Carbapenemase Testing for Carbapenem-Resistant Organisms (CRO)
A Primer for Clinical and Public Health Laboratories

Contents:

Introduction

The intent of this primer is to provide clinical and public health laboratorians with information about tests available for detection of carbapenemases among gram-negative bacteria. It does not describe when carbapenemase testing should be performed. Each facility should work with their antimicrobial stewardship team to implement a plan to detect carbapenemase-producing organisms that is appropriate for the facility and stakeholders served. Recommendations and requirements from local public health departments should be taken into consideration when developing this plan.

Acronyms

AST, Antimicrobial susceptibility test

CRO, carbapenem-resistant organism
CRAB, carbapenem-resistant *Acinetobacter baumannii*
CRE, carbapenem-resistant *Enterobacterales*
CRPA, carbapenem-resistant *Pseudomonas aeruginosa*

CPO, carbapenemase-producing or carbapenemase gene-positive organism
CP-CRAB or CPAB, carbapenemase-producing *Acinetobacter baumannii*
CP-CRE or CPE, carbapenemase-producing *Enterobacterales*
CP-CRPA or CPPA, carbapenemase-producing *Pseudomonas aeruginosa*
Non-CP-CRO, non carbapenemase-producing, carbapenem-resistant organism

Note: Not all **carbapenem-resistant organisms** are carbapenemase producers. Most carbapenemase-producing organisms will test resistant to one or more carbapenems but may test intermediate or susceptible

to one or more carbapenems. Carbapenem resistance mediated by non-carbapenemase mechanisms often involves extended-spectrum beta-lactamase (ESBL) or AmpC beta-lactamase production in combination with permeability defects (e.g., porin mutations or efflux). Carbapenem-resistant organisms with these mechanisms are referred to as non-carbapenemase producing carbapenem-resistant organisms (non-CP-CRO). A phenotypic and/or genotypic test for carbapenemase MUST be performed before reporting an isolate as a **carbapenemase-producing organism**.

CDC provides antimicrobial resistance data (arpsp.cdc.gov/profile/antibiotic-resistance?tab=ar-lab-network) that demonstrate the percentages of CRO that are CPO. Generally, about a third of CRE are CPE. In contrast, fewer than 5% of CRPA produce carbapenemase. CRAB are more complicated as approximately 90% harbor OXA-23 OXA-24/40 and/or OXA-58 etc., but few CRAB harbor one of the most common carbapenemase genes (KPC, NDM, VIM, IMP, OXA-48).

The main methods (CLSI endorsed, or FDA cleared) for detection of carbapenemases when testing isolates, positive blood cultures and rectal swabs are listed in Table 1 along with their applicability for use with Enterobacterales, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.

Table 1. Tests for Carbapenemases in Gram-Negative Bacteria

Method	Routinely performed on[1]			Enterobacterales	*Pseudomonas aeruginosa*	*Acinetobacter baumannii*
	Isolates	Positive blood cultures	Rectal Swabs			
Phenotypic (for isolates)						
Modified Carbapenem Inactivation Method (mCIM) with or without EDTA Carbapenem Inactivation Method (eCIM)	yes	no	no	yes	yes (mCIM only)	no
CarbaNP[2]	yes	no	no	yes	yes	no
BioMerieux Rapidec® Carba NP	yes	no	no	yes	yes	no
BD Phoenix™ CPO Detect	yes	no	no	yes	yes	yes
Genotypic / Other						
Cepheid Xpert® Carba-R	yes	no	yes	KPC, NDM, VIM, IMP, OXA-48-like[3]	KPC, NDM, VIM, IMP, OXA-48-like	KPC, NDM, VIM, IMP, OXA-48-like
Hardy NG-Test® CARBA 5[4]	yes	no	no	KPC, NDM, VIM, IMP, OXA-48-like	KPC, NDM, VIM, IMP, OXA-48-like	no
OpGen Acuitas AMR Gene Panel	yes	no	no	KPC, NDM, VIM, IMP, OXA-48-like, OXA-1, OXA-9[5]	KPC, NDM, VIM, OXA-1	no
Biofire® FilmArray® BCID2 Panel[6]	no	yes	no	KPC, NDM, VIM, IMP, OXA-48-like	KPC, NDM, VIM, IMP, OXA-48-like	KPC, NDM, VIM, IMP, OXA-48-like
GenMark® ePlex BCID[6]	no	yes	no	KPC, NDM, VIM, IMP, OXA (groups 23 & 48)	KPC, NDM, VIM, IMP, OXA (groups 23 & 48)	KPC, NDM, VIM, IMP, OXA (groups 23 & 48)
Luminex® VERIGENE gene detection[6,7]	no	yes	no	KPC, NDM, VIM, IMP, OXA (groups 23, 40, 48 and 58)	KPC, NDM, VIM, IMP, OXA (groups 23, 40, 48 and 58)	KPC, NDM, VIM, IMP, OXA (groups 23, 40, 48 and 58)
Check-Points CPO for BD MAX™	no	no	yes	KPC, NDM, VIM/IMP, OXA-48	KPC, NDM, VIM/IMP, OXA-48	KPC, NDM, VIM/IMP, OXA-48

[1] "Yes" indicates acceptable for specimen / organism group; some laboratories may validate the method for additional specimen types

[2] Performs poorly for OXA-48
[3] Gene targets as described with product label; contact manufacturer for additional information on gene variants targeted
[4] Phenotypic immunological assay that detects specific antigens associated with the 5 main carbapenemases
[5] Varies by species, check product label
[6] Includes organism identification targets for major gram-negative pathogens
[7] *Acinetobacter* target is *Acinetobacter* spp.

Notes:
This list is not exhaustive nor an endorsement of specific products.
Modified Hodge Test (MHT) (PDF) (clsi.org/media/nszl4tbc/_m100_archived_methods_table.pdf) is no longer recommended by CLSI as a reliable method for carbapenemase detection.

Table 2. Features of Various Tests for Carbapenemases

Feature	Phenotypic				Genotypic						
	mCIM / eCIM	**CarbaNP**	**bioMerieux Rapidec® Carba NP**	**BD Phoenix™ CPO Detect**	**Cepheid Xpert® Carba-R**	**Hardy NG-Test® CARBA 5**[1]	**OpGen Acuitas® AMR Gene Panel**	**Biofire® FilmArray® BCID Panel**	**GenMark® ePlex BCID**	**Luminex® VERIGENE**	**Check-Points Check-Direct CPO for BD MAX™**
Test system											
Special equipment needed	No[2]	Yes (pH meter)	No	Yes (BD Phoenix)	Yes	No	Yes	Yes	Yes	Yes	Yes
Kit storage temperature	NA	NA	2-8°C	≈20°C (RT)	2-28°C	4-30°C	15-25°C 2-8°C	15-25°C	2-8°C	2-30°C -20°C	2-25°C
Relative cost / test	$	$ - $$$	$$	$$$	$$$	$$	$$$	$$$$	$$$$	$$$$	$$$
Time to Result	Overnight	≈0.5-2 hr	≈0.5-2 hr	Overnight	≈75 min	≈25 min	≈2.5 hr	≈1 hr	≈1.5 hr	≈2 hr	≈5 hr
Relative expertise / training requirement	++	+++	++	++	+	+	+++	+	+	+++	+++
Test specimen[2]											
Bacterial colonies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No
Positive blood cultures (GNR)	No	No	No	No	No	No	No	Yes	Yes	Yes	No
Rectal swabs	No	No	No	No	Yes	No	No	No	No	No	Yes
Performance											
Results and differentiates big 5 carbapenemases	No	No	No	somewhat[3]	Yes	Yes	Not all[4]	Yes	Yes	Yes	Yes
Allows detection of “rare” or “new” carbapenemases / carbapenemase variants[5]	Yes	Yes	Yes	Yes	No	No	No	No	No	No	No
Impacted by weak carbapenemases (possible false negatives)	Yes	Yes	Yes	Yes	No	Yes	No	No	No	No	No
Impacted by presence of other beta-lactamases (possible false positives)	Yes	Yes	Yes	Yes	No	No	No	No	No	No	No

NA, not applicable; gram-negative rods

[1] Phenotypic immunological assay that detects specific antigens associated with the 5 most common carbapenemases

[2] "Yes" indicates intended specimen type according to test standard (e.g., CLSI) and/or FDA clearance; some laboratories may validate for other specimen types and implement as a laboratory developed test (LDT)

[3] Differentiates Ambler classes (A, B, D)

[4] Varies by species

[5] Broad detection of any carbapenemase without further differentiation.

Notes:

This list is not exhaustive nor an endorsement of specific products.

Some content reflects arbitrary considerations based on experience of the authors.

Table 3. Current CLSI and FDA-recognized Carbapenem Breakpoints[1,2]

Organism Group	Antimicrobial Agent	MIC (µg/ml)			Zone Diameter (mm)		
		Susc	Int	Res	Susc	Int	Res
Enterobacterales	doripenem	≤1	2	≥4	≥23	20-22	≤19
	ertapenem	≤0.5	1	≥2	≥22	19-21	≤18
	imipenem	≤1	2	≥4	≥23	20-22	≤19
	meropenem	≤1	2	≥4	≥23	20-22	≤19
Pseudomonas aeruginosa	doripenem	≤2	4	≥8	≥19	16-18	≤15
	imipenem	≤2	4	≥8	≥19	16-18	≤15
	meropenem	≤2	4	≥8	≥19	16-18	≤15
Acinetobacter spp.	doripenem	≤2	4	≥8	≥18	15-17	≤14
	imipenem	≤2	4	≥8	≥22	19-21	≤18
	meropenem	≤2	4	≥8	≥18	15-17	≤14

[1] CLSI M100 32nd edition (clsi.org/standards/products/free-resources/access-our-free-resources)

[2] FDA STIC (Susceptibility Test Interpretive Criteria) (www.fda.gov/drugs/development-resources/antibacterial-susceptibility-test-interpretive-criteria)

Table 4. Potential Activities of Newer Agents for Bacteria Producing Common Carbapenemases[1,2]

Antimicrobial Agent	Carbapenemase (Ambler Classification)				
	KPC (A)	NDM (B)	IMP (B)	VIM (B)	OXA-48 (D)
Beta-lactam combination agents					
Ceftazidime-avibactam	Yes	No	No	No	Limited
Ceftolozane-tazobactam	No	No	No	No	No
Imipenem-relebactam[3]	Yes	No	No	No	No
Meropenem-vaborbactam	Yes	No	No	No	No
Aztreonam-avibactam[4]	Yes	Yes	Yes	Yes	Yes
Other Agents					
Cefiderocol	Yes	Yes	Yes	Yes	Yes

[1] Adapted from Tenover, FC. Front Cell Infect Microbiol. 2021.

[2] AST must be performed to confirm susceptibility as resistance to these agents can occur

[3] Does not apply to the members of the family *Morganellaceae*

[4] Not FDA approved as of 10/25/22

Tables 5. Strategies for Testing Isolated Colonies for Carbapenemase Production and/or Carbapenemase Genes and Results Reporting

Table 5A reflects testing that may be done to determine if a CRO isolate is a carbapenemase producer and/or harbors a carbapenemase gene and optional comments that may be included on a laboratory report.

Strategies for carbapenemase testing in a laboratory may include:
1. No carbapenemase testing
2. Phenotypic testing only (e.g., mCIM)
3. Genotypic testing only (generally for KPC, NDM, VIM, IMP, OXA-48 only)
4. Both phenotypic and genotypic testing concurrently

In select settings, another strategy would be performance of a phenotypic carbapenemase test first and reflex to genotypic testing when phenotypic test is positive.

Table 5A. Optional Report Comments for Carbapenemase Testing

	Phenotypic Test mCIM[1]	**Genotypic Test KPC, NDM, VIM, IMP, OXA-48[2]**	**Optional Report Comment(s)**
No carbapenemase testing			
1A	Not done	Not done	Carbapenem-resistant [ORGANISM] isolated. Contact laboratory if carbapenemase testing desired.
Phenotypic testing only (e.g., mCIM)			
2A	Negative	Not done	Carbapenem-resistant [ORGANISM] isolated. Carbapenem resistance NOT due to carbapenemase production.
2B	Positive	Not done	Carbapenemase-producing [ORGANISM] isolated. Contact laboratory if carbapenemase characterization desired.
Genotypic testing only (generally for KPC, NDM, VIM, IMP, OXA-48 only)			
3A	Not done	Negative	Carbapenem-resistant [ORGANISM] isolated; KPC, NDM, VIM, IMP, OXA-48 not detected.
3B	Not done	Positive	Carbapenemase-producing [GENE TARGET] [ORGANISM] isolated.
Both phenotypic and genotypic testing concurrently			
4A	Negative	Negative	Carbapenem-resistant [ORGANISM] isolated; KPC, NDM, VIM, IMP, OXA-48 not detected.
4B	Negative	Positive	Carbapenemase-producing [GENE TARGET] [ORGANISM] isolated. Note: There may be rare occasions where a gene target test is positive but phenotypic test is negative.
4C	Positive	Negative	Carbapenemase-producing [ORGANISM] isolated. KPC, NDM, VIM, IMP, OXA-48 not detected Note: Isolate my harbor a carbapenemase gene not included in the gene target tests or produce very large quantities of other beta-lactamases (e.g., AmpC).
4D	Positive	Positive	Carbapenemase-producing [GENE TARGET] [ORGANISM] isolated.

[1] Or other phenotypic test for carbapenemase production
[2] Isolates usually positive for one of the gene targets; occasional isolates may be positive for more than one target

Table 5B. Summary of Key Features of Phenotypic versus Genotypic Tests for Carbapenemases

Feature[1]	Phenotypic (mCIM)	Genotypic
Reagents readily available to most laboratories	√	
Perform with routine laboratory equipment / reagents	√	
Test time to result		√
Identifies specific carbapenemase gene		√
Likely to catch novel carbapenemase genes or gene variants	√	
Relatively low cost/test	√	

[1] May vary depending on the type of phenotypic or genotypic test employed

Carbapenemase Testing Strategy Considerations:

1. Decisions for carbapenemase testing strategies are best made by the clinical microbiology laboratory in consultation with the Antimicrobial Stewardship Team and Infection Control.
2. **If only AST is performed, it cannot be assumed that a CRO is a carbapenemase-producer; a result of "carbapenemase-producing" and/or a specific carbapenemase gene (KPC, NDM, VIM, IMP, OXA-48) must only be provided following testing for carbapenemase production and/or the presence of a carbapenemase gene.**
3. Depending on the prevalence of specific carbapenemases in a facility/region, a laboratory may choose to do a phenotypic carbapenemase test (e.g., mCIM) first on select CRO and subsequently reflex to a genotypic test only on isolates carbapenemase positive with a phenotypic test.
4. Most genotypic tests do not target all known carbapenemase variants. Isolates that are carbapenemase positive with a phenotypic test and negative for the 5 major carbapenemase genes likely harbor an uncommon variant, uncommon carbapenemase or a previously unrecognized carbapenemase. Contact your local public health department to discuss such unusual findings to determine if further testing such as whole genome sequencing may be warranted.
5. Even if an isolate that produces a specific carbapenemase tests susceptible to an agent that is generally targeted against the carbapenemase, resistance can occur. For example, although most *Klebsiella pneumoniae* that produce KPC are susceptible to ceftazidime-avibactam, some isolates can demonstrate resistance to ceftazidime-avibactam.
6. It is possible that a CRO may harbor more than one carbapenemase gene.

Table 6. CRO Examples

Scenario A. CR *Enterobacter cloacae* – mCIM negative
Scenario B. CR *Klebsiella pneumoniae* – KPC positive
Scenario C. CR *E. coli* – NDM positive
Scenario D. CR *Pseudomonas aeruginosa* – VIM positive
Scenario E. CR *Acinetobacter baumannii* [OXA-23 Positive]
Scenario F. CR *Klebsiella pneumoniae* – KPC and NDM positive
Scenario G. CR *Pseudomonas aeruginosa* – mCIM positive [GES positive]
Scenario H. CR *Acinetobacter baumannii* – NDM positive and OXA-23 positive

The following scenarios illustrate routine antimicrobial susceptibility test results that may be encountered for CRO and a few highlights about each profile. A publication by Tamma et al, 2022 (www.idsociety.org/practice-guideline/amr-guidance) suggests antimicrobial agents for treating infections due to highly resistant gram-negative organisms. This can be used as a guide for testing specific agents as well.

Scenario A. CR *Enterobacter cloacae* – mCIM negative

Antimicrobial Agent	MIC (µg/mL)
Amikacin	4 S
Ampicillin	>32 R
Cefazolin	>32 R
Cefepime	4 SDD
Ceftazidime-avibactam	**≤1/4 S**
Ceftriaxone	>32 R
Ciprofloxacin	>4 R
Ertapenem	**>4 R**
Gentamicin	2 S
Meropenem	**1 S**
Piperacillin-tazobactam	>128/4 R
Tobramycin	2 S
Trimethoprim-sulfamethoxazole	>4/76 R

Highlights for Scenario A.

- Resistance to ertapenem but susceptibility to meropenem can occur when beta-lactamases (e.g., AmpC) other than carbapenemases are produced in large quantities. This is not an unusual finding in *Enterobacter* species, particularly *E. cloacae*.
- Phenotypic carbapenemase tests such as mCIM may be positive due to hyperproduction of AmpC. (Pierce et al, 2017)
- Results for other drug classes can vary in isolates resistant to ertapenem but susceptible to meropenem.
- On rare occasions, one of the most common carbapenemases (KPC, NDM, VIM, IMP, OXA-48) may confer resistance to ertapenem but not to other carbapenems.

Scenario B. *Klebsiella pneumoniae* – KPC positive

Antimicrobial Agent	MIC (µg/mL)
Amikacin	16 S
Ampicillin	>32 R
Cefazolin	>32 R
Cefepime	>32 R
Ceftazidime-avibactam	**≤1/4 S**
Ceftriaxone	>32 R
Ciprofloxacin	>4 R
Ertapenem	**>4 R**
Gentamicin	8 I
Meropenem	**>4 R**
Piperacillin-tazobactam	>128/4 R
Tobramycin	8 I
Trimethoprim-sulfamethoxazole	>4/76 R

Highlights for Scenario B.

- Resistant results from phenotypic testing for beta-lactams shown here are consistent for a KPC producer, however, resistance mechanisms other than KPC may produce similar phenotypic results.
- Most, but not all, isolates that produce KPC, a serine carbapenemase, are susceptible to ceftazidime-avibactam.
- Other beta-combination agents that may warrant testing against isolates harboring serine carbapenemases include imipenem-relebactam and meropenem-vaborbactam.

Scenario C. *E. coli* – NDM positive

Antimicrobial Agent	MIC (µg/mL)
Amikacin	>64 R
Ampicillin	>32 R
Cefazolin	>32 R
Cefepime	>32 R
Ceftazidime-avibactam	**>16/4 R**
Ceftriaxone	>32 R
Ciprofloxacin	>4 R
Ertapenem	**>4 R**
Gentamicin	>16 R
Meropenem	**>4 R**
Piperacillin-tazobactam	>128/4 R
Tobramycin	>16 R
Trimethoprim-sulfamethoxazole	>4/76 R

Highlights for Scenario C.

- Resistant results from phenotypic testing for beta-lactams shown here are consistent for a NDM producer, however, resistance mechanisms other than NDM may produce similar phenotypic results.

- Isolates that produce NDM, a metallo-beta-lactamase, are resistant to ceftazidime-avibactam, imipenem-relebactam and meropenem-vaborbactam.
- Special testing for aztreonam-avibactam may be warranted.[Bhatnagar, 2021; AR Lab Network ExAST (www.cdc.gov/drugresistance/ar-lab-networks/domestic/expanded-ast.html].

Scenario D. *Pseudomonas aeruginosa* – VIM positive

Antimicrobial Agent	MIC (µg/mL)
Amikacin	>64 R
Cefepime	>32 R
Ceftazidime	>32 R
Ceftolozane-tazobactam	>16/4 R
Ciprofloxacin	>4 R
Gentamicin	>16 R
Meropenem	**>4 R**
Piperacillin-tazobactam	>128/4 R
Tobramycin	>16 R

Highlights for Scenario D.

- Most CRPA are carbapenem resistant by mechanisms other than carbapenemase production.
- Intermediate or resistant results for ceftolozane-tazobactam and also cefepime and ceftazidime are a clue that a *P. aeruginosa* isolate may produce a carbapenemase. (Vallabhaneni, 2021)
- The most common carbapenemase reported in the USA for *P. aeruginosa* is VIM
- CRPA are resistant to newer beta-lactam combination agents including imipenem-relebactam and ceftazidime-avibactam in addition to ceftolozane-tazobactam.

Scenario E. *Acinetobacter baumannii* – [OXA-23 positive]

Antimicrobial Agent	MIC (µg/mL)
Amikacin	>64 R
Cefepime	>32 R
Ceftazidime	>32 R
Ciprofloxacin	>4 R
Gentamicin	>16 R
Meropenem	**>4 R**
Minocycline	1 S
Piperacillin-tazobactam	>128/4 R
Tobramycin	>16 R
Trimethoprim-sulfamethoxazole	>4/76 R

Highlights for Scenario E.

- Most phenotypic tests for carbapenemase production are not reliable for CRAB.
- Most CRAB produce a carbapenemase, usually OXA-23, a variant which is not included in most commercially available molecular test kits for carbapenemases. OXA-23 was detected with additional molecular testing.
- The only OXA gene target in most commercially available molecular test kits is OXA-48, a gene which is uncommon in *A. baumannii*

Scenario F. *Klebsiella pneumoniae* – KPC and NDM positive

Antimicrobial Agent	MIC (µg/mL)
Amikacin	32 I
Ampicillin	>32 R
Cefazolin	>32 R
Cefepime	>32 R
Ceftazidime-avibactam	**>16/4 R**
Ceftriaxone	>32 R
Ciprofloxacin	>4 R
Ertapenem	**>4 R**
Gentamicin	>16 R
Meropenem	**>4 R**
Piperacillin-tazobactam	>128/4 R
Tobramycin	>16 R
Trimethoprim-sulfamethoxazole	>4/76 R

Highlights for Scenario F.

- Resistant results from phenotypic testing for beta-lactams shown here are consistent for a NDM producer and it would be difficult to suspect the concomitant presence of KPC from this AST profile.
- Isolates that produce NDM, a metallo-beta-lactamase, are resistant to ceftazidime-avibactam, imipenem-relebactam and meropenem-vaborbactam.
- Special testing for aztreonam-avibactam is not warranted when a serine carbapenemase (e.g., KPC) is present together with a metallo-beta-lactamase (e.g., NDM).

Scenario G. *Pseudomonas aeruginosa* – mCIM positive and [GES positive]

Antimicrobial Agent	MIC (µg/mL)
Amikacin	>64 R
Cefepime	>32 R
Ceftazidime	>32 R
Ceftolozane-tazobactam	>16/4 R
Ciprofloxacin	>4 R
Gentamicin	>16 R
Meropenem	**>4 R**
Piperacillin-tazobactam	>128/4 R
Tobramycin	>16 R

Highlights for Scenario G.

- Most CRPA are carbapenem resistant by mechanisms other than carbapenemase production.
- Intermediate or resistant results for ceftolozane-tazobactam and also cefepime and ceftazidime are a clue that a *P. aeruginosa* isolate may produce a carbapenemase. (Vallabhaneni, 2021)
- Carbapenemases such as GES may be found in *P. aeruginosa* but this target is not included in most commercially available molecular test kits for carbapenemases. GES was detected with additional molecular testing.

Scenario H. CR *Acinetobacter baumannii* – NDM positive and [OXA-23 positive]

Antimicrobial Agent	MIC (µg/mL)
Amikacin	>64 R
Cefepime	>32 R
Ceftazidime	>32 R
Ciprofloxacin	>4 R
Gentamicin	>16 R
Meropenem	**>4 R**
Minocycline	>8 R
Piperacillin-tazobactam	>128/4 R
Tobramycin	>16 R
Trimethoprim-sulfamethoxazole	>4/76 R

Highlights for Scenario H.

- Most phenotypic tests for carbapenemase production are not reliable for CRAB.
- Most CRAB produce a carbapenemase, usually OXA-23, a variant which is not included in most commercially available molecular test kits for carbapenemases. OXA-23 was detected with additional molecular testing.
- The only OXA gene target in most commercially available molecular test kits is OXA-48, a gene which is uncommon in *A. baumannii.*
- Other non-OXA carbapenemases (e.g., NDM) are uncommon in *A. baumannii*

References

Bhatnagar A, S Boyd, S Sabour et al. 2021. Aztreonam-Avibactam Susceptibility Testing Program for Metallo-Beta-Lactamase-Producing Enterobacterales in the Antibiotic Resistance Laboratory Network, March 2019 to December 2020. Antimicrob Agents Chemother. 65(8): e00486-21. doi.org/10.1128/AAC.00486-21.

CDC Antimicrobial Resistance Lab Network ExAST Testing (Aztreonam-Avibactam) (www.cdc.gov/drugresistance/ar-lab-networks/domestic/expanded-ast.html)

CDC Antimicrobial Resistance and Patient Safety Portal (arpsp.cdc.gov/profile/antibiotic-resistance?tab=ar-lab-network)

CLSI. 2022. Performance Standards for Antimicrobial Susceptibility Testing, M100 32nd Edition. Clinical and Laboratory Standards Institute, Wayne, PA.

Pierce VM, Simner PJ, Lonsway DR et al. 2017. Modified Carbapenem Inactivation Method for Phenotypic Detection of Carbapenemase Production among Enterobacteriaceae. J Clin Microbiol. 55:2321-2333. doi.org/10.1128/JCM.00193-17.

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Antimicrobial-Resistant Treatment Guidance: Gram-Negative Bacterial Infections. Infectious Diseases Society of America **2022**; Version 1.1. Available at www.idsociety.org/practice-guideline/amr-guidance/. Accessed 26 OCT 2022.

Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America Guidance on the Treatment of AmpC β-lactamase-Producing Enterobacterales, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Infectious Diseases Society of America **2022**; Version 2.0. Available at www.idsociety.org/practice-guideline/amr-guidance-2.0/. Accessed 26 OCT 2022.

Tenover FC. 2021. Using Molecular Diagnostics to Develop Therapeutic Strategies for Carbapenem-Resistant Gram-Negative Infections. Front Cell Infect Microbiol. 11:715821. doi.org/10.3389/fcimb.2021.715821.

Vallabhaneni, S, JY Huang, JE Grass et al. 2021. Antimicrobial Susceptibility Profiles to Predict the Presence of Carbapenemase Genes among Carbapenem-Resistant *Pseudomonas aeruginosa* Isolates. J Clin Microbiol. 19;59(6):e02874-20. doi.org/10.1128/JCM.02874-20.

Additional Resources:

1. CDC Antimicrobial Resistance Lab Network (www.cdc.gov/drugresistance/laboratories.html)

2. CDPH/LACDPH "Testing for Carbapenemase Production Among Carbapenem-Resistant Organisms: When and How?" 10/27/22 Webinar Slides (PDF) (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CPO_webinar_102722.pdf) and Webinar Recording (youtu.be/I6LPBB9EQ8c)

3. CLSI Outreach Working Group Newsletters (clsi.org/meetings/susceptibility-testing-subcommittees/newsletter-archives/)

4. LACDPH MDRO Newsletters for Laboratorians (publichealth.lacounty.gov/acd/Diseases/NMDRO.htm)

5. Sabour S, JY Huang, A Bhatnagar et al. 2021. Detection and Characterization of Targeted Carbapenem-Resistant Health Care-Associated Threats: Findings from the Antibiotic Resistance Laboratory Network, 2017 to 2019. Antimicrob Agents Chemother. 65:e01105-21. doi.org/10.1128/AAC.01105-21

6. Tamma, PD, KE Goodman, AD Harris et al. 2017.Comparing the Outcomes of Patients with Carbapenemase-Producing and Non-Carbapenemase-Producing Carbapenem-Resistant *Enterobacteriaceae* Bacteremia. Clin Infect Dis. 64:257-264. doi.org/10.1093/cid/ciw741

7. Tamma, PD and PJ Simner. 2018. Phenotypic Detection of Carbapenemase-Producing Organisms from Clinical Isolates. J Clin Microbiol. 56: e01140-18. doi.org/10.1128/JCM.01140-18

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