
Analyte/Drug	<u>Value</u>	Units	Results/Interpretation
Amphotericin B (E-Test)	0.5	μg/mL	No CLSI Interpretation
Anidulafungin	4	µg/mL	No CLSI Interpretation
Caspofungin	2	µg/mL	No CLSI Interpretation
Fluconazole	256	µg/mL	No CLSI Interpretation
Isavuconazole	0.12	μg/mL	No CLSI Interpretation
Itraconazole	0.5	μg/mL	No CLSI Interpretation
Micafungin	4	µg/mL	No CLSI Interpretation
Posaconazole	0.12	µg/mL	No CLSI Interpretation
Voriconazole	2	µg/mL	No CLSI Interpretation

Note that <u>CDC-provided breakpoints</u> are used until CLSI develops interpretive criteria.

#### **Examples of CPO lab reports**

#### Reportable Tests: Blood Culture Gram Negative Pathogen Panel See Values: Klebsiella pneumoniae, DNA (A), OXA (CRE resistance gene), DNA (A) Blood Culture GN Panel, PCR (Final result) Test Analyte Result Value Escherichia coli, DNA Not Detected Pseudomonas aeruginosa, DNA Not Detected Klebsiella pneumoniae, DNA Detected (A) Klebsiella oxytoca, DNA Not Detected CTX-M (ESBL resistance gene), DNA Not Detected Not Detected Proteus species, DNA Not Detected Acinetobacter species, DNA Not Detected Citrobacter species, DNA Not Detected OXA (CRE resistance gene), DNA Detected (A) Not Detected IMP (CRE resistance gene), DNA KPC (CRE resistance gene), DNA Not Detected VIM (CRE resistance gene), DNA Not Detected NDM (CRE resistance gene), DNA Not Detected

Light growth Pseudomonas aeruginosa, Carbapenem-resistant
Multi-Drug Resistant Organism
Positive for NDM carbapenemase by immunochromatographic assay

# General Infection Control Guidance for MDROs

In healthcare settings, MDROs are spread by contact, either through person-to-person contact, contaminated surfaces and medical equipment that was not properly disinfected, or via the hands of healthcare workers who did not perform proper hand hygiene. This is why it is important for all healthcare staff to follow transmission-based precautions and thoroughly clean surfaces. When LTACHs consistently adhere to these basic elements of infection control, they can curb transmission of MDROs and other healthcare-associated infection (HAI).

Table 2: Infection Control Guidance for MDROs

IC Practices	Additional Information
Transmission-Based Precautions: Place the patient on the appropriate level of transmission-based precautions	Contact precautions are recommended for MDROs. Ensure that staff perform hand hygiene (HH) and don/doff personal protective equipment (PPE) appropriately upon entering/exiting the patient's room or dedicated area in accordance with the recommended guidelines set for the different transmission-based precautions:  Contact Precautions (CP)  Standard Precautions (SP)
Environmental Cleaning and Disinfection: Use the disinfectant most effective against the specific MDRO	Frequent and thorough cleaning of all high-touch surfaces in rooms, common areas, and shared equipment using products according to the manufacturer's instructions.  Ensure the disinfectant is effective against the MDRO. For example, use approved products from <a href="EPA List P">EPA List P</a> to disinfect against <i>C. auris</i> . If List P is not available, use products from <a href="EPA List K">EPA List K</a> and follow instructions for <i>C. difficile</i> .
Education: Frequent and consistent education of healthcare workers, patients, and their visitors on ways to reduce the spread of MDROs.	Regular in-service trainings to staff on IPC policies of hand hygiene, environmental cleaning, personal protective equipment, and device reprocessing.  Inform patients and their family of their MDRO status and educate on ways to reduce transmission.
Communication: When the patient is discharged, notify the receiving HCF of the patient's MDRO status	Use an <u>inter-facility transfer</u> form and provide all required documents (including laboratory reports and medication records). Ensure the patient is aware of their MDRO status and provide educational materials as needed. Flag patients' charts/EMR for MDRO so that appropriate precautions are taken upon readmission.  Facility IPs are encouraged to communicate Patient's MDRO status with other facility IPs with patient sharing/transfer.
MDRO Surveillance: Surveillance and monitoring of MDRO cases inform MDRO patterns and detects outbreaks and clusters.	<ul> <li>Maintain ongoing MDRO surveillance:         <ul> <li>Implement a laboratory monitoring system to identify MDROs.</li> <li>Maintain a list of each MDRO case on a line list to calculate MDRO rates and determine when further investigation needed.</li> <li>Share surveillance information with staff and infection control practitioners. Identify areas for intervention.</li> <li>Use surveillance data to detect outbreaks and patterns of transmission</li> </ul> </li> <li>Facilities can utilize LA County's Patient Safety Information Exchange (PSIE) to check a patient's MDRO history upon admission.</li> </ul>

#### Transmission-Based Precautions for MDROs

While LACDPH generally recommends Contact Precautions (CP) for most MDROs, CP is no longer recommended for common MDROs such as MRSA, ESBL, and VRE. LACDPH suggests LTACHs review the LACDPH Rethinking Contact

Precautions for MRSA and VRE guidance to determine if the use of Contact Precautions is necessary for these organisms.

# **Determining Transmission Based Precautions and Cohorting Strategy**

The practice of **cohorting** patients, which is the grouping of patients based on their MDRO status, is a strategy recommended for patients infected or colonized with most MDROs, especially novel and targeted MDROs. LTACHs can prioritize placing these patients in a single room if there are any available.

If single rooms are not available, patients can be cohorted in the same room based on their MDRO status. When assigning rooms, it's important that patients' MDRO status is known, and that specimens that test positive for CROs are tested for carbapenemase production. Cohorting patients with the same carbapenemase is preferred, but may not always be possible. Note that patients with the same MDRO(s) can be cohorted together regardless of their infection status or specimen source.

Facilities can also cohort patients with certain MDROs together in a dedicated unit or part of a unit (e.g., end of a hallway) with dedicated healthcare personnel, equipment, and medical devices as much as possible. Dedicating healthcare personnel (e.g., nurses, nursing assistants) who provide regular care to patients with MDROs can decrease the risk of spread within the facility.

When there is active transmission and/or an outbreak is confirmed or suspected, Contact Precautions are strongly recommended. For single cases, facilities can use the MDRO Cohorting Flowchart (*Figure 1*) and the Cohorting Recommendations by MDRO Type (*Table 3*) on how to best cohort with other patients. Avoid excessive patient movement as this can lead to additional transmission.

In general, prioritize single rooms and cohorting for patients with the most MDROs or the more concerning MDROs.

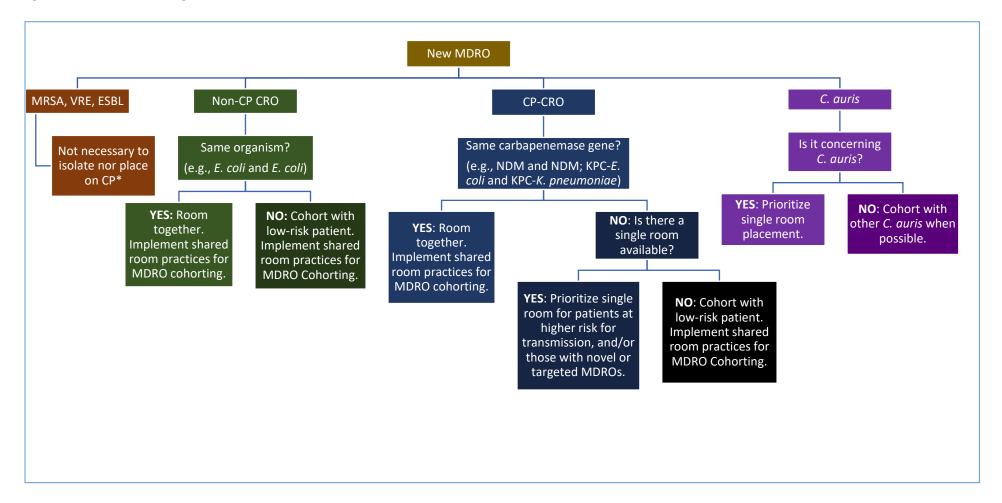
#### High-risk patients for MDRO acquisition

In general, persons who have one or more factors listed below tend to be at higher risk for MDRO acquisition. Facilities should consider these when determining if and how to cohort patients together, especially when they don't share the same MDRO status. Ideally, if you need to cohort patients with different MDROs together, select patients with the <u>fewest</u> amount of risk factors to minimize the risk of transmission. Risk factors include:

- Medical Services involving: Respiratory therapy, Mechanical Ventilation, Wound Care, PT/OT, Dialysis.
- Indwelling Devices: Midline catheter/PICC line, Central venous catheter, Other central line, PEG, Foley, Other invasive urinary catheter, ET tube, Trach, Ostomy.
- Wounds: surgical wounds, inserted medical devices sites, wound drain.

Patients with fewer or none of these factors are considered to be lower risk.

Figure 1. MDRO Cohorting Flowchart



<sup>\*</sup>see LACDPH Rethinking Contact Precautions for MRSA and VRE for more guidance: http://publichealth.lacounty.gov/acd/RethinkingContactPrecautions/index.htm

#### For additional definitions:

- Concerning *C. auris*: page 3.
- Shared room practices for MDRO cohorting: page 9.
- Lower risk patients: page 6.

Table 3: TBP and Cohorting Recommendations by MDRO Type

MDRO Type		DPH Recommendation	
Organism	Is it Novel or Targeted MDRO?	TBP Type	How to cohort⁺
MRSA, VRE, ESBL	No	SP	No special cohorting guidance is recommended, unless the facility is experiencing an outbreak. See LACDPH Rethinking Contact Precautions for MRSA and VRE for more guidance: <a href="http://publichealth.lacounty.gov/acd/RethinkingContactPrecautions/index.htm">http://publichealth.lacounty.gov/acd/RethinkingContactPrecautions/index.htm</a>
CRE, CRPA, CRAB	Yes	СР	Cohort only with other patients with the same carbapenemase gene.
(CROs) and CPOs	No or unknown	СР	Cohort only with other patients with the same carbapenemase gene unless there is an outbreak with another organism (e.g., targeted MDRO, COVID-19) for which cohorting needs to be prioritized.  If LTACH unable to admit new MDRO patient due to lack of compatible roommate^, new patient can be placed in a room with a non-positive patient with lowest risk for infection. †
C. auris	Yes	СР	Cohort only with other patients with the same organism.
	No or unknown	СР	Cohort only with other patients with the same organism unless there is an outbreak with another organism (e.g., targeted MDRO, COVID-19) for which cohorting needs to be prioritized.  If LTACH unable to admit new MDRO patient due to lack of compatible roommate^, new patient can be placed in a room with a non-positive patient with the fewest risk factors for MDRO transmission. †
VRSA	No	СР	Cohort only with other patients with the same organism.

<sup>\*</sup>regardless of which type of cohorting is done, ensure that staff treat each bed as a separate room (i.e., perform HH and change PPE between each patient, beds at least 3 feet apart). Additional guidance should be provided when facilities are unable to cohort by same organism/gene. See Cohorting Considerations.

<sup>^</sup>compatible roommate = someone with the same MDRO/infectious organism.

<sup>+</sup> patient with the fewest risk factors for MDRO transmission= patient with the least amount of indwelling devices, unhealed wounds, dependence on others for activities of daily living.

# Shared room practices for MDRO cohorting

In situations where LTACHs are unable to cohort patients whose MDRO status matches exactly, ensure the following conditions are met to minimize the risk of transmission:

<b>Cohorting Considerations</b>	Considerations Expanded
Only cohort positive     patients with non-positive     patients in rooms that can     allow for sufficient     physical separation.	<ul> <li>Provide 3-6 feet separation with a privacy curtain between beds.</li> <li>For rooms with 3+ beds, leave the middle bed empty.</li> </ul>
2. Round the floor regularly to directly observe (aka adherence monitoring or auditing) and improve adherence with hand hygiene (HH) and personal protective equipment (PPE) among frontline staff*.	<ul> <li>This should be done using secret observers from all departments (environmental services, house supervisor, charge nurses, rehab staff, etc.) regardless of the facility size or bed capacity.</li> <li>Please ensure all shifts (daytime, evening, overnight, weekend) are covered.</li> <li>Once daily is recommended for HH rounds/audits and at least 1-2 times per week for other rounds/audits (contact precautions, wound care, environmental cleaning &amp; disinfection (including fluorescent marker)).</li> </ul>
3. Frontline staff* should have consistently high adherence rates to the following:	<ul> <li>Treating each bed space in a multi-occupancy room as a separate room.</li> <li>Doffing and re-donning PPE between each bed space in multi-occupancy rooms.</li> <li>Performing HH between each bed space in multi-occupancy rooms.</li> <li>Using a fresh set of supplies (microfiber cloth, wipes, mop) for each bed space in multi-occupancy rooms during cleaning and disinfection.</li> </ul>
4. Treat each bed space within a multi-occupancy room as if it's a separate room.	<ul> <li>Clean and disinfect as if each bed area was a different room.</li> <li>Clean and disinfect any shared or reusable equipment with the appropriate disinfectant.</li> <li>Have healthcare personnel change personal protective equipment, including gloves, and perform hand hygiene before and after interaction with each roommate.</li> </ul>

<sup>\*</sup>Frontline staff is defined as any worker that enter patient rooms or patient care areas regardless of whether they provide direct care including the following: licensed clinical staff including wound treatment nurses and outside consultants, CNA, environmental services, respiratory therapists, rehab services (PT, OT, SLT), phlebotomists etc.

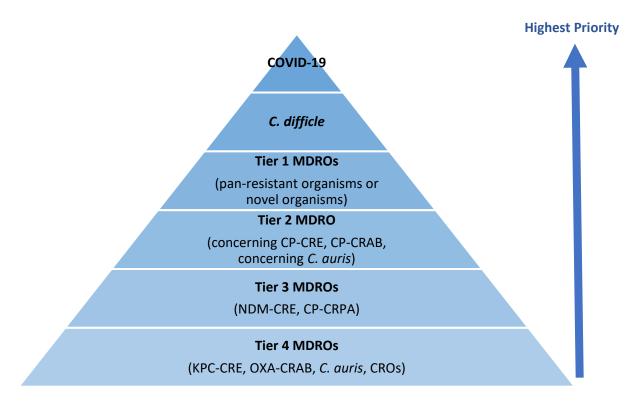
## What do with multiple organisms or outbreaks?

For patients who are positive for more than 1 organism of concern, or when a facility is experiencing multiple outbreaks, use the following <u>Prioritization Scheme</u> to create cohorts. Factors used to rank these organisms include endemicity in LAC, transmissibility, environmental hardiness, difficulty to treat, and restrictive guidance. Refer to <u>Table 1</u> and/or the <u>LACDPH MDRO Tiers Guidance</u> to find the most updated organism that fall into each Tier outlined below.

To use this scheme, patients with organisms that are ranked higher should be prioritized for single rooms or prioritized when creating cohorts. Consider other disease status such as COVID-19 and *C. difficile* when cohorting MDRO patients. For patients with multiple organisms, let the highest priority organism guide the cohorting strategy. In every situation, follow best practices to limit transmission.

See an example of how to implement this guidance in Appendix A: Sample Scenarios, Case #2.

Figure 2: Cohorting prioritization matrix



# How to implement this guidance

When implementing this guidance, especially when cohorting patients together with different infectious organisms, it is critical to ensure that staff are aware of the facility's expectations on how to limit transmission as much as possible. To accomplish this:

- 1. Train and educate staff on MDRO prevention practices, including any changes in policy or procedure.
- 2. Post clear signage on the door or wall outside of the patient room indicating the type of Precautions and required PPE (e.g., gown and gloves).
- 3. Ensure the patient care environment and shared equipment/devices are cleaned thoroughly with an appropriate EPA-registered disinfectant. Train EVS staff and clinical staff on when and how to clean, including which surfaces/devices each is responsible for.
- 4. Ensure access to PPE, including gowns and gloves, are available outside of each room.
- 5. Ensure access to alcohol-based hand rub in every room (ideally both inside and outside of the room).
- 6. Place a trash can inside the patient room and near the exit for discarding PPE after removal, prior to exit of the room or before providing care for another resident in the same room.
- 7. Work to keep beds at least 3 feet apart, separated by curtains that are replaced regularly.
- 8. Provide MDRO education to patients and visitors.
- 9. Conduct regular monitoring and assessment of adherence to the following practices to determine the need for additional training and education on:
  - Hand hygiene
  - o Use of PPE
  - Cleaning of shared equipment and/or devices
  - Cleaning of patient rooms
  - Staff ability to consistently treat each bed as a separate room (i.e., changing PPE and performing HH in between patients in the same room)

## Resources:

#### **Infection Control**

- CDC Type and Duration of Precautions Recommended for Selected Infections and Conditions (Appendix A): <a href="https://www.cdc.gov/infection-control/hcp/isolation-precautions/appendix-a-type-duration.html">https://www.cdc.gov/infection-control/hcp/isolation-precautions/appendix-a-type-duration.html</a>
- CDC Project Firstline: https://www.cdc.gov/infectioncontrol/projectfirstline/index.html

#### **MDRO-specific**

- LACDPH MDRO website: http://publichealth.lacounty.gov/acd/mdro/index.htm
- CDPH Prevention of MDROs in Healthcare Facilities:
   https://www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/C\_auris\_AHR\_C
   DC CDPHshareWebinarcCombined\_ADA\_121020.pdf
- LACDPH Transferring Guidance for MDROs: http://publichealth.lacounty.gov/acd/docs/LACDPH\_TransferringGuidanceforMDROs.pdf
- CDC Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrugresistant Organisms (MDROs): <a href="https://www.cdc.gov/hai/mdro-guides/containment-strategy.html?CDC\_AA\_refVal=https%3A%2F%2Fwww.cdc.gov%2Fhai%2Fcontainment%2Fguidelines.html">https://www.cdc.gov%2Fhai%2Fcontainment%2Fguidelines.html</a>

#### C. auris

- LACDPH Mitigating the Spread of C. auris in Los Angeles County: <a href="http://publichealth.lacounty.gov/acd/docs/MitigatingSpreadofC.aurisLAC.pdf">http://publichealth.lacounty.gov/acd/docs/MitigatingSpreadofC.aurisLAC.pdf</a>
- CDPH Candida auris: https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/Candida-auris.aspx
- CDC Candida auris: https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/Candida-auris.aspx

#### CROs/CPOs

- CDPH CRO and CPO for Public Health and Healthcare Providers: <a href="https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CRE">https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CRE</a> InfectionPreventionStrategies.aspx
- VDOH Simplifying CROs vs CPOs: <a href="https://www.vdh.virginia.gov/content/uploads/sites/174/2022/08/MidAtlantic-Webinar-simplifying-CROs\_cleared.pdf">https://www.vdh.virginia.gov/content/uploads/sites/174/2022/08/MidAtlantic-Webinar-simplifying-CROs\_cleared.pdf</a>

#### CDI:

CDPH CDI Prevention for Public Health and Healthcare Providers:
 <a href="https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CDI\_PREVENTION\_STRATEGIES.aspx">https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CDI\_PREVENTION\_STRATEGIES.aspx</a>

# Appendix A: Sample scenarios

# **Case 1: New patient admitted**

#### Situation:

- Male patient positive for NDM-producing carbapenem-resistant *P. aeruginosa* (NDM-CRPA) admitted from hospital. Positive in a sputum specimen collected one month prior.
- Upon review of bed board, no other NDM-CRPA positive male patients in the facility at the time. No single rooms available either.

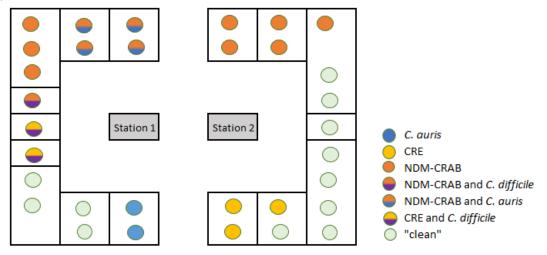
## **Resolution:**

- 1. Rather than refusing, identify a patient with CRPA or no MDROs, and the fewest amount of risk factors to cohort this patient with.
- 2. Make sure staff are aware to treat each bed as a different room. Follow <u>best practices to limit</u> transmission.

# Case 2: New outbreak

#### Situation:

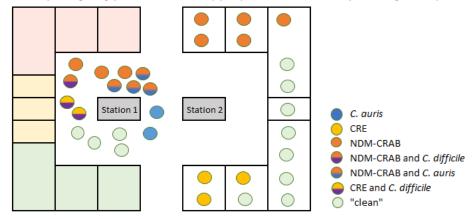
• You have a lot of MDRO positive patients in your facility. This is how you currently have them placed:



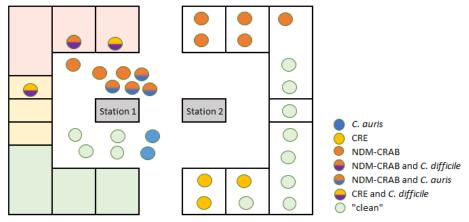
• You now have a COVID-19 outbreak among patients in station 1. Per DPH recommendations, you need to prioritize cohorting by COVID-19 status as part of an outbreak control measure.

## **Resolution:**

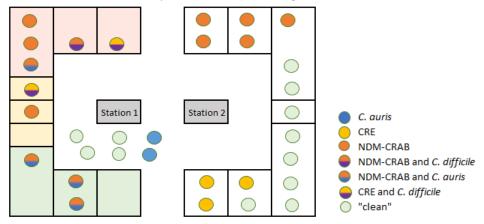
- 1. Use the Cohorting Prioritization Matrix (Figure 2) to help decide how to create cohorts.
- 2. Start by assigning patients to the appropriate zones (red, yellow, green) per COVID-19 status.



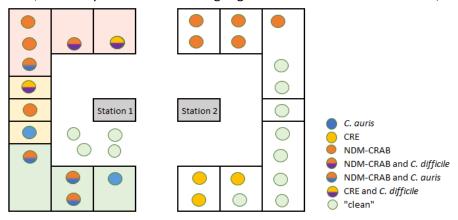
3. Then, start by assigning by the next most clinically-concerning organism: *C. difficile*.



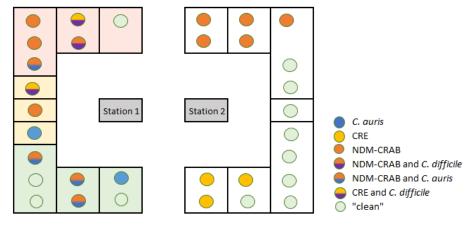
4. Then, cohort by the next concerning organism: Tier 1 or Tier 2 MDROs, like NDM-CRAB. However, the NDM-CRAB patients are different genders so not all can be in the same room.



5. Then, cohort by the next concerning organism: Tier 3 then Tier 4 MDROs, like C. auris and CRE.



6. Finally, place the clean patients where you can. Consider risk factors for MDRO acquisition, making sure to place clean patients with the fewest amount of these risk factors in rooms with MDRO-positive patients as much as possible.



7. Make sure staff are aware to treat each bed as a different room. Follow <u>best practices to limit transmission</u>.