

MDCH Confirmatory Testing for Carbapenem-Resistant *Enterobacteriaceae* (CRE)

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Background

- Carbapenem resistance is serious concern
 - Very sick patients
 - MDRO, few options left for treating
 - High morbidity and mortality
 - Infection prevention and control emergency
- Two mechanisms of resistance:
 - Production of a carbapenemase enzyme (“B-lactamase on steroids”)
 - KPC, NDM-1, (others, but these two are current concern in US)
 - Other B-lactamases + porin loss
- Laboratory detection is complex

Background

- All Michigan clinical micro labs have rec'd CLSI documents 2012
 - M02 – A11 (Disk Diffusion)
 - M07 – A9 (MIC reference methods)
 - M100 – S22 (Interpretive Breakpoints, Quality Control ranges, summary of screening and confirmatory test recommendations)
- 2013 CLSI document M100-S23 is on order for MI labs

Background

- Current FDA-cleared breakpoints on automated susceptibility testing instruments may miss some isolates that are producing carbapenemase but still test as “S”
- Carbapenem breakpoints were revised by CLSI in June 2010
 - Cephalosporin (not all) & aztreonam breakpoints had been revised previous January 2009
- Labs were advised to “validate” the new CLSI breakpoints against a reference method
 - Disk-diffusion performed per CLSI M02-A11
 - Broth microdilution performed per CLSI M07-A9
- Hard to find MIC panels with lower breakpoint dilutions

Funding Opportunity

- Healthcare-associated Infections are top priority at CMS
- Michigan's Healthcare-Associated Infection (HAI) Prevention Plan recognized need for confirmatory testing for CRE
- Grants awarded to two state public health labs (MI and IN) through June 2013

Goal

- Develop non-automated AST capacity in state PHLs for CRE and VRSA to provide confirmatory testing for clinical laboratories w/in jurisdiction

Activities

- Implement non-automated methods to confirm CRE and VRSA
- Implement PCR for most common mechanisms of carbapenem and vancomycin resistance using CDC protocols
- Develop and maintain partnerships w clinical laboratories
- Foster situational awareness of antimicrobial resistance (AR), including real-time communication with state epi and HAI coordinator
- Pilot CDC framework for PH surveillance for critical bacterial AR

MI Project Design

- Perform MIC testing by CLSI reference microbroth dilution method
 - Four carbapenems (imipenem, meropenem, ertapenem, doripenem)
 - 3rd gen ceph (ceftriaxone)
 - cephamycin (cefoxitin)
 - monobactam (aztreonam)
- Interpret and report using newest CLSI breakpoints

MI Project Design (cont'd)

- Perform Modified Hodge Test (w meropenem)
- Perform PCR testing
 - KPC gene bla_{KPC}
 - NDM-1 gene bla_{NDM-1}
- Also a VRSA component:
 - PCR testing for *vanA* gene in *Staphylococcus aureus*

MI Project Design (cont'd)

- Perform Modified Hodge Test if any carbapenem I or R
- Perform PCR for KPC and NDM-1 genes if:
 - carbapenem I or R
 - 3rd generation cephalosporins R
 - Modified Hodge Test positive
- Report to submitter
- Share results with state HAI coordinator
 - Jennie Finks and SHARP Unit

Clinical Lab Role

- Sentinel Partner:
 - Detect possible carbapenem resistance in isolates of *Enterobacteriaceae*
 - Detect possible vancomycin resistance in isolates of *S. aureus*
 - Use newest recommendations from CLSI to the extent possible
 - Send all** suspect isolates to MDCH laboratory in Lansing for confirmation

**depending on number of isolates rec'd, guidance may change

Labs using “older” CLSI breakpoints

- Instrument result = carbapenem I or R
- If carbapenem = S, look at results for cephalosporins:
 - One or more 3rd generation ceph = resistant, consider MIC value for carbapenem
 - MIC of 2 or 4 may indicate carbapenemase production
- Follow up with MHT as recommended

Flowchart for “older” breakpoints

I or R to at least one carbapenem reported

OR

Imipenem/ meropenem/ ertapenem MIC ≥ 2

AND

R to one or more cephalosporin III

cefoperazone, cefotaxime, ceftazidime, ceftizoxime, ceftriaxone

regardless of

Modified Hodge Test (MHT) result, if performed

Send isolates to MDCH

Labs using “newer” CLSI breakpoints

- Interpret and report carbapenems according to Table 2A in 2012 version of CLSI document M100-S22
- Send any I or R isolates to MDCH

What to Submit

- Pure culture of any species of *Enterobacteriaceae* that fits criteria
 - *E coli*
 - *Klebsiella*
 - *Enterobacter*
 - *Citrobacter*
 - **NOT** *Pseudomonas*
 - *Serratia*
 - *Proteus*
 - *Providencia*
 - *Morganella*
 - **NOT** *Acinetobacter*
- Please email or call Marty Boehme if you're not sure:
boehmem@michigan.gov 517-335-9654
- Also include copy of instrument printout and MHT results

Notes

- Imipenem MICs for *Proteus*, *Providencia* and *Morganella* may be higher than meropenem or doripenem
- Intrinsic resistance, not due to carbapenemase mechanism

How to Submit

- Agar *slants* only, no agar plates will be accepted
- Please include copy of your ID and AST results (e.g., printout from automated instrument)
- Also include MHT result, if performed
- Enter “CRE Confirmation” in Other _____ test area on MDCH lab requisition

Transport to Lansing

- Send to MDCH Lansing
 - Hospital courier
 - US Mail
 - FedEx
- Follow regulations for shipping Infectious Substances, category B (UN 3373)

Testing at MDCH

- Gram Stain
- Confirm organism ID (after subculture for fresh growth)
- Reference method MIC (CLSI broth microdilution using frozen panels)
- Modified Hodge Test
- PCR for KPC and NDM-1 genes as indicated by results of above testing

Reporting

- Gram Stain and organism identification
- MIC value and interpretation (S, I, or R) for antimicrobials:
 - Aztreonam
 - Cefoxitin
 - Ceftriaxone
 - Doripenem
 - Ertapenem
 - Imipenem
 - Meropenem
- Modified Hodge Test result (pos or neg)

Reporting (cont'd)

- KPC PCR result
 - KPC (*bla*_{KPC}) gene DNA Detected
 - KPC (*bla*_{KPC}) gene DNA Not Detected
- NDM-1 PCR result
 - NDM (*bla*_{KPC}) gene DNA Detected
 - NDM (*bla*_{KPC}) gene DNA Not Detected

Notification

- Positive KPC and/or NDM-1
 - Submitter
 - Bureau of Epi SHARP Unit

Where to find.....

MDCH Department of Community Health MICHIGAN.GOV Michigan's Official Website

Michigan.gov Home MDCH Home Sitemap Contact MDCH Search

Providers

- HIPAA
- Health Professional Shortage Area
- Institutional Review Board
- International Medical Graduate Programs
- M-SEARCH
- State Loan Repayment Program
- Lab Services**
- Laboratory Services Guide
- Outreach
- Specimen Submission
- Guidelines for Labs
- Regional Labs
- Communications
- Training
- Biomonitoring Opportunities
- Communicable & Chronic Diseases
- Departmental Forms
- Community Mental Health Services
- Certificate of Need
- Substance Abuse Providers

Bureau of Laboratories

- [MDCH 24/7 EMERGENCY PHONE NUMBER: 517-335-9030](#)
- [What's New?](#)
- [A-Z Test Listing](#)
- [Bureau of Laboratories Holiday Business Hours](#)
- [Laboratory Influenza Page](#)
- [Test Request Forms](#)
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Quick Links

- [Disaster Preparedness in Michigan](#)
- [Michigan Public Health Institute](#)
- [Bureau of Laboratories - Laboratory Services Guide](#)

OPEN MICHIGAN MDCH SCORECARD

Laboratory Services Guide
[Click here for:](#) Guide to Laboratory Services

Outreach
[Click here for:](#) outreach information and activities

Specimen Submission
[Click here for:](#) Information on specimen submission, including specimen collection instructions, test request forms and specimen submission guidelines.

Guidelines for Labs
[Click here for:](#) Guidelines for Labs

Regional Labs
[Click here for:](#) The Michigan Regional Lab System

Communications
[Click here for:](#) our Newsletter and Urgent Notification archive

Training
[Click here for:](#) training information

Biomonitoring Opportunities
[Click here for:](#) General information about lab services relating to chemical and toxicological testing.

<http://www.michigan.gov/mdchlabs>



Providers

HIPAA

Health Professional Shortage Area

Institutional Review Board

International Medical Graduate Programs

M-SEARCH

State Loan Repayment Program

Lab Services

Laboratory Services Guide

Outreach

Specimen Submission

Guidelines for Labs

Regional Labs

Communications

Training

Biomonitoring Opportunities

Communicable & Chronic Diseases

Departmental Forms

Community Mental Health Services

Certificate of Need

Substance Abuse Providers

Test Request Forms

The Bureau of Laboratories is pleased to offer you the option of downloading test requisitions directly to your printer. Some of these forms are fillable prior to printing. All forms are in the process of being converted to fillable forms.

Download a test requisition form from the selection below:

For best printing of forms, use the print button on the Adobe Acrobat software instead of your browsers print button. Please note that most forms are two pages. It is essential to print and submit the entire form.

- Blood Lead Test Request [DCH-0696 \(Instructions for completing form DCH-0696\)](#) - updated 4/20/2011
- CD4/CD8 & HIV-1 Viral Load Testing [DCH-0583](#) (form change) - updated 05/02/2012
- CDC Submission Form, [CDC 50.34](#)
- CDC Lyme Disease Case Report Form, [CDC 52.60](#)
- *Chlamydia trachomatis/Neisseria gonorrhoeae* (non-culture), [DCH-1248](#) - updated 01/10/2012
- Environmental Lead Sampling [DCH-0558](#) (The form prints best using a color printer) - updated 5/5/2011
- HIV-1 Genotyping [DCH-0583](#) (form change) - updated 05/02/2012
- Microbiology/Virology [DCH-0583](#) - updated 10/23/2012 **NOTE: This is a 2 page form. Both pages must be printed, completed and submitted to avoid testing delays.**
- Multiple Patient/Sample - Same Test [DCH-1052](#) - updated 2/2/2012
- PCB & Pesticide Test Request [DCH-0571](#) - updated 9/15/2011
- Rabies Testing - Lower Peninsula [DCH-1053](#) - updated 8/13/2010
- Sentinel Physician [DCH-1583Sent](#) - updated 9/11/2009
- Tick Identification and Test Form ([MDARD form](#)) - updated 09/28/2012
- Trace Metals Test Requisition [DCH-0976](#)
- Vaccinia/Variola/Pox Virus [DCH-1396](#) - updated 2/2/2012

The following test requisition cannot be downloaded from this site. To order, please contact Mark Warstler at the MDCH Lab Support Unit by Fax 517-335- 9039, phone 517-335-9040, or E-mail at WarstlerMI@michigan.gov.

- Dried Blood Spot; HIV - DCH-0689 ([Instructions](#)) - updated 8/29/2012

The following test requisitions must be ordered by contacting Accounting, as there is a fee associated with the testing. Please call 517-241-5583 for more information.

Related Content

- Explore Lab Science Program
- MDCH BOL CLIA Certificate **FOR**
- Bioterrorism Laboratory Preparedness
- Radiological Preparedness
- What's New?
- Laboratory Influenza Page
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- Specimen Submission Guidelines
- Specimen Collection Instructions
- Clinical Specimen Collection Units
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Microbiology/Virology Test Requisition

Bureau of Laboratories Michigan Department of Community Health

PO Box 30035 3350 North Martin Luther King Jr. Blvd. Lansing Michigan 48909

Laboratory Records: 517-335-8059 Fax: 517-335-9871 Technical Information 517-335-8067 Web: [HTTP://www.Michigan.gov/mdchlab](http://www.Michigan.gov/mdchlab)

Date Received at MDCH										MDCH Sample #																	
AGENCY - SUBMITTER INFORMATION										ENTER STARLIMS AGENCY CODE																	
Return Results to:					FP <input type="radio"/>					Phone (24/7)																	
					STD <input type="radio"/>					FAX																	
PHYSICIAN OF RECORD/LEGALLY AUTHORIZED PERSON ORDERING TEST										NATIONAL PROVIDER IDENTIFIER:																	
PATIENT INFORMATION - NAME (LAST, FIRST, MIDDLE INITIAL OR UNIQUE IDENTIFIER) Must Match Specimen Label Exactly																											
SUBMITTER'S PATIENT #-IF APPLICABLE																											
PATIENT'S CITY-RESIDENCE										ZIP CODE					GENDER <input type="radio"/> Female <input type="radio"/> Male												
RACE		<input type="radio"/> BLACK/AA <input type="radio"/> WHITE <input type="radio"/> NATIVE AMERICAN OR ALASKAN <input type="radio"/> ASIAN <input type="radio"/> HAWAIIAN/PI <input type="radio"/> UNKNOWN <input type="radio"/> OTHER (SPECIFY): _____																									
ETHNICITY					HISPANIC <input type="radio"/> YES <input type="radio"/> NO <input type="radio"/> UNKNOWN ARAB DESCENT <input type="radio"/> YES <input type="radio"/> NO <input type="radio"/> UNKNOWN					DATE OF BIRTH		M		M		D		D		Y		Y		Y		Y	
SUBSCRIBER INFORMATION <input type="radio"/> MEDICAID <input type="radio"/> PLAN FIRST! <input type="radio"/> ADAP <input type="radio"/> DOC <input type="radio"/> OTHER _____																											
SUBSCRIBER NUMBER																											

SUBMITTER'S SPECIMEN # - IF APPLICABLE

DATE COLLECTED

M

M

D

D

Y

Y

Y

Y

TIME COLLECTED

O
A.M.

O
P.M.

INDICATE TEST REQUESTED

(complete specimen source information on back)

SEROLOGY

- ARBOVIRUS ENCEP PANEL(IgM)§
- BRUCELLA SEROLOGY
- FUNGAL SEROLOGY
COMPLEMENT FIXATION
- FUNGAL IMMUNODIFFUSION
- FRANCISELLA SEROLOGY
- LEGIONELLA - HA
- LYME DISEASE - EIA
Complete # 4 (reverse)
- MEASLES IgG
- MUMPS IgG
- RABIES AB SEROLOGY
Complete # 3 (reverse)
- RUBELLA IgG
- TETANUS TOXIN EIA
- VARICELLA ZOSTER IgG
§ May – October Includes Eastern Equine, California, St. Louis and West Nile. CSF only

SERUM STATUS - If Applicable

- Acute Convalescent

MISCELLANEOUS

- AUTOCLAVE TEST STRIPS
- LEGIONELLA - DFA
- LYME DISEASE EIA (TEA)

SYPHILIS TESTING

- SYPHILIS (USR Test)
- SYPHILIS VDRL - CSF Only
- SYPHILIS DFA
Complete # 2 (reverse)
- SYPHILIS FTA - ABS DS+
- SYPHILIS IgM WESTERN BLOT*
- SYPHILIS TP-PA*
(* Prior Approval Required)

HIV TESTING

- HIV AB/AG – Serum
- HIV AB - Oral Mucosal Transudate
- CD4/CD8
(EDTA whole blood)
- HIV-1 VIRAL LOAD
(EDTA plasma)
- HIV-1 GENOTYPING
(EDTA plasma)

HEPATITIS TESTING

- HEPATITIS C SCREEN
- HBsAg Complete #1 (reverse)
- HEPATITIS B SURFACE AB
(Anti-HBs)
- HEPATITIS A VIRUS (IgM)

MICROBIOLOGY

- AEROBIC ISOLATE ID
Complete # 5 (Reverse)
- AFB SUSCEPTIBILITY
- AFB SLIDE/CULTURE-CLINICAL SPECIMEN
- AFB Identification – Isolate ID
- C. trachomatis (Non-culture)¹
- E. coli (SLT) TOXIN & SEROLOGY
- ENTERIC BACTERIAL CULTURE
- FOODBORNE ILLNESS - Stool or Food Complete # 6 (Reverse)
- FUNGAL IDENTIFICATION– Isolate ID
- LEGIONELLA CULTURE
- NEISSERIA GONORRHOEAE - Isolation
- NEISSERIA - REFERRED CULTURE
- PARASITOLOGY – BLOOD
- PARASITOLOGY – STOOL
- PARASITOLOGY – WORM
- PERTUSSIS PCR
- Salmonella/Shigella SEROTYPING-Human

VIROLOGY

- ENTEROVIRUS PCR
- INFLUENZA (PCR/Culture)
Complete #7 (Reverse)
- RESPIRATORY PCR PANEL
- VIRAL CULTURE

Tests That Require Prior MDCH Approval

- BACTERIAL TYPING – PFGE Complete # 6 (Reverse)
- BOTULISM TOXIN
- MUMPS - PCR
- MEASLES IgM @ CDC
- NOROVIRUS PCR
Complete # 6 (Reverse)
- PERTUSSIS CULTURE
- RUBELLA IgM
- SALMONELLA SEROTYPING (Non-Human)
- TOXIC SHOCK TESTING

CRE Confirmation

Other: _____

Other: _____

Write test name CRE Confirmation in box for “other”

2 IF REQUESTING EXAMINATION FOR: SYPHILIS - DFA COMPLETE THIS SECTION

Duration of Lesion				<input type="radio"/> Days <input type="radio"/> Months <input type="radio"/> Years	Specify Site:
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3 IF REQUESTING EXAMINATION FOR: RABIES ANTIBODY SEROLOGY COMPLETE THIS SECTION

Date of Last Rabies Vaccination	<input type="text"/>									
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4 IF REQUESTING EXAMINATION FOR: LYME BORRELIOSIS COMPLETE THIS SECTION

ONSET DATE	<input type="text"/>	State/County/Country of Exposure	<input type="text"/>								
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EARLY DISEASE	<input type="checkbox"/> Erythema migrans	<input type="checkbox"/> Symptoms (Specify): _____ (5 cm at least in diameter) (Ex., Rash, Fever, Headache, Joint Pain)	LATE DISEASE	<input type="checkbox"/> Neurologic	<input type="checkbox"/> Cardiac	<input type="checkbox"/> Rheumatologic
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5 IF REQUESTING EXAMINATION FOR: AEROBIC CULTURE COMPLETE ALL THAT APPLY

Aerobe Microaerophile Gram Positive Negative Variable Rod Coccus Diplococcus

Bacterial Growth Char.: MacConkey Pos Neg Oxidase Pos Neg Catalase Pos Neg Dextrose Oxidation Fermentation

Other: _____

Enter organism ID, Modified Hodge Test result.

Attach copy of Microscan or Vitek printout

6 IF REQUESTING EXAMINATION FOR: OUTBREAK INVESTIGATION COMPLETE THIS SECTION

ONSET DATE	<input type="text"/>								
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OUTBREAK IDENTIFIER (Foodborne ONLY - If Applicable)

ORGANISM SUSPECTED (If Applicable)

MDCH Prior Approval: Name, date or code

7 IF REQUESTING EXAMINATION FOR: ... COMPLETE THIS SECTION

Questions?