

# Carbapenem-resistant Enterobacteriaceae (CRE) Investigations – Part One

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# Objectives

1. Why you should care more about CRE now than you did before
2. Background info on CRE to whet your palate
3. Preview public health response and upcoming activities

A circular inset image showing a microscopic view of Clostridium difficile (CRE) bacteria. The bacteria are rod-shaped with long, thin flagella extending from them. The background is a light blue, textured surface.

# **Why you should care more about CRE now than you did before**

# Antibiotic Resistance Threats in the U.S., 2013 (CDC)

## HAZARD LEVEL URGENT



These are high-consequence antibiotic-resistant threats because of significant risks identified across several criteria. These threats may not be currently widespread but have the potential to become so and require urgent public health attention to identify infections and to limit transmission.

*Clostridium difficile* (*C. difficile*), Carbapenem-resistant Enterobacteriaceae (CRE), Drug-resistant *Neisseria gonorrhoeae* (cephalosporin resistance)

## HAZARD LEVEL SERIOUS



These are significant antibiotic-resistant threats. For varying reasons (e.g., low or declining domestic incidence or reasonable availability of therapeutic agents), they are not considered urgent, but these threats will worsen and may become urgent without ongoing public health monitoring and prevention activities.

Multidrug-resistant *Acinetobacter*, Drug-resistant *Campylobacter*, Fluconazole-resistant *Candida* (a fungus), Extended spectrum  $\beta$ -lactamase producing Enterobacteriaceae (ESBLs), Vancomycin-resistant *Enterococcus* (VRE), Multidrug-resistant *Pseudomonas aeruginosa*, Drug-resistant Non-typhoidal *Salmonella*, Drug-resistant *Salmonella* Typhi, Drug-resistant *Shigella*, Methicillin-resistant *Staphylococcus aureus* (MRSA), Drug-resistant *Streptococcus pneumoniae*, Drug-resistant tuberculosis (MDR and XDR)

## HAZARD LEVEL CONCERNING



These are bacteria for which the threat of antibiotic resistance is low, and/or there are multiple therapeutic options for resistant infections. These bacterial pathogens cause severe illness. Threats in this category require monitoring and in some cases rapid incident or outbreak response.

Vancomycin-resistant *Staphylococcus aureus* (VRSA), Erythromycin-resistant *Streptococcus* Group A, Clindamycin-resistant *Streptococcus* Group B

Although *C. difficile* is not currently significantly resistant to antibiotics used to treat it, it was included in the threat assessment because of its unique relationship with resistance issues, antibiotic use, and its high morbidity and mortality.

# Antibiotic Resistance Threats in the U.S., 2013 (CDC)

## HAZARD LEVEL

### URGENT



These are high-consequence antibiotic-resistant threats because of significant risks identified across several criteria. These threats may not be currently widespread but have the potential to become so and require urgent public health attention to identify infections and to limit transmission.

*Clostridium difficile* (*C. difficile*), Carbapenem-resistant Enterobacteriaceae (CRE), Drug-resistant *Neisseria gonorrhoeae* (cephalosporin resistance)

- *Clostridium difficile* (*C. diff*)
- Carbapenem-resistant *Enterobacteriaceae* (CRE)
- Drug-resistant *Neisseria gonorrhoeae*



Council of State and Territorial Epidemiologists

17-ID-04

**Committee:** Infectious Disease

**Title:** Public Health Reporting and National Notification of Carbapenemase Producing Carbapenem-Resistant Enterobacteriaceae (CP-CRE) for *E. coli*, *Klebsiella* spp. and *Enterobacter* spp.



Council of State and Territorial Epidemiologists

## II. Background and Justification

In this position statement, CP-CRE is defined as:

- *E. coli*, *Klebsiella* spp., or *Enterobacter* spp. where the isolate is:
  - Positive for carbapenemase production by a phenotypic method

OR

- Positive for a known carbapenemase resistance mechanism by a recognized test

# Bureau of Laboratories



A circular inset image showing a microscopic view of a bacterium, likely a Gram-negative rod, with numerous flagella extending from its surface. The bacterium is the central focus, with other similar structures visible in the background.

# Background info on CRE

# CRE: What is it?

Carbapenem-Resistant

*Enterobacteriaceae*

“Entero-bact-teary-A-see-A”

# CRE: What is it?

*Enterobacteriaceae*

- *Family of Bacteria*
  - ▣ *Klebsiella* species
  - ▣ *Escherichia coli* (*E. coli*)
  - ▣ *Enterobacter* species

# CRE: What is it?

Carbapenem-Resistant

*Enterobacteriaceae*

# CRE: What is it?

## Carbapenem

- *Class of antibiotics that are:*
  - ▣ *Extremely broad-spectrum*
  - ▣ *Among the most powerful*
  - ▣ *Include:*
    - ▣ *Imipenem*
    - ▣ *Meropenem*
    - ▣ *Ertapenem*
    - ▣ *Doripenem*

# CRE: What is it?

Carbapenem-resistant

- The bacteria do not respond to treatment with carbapenem antibiotics

# CRE: What is it?

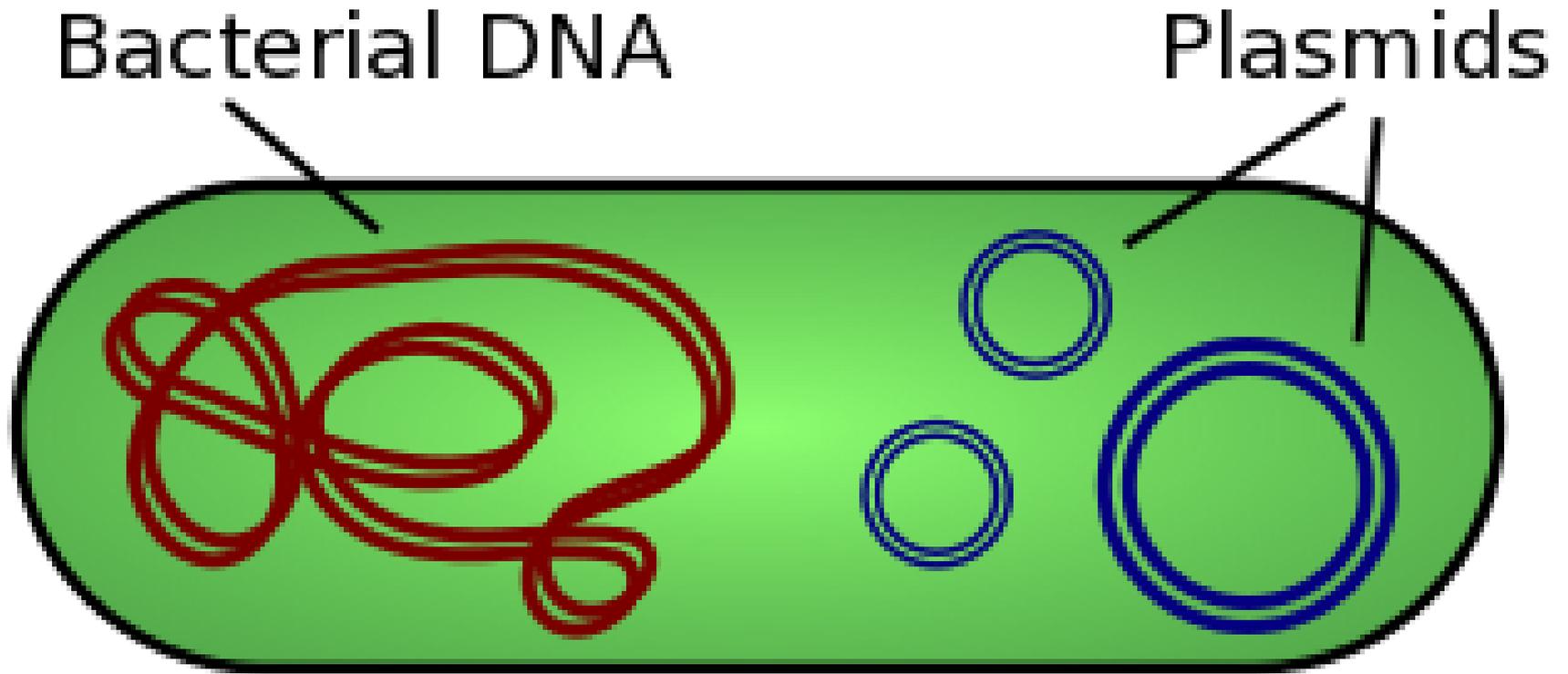
Carbapenem-Resistant

*Enterobacteriaceae*

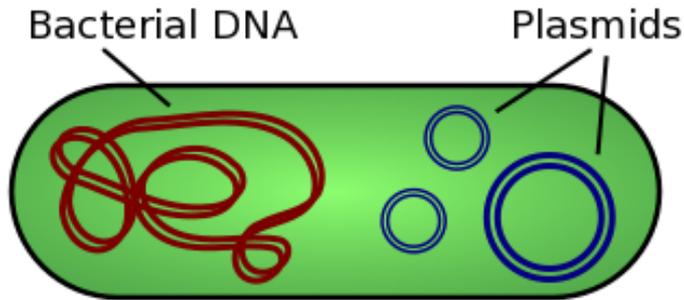
## 2 ways to Carbapenem-resistance

- Intrinsic
  - ▣ Mutations are random errors when chromosomal DNA is copied
  - ▣ Allows the bacteria to become resistant
- Acquired
  - ▣ It is common for bacteria to carry plasmids
  - ▣ Sometimes plasmid DNA contains genes that eliminate the poisonous effects of antibiotics

# ▶ Plasmids: Extra Swappable Genes



# Plasmids: Extra Swappable Genes



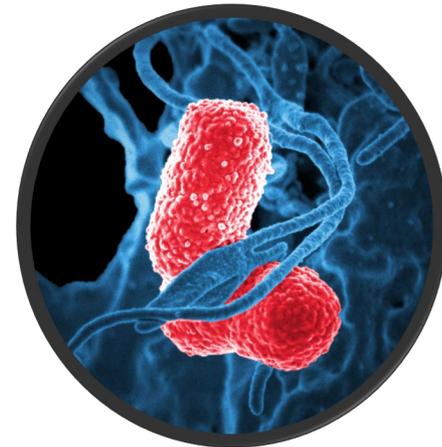
- Plasmids can carry genes to make carbapenemases
  - ▣ Carbapenemase is an enzyme that chews up Carbapenems
    - ▣ KPC- *Klebsiella pneumoniae* carbapenemase
    - ▣ NDM
    - ▣ VIM
    - ▣ OXA-48

# CRE vs. CP-CRE

Carbapenem-resistant  
*Enterobacteriaceae*

vs.

Carbapenemase-  
producing  
carbapenem-resistant  
*Enterobacteriaceae*



# ➤ CRE vs. CP-CRE

## CP-CRE



*"Identifying and containing bacteria which produce carbapenemase will prevent the spread of resistance to other people and other organisms"*

*-Stone, N. (CDC, 2016)*

# CRE vs. CP-CRE

- Specific testing is needed for carbapenemases
  - Many labs don't test
- Therefore, we recommend treating all CRE like they are highly transmissible.

# Transmission



CP-CRE is transmitted person-to-person through contact with contaminated hands, equipment, or environmental surfaces.

Usually contamination is fecal.

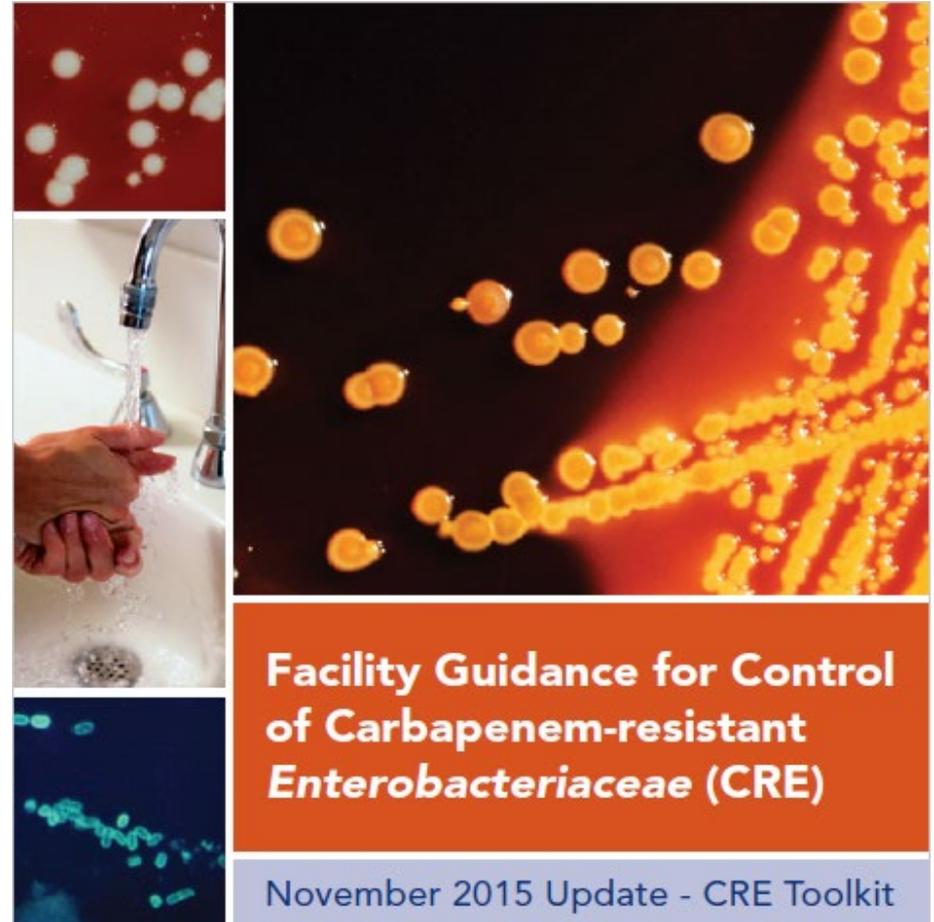
# Colonization vs. Infection

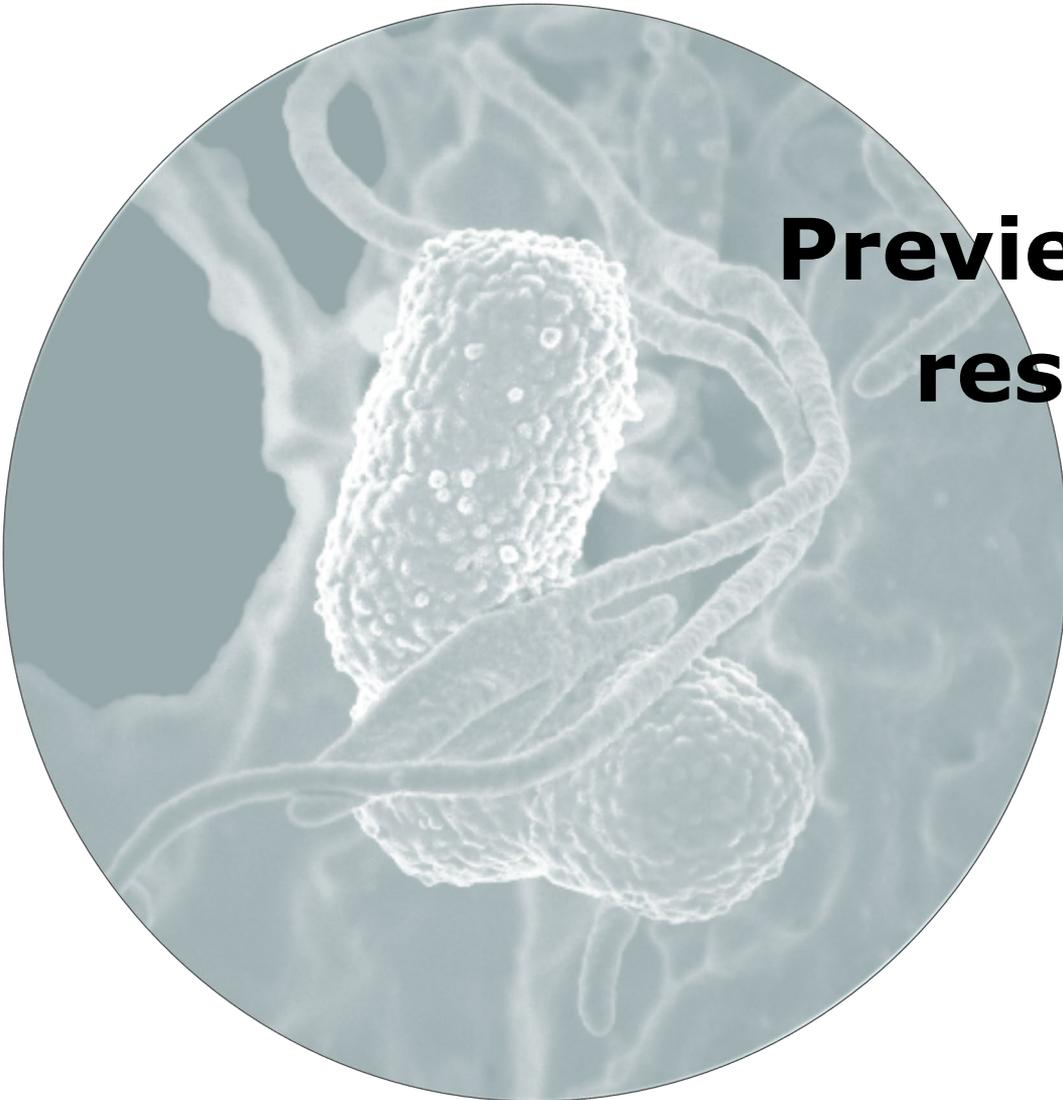
- Even antibiotic-resistant bacteria might not be harmful to a patient
  - Example: CRE cultured from a rectal swab
  - No treatment indicated if there are no signs/symptoms
- Separating colonization and infection can be difficult
- Both colonized and infected persons can spread the organism

# CRE Control Strategies

## CDC Toolkit Updated 2015

(<https://www.cdc.gov/hai/pdfs/cre/cre-guidance-508.pdf>)

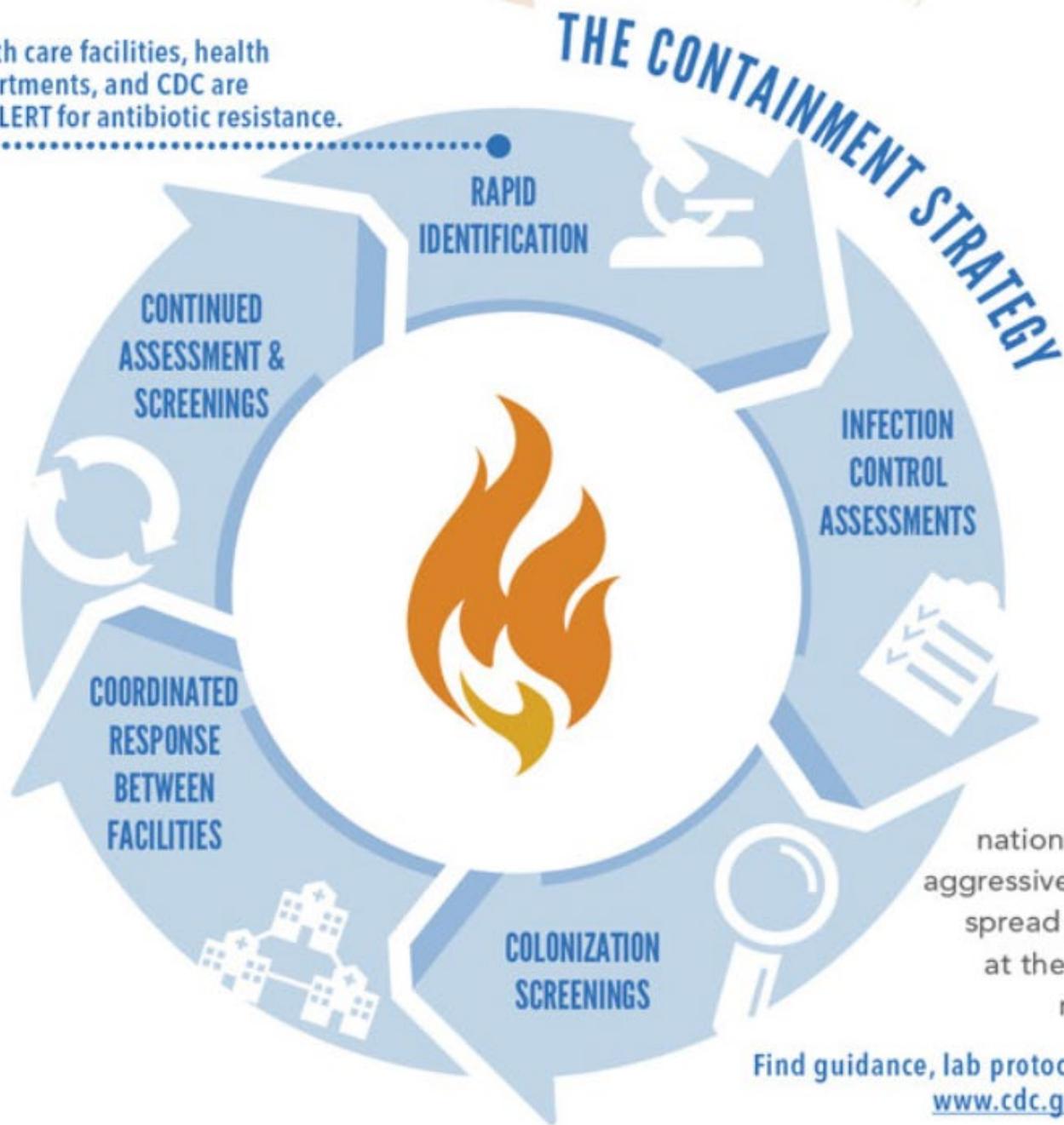


A circular inset image showing a microscopic view of a bacterium with a textured, cylindrical body and several long, thin flagella extending from it. The background is a light blue, semi-transparent circular area.

# **Preview public health response activities**



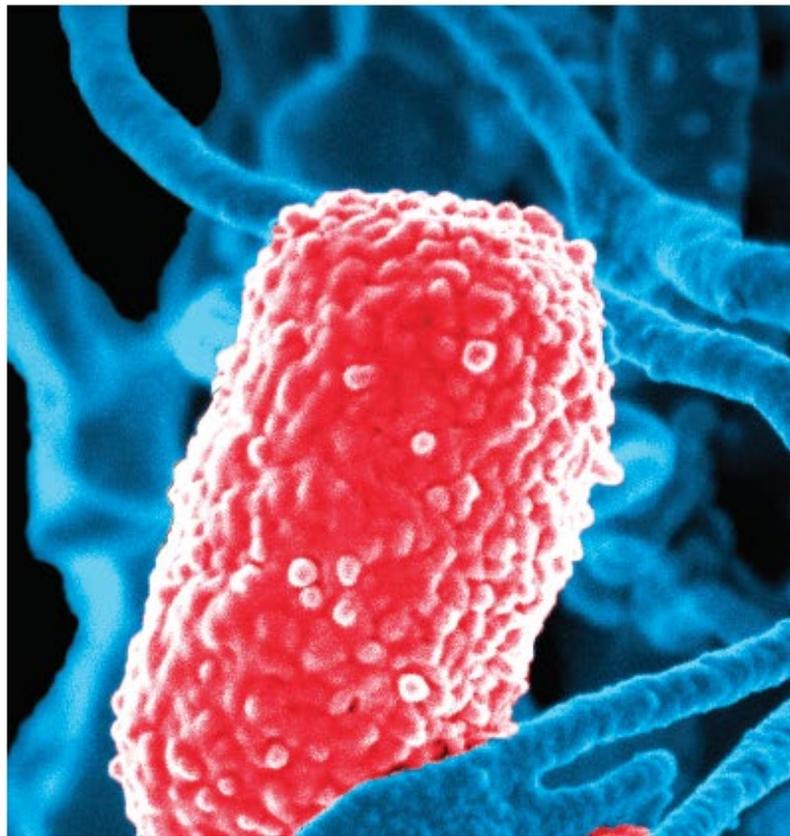
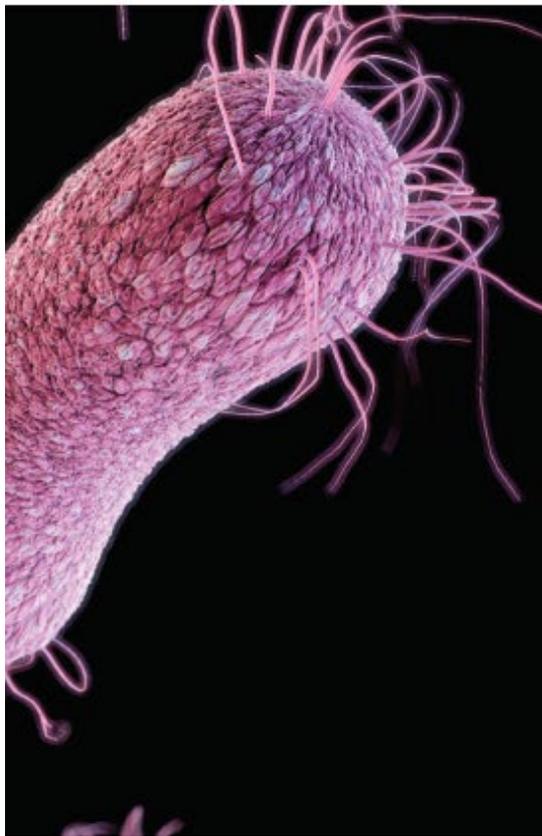
Health care facilities, health departments, and CDC are **ON ALERT** for antibiotic resistance.



Public health teams nationwide can launch early, aggressive responses to contain spread and protect people— at the first sign of antibiotic resistance, every time.

Find guidance, lab protocols, and more resources: [www.cdc.gov/HAI/Outbreaks/MDRO](http://www.cdc.gov/HAI/Outbreaks/MDRO)

# Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs)



# ▶ Example from interim guidance



## Tier 1 organisms:

Organisms in this group include those with resistance mechanisms novel to the United States (i.e., never previously or only very rarely identified in the United States) or organisms for which no current treatment options exist (pan-resistant) and that have the potential to spread more widely within a region. This category also includes organisms and resistance mechanisms for which reports and therefore experience in the United States is extremely limited and a more extensive evaluation might better define the risk for transmission. Examples of organisms in this category include vancomycin-resistant *Staphylococcus aureus* (VRSA).

## Strategies:

- **Upon identification of the organism or mechanism in a laboratory, the laboratory or healthcare facility should promptly notify:**
  - The patient's primary caregiver, patient care personnel, other healthcare staff per facility policies/procedures; generally, local and state public health departments, and federal public health authorities should also be notified.

**Source:** CDC's Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs)

# ▶ Upcoming PA DOH Activities

- CP-CRE testing at BOL
  - ▣ Reported into LIMS
  - ▣ Message mapping to report into NEDSS
  - ▣ Investigation questionnaire in NEDSS
- (Eventually) CP-CRE reports into NEDSS from outside micro labs

**THANK YOU!**

Healthcare-associated Infection  
Prevention/Antimicrobial  
Stewardship (HAIP/AS) team

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