Carbapenem-Resistant Organisms

Key Info	**Public health should investigate all CRO that test positive for carbapenemase**. Public health investigation is not required for carbapenemase-negative CRO except for suspected outbreaks.
Signs and Symptoms	CRO have no definitive clinical symptoms. Common infections caused by these organisms include wound, urine and blood stream, but can colonize and cause no symptoms.
Incubation	CRO can colonize the stool, skin, and other body sites without causing infection, therefore the incubation period is not well defined.
Case classification	**Clinical criteria**: None
	Confirmed: Patient with a clinical or surveillance culture yielding *E. coli*, *Klebsiella* spp., and *Enterobacter* spp., other Enterobacterales, or *Pseudomonas* or *Acinetobacter* positive for known carbapenemase gene or positive on phenotypic test for carbapenemase. Any other genera that test positive for carbapenemase should be classified as confirmed.
	CR-isolates that complete testing and are not confirmed should be classified as "ruled out."
Differential diagnosis	NA
Treatment	Antibiotic agents for treating CRE and CRO infections are extremely limited and often associated with adverse reactions. Colonization should not be treated except in extremely rare situations. Infectious disease consultation is recommended when treating infections due to CRO. PHL offers expanded antimicrobial susceptibility testing (EXAST) for hard to treat infections.
Duration	Can silently colonize intestine, skin and other body sites. Persistence related to healthcare and antibiotic exposure. Colonization may lead to endogenous infection and can spread to others.
Exposure	• Healthcare settings, particularly high acuity healthcare. • Can survive on inanimate surfaces for long periods. • Spreads via close contact, in healthcare facilities via healthcare workers' hands, shared/mobile medical equipment, and contaminated surfaces. • Travel
Laboratory testing	• Isolate genus and species identification, antimicrobial susceptibility testing (AST), carbapenemase testing. • Screening testing for colonization *Submission:* • Use Antibiotic Resistance Lab Network (ARLN) Requisition Form • Ship isolates on Choc, HIA, BHI slant (plate ok if submitted via courier), ambient, category B. • Screening stool/rectal swab provided in collection kit provided, ambient, category B. • When antibiotic treatment options are very limited, clinicians can request expanded antimicrobial susceptibility testing (EXAST). Pre-approval is required.
Public health actions	Local health jurisdictions: notifiable to Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (CDE) within 7 days of completing the investigation or 21 days of receipt of case or lab report. **Only carbapenemase positive must be investigated by public health.** *Infection Control:* • Cases should be placed on Contact Precautions ideally in a private room (see Appendix). • Reinforce hand hygiene, proper PPE use, and environmental cleaning. • See What to do if you identify a targeted multidrug resistant organism in your facility

Carbapenem-Resistant Enterobacterales (CRE) and other Carbapenem-Resistant Organisms

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To increase awareness of carbapenem-resistant Enterobacterales (CRE) and other carbapenem-resistant organisms (CRO) by public health and healthcare professionals.
2. To promote appropriate infection control interventions to prevent transmission of CRE and other CRO within and between healthcare facilities, and between healthcare facilities and the community.
3. To rapidly identify carbapenemase-producing CRE (CP-CRE) and other carbapenemase-producing-organisms (CPO) and prevent or eliminate sources or sites of ongoing transmission within Washington.
4. To better characterize the epidemiology of these infections in Washington to guide response.

B. Required Reporting

1. Laboratories: lab report to the local health jurisdiction (LHJ) and isolate submission to PHL required (2 business days) for *E. coli, Klebsiella* spp., and *Enterobacter* spp.
    - Positive for known carbapenemase resistance gene (including but not limited to KPC, NDM, VIM, IMP, or OXA-48) demonstrated by nucleic acid detection (NAT or NAAT) or whole genome sequencing;
    - Positive on a phenotypic test for carbapenemase production including but not limited to Metallo-B-lactamase test, modified Hodge test (MHT) (for *E. coli* and *Klebsiella* species only), CarbaNP, Carbapenem Inactivation Method (CIM) or modified CIM (mCIM);
    - Resistant to any carbapenem including but not limited to doripenem, ertapenem, imipenem or meropenem (minimum inhibitory concentrations of ≥ 4 mcg/ml for meropenem, imipenem, and doripenem or ≥ 2 mcg/ml for ertapenem).

    Isolates should be accompanied by a Public Health Laboratories (PHL) Antibiotic Resistance Lab Network (ARLN) Requisition Form and clinical lab antimicrobial susceptibility test result. See ARLN Test Menu and Specimen Collection and Submission Instructions for details on isolate submission.
2. Healthcare facilities and providers: notifiable to the local health jurisdiction (LHJ) within 3 business days for *E. coli, Klebsiella* spp., and *Enterobacter* spp.

- Positive for known carbapenemase resistance gene (including but not limited to KPC, NDM, VIM, IMP, or OXA-48) demonstrated by nucleic acid detection (NAT or NAAT) or whole genome sequencing;
- Positive on a phenotypic test for carbapenemase production including but not limited to Metallo-B-lactamase test, modified Hodge test (MHT) (for E. coli and Klebsiella species only), CarbaNP, Carbapenem Inactivation Method (CIM) or modified CIM (mCIM);
- Resistant to any carbapenem including but not limited to doripenem, ertapenem, imipenem or meropenem (minimum inhibitory concentrations of ≥ 4 mcg/ml for meropenem, imipenem, and doripenem or ≥ 2 mcg/ml for ertapenem).

3. Local health jurisdictions: notifiable to Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (CDE) within 7 days of case investigation completion or summary information required within 21 days for *E. coli, Klebsiella* spp., and *Enterobacter* spp.
   - Positive for known carbapenemase resistance gene (including but not limited to KPC, NDM, VIM, IMP, or OXA-48) demonstrated by nucleic acid detection (NAT or NAAT) or whole genome sequencing;
   - Positive on a phenotypic test for carbapenemase production including but not limited toy Metallo-B-lactamase test, modified Hodge test (MHT) (for *E. coli* and *Klebsiella* spp. only), CarbaNP, Carbapenem Inactivation Method (CIM), or modified CIM (mCIM).

Reporting and submission of other CRO isolates, including other CR-genera in the order Enterobacterales, CR-*Pseudomonas* spp., and CR-*Acinetobacter* spp., is strongly *encouraged* but not *required*. See Table 1 on page 4 for details about resistance criteria to guide submission. For information about sentinel labs, please contact the Washington Antibiotic Resistance Lab Network at ARLN@doh.wa.gov. Any CPO identified at PHL will be reported to the LHJ for a public health investigation.

C. Local Health Jurisdiction (LHJ) Investigation Responsibilities

1. LHJs should investigate and report all carbapenemase producing organisms (CPO) in order to identify the source and whether transmission to additional patients has occurred. Enter the case into the Washington Disease Reporting System (WDRS) under Highly Antibiotic Resistant Organism (HARO).

   LHJs should be notified by laboratories, healthcare providers, or infection preventionists of CRO isolates submitted to PHL; it is not necessary for LHJs to investigate all CRO reports but may choose to perform a preliminary investigation before phenotypic or mechanistic testing for carbapenemase production is completed.

2. Any outbreak or suspected outbreak of CROs in a healthcare facility is mandated to be reported immediately to LHJs and should be investigated.

Table 1: Species, Resistance Criteria, and Submitters for Washington State Targeted Multidrug Resistant Bacterial Surveillance

Family or Genus	Antibiotic Resistance	Submitters
CR-Enterobacterales: *E. coli* *Klebsiella* spp. *Enterobacter* spp.	Resistant to ≥1 carbapenem: Minimum inhibitory concentrations (MIC) ≥4 μg/ml for meropenem, imipenem, and doripenem, and ≥ 2 μg/ml for ertapenem **OR** Kirby-Bauer zone of inhibition diameter (ZID) ≤19 mm for meropenem, imipenem, and doripenem, and ≤18 mm for ertapenem	All labs
CR-*Acinetobacter* spp.	Resistant to ≥1 carbapenem: MIC ≥8 μg/mL for any carbapenem **OR** Kirby-Bauer ZID ≤14 mm for doripenem and meropenem, and ≤18 mm for imipenem	All labs
CR-*Pseudomonas* spp.[1]	Resistant to ≥1 carbapenem, excluding ertapenem: MIC ≥ 8 μg/mL for any carbapenem **OR** Kirby-Bauer ZID ≤ 15 mm for any carbapenem **AND** Non-susceptible or resistant (I or R) to ceftazidime (MIC ≥ 16 μg/mL or Kirby Bauer ZID ≤ 17 mm) and cefepime (MIC ≥ 16 μg/mL or Kirby Bauer ZID ≤ 17 mm)	Sentinel labs[2]
Carbapenem-resistant *Citrobacter* spp.	Resistant to ≥1 carbapenem: MIC ≥4 μg/ml for meropenem, imipenem, and doripenem, and ≥ 2 μg/ml for ertapenem **OR** Kirby-Bauer ZID ≤19 mm for meropenem, imipenem, and doripenem, and ≤18 mm for ertapenem	Sentinel labs[2]
Carbapenem-resistant *Morganella, Proteus* and *Providencia* spp. [3]	Resistant to 1 carbapenem in addition to imipenem: MIC ≥4 μg/ml for meropenem and doripenem, and ≥ 2μg/ml for ertapenem **OR** Kirby-Bauer ZID ≤19 mm for meropenem and doripenem, and ≤18 mm for ertapenem	Sentinel labs[2]

[1] If the number of each isolate-type for submission is too burdensome, sentinel labs may submit only a subset.
[2] All labs are encouraged to submit these isolate types but are not required to do so.
[3] Note: These genera may have intrinsic resistance to imipenem. Only those that are resistant to a carbapenem other than imipenem should be submitted.

3. Because of the potential for transmission of CRO to vulnerable patients in healthcare settings, providers, infection preventionists, and facilities should institute appropriate infection control precautions when CRO are identified. These actions are described in national expert guidance; see Section 5B and the Appendix for detailed recommendations about infection prevention in healthcare settings. The LHJ may reinforce appropriate infection preventions messaging but implementation and communication of CRO status to the patient or home caregivers, including how to prevent transmission, is the responsibility of healthcare providers, infection preventionists, and facilities.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Enterobacterales constitute a large order of Gram-negative bacilli, many of which are normal inhabitants of the intestinal tract in humans, other mammals, and birds. Enterobacterales most commonly encountered in healthcare settings include the taxonomic families, Enterobacteriaceae, Morganellaceae, and Yersiniaceae (see NCBI Taxonomy Browser for more details), including the genera *Citrobacter, Enterobacter, Escherichia, Klebsiella, Morganella, Proteus, Providencia, and Serratia.* These bacteria may be harmless or can cause serious infections in humans, particularly those with healthcare exposure and who are debilitated due to serious illness, old age, invasive procedures, or indwelling catheters.

Acinetobacter and *Pseudomonas* are also Gram-negative bacilli (not in the order, Enterobacterales). They are common inhabitants of soil and water, may colonize human skin (both) and intestines (*Pseudomonas*), frequently contaminate the hospital environment, and may cause opportunistic infections in debilitated hosts.

Carbapenem antibiotics (doripenem, ertapenem, imipenem, and meropenem) are broad spectrum (active against many different groups of bacteria) and usually reserved for severe life-threatening infections. Certain Gram-negative bacilli, including the order, Enterobacterales, and genera, *Pseudomonas* and *Acinetobacter*, have developed carbapenem resistance which limits options for treating infections due to these organisms. The mechanism of resistance can be varied; most concerning are carbapenemases, enzymes produced by bacteria that inactivate carbapenems directly. Carbapenemase genes transmitted on plasmids are primarily responsible for the worldwide spread of CP-CRE. Plasmids are mobile pieces of genetic material that can be passed between bacterial species, otherwise known as horizontal inheritance. This type of inheritance can rapidly and greatly increase the prevalence of the trait in a population, particularly where there is high risk of transmission such as in a healthcare environment.

Carbapenemases of global importance include *Klebsiella pneumoniae* carbapenemase (KPC), New Delhi metallo-β-lactamase-type 1 (NDM-1), Verona integron encoded metallo-β-lactamase (VIM), imipenemase metallo-β-lactamase (IMP), and oxacillinase-48 (OXA-48). As of 2021, KPC is the most common carbapenemase in Enterobacterales in the United States and in Washington.

Non-carbapenemase carbapenem resistance in the Enterobacterales and other Gram-negative bacteria, such as Pseudomonas and Acinetobacter, is mediated by a combination of mechanisms, typically via production of an extended-spectrum β-lactamase or extended-spectrum cephalosporinase (also called ESBL or AmpC) plus decreased permeability of the bacterial cell wall (e.g., porin mutations) to influx of carbapenem antibiotics. Although also multidrug resistant, these organisms are currently thought to have local rather than global importance; unlike carbapenemases which have increased significantly over the past 10-15 years, the frequency of non-carbapenemase carbapenem resistance has increased gradually over time. CP-CRE, CP-Pseudomonas and CP-Acinetobacter are becoming more common in Washington and require the most

aggressive infection control measures and coordinated response between healthcare facilities and public health in order to prevent them from becoming endemic.

C. Description of Illness

Infections due to carbapenem resistant (CR) Enterobacterales and other CR-Gram negative bacteria, such as *Pseudomonas* and *Acinetobacter,* are associated with high rates of morbidity and mortality and occur most frequently among persons with prolonged hospitalization, and those who are chronically or critically ill, or exposed to invasive devices such as ventilators, urinary catheters, or central venous catheters. These infections may manifest as urinary tract, blood stream, surgical site, and lung infections. Colonization with these bacteria can also occur and *does not require treatment,* though similar infection control precautions should be used for colonized persons in healthcare settings and in the home environment in order to prevent transmission to other patients or family members. Colonized patients are at risk for invasive infection from their own endogenous colonization and this risk increases when indwelling devices are present.

D. CRE in Washington State

In Washington, CRE and other CRO are routinely detected by commercial laboratories but CP-CRE and other CPO are relatively infrequent. Before systematic reporting began in 2012, 8 CP-CRE had been identified in Washington. The DOH MDRO Dashboard provides a summary of CRO and CPO surveillance in Washington since 2012.

As of 2021, DOH has received reports of 8 different carbapenemases in CRE, Acinetobacter, and Pseudomonas: KPC, NDM, VIM, IMP and OXA-48, OXA-23, OXA 24/40, and IMI/NMC. Inpatient healthcare remains the most likely reported source of acquisition for carbapenemases.

D. Reservoirs

Enterobacterales are normally carried in the intestines of many mammals and birds. *Acinetobacter* and *Pseudomonas* exist in water and soil. Carbapenem-resistant infections in the United States are generally associated with healthcare exposures and occur most commonly in debilitated persons with chronic illness. These Gram-negative organisms can survive on inanimate objects for many months. Humans can be colonized in wound drainage; on catheter exit sites; in stool, urine, and sputum; and may transmit in the healthcare environment. Colonized persons are at risk for infection from endogenous carriage.

E. Modes of Transmission

Transmission of CRE and other CRO may occur through direct contact with bodily fluids or by skin contact. In healthcare settings, CRE and CRO can be spread via the hands of healthcare workers, by inanimate objects such as medical equipment, bed rails, computer keyboards, cleaning supplies, and colonized sink drains. Transmission has occurred in healthcare settings even when contact precautions were in place, although infection control lapses cannot be ruled out. The attack rate for household contacts of cases has not been defined. Persons who are infected or colonized may be a source of transmission to others.

F. Incubation Period

Because CRE and other CRO can colonize the intestines and other sites without causing infection, the incubation period is not well defined.

G. Period of Communicability

Persons can potentially transmit CRE and other CRO to others as long as the organisms are present in bodily fluids or on the body. Patients can be intermittently positive on serial surveillance cultures and may be colonized for long periods of time. Persons at highest risk for transmitting and contracting CRE and CRO are those who require intensive care or assistance with activities of daily living or have wounds or indwelling devices. Epidemiologically linked patients within the healthcare environment (roommates, those who shared healthcare staff before infection precautions were implemented) are thought to be at highest risk for contracting the organism.

H. Treatment

The antibiotic agents for treating CRE and CRO infections are extremely limited and are often associated with adverse reactions. In general, colonization should not be treated except in extremely rare situations such as planned bone marrow transplant. Infectious disease consultation is recommended for treatment decisions and especially when decolonization is being considered.

3. CASE AND CONTACT DEFINITIONS

A. Clinical Criteria for Diagnosis of Cases

Carbapenem-resistant (CR) and carbapenemase-producing (CP) Enterobacterales and other CR and CP organisms may cause a variety of clinical syndromes including urinary tract, blood stream, surgical site, pulmonary and intra-abdominal infections similar to other invasive bacterial infections. Persons who are colonized with CRE and CRO may appear healthy and have no symptoms but still require infection control precautions when in healthcare settings to prevent spread to vulnerable patients.

B. Laboratory Criteria for Diagnosis of Cases

CP-CRE and other carbapenemase producing organisms: A confirmed carbapenemase-producing CRE (CP-CRE) or CPO case is a patient with a clinical or surveillance culture yielding *E. coli*, *Klebsiella* spp., *Enterobacter* spp., other Enterobacterales, *Acinetobacter*, or *Pseudomonas*

1. Positive for known carbapenemase gene (including but not limited to KPC, NDM, VIM, IMP, OXA-48) demonstrated by nucleic acid detection (NAT or NAAT) or whole genome sequencing;
2. Positive on a phenotypic test for carbapenemase production by Metallo-B-lactamase test, modified Hodge test (MHT) (for E. coli and Klebsiella species only), CarbaNP, Carbapenem Inactivation Method (CIM) or modified CIM (mCIM).

For public health surveillance, each unique genus/species/carbapenemase combination in a clinical culture should be counted as a new case no more than once per 12 months. See

the Council of State and Territorial Epidemiologist Position Statement, 17-ID-04 for more details about surveillance case counting.

Only CP-CRE *E. coli*, *Klebsiella* spp., and *Enterobacter* spp. are mandated to be reported to public health, but any other carbapenemase-positive CRE or CRO should be classified as a confirmed case.

C. Case Classification

Confirmed: Meets lab criteria as described in section 3B above.
CR-isolates that complete testing and are negative for carbapenemase gene are not confirmed should be classified as "ruled out" or "not reportable."

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

CRE are most commonly diagnosed by bacterial isolation with antibiotic susceptibility testing. See laboratory criteria for definition of a CRE and CRO in Section 1B and of CP-CRE and CPO in Section 3B. Most clinical laboratories use automated susceptibility testing methods (Vitek 2, Trek, Microscan, Phoenix). Traditional methods for determining resistance include broth dilution, disk diffusion or E test. Resistance should be determined using the most up-to-date resistance breakpoints as set by Clinical Laboratory Standards Institute (CLSI) M100-S25. Other phenotypic and genetic tests are used to confirm carbapenemase production. Consult the DOH Healthcare Associated Infections and Antimicrobial Resistance Program at 206-418-5500 for questions about determining whether a case meets the definition for CRE, CRO, CP-CRE, or CPO, or for submission to PHL for confirmatory testing.

B. Services Available at the Washington State Public Health Laboratories (PHL)

At PHL, all isolates have identification confirmed and undergo antimicrobial susceptibility testing (AST). In addition, submitted CR-Enterobacterales and CR-*Pseudomonas* isolates undergo modified carbapenemase inactivation method (mCIM) phenotypic testing as well as nucleic acid testing (NAT) for the most common carbapenemase genes. Isolates with positive mCIM, indicating carbapenemase production, and negative NAT are sent to CDC for additional testing to identify if a novel carbapenemase is present that is not detected by the NAT testing at PHL. CR-*Acinetobacter bauamanii* are tested with PCR for carbapenemase production. *Acinetobacter baumanii* can harbor some variant carbapenemases not found in CRE or CRPA, thus these isolates receive additional testing for these carbapenemase variants.

Specimens submitted from patients for carbapenemase screening undergo RT-PCR performed to identify carbapenemase production. Culture based testing is performed on positive specimen. PHL provides appropriate screening supplies and instructions for collection. **Pre-approval is required for carbapenemase screening** through the HAI program (206-418-5500).

For clinical purposes, PHL also offers expanded antimicrobial susceptibility testing (EXAST) for hard to treat infections. Isolates eligible for submission include Enterobacterales not susceptible to all β-lactams tested, including either

ceftazidime/avibactam or meropenem/vaborbactam (these may be MBL-producing isolates that cause infections with few effective treatment options) OR possess at least one MBL gene (blaNDM, blaVIM, or blaIMP) confirmed by a molecular test. Preapproval is required by emailing ARLN@doh.wa.gov. See details at Expanded Antimicrobial Susceptibility Testing.

When submitting specimens to PHL, include the Antibiotic Resistance Lab Network (ARLN) Requisition Form. Note that PHL requires all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth), on both the specimen label and the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

5. CASE INVESTIGATION

Review laboratory results to confirm genus and species and antimicrobial susceptibility testing to ensure the isolate meets the CRE, CRO, CP-CRE or CPO surveillance case definition, see section 3B. CRE isolates of *E. coli*, *Klebsiella*, and *Enterobacter* must be submitted to PHL for additional testing to determine whether the mechanism of resistance is due to carbapenemase. Other CR-isolates are *strongly encouraged* to be submitted to PHL but are not mandated by Washington Administrative Code.

The guidance, What to do if you identify a targeted multidrug resistant organism in your facility, provides response actions for LHJs and healthcare facility infection preventionists in order to quickly collect data for CPO investigations and to prevent transmission to others. DOH HAI Program staff are available to assist and can be reached at 206-418-5500.

A. Case Management

Consult an Infectious Disease specialist for treatment recommendations. In almost all cases, decolonization is not recommended but may be considered prior to immune-modulating therapy such as chemotherapy or bone marrow transplant. For cases with very limited treatment options, the PHL can perform expanded antimicrobial susceptibility testing but pre-approval is required.

B. Case Follow Up

Conduct a public health investigation for all confirmed CP-CRE and CPO cases. Case isolates that test negative for carbapenemase do not require public health investigation unless there is suspicion of an outbreak. The DOH HAI Program staff is available to lead investigations as the request of the LHJ. Review clinical history, medical records and laboratory records and interview the case, parent/guardian, power of attorney, close family members, or others who may be able to provide pertinent information, if necessary. Enter case's name; demographics; address, dates of notification, investigation start, birth and onset; organism identified; and investigator's name into the electronic surveillance system WDRS under "Highly antibiotic resistant organism" (HARO) and complete the HARO wizard question package including the "Clinical and Laboratory" tab.

B. Ensure Infection Control

Because of the potential for transmission of CRE and other CRO to vulnerable patients in healthcare settings, action is required by healthcare providers, infection preventionists and facilities to institute appropriate infection control precautions when these resistant organisms are identified by a clinical lab even if reporting to local health is not required (e.g., reporting is not mandated for CR-*Pseudomonas* or CR-*Acinetobacter*). Providers should also communicate infection or colonization status to patients and family members and educate about how to prevent transmission in the home using a CRO Patient Notification form, and to receiving facilities and providers when patients transfer care using an inter-facility infection control transfer form.

For patients with CRE and CRO, the intensity of infection control measures should be based on mechanism of carbapenem resistance (e.g., CP versus non-CP), healthcare setting, and patient's clinical status. More intensive infection prevention should be implemented for carbapenemase-producing organisms, acute care, and for patients with active infections, indwelling devices, wounds, diarrhea, uncontained drainage or incontinence, or require assistance with activities of daily living that involve close contact between patient and caregiver (e.g., dressing, bathing, toiling).

In general, in acute care settings such as hospitals and long-term acute care hospitals, carbapenemase positive patients should be cared for in private rooms with indefinite application of contact precautions, and carbapenemase negative patients for a minimum of 1 year since most recent detection. Cohorting of patients may be used if private rooms are unavailable.

In LTC settings, residents who are infected with CRE or CRO should be on contact precautions. For residents colonized with CRE or CRO, Enhanced Barrier Precautions should be used for all carbapenemase positive cases and should be *strongly considered* for carbapenemase negative cases for a minimum of 1 year since most recent detection.

See the Appendix for more detailed infection prevention guidance and refer to national expert guidance:

- Management of Multidrug-Resistant Organisms in Healthcare Settings, 2006 https://www.cdc.gov/infectioncontrol/pdf/guidelines/mdro-guidelines.pdf
- Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings https://www.cdc.gov/infectioncontrol/pdf/guidelines/isolation-guidelines.pdf
- CDC Facility Guidance for Control of Carbapenem-resistant Enterobacteriaceae https://www.cdc.gov/hai/pdfs/cre/CRE-guidance-508.pdf
- Interim Guidance for a Health Response to Contain Novel or Targeted MDROs https://www.cdc.gov/hai/outbreaks/docs/Health-Response-Contain-MDRO.pdf
- Duration of Contact Precautions for Acute-Care Settings https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/duration-of-contact-precautions-for-acutecare-settings/94E38FDCE6E1823BD613ABE4E8CB5E56

C. Identify Potential Sources of Infection or Colonization

Public health should investigate all CP-CRE and CPO cases to identify the source, evaluate for lapses in infection control in healthcare settings, detect potential transmission to other patients, ensure the patient is educated and appropriate communication of CP-CRE or CPO status occurs to healthcare providers and facilities where the patient receives care. Identify current and past healthcare and underlying conditions, including any hospital or long-term care admissions, surgeries, dialysis, indwelling catheters, or international healthcare or travel, focusing particularly on the 12 months prior to diagnosis. If the index case has had many healthcare encounters and public health resources are limited, focus the investigation on the 1 month prior to diagnosis. The guidance What to do if you identify a targeted multidrug resistant organism in your facility will help LHJs and facilities quickly perform the investigation.

6. CONTROLLING FURTHER SPREAD

A. Infection Control Recommendations

See section 5B above and the Appendix for healthcare setting-specific infection prevention recommendations.

Providers should communicate information about patients' carriage of CRE and CRO to receiving facilities, as is done for *C. difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA) and other epidemiologically important organisms, using an inter-facility infection control transfer form or other standardized method. Patients, power of attorney, and their home caregivers should also be informed of multidrug resistant organism (MDRO) carriage and instructed in infection prevention, particularly stressing hand hygiene. A CRO Patient Notification form is available to educate patients.

Patients with CRE or CRO who return to a home setting should be instructed in good hand hygiene, especially after touching the infected area, contaminated dressings, and after using the bathroom. See patient education information that can be used. People providing care at home for patients with CRE and CRO should be careful about washing their hands, especially after contact with wounds, dressings and other contaminated objects or surfaces or helping the CRE or CRO patient with toileting. Gloves should be used when anticipating contact with body fluids or blood. This is particularly important if the caregiver is caring for more than one ill person. Healthy people usually don't become infected with CRE or CRO but can become colonized. Communicate CRE or CRO status to healthcare providers in outpatient settings, particularly those where invasive procedures are performed (i.e., urology) and upon return to healthcare facility to avoid spread.

C. Contact Management

Epidemiologically-linked contacts (defined in section 5D) of a CP-CRE or CPO case who have symptoms or signs compatible with infection (fever, pneumonia, sepsis, draining wound, dysuria) should be placed in contact precautions and evaluated promptly by a healthcare provider.

Since the SARS-CoV-2 pandemic, there have been many reported instances of CPO transmission in intensive care units despite the use of transmission-based precautions.

When there is potential for spread to others in a healthcare setting, screening of those at risk should be performed, including:

- All roommates and those who shared a bathroom with the case, even if they have been discharged from the facility.
- Other patients or residents who shared healthcare staff or were in nearby rooms while the index case was not on contact precautions.
- Other patients or residents who overlapped with the case on the same wing or hallway who have high care needs for activities of daily living, wounds, or indwelling devices.
- In some situations, all patients or residents in the unit or facility should be screened.

Screening cultures of healthcare personnel and healthy household contacts is not recommended unless implicated in transmission or in other unique situations.

For further guidance on surveillance screening, see

- CDC Facility Guidance for Control of Carbapenem-resistant Enterobacteriaceae https://www.cdc.gov/hai/pdfs/cre/CRE-guidance-508.pdf
- Interim Guidance for a Health Response to Contain Novel or Targeted MDROs https://www.cdc.gov/hai/outbreaks/docs/Health-Response-Contain-MDRO.pdf

Surveillance screening testing can be performed free of charge at PHL. The only validated method for screening is from rectum or stool but other sites may be considered with advance planning. Consult with HAI Program staff available at 206-418-5500 for guidance on screening recommendations, instructions, and proper collection materials.

D. Environmental Evaluation

In healthcare settings, ensure that environmental cleaning procedures adhere to CDC and HICPAC Guidelines for Environmental Infection Control in Health-Care Facilities.

Since environmental cleaning is such a vital component of infection prevention, the identification of CRE or other target MDROs in a facility should prompt communication to environmental services staff reinforcing their important role in protecting patients, an audit of cleaning practices, ensuring use of EPA-approved disinfectants, adherence to proper contact time, and completeness of cleaning. Consideration should be given to providing disinfectant wipes so that bedside staff can clean and disinfect high touch surfaces such as—bedside table, remote control, call button, bedside rails, doorknobs, faucet and toilet handles, and light switches—at least once a shift. Ensure that reusable medical equipment is properly cleaned and disinfected between use, and there is a clear procedure for identifying whether equipment is clean and ready for use.

7. ROUTINE PREVENTION

A. Routine Prevention

Prevention of CRE transmission requires collaboration and coordination between public health agencies and healthcare facilities. Controlling transmission necessitates knowing

local and regional prevalence of these organisms through surveillance, rapid identification of colonized and infected patients in healthcare settings and implementing facility-specific and regional interventions to prevent transmission.

Core measures that facilities should follow include hand hygiene, contact precautions, education of healthcare personnel, minimizing device use, cohorting staff and patients, laboratory notification, antimicrobial stewardship, and screening for CRE or CRO when indicated.

B. Prevention Recommendations

All persons can adhere to good health hygiene to stop the spread of pathogens by washing hands frequently, especially

- Before preparing or eating food
- After using the bathroom or helping another person with toileting or diapers
- After blowing the nose, coughing or sneezing
- After touching used tissues or handkerchiefs
- Before and after changing wound dressings or bandages

ACKNOWLEDGEMENTS

We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

UPDATES

March 2014: Updates include submission and reporting requirements for CRE surveillance and local health responsibilities for investigation and infection control; updates are interspersed throughout but affected mainly sections 1B and C, 2A and C, 3B, 4B, and 5B and C.

April 2015: Updates include a change in CRE surveillance case definition, and submission and reporting requirements; updates are interspersed throughout but affected mainly sections 1B, 3B, and 4B.

November 2016: Updates include changes in case definitions, and added detail about infection control recommendations for different healthcare settings in section 5B and Appendix B. Other updates are interspersed throughout but affected mainly sections 1B, 3B and 5B.

May 2018: Updates include case definitions in section 3B, reporting requirements in section 1B, and new infection prevention guidance resources in section 5B. We have updated the guidance to be applicable to both CRE and other CRO.

June 2021: Updates include changing the taxonomic family name, Enterobacteriaceae, to the more inclusive order name, Enterobacterales, removing Appendix B, table of genera included under Enterobacteriaceae; making the document applicable to other carbapenem resistant organism, and providing links to new guidance materials, including "What to do if you identify a targeted multidrug resistant organism in your facility."

August 2021: Added Table 1 that defines resistance criteria of bacterial isolates for submission to PHL for carbapenemase testing; clarified that any carbapenemase-producing Enterobacterales, *Acinetobacter* or *Pseudomonas* isolates should be classified as "confirmed" and those testing negative as "not reportable."

November 2021: Reorganized sections 5 and 6 to remove repetition. Updated infection control recommendations in the appendix to better align with national guidance.

Appendix:

Highly antibiotic resistant organisms, and particularly carbapenemases, are more common among people who have had a lot of healthcare exposures, invasive procedures, and antibiotics. Often, these risk factors are chronic and ongoing, therefore once a patient is colonized with a carbapenem-resistant Enterobacterales (CRE) or other carbapenem-resistant organism (CRO), long-term carriage may occur and should be factored into decisions about duration of transmission-based precautions (TBP).

Carbapenemase negative CRE or CRO
In general, for people colonized or infected with **carbapenemase negative CRE or CRO**, hospitals should consider maintaining Contact Precautions (CP) for the duration of the index hospitalization when the infection or colonization is first detected, and for a minimum of 1 year following the most recent detection(1). In nursing homes, CP should be maintained for residents being treated for an infection. After treatment is completed and for all other residents who have a history of infection or colonization with a non-carbapenemase producing CRE or CRO**,** nursing homes should strongly consider using Enhanced Barrier Precautions (EBP) (2) for a minimum of 1 year following most recent detection. EBP means using gown and gloves for care involving close physical contact (dressing, bathing, toileting, changing linens, device and wound care).

Carbapenemase positive CRE or CRO,
For people colonized or infected with **carbapenemase positive CRE or CRO**, hospitals should maintain TBP indefinitely (1). In nursing homes, CP should be maintained for any residents being treated for infections and use Enhanced Barrier Precautions (EBP) for a minimum of 1 year following the most recent detection. Nursing homes may then consider discontinuing EBP for residents with a history of carbapenemase-producing CRE or CRO who meet the following criteria.

- They have recovered from their acute illness.
- They do not have indwelling devices, wounds or incontinence.
- They have no significant need for assistance with activities of daily living,

AND:

- At least 1 year has elapsed since the most recent positive culture (either screening or clinical).
- The patient is not currently being treated with antibiotics, and
- Two or more consecutive rectal screening sample swabs collected at least a week apart are negative.

Facilities should discuss any plans to discontinue TBP for patients with carbapenemase-positive CRE or CRO with their local health jurisdiction.

Carbapenemases have been identified in Enterobacterales, and *Pseudomonas* and *Acinetobacter* species. Though all three groups may colonize the intestines, Enterobacterales are most likely to maintain colonization in the intestines whereas *Pseudomonas* species are more likely to colonize the respiratory tract, and *Acinetobacter* species to colonize wounds or skin. Therefore, risk of transmission from a colonized patient may vary based on site of colonization and type of care the patient requires; these factors should be considered when assessing need for TBP.

1. Banach DB, et al. Duration of Contact Precautions for Acute-Care Settings. Infect Control Hosp Epidemiol.2018 Feb;39(2):127-144.).
2. CDC, Implementation of Personal Protective Equipment in Nursing Homes to Prevent Spread of Novel or Targeted Multidrug resistant Organisms (MDROs). Available at: https://www.cdc.gov/hai/containment/PPE-Nursing-Homes.html.

Table 1. Infection prevention recommendations for CRE and CRO cases in acute care settings

Acute Care				
Infection Prevention Measure	**Carbapenemase positive CRE/CRO**		**Carbapenemase negative CRE/CRO**	
	Infected	**Colonized**	**Infected**	**Colonized**
Standard Precautions	Yes	Yes	Yes	Yes
Contact Precautions	Yes	Yes, indefinitely	Yes	Yes, for minimum 1 year following most recent detection
Private Room	Yes	Yes	Yes; if feasible	Yes; if feasible
Door signage	Yes	Yes	Yes	Yes
Dedicated or disposable equipment	Yes	Yes	Yes	Yes
Visitor Recommendations				
Perform hand hygiene often, and always after leaving resident's room.	Yes	Yes	Yes	Yes
Wear gown/gloves if contact with body fluids is anticipated	Yes	Yes	Yes	Yes
Wear gown/gloves if no contact with body fluids is anticipated	No	No	No	No

Table 2. Infection prevention recommendations for CRE cases in long-term care settings

Long-term Care				
Infection Prevention Measures	**Carbapenemase positive CRE/CRO**		**Carbapenemase negative CRE/CRO**	
	Infected	**Colonized**	**Infected**	**Colonized**
Standard Precautions	Yes	Yes	Yes	Yes
Contact Precautions	Yes	CP not required, EBP for minimum 1 year since most recent detection	Yes	CP not required, strongly consider EBP for minimum 1 year since most recent detection
Private Room or Cohort	Yes	Yes	Yes, if feasible	Yes, if feasible, for duration of EBP
Restricted to Room	Yes	No, unless unable to maintain clean hands, clothes, equipment.	Yes	No, unless unable to maintain clean hands, clothes, equipment.
Door signage	Yes	Yes	Yes	Yes, for duration of EBP
Dedicated or disposable equipment	Yes	Yes	Yes	Yes, for duration of EBP
Visitor Recommendations				
Perform hand hygiene often, and always after leaving resident's room.	Yes	Yes	Yes	Yes
Wear gown/gloves if contact with body fluids is anticipated	Yes	Yes	Yes	Yes
Wear gown/gloves if no contact with body fluids is anticipated	No	No	No	No