**University of Washington Medical Center**

Clinical Microbiology Laboratory Document # 601.U.115.02

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| Antibiotics Manual  **Carbapenem-Resistant Gram-Negative Rod Reporting and DOH Surveillance** | | Effective: 4/20/18 |
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| Revises or supersedes: 6/1/2015 | | Revised by: Heather Berger |

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| ANNUAL REVIEW | | | |
| Reviewed by: | Date | Reviewed by: | Date |
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# Purpose

# Washington State Department of Health has conducted ongoing surveillance for carbapenem-resistant Enterobacteriaceae (CRE) since 2012. CRE are highly antibiotic resistant bacteria that have been deemed an “urgent threat” due to the associated high morbidity and mortality and their ability to spread readily in healthcare settings. CRE can develop resistance to carbapenems by a variety of mechanisms; most concerning among these mechanisms is the ability to produce carbapenemase because the genes involved are located on mobile pieces of DNA called plasmids that can easily spread to other bacterial species and genera. This document describes how the University of Washington clinical microbiology laboratory will test, report and send Enterobacteriaceae isolates for further testing at the DOH state laboratory. This document uses the term and taxonomic classification Enterobacteriales (an order) in place of the family Enterobacteriaceae to include other families, specifically Morganellaceae (which includes *Proteus* spp.). All Enterobacteriales are approved for clinical use. Other organisms such as, non-mucoid *Pseudomonas* species from non-cystic fibrosis specimens, and *Acinetobacter* species are further sent for carbapenemase testing, but will only be documented in the culture workup and not reported.

# Procedure

1. Preliminary reporting by the routine benches.
2. The [MDROC] code will be added to the organism line when the required phenotypic testing criteria are met see 601.U347 MDRO Reporting criteria for Gram Negative Rods.
3. For *Enterobacteriales* isolates that have non-susceptible imipenem or meropenem results, all beta-lactam antibiotic results will be suppressed by the Trek system.

***Exception***

* If ertapenem is non-susceptible, and imipenem and meropenem test susceptible, sensitivity results will not be suppressed and will be reported as tested. The organism will be sent for carbapenemase testing.
* If imipenem is non-susceptible for *Proteus, Providencia* or *Morganella* and the other carbapenems test susceptible, the susceptibility will be reported as tested. This phenotype is not considered to be an MDRO, and the organism will not be sent for rule out carbapenemase testing.

1. The technologist will have to manually un-suppress and report the resistant drugs and keep the sensitive and intermediate drugs suppressed. See the process document Trek GN Panel and Reporting Guidelines for information of reporting panels from the Trek system. The following list of drugs are beta-lactam antibiotics that may be reported for urines and non-urine sites:

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| Enterobacteriales | | Enterobacteriales | |
| (urine, non-Salm) | | (non-urine, non-Salm) | |
| Ampicillin | Ampicillin | |
| Amp/sulbactam | Amp/sulbactam | |
| Aztreonam | Aztreonam | |
| Cefazolin | Cefazolin**1** | |
| Cefepime | Cefepime | |
| Cefotetan **3** | Cefotetan**1,3** | |
| Ceftazidime | Ceftazidime | |
| Ceftazidime-avibactam **4** | Ceftazidime-avibactam **4** | |
| Ceftolozane-tazobactam **4** | Ceftolozane-tazobactam **4** | |
| Ceftriaxone | Ceftriaxone | |
| Ertapenem | Ertapenem | |
| Imipenem**2** | Imipenem**2** | |
| Meropenem | Meropenem | |
| Pip/tazobactam | Pip/tazobactam | |

1. Not reported on isolates from CSF

2. Not reported if both meropenem and imipenem are susceptible

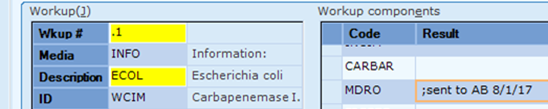
3. Do not report on *C.freundii* isolates when using Sensititre panels

4. Do not report unless requested or automatically released when resistant to all

tested beta-lactams (not to include aztreonam).

1. All sensitive beta-lactam antibiotics which may include ampicillin, amp-sulbactam, aztreonam, cefazolin, cefepime, cefotetan, ceftazidime, ceftriaxone, ertapenem, imipenem and meropenem are suppressed and not reported until at least ***one negative*** rule out carbapenemase test results are available, generally this will be the more rapid Carba-R test.
2. Report FSTF {further sensitivities to follow} in the culture report if any beta-lactam sensitivities are pending rule out carbapenemase testing. Do not report FSTF if all beta-lactam antibiotics are resistant and only carbapenemase testing is pending.
3. Non-mucoid, non-cystic *Pseudomonas* and *Acinetobacter* species will not have susceptibility results altered if any of the tested carbapenems show non-susceptible results. The full susceptibilities will be reported as tested by the Trek system.
4. Submission of isolates to the antibiotics section for carbapenemase testing.
5. There is a one month referral time period between previous rule out carbapenemase testing as long as the identification and susceptibility match the previously tested isolate from the same site. If the organism is isolated from a different site carbapenemase testing should be performed.
6. The following phenotypic susceptibility criteria should be met to initiate carbapenemase testing (See **attached document: 601.U.339 Carbapenemase Testing Chart**):
7. Testing (CIM and Carba-R PCR) is performed on all *Enterobacteriales*which are non-susceptibleto one or more of the following carbapenem antibiotics; ertapenem, imipenem or meropenem.
8. Exception: *Proteus* species, *Providencia* species, and *Morganella morganii*, which have higher imipenem MICs should be either ertapenem or meropenem non-susceptible, unless ordered by special request.
9. Non-mucoid imipenem or meropenem non-susceptible ***Pseudomonas* species** from non-cystic fibrosis patients, unless ordered by special request will be tested by CIM test only and is considered RUO-*research use only*. Do not report results in the LIS.
10. Imipenem or meropenem non-susceptible ***Acinetobacter* species** unless ordered by special request will be tested by CIM test only and is considered RUO-*research use only*. Do not report results in the LIS.
11. Place a meropenem disk whenever possible on any blood agar sub-cultures, to exert selective pressure on the isolate for testing. Sub-culture plates with a meropenem disk are preferred for PCR/CIM testing, but not absolutely required (see Procedure for Carbapenemase Inactivation Method).
12. The routine bench will create a workup for carbapenemase testing as follows:
13. Enter the result on workup number 80.\_#\_ = the organism’s culture line number, e.g., 80.1 if on line 1, 80.2 if on line 2, etc.).
14. At the <Media>: enter {INFO}.
15. At the <Description>: enter the organism code e.g., {ECOL}, {KPNE}, {PAER}, {ABCC} etc.
16. At the <ID>: enter WCIM, this will prompt for several workup component code.
17. At workup code <MDRO>: enter {date sent to the antibiotics section for CIM testing}

**Example of workup for carbapenemase testing:**



1. Print a culture report and send a pure culture of the organism. Effort should be taken to reduce sub-culturing of isolates because there may be a loss of resistance mechanisms contained on plasmids.
2. All isolates sent to the antibiotic’s section for carbapenemase testing will be stocked according to routine bench stocking protocol (ie; S or BB stocking numbers and documented in W60.1 workup numbers). See general laboratory stocking procedure for further information.
3. Isolates must be sent to the antibiotic’s section by 1:00 pm in order for the Gene Xpert Carba-R PCR test to be performed the same day. Typical run time is 69 minutes.
4. Genotypic testing is performed for all *Enterobacteriales*using the Gene Xpert Carba-R assay, unless by special request for *Pseudomonas* spp. or *Acinetobacter* spp. See section C for reporting results from genotypic testing.
5. After genotypic testing is performed on all submitted *Enterobacteriales*, phenotypic carbapenemase testingshall be done by the antibiotic’s section using the Carbapenemase Inactivation Method Test (CIM), see Procedure for Carbapenemase Inactivation Method for specific testing information.
6. *Acinetobacter* and *Pseudomonas* species: perform the CIM test only and document in the workup. Do not report CIM results for *Pseudomonas* species and *Acinetobacter* species in the electronic medical record or report in the LIS, and do not charge for the test. Positive or questionable results should be reported to the Lead, microbiology fellow or Director.
7. After carbapenemase testing is performed the following results will be entered by the antibiotics section:
8. **CINM**: enter [POS, NRN, or INDET] positive, negative or indeterminate as a result for this field.
9. **ZNCIM**: enter the zone size for the CIM.
10. **INCIM**: enter the zone size if there are inner colonies within the zone of inhibition around the meropenem disk.
11. **CARBAR**: enter results of Carba-R PCR testing.
12. **NOTIFY**: if the CIM is positive enter who is notified ie: floor/provider, infection control, and state lab.
13. See section D for further information on Carbapenemase Inactivation Method (CIM) reporting.
14. Genotypic carbapenemase PCR result reporting (Carba-R) by the routine benches:
15. **Negative PCR testing and reporting:**
16. The antibiotics section will enter the negative results into the workup at the <CARBAR> prompt with the NRN code.
17. Always send *E.coli, Klebsiella sp, and Enterobacter sp* to the DOH for further testing if resistant to any carbapenem. Do not send if carbapenem results are intermediate only.
18. In the <Workup components:> section, enter MDRO: NOKPC. Add the following comment to the workup only with the date sent: SSPHL- {Sent to Washington State Public Health Lab for confirmation-;date.}
19. Release the suppressed susceptible/intermediate beta-lactam MIC values as tested by the Trek system.
20. Setup the phenotypic CIM test. See section D for reporting.
21. Do not final the cultures until all results are entered for carbapenemase testing, including the DOH results.
22. For stand-alone rule out carbapenemase testing for outside clients, or by request only, the Carba-R negative test can be reported: {CARBNG} *IMP, VIM, NDM, KPC, and OXA-48 carbapenemase DNA sequences not detected by PCR*.
23. **Positive testing by PCR and State Laboratory notification:** results will be entered in the workup of the culture and the report by the antibiotics section.
24. Positive PCR resulting codes are to be reported as follows:
25. **IMPCAR** (GNIMP-PCR-MDRO-ICCOMC-REPT0): *Imipenem-resistant metallo-beta-lactamase (IMP) gene detected. Likely resistant to penicillins, cephalosporins, and carbapenems (but not aztreonam).(Methodology: real time PCR). Multi-Drug Resistant Organism – For inpatients, isolate using contact precautions per institutional policy. Contact Infection Control if you have any questions. - This result is a Washington state Notifiable condition. Contact public health authorities in accordance with WAC 246-101.*

<http://www.doh.wa.gov/Portals/1/Documents/5100/210-001-Poster-HCP.pdf>

1. **VIMCAR** (GNVIM-PCR-MDRO-ICCOMC-REPT0): *Verona integron-encoded metallo-beta-lactamase (VIM) gene detected. Likely resistant to penicillins, cephalosporins, and carbapenems (but not aztreonam). (Methodology: real time PCR). Multi-Drug Resistant Organism – For inpatients, isolate using contact precautions per institutional policy. Contact Infection Control if you have any questions. - This result is a Washington state Notifiable condition. Contact public health authorities in accordance with WAC 246-101.*

<http://www.doh.wa.gov/Portals/1/Documents/5100/210-001-Poster-HCP.pdf>

1. **NDMCAR** (GNNDM-PCR-MDRO-ICCOMC-REPT0) : *New Delhi metallo beta-lactamase (NDM) gene detected. Likely resistant to penicillins, cephalosporins, and carbapenems (but not aztreonam). (Methodology: real time PCR). Multi-Drug Resistant Organism – For inpatients, isolate using contact precautions per institutional policy. Contact Infection Control if you have any questions. - This result is a Washington state Notifiable condition. Contact public health authorities in accordance with WAC 246-101.*

<http://www.doh.wa.gov/Portals/1/Documents/5100/210-001-Poster-HCP.pdf>

1. **KPCCAR** (GNKPC-PCR-MDRO-ICCOMC-REPT0): *KPC (Klebsiella pneumonia carbapenemase) gene detected. Likely resistant to penicillins, cephalosporins, carbapenems, and aztreonam. (Methodology: real time PCR). Multi-Drug Resistant Organism – For inpatients, isolate using contact precautions per institutional policy. Contact Infection Control if you have any questions. - This result is a Washington state Notifiable condition. Contact public health authorities in accordance with WAC 246-101.*

<http://www.doh.wa.gov/Portals/1/Documents/5100/210-001-Poster-HCP.pdf>

1. **OXACAR** (GNOXA-PCR-MDRO-ICCOMC-REPT0) : *OXA-type beta-lactamase (OXA) gene detected. Possibly resistant to penicillins, cephalosporins, and carbapenems (but not aztreonam). (Methodology: real time PCR). Multi-Drug Resistant Organism – For inpatients, isolate using contact precautions per institutional policy. Contact Infection Control if you have any questions. - This result is a Washington state Notifiable condition. Contact public health authorities in accordance with WAC 246-101.*

<http://www.doh.wa.gov/Portals/1/Documents/5100/210-001-Poster-HCP.pdf>

1. Positive results are called to the floor, infection control (IC). The DOH State Laboratory will be alerted electronically through the LIS.
2. The following information should be entered in the already created culture workup as follows: Workup code<CARBAR>{Target code} for a positive result.
3. Page the micro fellow or director and communicate the positive result. If susceptibility results are hidden for susceptible beta-lactam drugs, have the microbiology fellow determine how the results will be reported.
4. Setup the phenotypic CIM test. See section D for reporting.
5. Within 2 business days the antibiotics section will send the isolate by courier to the state DOH laboratory. See section 7 for further instruction on sending the isolate.
6. Do not final the cultures until the results return from the state lab.
7. Confirm that the organism has been stocked and the ADCARB charge has been added to the culture.

1. **Reporting CIM phenotypic testing for *Enterobacteriales* only.**
2. **Positive CIM resulting, and additional testing for *Enterobacteriales***
3. Positive results for *Enterobacteriales* are reported on the organism line of the culture report:

*{**POSCIM-MDRO-ICCOMC-REPT0-LDTD }*

*“Phenotypic testing is POSITIVE for carbapenemase production by the carbapenem inactivation method. Multi-Drug Resistant Organism-For inpatients, isolate using contact precautions per institutional policy. Contact Infection Control if you have any questions. This result is a Washington state Notifiable condition. Contact public health authorities in accordance with WAC 246-101.* [*http://www.doh.wa.gov/Portals/1/Documents/5100/210-001-Poster-HCP.pdf*](http://www.doh.wa.gov/Portals/1/Documents/5100/210-001-Poster-HCP.pdf) *This test was developed and its performance characteristics determined by the University of Washington Department of Laboratory Medicine in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. FDA.”*

1. Page the Micro Fellow, the floor for in-patients, and hospital Infection Control (IC) to communicate results, if not already done for the PCR results. Document the calls in the workup and in the report.
2. The state lab should be notified of the positive CIM/PCR and asked if they want the isolate forwarded. See section E of this procedure for further information on sending isolates to the state lab.
3. **Indeterminant CIM Resulting and further PCR testing for *Enterobacteriales***
4. Indeterminant results for *Enterobacteriales* are reported on the organism line of the culture report:

{*INDCIM -LDTD}* “*Phenotypic testing is INDETERMINANT for carbapenem production by the carbapenem inactivation method. This test was developed and its performance characteristics determined by the University of Washington Department of Laboratory Medicine in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. FDA.”*

1. **Negative CIM Resulting**
2. Negative results are not routinely reported andwill be documented in the workup under the {CINM} workup code.
3. The following reporting codes may be reported only if the test has been ordered as a stand-alone rule out carbapenemase test.

{NEGCIM-LDTD}: *“Phenotypic testing is negative for carbapenem production by the carbapenem inactivation method. This test was developed and its performance characteristics determined by the University of Washington Department of Laboratory Medicine in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. FDA.”*

1. Discrepant genotypic Carba-R and phenotypic CIM testing
2. If carbapenemase testing is discrepant (ie, PCR negative, CIM positive) consult with antibiotic lead, fellow or director prior to reporting the second result. Reporting of the second carbapenemase test will be determined at the discretion of the Fellow or director.
3. Sending specimens to the State Laboratory for CRE surveillance by the antibiotics section
4. Washington State Department of Health will be notified electronically for CP-CRE (Carbapenemase producing-carbapenemase resistant Enterobacteriales), whether determined by genotypic or phenotypic testing.
5. CP-CRE isolates should be sent to the Washington State Public Health Laboratory within two business days. Other isolates that will routinely be sent are *E. coli, Klebsiella spp., or Enterobacter spp*. resistant to any carbapenem. Other isolate types with questionable or discrepant CIM/PCR results should be discussed with Director/Fellow before sending to the state laboratory.
6. The antibiotic’s section may call the Office of Communicable Disease Epidemiology (OCDE) Phone#: 206-418-5595, to relay questionable results and to inquire if the isolate should be sent for further testing.
7. For non-UW outpatients ask the ordering location to send the isolate to the state lab in order for results to be reported directly to the outside lab.
8. A Public Health Laboratory Microbiology submission form should be completed and faxed to 206-418-5515 along with a copy of the laboratory sensitivity. Forms can be found at: http://www.doh.wa.gov/Portals/1/Documents/5230/302-013-Micro.pdf. In the comments section of the form, indicate the PCR results. It is important that the county that the patient resides in is written on the form, this will allow the DOH to contact the Local Health Jurisdiction of the patient’s residence.
9. A fresh subculture should be packaged as a Biological Substance Category B and sent via UW courier (leaves SPS at 08:00).
10. A copy of the patient report including the full susceptibility results should accompany the isolate and the Public Health Laboratory Microbiology submission form.
11. The antibiotic’s CRE log sheet will be filled out and a copy of the submission form will remain in the Antibiotics section for record keeping.
12. See 601.U.118 Procedure for Send out Responsibilities of the Antibiotic Section for information about sending isolates to the PHL via internal courier.
13. The state lab may decide to send the organism to the CDC for further PCR testing, if this happens add to the workup: SPCDC {*Specimen was sent to the CDC for further evaluation*}.
14. The state lab has a one month referral time between testing specimens from specific patients. This referral includes isolates from different sites such as urine vs. wound cultures. Any questions about referrals should be called to the OCDE.
15. Testing by the State Public Health Laboratory or CDC.
16. If the result is a new positive generated by the state lab, the Micro Fellow/Director must be paged. Inpatient results need to be called to the floor, IC and stock the isolate. The Fellow/Director will determine if the susceptibility results need to be amended.
17. Enter all additional information in the workup and log onto the CRE log sheet in the antibiotic’s bench.
18. Final the culture if all work has been completed.
19. Billing for genotypic and phenotypic carbapenemase testing
20. Billing for Carbapenemase Inactivation Method (CIM) test, add one of the following billing codes to the billing section of the culture for testing *Enterobacteriales* only.

a. **AD1CIM**=first isolate tested.

b. **AD2CIM**=Second isolates tested.

c. **AD3CIM**=Third isolates tested.

1. Billing for Carba-R Carbapenemase PCR testing
2. Add the **ADCARB** billing code to the billing section of the culture.
3. **Attachments**
4. Public Health Laboratory Microbiology submission form
5. 601.U.339 Carbapenemase testing flow chart
6. 601.U.347 MDRO Reporting Criteria for GNRs
7. **Revisions**

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| 6/27/17 | II,2 Rapid carb testing deleted from the procedure and retired. PCR testing by HMC microbiology added.  II,2,e-f: Information about how prepare and send the isolate for PCR testing at HMC Microbiology.  II,4-6: Expanded information on reporting.  Information about CIM testing added.  Revised MDRO definitions added. |
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