Workgroup A: Proposed Investigation/Reporting Thresholds and Outbreak Definition for Carbapenem Resistant Enterobacteriaceae (CRE)
August 16, 2018

The thresholds and definitions below are intended to be a guideline and are based on expert opinion except as noted otherwise. States and local jurisdictions may have their own requirements for reporting and outbreak definitions. Healthcare facilities should consult public health if they have questions about the definition or its application.

- CRE numbers include both colonized and infected patients.
- Prevalence definitions are intended as examples based on the average facility in a region. The CRE prevalence may vary among facilities in a region due to facility bed size, patient population, whether a facility conducts admission screening or active surveillance, and other factors. Some facilities might fall into one prevalence group for CP-CRE and a different prevalence group for CRE. Please see points for consideration for further discussion of this issue.

	Acute Care Hospitals	Long-Term Acute Care Hospitals and Long-Term Care Facilities with Ventilated Patients	Long-Term Care Facilities (LTCF)	Critical Access Hospitals	Dialysis Facilities	Outpatient
Threshold for facility to start investigation	*In regions with high prevalence CRE and/or endemic KPC[1]:* • 1 non-KPC CP-CRE (NDM, VIM, IMP, OXA-48 type) • 2 KPC-CRE, 2 CP-CRE (unknown mechanism*), or 2 CRE (non-CP or mechanism testing not performed) of same organism in a 4-week period in patients on the same unit who were not previously known to be infected or colonized**. Some facilities in high prevalence areas might wish to use their facility and regional data in collaboration with public health to define a threshold for additional investigation, as 2 CRE might be too sensitive. *In a region with lower prevalence CRE[2]:* • 1 CP-CRE (KPC, NDM, VIM, IMP, OXA-48 type, or positive by phenotypic test) • 2 CRE (non-CP or mechanism testing not performed*) of same organism in a 4-week period in patients on the same unit** *In regions with very low CRE prevalence[3]:* • 1 CRE (CP, non-CP, or unknown CP)		1 CRE (CP, non-CP, or unknown CP in patient not previously known to be infected or colonized)			

Threshold for reporting to PH	*In regions with high prevalence CRE and/or endemic KPC*[1]*:* • 1 non-KPC CP-CRE (NDM, VIM, IMP, OXA-48 type) • 2 KPC-CRE, 2 CP-CRE (unknown mechanism*), or 2 CRE (non-CP or mechanism testing not performed) of same organism in a 4-week period in patients that are epidemiologically-linked[#] and were not previously known to be infected or colonized. *In regions with lower prevalence CRE*[2]*:* • 1 CP-CRE (KPC, NDM, VIM, IMP, OXA-48 type, or positive by phenotypic test) • 2 CRE (non-CP or mechanism testing not performed*) of same organism in a 4-week period in patients that are epidemiologically-linked[#] with confirmatory laboratory testing *In regions with very low CRE prevalence*[3]*:* 1 CRE (CP, non-CP, or unknown CP*)	1 CRE (CP, non-CP, or unknown CP in patient not previously known to be infected or colonized)
Outbreak definition	≥ 2 CRE of same organism (or mechanism, if mechanism testing performed) in a 4-week period in patients that are epidemiologically-linked[#] or determined to be genetically related by laboratory testing.[$] Facilities in high prevalence or endemic areas whose baseline exceeds this level should work with public health to select a threshold based on historic CRE rates.	

CP=carbapenemase-producing; non-CP = non carbapenemase-producing; KPC=*Klebsiella pneumoniae* carbapenemase; NDM = New Delhi Metallo-β-Lactamase; OXA-48-type = oxacillinase; VIM = Verona-Integron encoded carbapenemase; IMP = active-on-Imipenem Metallo- β-lactamase

[1]Regions with high prevalence or endemic CRE are defined as areas where CRE are routinely identified (e.g., on average, acute care facilities and high acuity skilled nursing facilities in high prevalence regions would have more than one CRE case per month and those in endemic regions would have one or more CRE cases per week).

[2]Regions with lower prevalence CRE are defined as areas where CRE are identified with some regularity (e.g., on average, acute care facilities in these regions would have more than a few cases per year to one case per month).

[3]Regions with very low prevalence CRE are defined as areas where CRE are seldom identified (e.g., on average, acute care facilities in these regions have one or a few CRE cases per year).

*When CP mechanism is unknown, facilities should consider testing via the public health laboratory in their state or the Antibiotic Resistance Laboratory Network.

**At minimum, patients admitted to a common unit should be investigated, but additional factors that might indicate a common exposure, such as invasive procedures, could also be used. Patients do not need to have overlapping stays to meet the threshold for additional investigation.

[#]Epidemiologically-linked = Including but not limited to the following examples: residing on same unit (or within same facility if facility is small, transferred from same outside facility, assigned to same primary or consultative service, facility staff in common, had same procedure, seen at same facility, etc.
[$]Laboratory testing methods commonly used for assessing genetic relatedness include pulsed field gel electrophoresis (PFGE) and whole genome sequencing (WGS).

Points for consideration:

- CRE prevalence is highly heterogeneous in the United States. For this reason,
    - In high prevalence or endemic areas, the threshold for investigation of 2 CRE on the same unit was selected for greatest sensitivity. For some facilities in KPC endemic settings, this threshold might prove too burdensome. In this case, facilities should know their baseline CRE prevalence and choose a threshold for investigation that represents a rise above the baseline and that carefully balances sensitivity with specificity. Facilities in these regions might have a lower threshold for investigating non-*K. pneumoniae* CRE, which could carry less common carbapenemases, compared to carbapenem-resistant *K. pneumoniae.*
    - Some facilities may have a prevalence that differs from other facilities in the region. For example, for an ACH in a lower prevalence region that receives patients from facilities in higher prevalence regions, the higher prevalence thresholds might be more appropriate than those for the lower prevalence region.

Facilities should consult with public health for guidance about which prevalence threshold they should use. If the prevalence threshold is unknown, a facility should start with the thresholds for low CRE prevalence and modify as more information becomes available.

- Mechanism testing for CRE is available at 50 state public health laboratories and 7 local health departments. Facilities that do not regularly send isolates for mechanism testing should request mechanism testing for CRE that meet the following criteria 1) isolated from patients with a history of hospitalization outside the U.S. in the 6 months prior to culture collection, 2) resistant to all antibiotics tested at the clinical laboratory, 3) part of a suspected outbreak (i.e., 2 isolates that meet the criteria for further investigation by a facility).
- Non-KPC CRE remain rare throughout the U.S. Identification of any non-KPC CP-CRE, or KPC CRE in non-endemic areas, should result in a public health investigation as described in the CDC Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms.
- Screening tests to identify asymptomatic carriers are available at no cost to facilities through the Antimicrobial Resistance Laboratory Network.
- This definition does not replace reporting of CP-CRE as part of the Nationally Notifiable Disease Surveillance System. The definition adds additional guidance for thresholds for facilities to investigate and report to public health to ensure possible outbreaks are detected early.