Carbapenemase-Producing Carbapenem Resistant *Enterobacteriaceae* (CP-CRE) Statewide Reporting Webinar

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The SHARP Unit

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Carbapenem-resistant Enterobacteriaceae

• Enterobacteriaceae – enteric organisms, gram negative bacilli

- Carbapenems class of broad-spectrum, β-lactam antibiotics
 - Agents of last resort one of the few remaining effective therapies
 - Only 4 carbapenems: Doripenem, Ertapenem, Imipenem, and Meropenem

 Infections - responsible for urinary tract infections, bacteremia, pneumonia, wound infections

Mechanisms of Carbapenem Resistance

- 1. Carbapenemases
- 2. Acquired resistance
- 3. Naturally imipenem-resistant *Enterobacteriaceae*

Not all CRE are carbapenemase producers...

CRE and Novel Resistance Activity

Carbapenemases:

- Klebsiella pneumoniae carbapenemase (KPC)
- New Delhi metallo-β-lactamase (NDM)
- Verona integron encoded metallo-β-lactamase (VIM)
- Imipenemase metallo-β-lactamase (IMP)
- Oxacillinase-48 (OXA-48)

Other resistance elements:

Mobile colistin resistance (mcr)

Public Health Threat of CRE Infections

- Treatment options are more limited
 - New antibiotics have been slow to develop and come to market
 - Although several new agents are now/soon to be available
 - Pan-resistant strains identified
- CRE infections associated with high mortality rates
- Resistance is highly transmissible
 - Between organisms plasmids
 - Between patients hands, healthcare workers
- Potential for spread into the community
 - E. coli a common cause of community infection

Carbapenem-resistant *Enterobacteriaceae* (CRE) Surveillance and Prevention Initiative

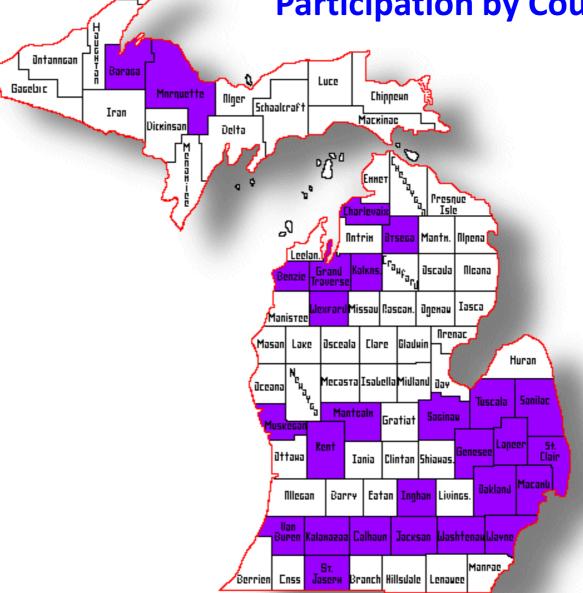
CRE Surveillance and Prevention Initiative Voluntary Participation

	Baseline Period	Intervention Period	Acute Care	LTAC	LTC/SNF	Total
Phase 1	Sept 2012-Feb 2013	Mar 2013- Aug 2014	17	4	0	21
Phase 2	Mar 2014-Aug 2014	Sept 2014-Feb 2016	7	2	0	9
Phase 3	Sept 2015-Feb 2016	Mar 2016-Aug 2017	4	4	2	10
New facilities	Sept 2017-Feb 2018	Mar 2018-Aug 2019	14	7	0	21
Combined Cohort	Sept 2017-Feb 2018	Mar 2018-Aug 2019	42	17	2	61

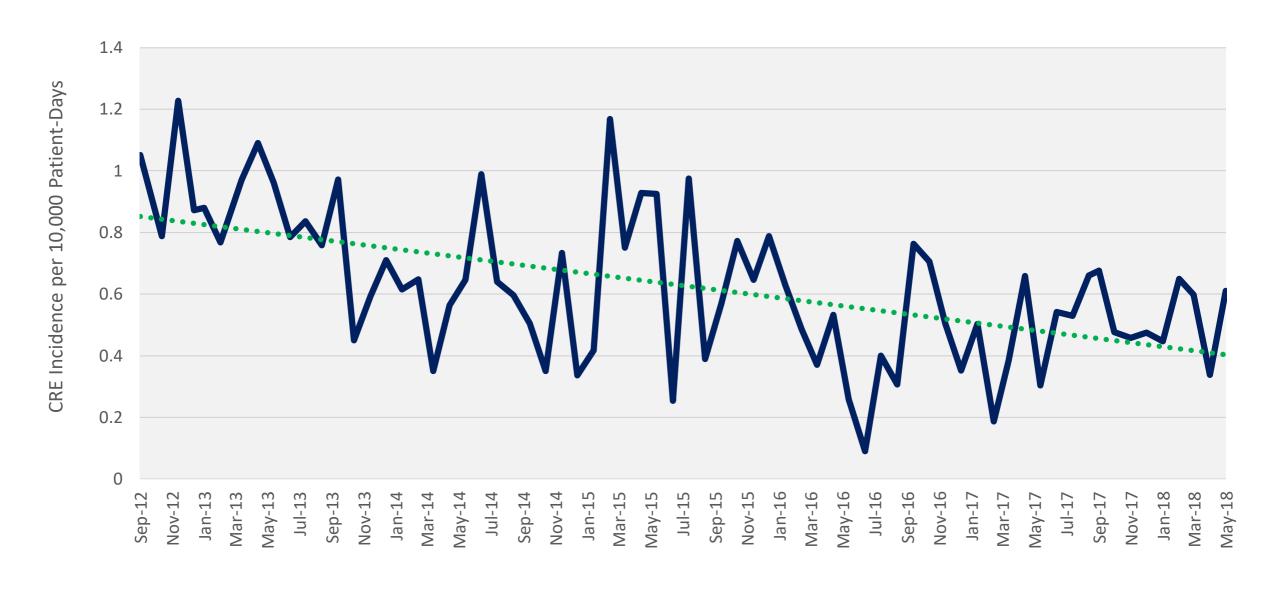


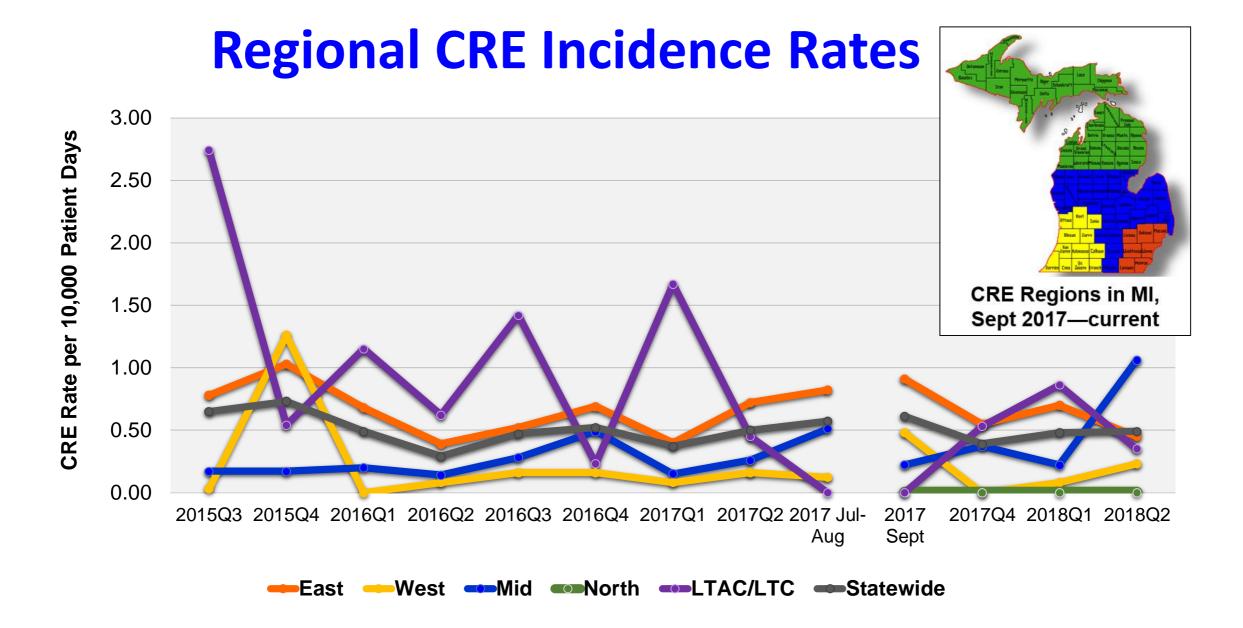
Participation by County, 2012-2017

CRE Surveillance and Prevention Initiative Participation by County, Sept 2018



Overall CRE Incidence





Regional CRE Incidence Rates

	Number of Facilities	2018 Q2			
Region		Number of CRE Cases	Total Patient Days	Overall Rate	
East	19	17	380,099	0.45	
West	7	3	128,213	0.23	
Mid	9	14	132,127	1.06	
North	7	0	43,235	0.00	
LTAC/LTC	19	2	57,431	0.35	
Statewide	61	36	741,105	0.49	

Prevention Measures Implemented

Category	Specific Measure
Procedure Changes	 Screening and presumptive isolation of all patients admitted from an LTAC PICU CHG Bath Audits Development of practitioner-specific reports to describe infectious diseases specialist approvals of carbapenem use In-house laboratory will be performing phenotypic testing to confirm carbapenamase production Flagging of CRE patient in our IC surveillance system (RL systems) so that they can be isolated more quickly on subsequent admissions Daily CHG bathing of all ICU patients Terminal Clean/Bed exchange for patient who has occupied a room for greater than 45 days Prompt discontinuance of unnecessary invasive devices CHG bathing in confirmed CRE cases for 3 days Sending CRE isolates to MDHHS BOL for lab confirmation
Education	 Improved physician education on prevention and control of MDRO organisms, infection, and colonization MDRO Component in 2013 Annual CHM Infection Prevention (IP) Nursing Intranet Learning (NL) Competency, Education Hand Hygiene Impact on MDRO/CRE Educating new/transitioning staff in the proper process of CHG bathing of patients in ICU Educational pamphlet will be developed to educate patients and visitors about CRE Educate patient care services (RNs, and PCAs) about preventing transmission of CRE, compliance with signage and supplies for Contact Precautions while screening patients for CRE or for a patient that is positive for CRE Education to raise awareness of the resistance mechanisms of emerging pathogens Present MDRO (including CRE) education for Medical Residents and reach other healthcare personnel (RNs, support services, MDs, etc.) using forums such as unit huddle
Compliance	Evaluating compliance with isolation practices (i.e., posting of proper signage, availability of gloves, masks, and gowns as well as proper use of these supplies) for all patients that are in isolation
Communication	Rapid communication between lab, IP and ID physicians, inter-facility communication, Inter-facility communication for CRE positive patients: When a CRE is identified, communication will occur to any outside transferring facility by communication transfer form and/or phone communication
Pilot project	Project using Dazo fluorescent marking gel to objectively measure thoroughness of disinfection cleaning on critical surfaces

CRE Infections Prevented2012-current

Initiative Phase	All Facilities	Acute Care	LTAC/LTC
Phase 1 Facilities	280	235	45
Phase 2 Facilities	68	50	18
Phase 3 Facilities	14	0	14
Combined Cohort (Mar 2018 - current)	3	4	-1
Total Initiative	365	289	76

CP-CRE Reporting

CRE Surveillance & Prevention Initiative vs. CP-CRE Reporting

- CRE Surveillance and Prevention Initiative
 - Klebsiella pneumoniae and Escherichia coli that are resistant to ANY carbapenem
 - Voluntary reported through the CRE S&PI only
 - 61 facilities
- New Communicable Disease Reporting for CP-CRE
 - Klebsiella spp., Enterobacter spp., Escherichia coli positive for carbapenemase production by a phenotypic test or positive for carbapenem resistance mechanism (KPC, NDM, VIM, OXA-48, IMP or other carbapenemase gene) and those resistant to ANY carbapenem
 - Mandatory reported through ELR or manual entry into MDSS
 - Statewide

CP-CRE Reporting Requirements

- Laboratories, infection prevention and Local Health Departments are required to report all cases of **CP-CRE** according to the following criterion for *Klebsiella* spp., *E. coli*, or *Enterobacter* spp.:
 - Healthcare record contains a diagnosis of Carbapenemase-producing Carbapenem-resistant Enterobacteriaceae (CP-CRE), KPC, NDM, OXA-48, IMP or VIM or other novel carbapenemase
 - Any isolate of Klebsiella spp., E. coli, or Enterobacter spp. demonstrating carbapenemase production by a phenotypic test (e.g., Carba NP, CIM, mCIM)
 - Any isolate of *Klebsiella* spp., *E. coli*, or *Enterobacter* spp. with a known carbapenemase resistance mechanism (e.g., KPC, NDM, OXA-48, IMP, VIM, or other carbapenemase gene) by a recognized molecular test (e.g., PCR, Expert Carba-R)

CP-CRE Reporting Requirements

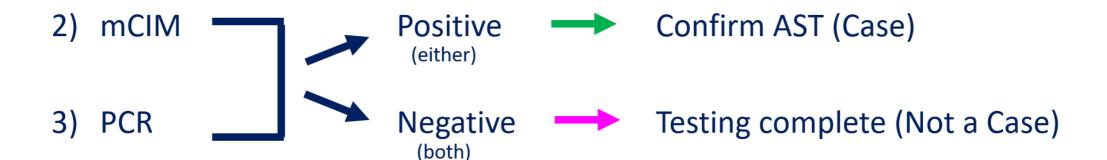
- If laboratories are <u>unable to detect</u> **CP-CRE**, (*i.e.*, cannot test for carbapenemase production (phenotypic) or resistance mechanism (molecular test):
 - Report any isolate of Klebsiella spp., E. coli, or Enterobacter spp. with a minimum inhibitory concentration (MIC) of any of the following:
 - ≥4 mcg/ml for Meropenem
 - ≥4 mcg/ml Imipenem
 - ≥4 mcg/ml Doripenem
 - ≥ 2 mcg/ml for Ertapenem

Carbapenemase and Resistance Mechanism Testing

- Laboratories are strongly encouraged to submit CRE isolates to the MDHHS Bureau of Laboratories
 - Confirm organism identification
 - Perform mCIM testing
 - Perform PCR testing for KPC, NDM, OXA-48, IMP, VIM
 - If mCIM or PCR are positive, antimicrobial susceptibility testing (AST) will be performed

MDHHS Bureau of Laboratories Report

1) Confirm ID



MDHHS Bureau of Laboratories Report

Antimicrobial Resistance Confirmation (ARC)

Gram Stain

Gram negative bacilli

Culture Results

Confirmed as Klebsiella pneumoniae

Identification Performed by MALDI-TOF.

Antimicrobial Susceptibility Results

	Klebsiella pneumoniae		
	MIC - Interpretation		
Amikacin	<=4	S	
Aztreonam	>16	R	
Cefepime	4	SDD	
Cefotaxime	32	R	
Ceftazidime	>16	R	

Modified Carbapenem Inactivation Method

Positive

Phenotypic test

Modified Carbapenem Inactivation Method (mCIM) screen positive - this isolate demonstrates carbapenemase production. The clinical efficacy of the carbapenems has not been established for treating infections caused by Enterobacteriaceae and Pseudomonas aeruginosa that test carbapenem susceptible but demonstrate carbapenemase production in vitro. ISOLATES THAT ARE mCIM POSITIVE SHOULD BE CONSIDERED RESISTANT TO ALL CARBAPENEMS REGARDLESS OF MIC. MIC REPORTED FOR EPIDEMIOLOGIC PURPOSES ONLY.

PCR Result

KPC (bla-KPC) gene DNA Detected

Molecular test

NDM-1 (bla-NDM-1) gene DNA Not Detected

OXA-48 (bla-OXA-48 like) gene DNA Not Detected

VIM (bla-VIM) gene DNA Not Detected

KPC, NDM, OXA-48, and VIM are the most common carbapenemases in the United States, however there are other less common carbapenemases and other mechanisms of carbapenemase resistance not detected by this PCR assay.

IMP PCR Result

IMP (bla-IMP) gene DNA Not Detected

Tips on How to Report Cases into MDSS

MDSS Reporting

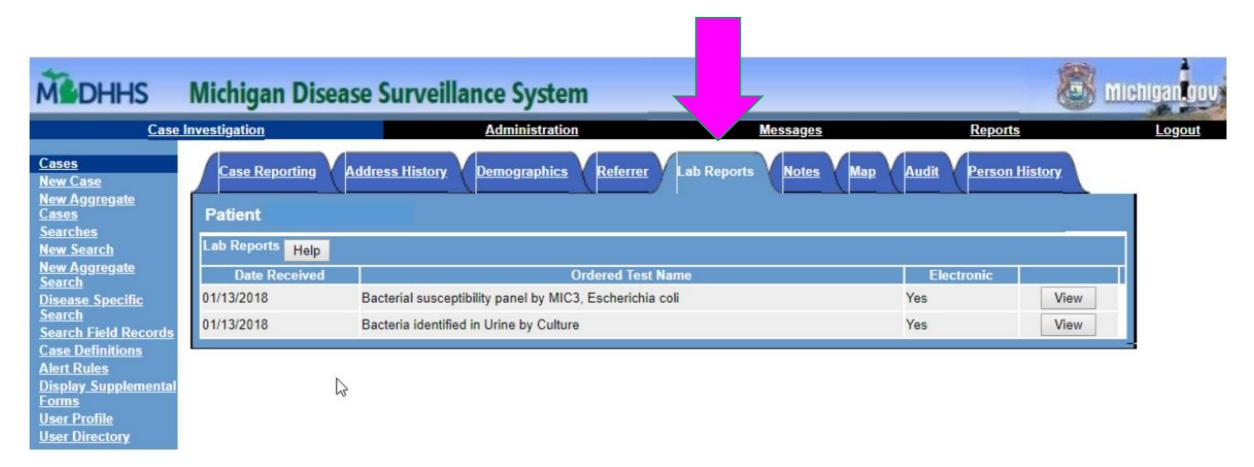
- CP-CRE cases should be reported using the Michigan Disease Surveillance System (MDSS)
 - Web-based communicable disease reporting system for the state of Michigan
 - Cases can be reported by:
 - Electronic laboratory report (ELR)
 - Manual case entry
 - Reporting and ELR Guidance available at <u>www.michigan.gov/hai</u>

Electronic Laboratory Reporting (ELR)

- BOL is now reporting all carbapenemase and resistance mechanism testing into MDSS!
 - Both positive and negative results are now reported into MDSS
 - Klebsiella spp., E. coli, or Enterobacter spp., only
 - Populate into Lab Reports tab for culture results, mCIM, PCRs, and AST
 - Allows local health departments to know if a case is Confirmed or Not a Case

Electronic Laboratory Reporting (ELR)

ELRs will populate into the Lab Reports tab – positive and negative results



ELR Example



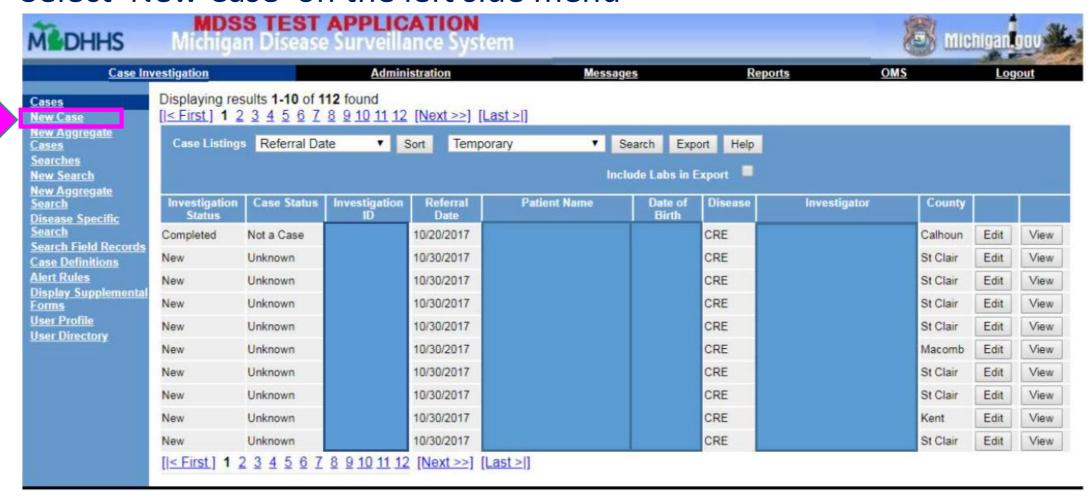
MDSS TEST APPLICATION Michigan Disease Surveillance System



Administration Case Investigation Messages Reports 8 1 Cases Address History **Demographics** Referrer Lab Reports Case Reporting Person History New Case New Aggregate Patient TEST10, CRE Cases Searches Lab Order Information **New Search New Aggregate** Test Name* : PCR Result Search Disease Specific Lab Report Date (mm/dd/yyyy): 03/28/2018 Search Search Field Records Case Definitions **Ordering Provider** Alert Rules Last: Display Supplemental Affiliation: MDHHS - QUALITY ASSURANCE SECTION - MARTY Street: 3350 N. MLK JR. BLVD. BLDG 44, RM 158 **User Profile User Directory** LANSING Michigan Phone number : 517-335-8074 Laboratory Information Lab Name*: MDHHS REGIONAL LAB - LANSING Street: 3350 N. Martin Luther King Jr. Blvd. Geocode Source : County: Michigan Lansing Phone number: 517-335-8063 Specimen Information Specimen Collection Date (mm/dd/yyyy): 03/28/2018 Specimen Source : Specimen Site: Specimen Site Text: Results Reported Test Name: bla(KPC) gene/null KPC (bla-KPC) gene DNA Detected Coded Result Numeric Result Abnormal Flags/Susceptibility Results:

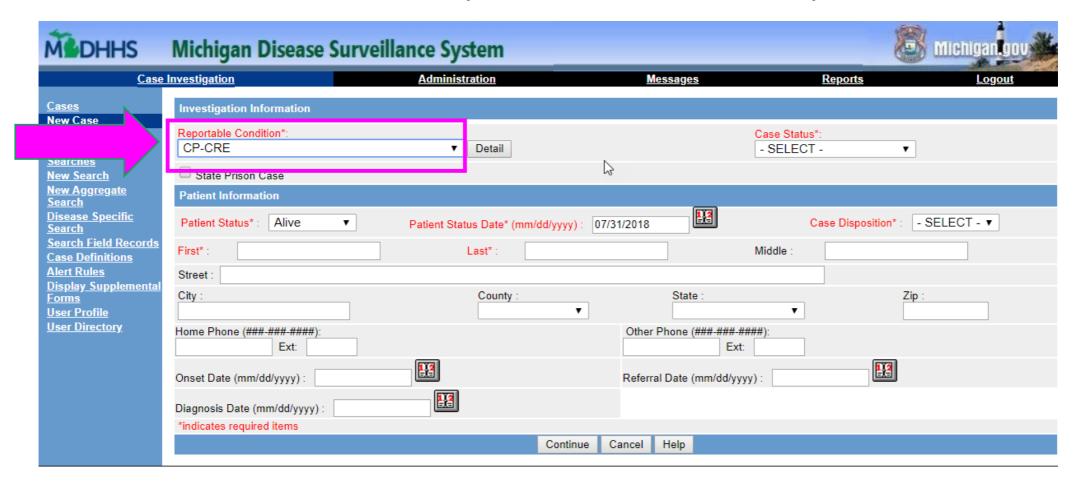
Manual Case Entry

Select 'New Case' on the left side menu



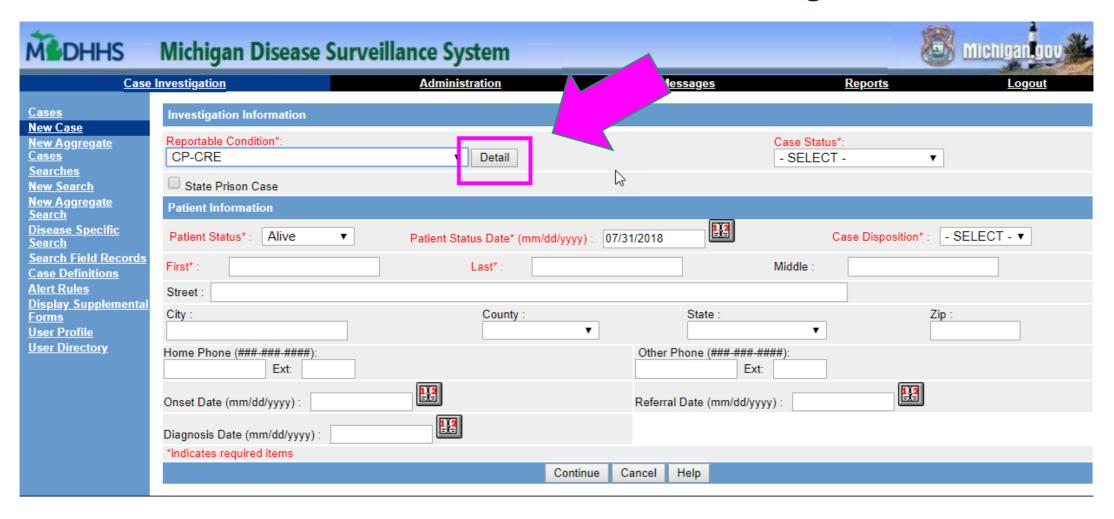
Manual Case Entry

Select 'CP-CRE' from the Reportable Condition drop-down menu



Manual Case Entry

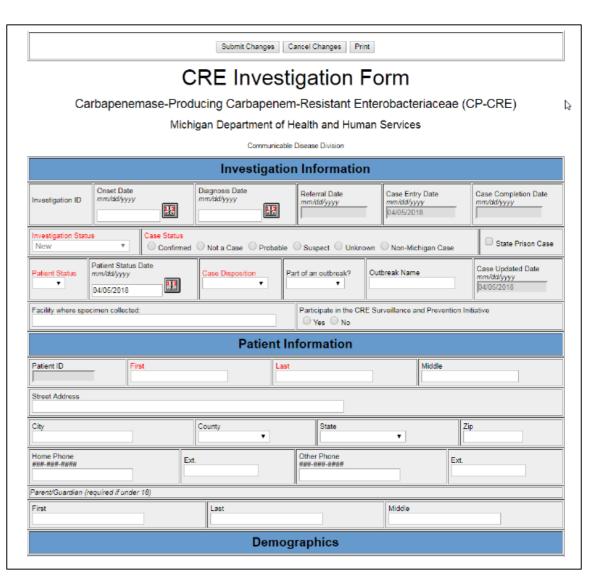
Select the 'Detail' button to launch the case investigation form



CP-CRE Case Investigation Form

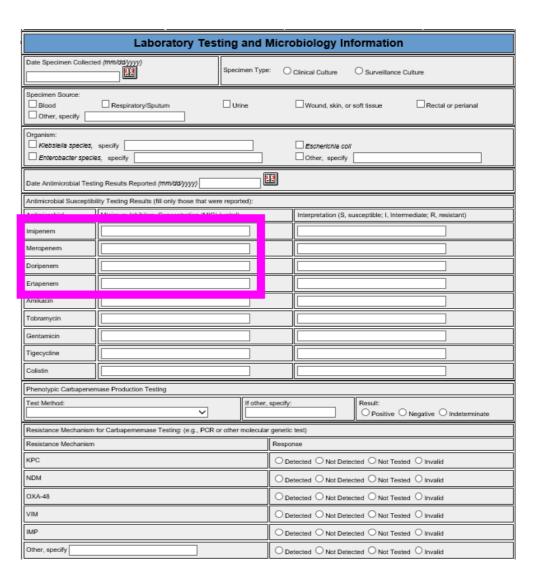
CRE Investigation Form Sections

- Patient Information
- Demographics
- Laboratory Testing
- Clinical Information
- Antimicrobial Therapy



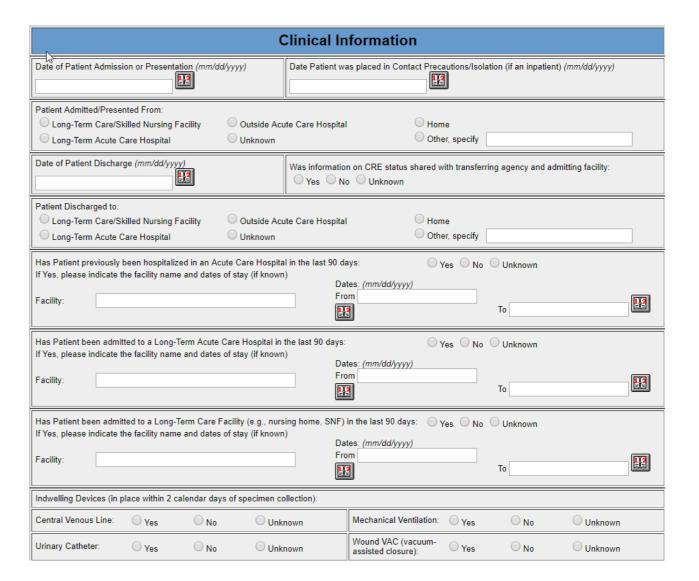
CP-CRE Laboratory Testing

- Laboratory Testing information is required to determine case classification
 - Enter lab data into Case Detail Form (instead of Lab Reports tab) for manual case entry
 - Date collected
 - Specimen source
 - Organism
 - MIC (need actual value)
 - Carbapenemase testing
 - Resistance mechanism testing



CP-CRE Clinical Information

- Clinical Information
 - Healthcare exposures
 - Travel
 - Particularly important for any confirmed NDM, OXA-48, IMP, or VIM cases



Case Classification

CONFIRMED CP-CRE

- Klebsiella spp., E. coli, Enterobacter spp.
 - Positive phenotypic test OR
 - Positive carbapenem resistance mechanism

SUSPECT CP-CRE

- Klebsiella spp., E. coli, Enterobacter spp.
 - Resistance to at least 1 carbapenem
 - No phenotypic or molecular testing done

NOT a CASE

- BOL report is negative for phenotypic and molecular tests
- All carbapenems are susceptible (MICs don't match case definition)
- Not Enterobactericeae

Actual CP-CRE Reporting

SUSPECT Cases

- Only MICs known
- Carbapenem Resistance

Enterobacteriaceae

CONFIRMED Cases

- Phenotypic or molecular mechanism known
- CP-CRE

Case Deduplication

Local Health Departments

- An individual should only be counted once per 12 months for the same organism and resistance mechanism
- When reviewing newly reported cases/lab results:
 - Search to see if the patient has already been reported
 - Confirm whether the organism identification is the same
 - Confirm whether the resistance mechanism present is the same
 - Choose the new detail form when merging cases

Frequently Asked Questions

- I can't find results for all of the antimicrobials listed on the case detail form
 - Just looking for the 4 carbapenems:
 - Doripenem
 - Ertapenem
 - Imipenem
 - Meropenem
- There are no MICs for the carbapenems, just a letter (S, I, R) or there are no carbapenems reported
 - Please call the laboratory and get the actual MICs and specifically ask for carbapenem results

- A report came in from BOL that was positive for Citrobacter freundii
 KPC. What do I do?
 - While this is a confirmed KPC CP-CRE it is not a *Klebsiella spp., E coli,* or *Enterobacter spp.* and is not required to be reported
- A report came in from BOL that was positive for VIM, but it is not a Klebsiella spp., E coli, or Enterobacter spp. What do I do?
 - That is a novel resistance case
 - Sara will be contacting you for follow-up
 - Case can be entered as CP-CRE
 - Organism: Other, specify

- Repeat cultures should facilities be sending every isolate regardless of if they sent it in the past?
 - BOL policy is that if it's the same organism from same patient, same lab, they will only do the repeat ARC testing every 6 months, unless specifically requested by the submitting lab (e.g., if the AST profile looks completely different, or more resistant than previously)
 - If it is a new species in the same patient then they will test
 - If it is the same patient, different lab then they will test
 - Example: tests with all the same organism within the 12 month time frame then subsequent cases can be merged, (even though we don't the know the mechanism for the later isolates)

- Does the Modified Hodge Test (MHT) count as a confirmatory test?
 - Yes, technically. However...
 - MHT often can produce false positive results for *Enterobacter* spp. (can pick up AmpC production or other mechanisms of resistance other than carbapenemase production) and therefore the positive results are not reliable
 - MHT does better job of detecting true carbapenemase production in Klebsiella spp. and E. coli, which are usually KPC
 - However it can miss the metallo-B-lactamase carbapenemases like NDM, giving false negative results
 - MHT is no longer being recommended for confirmatory testing, and it has been removed from the CLSI M100 guidelines for clinical laboratories
 - mCIM test is recommended instead

How long do we have to complete the case detail form?

- As with any CD, please try and get the information as soon as possible
- If anything, verify patient's chart is flagged and they are in contact precautions
- We do have time to investigate, but if a contact investigation is needed, it's
 easier to test patients still admitted than discharged

SUSPECT cases - How much of the form to complete?

- If you know the facility submits isolates to BOL for testing, you can wait to see the lab result.
- If you know they don't or are unsure, investigate the case (demographics, track down the MICs, check healthcare exposures (are they currently admitted and in contact precautions), if LTC/SNF patient – please document current and previous locations in the Notes

- Home address is used for hospital/LTC/SNF patients how do we detect clusters?
 - Initiative and non-initiative patients can be linked in MDSS
 - If you know the previous hospital/LTC/SNFs location(s), please document in Notes
- When should we put their home address versus facility address?
 - If specimen was collected at the LTC/SNF facility use facility address
 - If they have been a resident in a LTC/SNF within the past 3 months, please indicate the facility address in the Notes

- From the LHD perspective: How do I know which facilities participate in the CRE Surveillance and Prevention Initiative?
 - Brenda and Sara will be providing the Regional Epidemiologists a list of participating facilities in their jurisdictions/counties to pass along to LHDs

- Do facilities that participate in the CRE Surveillance and Prevention Initiative report twice?
 - No
 - Cases that meet the surveillance definition for the initiative are the same as the reporting requirement – no dual reporting
 - Cases are entered into MDSS (unless arrangement with Sara or LTAC)
 - Facilities do report # cases, # of patient-days and # of admissions monthly to Sara

Updated Guidance

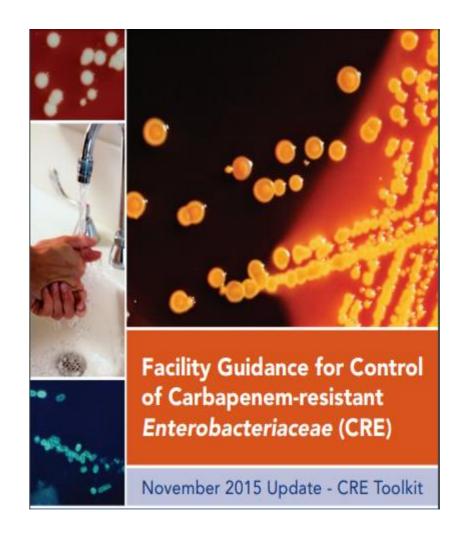
- Currently updating the Interim CP-CRE Case Reporting and Investigation Guidance
 - Reporting
 - Case Classification
 - Investigation
 - Prevention
- Planning to release January 2019

Investigation

- KPC Endemic vs. Non-Endemic Areas
 - Patient information, demographics, laboratory data, healthcare exposures, travel
 - Information important for prevention purposes
 - Revise MDSS form for needed vs. optional data in future?
- Novel CP-CRE resistance mechanisms, including NDM-1, OXA-48,
 VIM, and IMP:
 - Please complete the entire case detail form as best as possible
 - Documentation of healthcare exposures and international travel is crucially important

CP-CRE Prevention

- Hand Hygiene
- Contact precautions
- Environmental Cleaning
- Use of devices
- Antimicrobial stewardship
- Chlorhexidine bathing
- Laboratory notification
- Inter-facility communication
- Screening contacts of CRE Patients
- Active surveillance testing
- HCP, Patient & Family Education



CRE Brochures



CRE

Cabapenem-Resistant Enterobacteriaceae



WHAT ARE PENEM-RESISTANT OBACTERIACEAE (CRE)?

a family of germs that o treat because they resistant to many y used antibiotics.

main types of cteriaceae that may ant to carbapenems, siella species, robacter species, erichia coli (E. coli).

AT RISK FOR CRE

Ily affects people who: icute or long-term care s like hospitals, clinics ing homes. weak immune system. n item like tubes or ng machines going ir body.

V DOES CRE SPREAD?

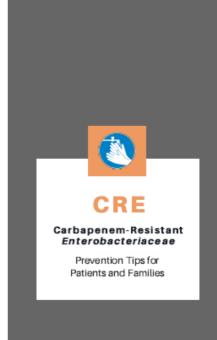
RE infections happen thcare settings like and nursing homes.

sick from CRE a person come in contact uch) the CRE germ.

reads when someone s an infected or colonized s body or body fluids.

t can be:

ect, by touching wounds eces (poop); OR rect, by way of dirty ds or touching dirty ects (like tubes that love liquid from the y or breathing chines).



HAT ARE CARBAPENEM-RESISTANT NTEROBACTERIACEAE (CRE)?

E are a family of germs t are hard to treat because y are often resistant to ny commonly used ibiotics.

re are three main types of erobacteriaceae that may esistant to carbapenems,

. Klebsiella species, .Enterobacter species, and .Escherichia coli (E. coli).

OUR TIPS FOR NG FOR SOMEONE WITH CRE

ear gloves whenever u are going to touch dy fluids or blood.

ash your hands.

is important to wash our hands after you: Touch wounds Help the person use the bathroom Clean up feces (poop)

ean surfaces and edical devices that ve touched a CRE tients body or body ids, with soap and ter and then a usehold disinfectant eaner).

sh all used clothes, eets, and linens using ndry detergent.

We Need Your Input!

• Questions, comments, suggestions...

Updated Guidance

- January 2019
- www.michigan.gov/hai
- www.michigan.gov/cdinfo
- Listserves (Communicable Disease, NHSN Users, clinical micro)

Thank You

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