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MC 6.014 Enterobacterales without concern for AmpC Susceptibility Reporting

Purpose

This procedure provides instruction and guidance for routine testing and selective and cascade susceptibility reporting on Enterobacterales, without concern for derepression of AmpC β -lactamase.

Principal and Clinical Significance

The decisions for the most appropriate antimicrobial agents to test and report are made with input from Pharmacy, Infectious Disease and the Clinical Laboratory. The goal is to provide clinically relevant information that will decrease the chance of developing antibiotic resistance, harmful effects of inappropriate antimicrobial use and avoid reporting results that could adversely affect patient care using selective and cascade reporting rules.

Policy Statements

This procedure applies to Microbiologists who perform susceptibility testing.

Special Safety Precautions

Microbiologists are subject to occupational risks associated with specimen handling.

- Biohazard Containment
- Biohazardous Spills
- Safety in the Microbiology Laboratory

Procedure

- 1. Enterobacterales with no concern for derepression of AmpC β-lactamase include:
 - Budvicia species
 - Buttiauxella species
 - Cedecea species
 - Citrobacter amalonaticus, farmeri, gilleni, koseri, sedlakii
 - Cronobacter species
 - Edwardsiella species
 - Escherichia species
 - Ewingella species
 - Erwinia species
 - Klebsiella species
 - Kluyvera species
 - Leclercia species
 - Moellerella species
 - Morganella species
 - Plesiomonas species
 - Providencia species
 - Proteus species
 - Rahenella species
 - Raoultella species
 - Shewanella species
 - Pantoea species
 - Serratia species
 - Tatumella species
 - Yersinia species
 - Yokenella species



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- 2. Antibiotics appropriate for routine testing and reporting for Enterobacterales without concern for derepression of AmpC β-lactamase include:
 - Ampicillin
 - Ampicillin Sulbactam
 - Amoxicillin Clavulanate
 - Cefazolin
 - Ceftriaxone
 - Cefotaxime
 - Ceftazidime
 - Cefepime
 - Piperacillin-tazobactam
 - Gentamicin
 - Tobramycin
 - Ciprofloxacin
 - Levofloxacin
 - Trimethoprim Sulfamethoxazole
 - Ertapenem
 - Imipenem
 - Meropenem
 - Cefiderocol
 - Ceftazidime-avibactam
 - Ceftolozane-tazobactam
 - Imipenem-relebactam
 - Meropenem-vaborbactam
 - Aztreonam
 - Amikacin
 - Nitrofurantoin-Urine only
- Perform susceptibilities using Vitek cards N806 and XN30, MicroScan NUC101 or Kirby Bauer Method.
- 4. Not all antibiotics are available on every panel.
 - Vitek will be the primary method of testing.
 - In most cases, only the N806 cards needs to be performed.
 - Perform XN30 for Cefpodoxime on E. coli, K. pneumoniae and P. mirabilis in urine cultures when cefazolin is resistant and ESBL is negative.
 - Perform XN30 for Imipenem when Meropenem is resistant.
 - MicroScan and Kirby Bauer are back up if testing fails.
 - Do not perform testing on multiple methods to cover all the antibiotics. It is acceptable if cascaded antibiotics are not reported.
 - Cefiderocol is not available in house and would need to be sent out if requested.
- 5. Vitek results will be accepted under the Online Results tab. Modifications will be under the **VITMIC** keyboard under the Susceptibility tab.
- 6. MicroScan and Kirby Bauer results will be entered manually under the **MMIC** and **KB** keyboards respectively under the Susceptibility tab.

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Selective Reporting

- Antibiotics will be reported in a specific order indicating the first and subsequent preferences of the Antimicrobial Stewardship Committee and Infectious Disease physicians
- Antibiotics will be reported depending on the source, if the sample is a urine or nonurine source.
- There will be exceptions based on the method used for testing.
- 4. For **urine sources**, these 7 antibiotics will be reported routinely, in this order.
 - 1. Ampicillin
 - 2. Cefazolin
 - 3. Trimethoprim-Sulfa
 - 4. Ciprofloxacin
 - 5. Gentamicin
 - 6. Nitrofurantoin
 - 7. ESBL

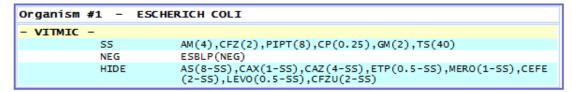
Figure 1 -Only AM, CFZ, TS, CP, GM, FD and ESBL are reported. All other antibiotics are in HIDE

Organism #1 -	ESCHERICH COLI
- VITMIC -	
SS	AM(8),TS(40),CP(0.25),GM(2),FD(32),CFZU(16)
NEG	ESBLP(NEG)
HIDE	CFZ(16-R),AS(8-SS),CAX(1-SS),CAZ(4-SS),ETP(0.5-SS),MERO(1- SS),CEFE(2-SS),LEVO(0.5-SS),PIPT(8-SS)

Figure 2-Only CFZ, TS, CP, GM, FD, ESBL are reported.

- Note: Cefazolin antibiotic code CFZU will report for EC, KLPN, PRMI.
 Code CFZ will be in Hide.
- Note: Cefazolin antibiotic code CFZ will report for all other organisms.
- 5. For **non-urine sources**, these 7 antibiotics will be reported routinely, in this order.
 - 1. Ampicillin
 - 2. Cefazolin
 - 3. Piperacillin-tazobactam
 - 4. Ciprofloxacin
 - 5. Gentamicin
 - 6. Trimethoprim-Sulfa
 - 7. ESBL

Figure 3-Only AM, CFZ, PIPT, CP, GM, TS and ESBL are reported. All other antibiotics are in HIDE.



6. If any carbapenem is resistant, confirm result by alternate method. Report in Sunquest if confirmed resistant and submit isolate to MDH. See Carbapenemase Detection section of procedure for further instructions. Resistant carbapenems will be reported regardless of selective or cascade reporting.

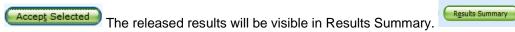
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Cascade Reporting- Vitek Method

If resistance is encountered, additional antibiotics will automatically be released.

1. For Vitek method, hidden antibiotics will be released when Accept Selected is clicked.



Results can be edited under the VITMIC keyboard but is not needed to report the cascaded antibiotics.

Method: Vitek -urine source

- o If Ampicillin is R → report Ampicillin-Sulbactam
 - If Cefazolin is R→ report Ceftriaxone and Cefpodoxime**
 - o If Ceftriaxone is R → report Ceftazidime
 - If Ceftazidime is R → report Ertapenem
 - o If Ertapenem is R → report Meropenem
 - If Gentamicin → report Amikacin***
- **Perform XN30 for Cefpodoxime.
- 4. ***Perform Amikacin testing using the KB method and perform day of use QC.

Figure 4-Ampicillin Sulbactam, Ceftriaxone, Ceftazidime and Ertapenem are released from HIDE due to resistance.

Organism	#6 -	ESCHERICH COLI (STRAIN 4)
- VITMIC (ZZO5)	-	
	SS	GM(<=1),FD(<=16),AS(8),ETP(<=0.12),MERO(<=0.25)
	POS	ESBLP(POS)
	R	AM(>=32),TS(>=320),CP(>=4),CAX(>=64),CFZU(>=32),CAZ(>=32)
	HIDE	CFZ(>=32-R),CEFE(2-R),LEVO(>=8-R),PIPT(<=4-SS)

Figure 5 -Ceftriaxone, Ceftazidime, Ertapenem and Meropenem are released from HIDE due to resistance.

Organism #2	- KLEB	SIELLA OXYTOCA
- VITMIC (ZZO1)	-	
	SS	TS(40),CP(0.25),GM(1),FD(32),MERO(1)
	POS	ESBLP(POS)
	R	CFZ(32),CAX(16),CAZ(16),ETP(2)
	HIDE	AS(8-SS),CEFE(2-SS),LEVO(0.5-SS)

Method: Vitek: -non-urine sources

- o If Ampicillin is R → report Ampicillin-Sulbactam
 - If Cefazolin is R→ report Ceftriaxone
 - o If Ceftriaxone is R → report Ceftazidime
 - If Ceftazidime is R → report Ertapenem
 - o If Ertapenem is R → report Meropenem
 - If Meropenem is R → report Imipenem**
- 5. ** Perform XN30 for Imipenem.

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Figure 6-Ampicilin Sulbactam, Ceftriaxone, Ceftazidime, Ertapenem is released due to resistance

Org #1. - VITMIC -	ESCHE	RICH COLI	
	SS	PIPT(8),CP(0.25),GM(2),TS(40),AS(8),ETP(0.5)	
	R	AM(32),CFZ(16),CAX(4),CAZ(16)	
	NEG	ESBLP(NEG)	
	HIDE	MERO(1-SS),CEFE(2-SS),LEVO(0.5-SS),CFZU(16-SS)	

- 6. All other antibiotics on the panel that are not part of the cascade are hidden. Do not release and report. Hidden antibiotics include:
 - Cefepime
 - Levofloxacin
- 7. Requested antibiotics may be released with a provider request
- 8. Techs will need to confirm the cascade with cefazolin resistance on *E. coli, P. mirabilis and K. pneumoniae*. Dependent on the interpretation of the CFZ and CFZU, the cascade may not work properly. Release antibiotics following the rules of the cascade.
- 9. There will be instances when some antibiotics are not reported due to intrinsic resistance and/or product limitations. One example is *Serratia marcescens*.
 - Ampicillin and Amp Sulbactam are intrinsically resistant and have product limitations and cannot be reported.
 - Piperacillin tazobactam has a product limitation and cannot be reported.
 - Cefazolin is intrinsically resistant but we can report the resistant Cefazolin which will start the cascade so other antibiotics can be reported.

Figure 7 Online and accepted data for Serratia marcescens

```
Organism #1
                       SERRATIA MARCESCENS
  VTTMTC -
                SS
                                CP(<=0.06),GM(<=1),TS(<=20),CAX(<=0.25)
                                CFZ(>=32)
CAZ(<=0.5-SS),ETP(<=0.12-SS),MERO(<=0.25-SS),CEFE(<=0.12-SS),LEVO(<=0.12-SS)
                HTDE
Online Instrument Data
       ID-N806(VK2)
                                                             SUS-N806 (VK2)
        SERRATIA MARCESCENS
                                                    SS
                                                            CP(<=0.06),GM(<=1),TS(<=20)
                                                             CFZ(>=32)
                                                    R
                                                            CAX(<=0.25-SS),CAZ(<=0.5-SS),ETP
(<=0.12-SS),MERO(<=0.25-SS),CEFE
(<=0.12-SS),LEVO(<=0.12-SS)
                                                     HIDE
```

Cascade Reporting-MicroScan Method

If resistance is encountered, additional antibiotics will automatically be released.

For MicroScan method, hidden antibiotics will be released when File

Results will be visible in Results Summary.

Results Summary.

Enter all results manually under the MMIC keyboard. Antibiotics will be released following the cascade rules.

Method: **MicroScan** – urine source

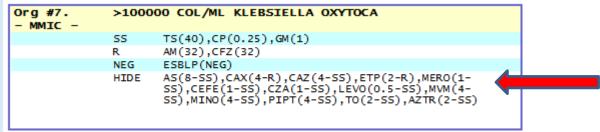
- If Ampicillin is R → report Ampicillin-Sulbactam
 - If Cefazolin is R→ report Ceftriaxone
 - o If Ceftriaxone is R → report Ceftazidime

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- o If Ceftazidime is R → report Ertapenem
 - o If Ertapenem is R → report Meropenem

Figure 8 Ampicillin Sulbactam, ceftriaxone, ceftazidime and meropenem still hidden



3. It will appear as the results are hidden but Sunquest will release from HIDE automatically after results are filed.

Figure 9 Ampicillin Sulbactam, ceftriaxone, ceftazidime and meropenem released from HIDE.

Organism #7	-	>100000 COL/ML KLEBSIELLA OXYTOCA	
- MMIC -		A	
	SS	TS(40),CP(0.25),GM(1),AS(8),CAZ(4),MERO(1)	
	R	AM(32),CFZ(32),CAX(4)	_
	NEG	ESBLP(NEG)	
	HIDE	ETP(2-R),CEFE(1-SS),CZA(1-SS),LEVO(0.5-SS),MVM(4-SS),MINO(4- SS),PIPT(4-SS),TO(2-SS),AZTR(2-SS)	

Method: MicroScan - non-urine sources

- If Ampicillin is R → report Ampicillin-Sulbactam
 - If Cefazolin is R→ report Ceftriaxone
 - If Ceftriaxone is R → report Ceftazidime
 - If Ceftazidime is R → report Ertapenem
 - o If Ertapenem is R → report Meropenem

Figure 10 Example of patient with resistance.

- MMIC -	
SS	PIPT(8),CP(0.25),GM(2),TS(40),AS(8),ETP(0.5)
R	AM(32),CFZ(8),CAX(4),CAZ(16)
NEG	ESBLP(NEG)
HIDE	TO(2-SS),MERO(1-SS),CEFE(2-SS),AZTR(4-SS),CZA(8-SS),LEVO(0.5-SS),MVM(4- SS),MINO(4-SS)

- 4. All other antibiotics on the panel that are not part of the cascade are hidden. Do not release and report. Hidden antibiotics include:
 - Cefepime
 - Tobramycin
 - Levofloxacin
 - Aztreonam
 - Minocycline
 - o Ceftazidime-avibactam
 - o Meropenem-vaborbactam
- 5. Requested antibiotics may be released with a provider request.

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Cascade Reporting- Kirby Bauer Method If resistance is encountered, additional antibiotics will automatically be released.

1. Enter **all** results manually under the **KB** keyboard. Antibiotics will be released following the cascade rules.

Method: Kirby Bauer – urine source

- Ampicillin is R → report Ampicillin-Sulbactam
 - o If Cefazolin is R→ report Ceftriaxone
 - If Ceftriaxone is R → report Ceftazidime
 - o If Ceftazidime is R → report Ertapenem
 - o If Ertapenem is R → report Meropenem
 - o If Gentamicin is R → report Amikacin**
- 2. ** Perform day of use QC for Amikacin.

Figure 11 No resistance

Org #1. - KB -	>1000	00 COL/ML ESCHERICH COLI
	SS	AM(18),CFZ(23),TS(16),CP(26),GM(18)
	HIDE	AS(15-SS),CAX(23-SS),CAZ(21-SS),ETP(22-SS),MERO(23- SS),AK(20-SS),CEFE(25-SS),IMP(23-SS),PIPT(25-SS),TO (17-SS)

Figure 12 -Resistance to Am so AS so is released

Organism #1 -	>100000 COL/ML ESCHERICH COLI
- KB -	
SS	TS(16),CP(26),GM(18),AS(15),CAX(23)
R	AM(13),CFZ(8)
HIDE	CAZ(21-SS),ETP(22-SS),MERO(23-SS),AK(20-SS),CEFE(25- SS),IMP(23-SS),PIPT(25-SS),TO(17-SS)

Method: **Kirby Bauer** – non-urine source

- If Ampicillin is R → report Ampicillin-Sulbactam
 - o If Cefazolin is R→ report Ceftriaxone
 - If Ceftriaxone is R → report Ceftazidime
 - o If Ceftazidime is R → report Ertapenem
 - If Ertapenem is R → report Meropenem
 - If Meropenem is R → report Imipenem

Figure 13 KB keyboard example with resistance

Will redictation
AS(18),ETP(22),GM(18),CP(26)
TS(15)
AM(13),CAX(19),CAZ(17),CFZ(19),PIPT(20)
AK(20-SS),IMP(24-SS),CEFE(21-I),MERO(25-SS),TO(17-SS)

- 3. All other antibiotics on the panel that are not part of the cascade are hidden. Do not release and report. Hidden antibiotics include:
 - Cefepime
 - Tobramycin
 - Amikacin



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4. Requested antibiotics may be released with a provider request.

Method Performance Specifications

- 1. Usually, only the Vitek card AST-N806 will be required for testing Enterobacterales with no concern for AmpC.
- 2. Report Cefpodoxime when Cefazolin is resistant on urine cultures that isolated *E. coli, Klebsiella pneumoniae, Proteus mirabilis* and is ESBL negative.
 - Set up a XN30 card to obtain a Cefpodoxime result and release only the Cefpodoxime. Refer to the MC 6.02 AST-XN30 for further reporting instructions.
- 3. Report Imipenem when Meropenem is resistant on non-urine sources.
 - Set up a XN30 card to obtain the Imipenem result and release only the Imipenem.
 Refer to the MC 6.02 AST-XN30 for further reporting instructions.
- 4. Mucoid isolate susceptibility testing should be performed with the Kirby Bauer method.

ESBL Detection

- . *E. coli, K. pneumoniae, K. oxytoca:* This is performed on Vitek AST-N806 card.
 - If Vitek AES phenotype is ESBL or ESBL (CTX-M LIKE) and ceftazidime and/or ceftriaxone MIC's are non-susceptible, report the ESBL as positive.
 - Confirm with MicroScan if questionable.
 - Change asterisk * results to R. Do not report MIC.
 - Report Meropenem
- 2. Proteus mirabilis: If the Vitek AST-N806 card has an AES finding for ESBL phenotype-
 - Perform MicroScan to confirm.
 - Report Meropenem
 - Refer to MC 6.40 MicroScan MIC procedure for reporting instructions.

Carbapenemase Detection

- 1. If a carbapenem exhibits resistance, confirm the resistant result with an alternate method before reporting results.
 - Confirmation is not needed if patient has known resistance.
- 2. If resistance is not confirmed, report the MicroScan or KB result.
- 3. With known or confirmed resistance:
 - o Report MIC results as tested. Do not change interpretations.
 - Label as MDRO
 - Notify provider
 - Send isolate to MDH Project 1380
 - o Add MDHADD comment
 - o Freeze isolate
- 4. Notify Infection Control with positive mCIM result.
- 5. Report MDH results with NCPO with negative mCIM result or the appropriate Carbapenemase Producer code. e.g. VIM, KPC, NDM, etc.

Carbapenemase Result Reporting

- 1. Result Enterobacterales with resistance to a carbapenem and negative mCIM result as: example-EC-MDRO-NCPO
- 2. Result Enterobacterales with resistance to a carbapenem and positive mCIM result as: example-KLOX-MDRO-KPC
- 3. Add SCAND when MDH reports are scanned.
- 4. Add PRAC with known or previous resistance.

Vitek Product Limitations

Results for an antibiotic/organism combination may have limitations and may be suppressed from reporting. Refer to table below for specific limitations.

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AST-N806 card for Enterobacterales without concern for AmpC

Antibiotic	Product Limitations
Ampicillin	Citrobacter spp., Klebsiella spp. Morganella morganii, Proteus vulgaris and penneri, Providencia rettgeri and stuartii, Raoultella spp., Serratia marcescens and Yersinia enterocolitica are intrinsically resistant. Perform alternate method for Citrobacter spp, Pantoea spp, Serratia spp, Cronobacter sakazakii.
Ampicillin/Sulbactam	Morganella morganii, Providencia rettgeri and stuartii Serratia marcescens and Yersinia enterocolitica are intrinsically resistant. Perform alternate method for Citrobacter spp, Pantoea spp, Serratia spp, Cronobacter sakazakii.
Cefazolin	Morganella morganii, Proteus vulgaris and penneri, Providencia rettgeri and stuartii., Serratia marcescens and Yersinia enterocolitica are intrinsically resistant.
Cefepime	Perform KB on Morganella spp. if requested
Ceftazidime	Perform alternate method on Morganella morganii
Ceftriaxone	Perform alternate method on Proteus vulgaris and Morganella spp.
Ciprofloxacin	Perform alternate method on <i>P. rettgeri</i> MIC = 0.25 or 0.5 Perform alternate method on <i>S. marcescens</i> and <i>K. pneumoniae</i> with MIC = 0.5
Ertapenem	Perform alternate method with MIC of 0.25-0.5
Gentamicin	If resistance is observed on <i>Proteus vulgaris, Citrobacter koseri,</i> Serratia marcescens, send isolate to MDH.
Meropenem	Perform alternate method on <i>Proteus vulgaris</i> Perform alternate method on resistant <i>Klebsiella oxytoca, Proteus mirabilis.</i>
Piperacillin /Tazobactam	Perform alternate method on Serratia marcescens on non-urine isolates.

AST-XN30 card for Enterobacterales without concern for AmpC

Antibiotic	Product Limitations
Amikacin	Not validated. Perform KB and day of use QC
Amoxicillin/Clavulanic	Perform alternate method on <i>Providencia</i> spp.
Acid	Perform alternate method on intermediate or resistant <i>Proteus</i> spp.
Cefpodoxime	Perform alternate method on Morganella morganii, Serratia spp.
Ceftazidime/	Perform alternate method on Providencia rettgeri.
Avibactam	-
Ceftolozane/	Perform alternate method on Morganella morganii, Providencia rettgeri,
Tazobactam	Serratia marcescens
	If resistance is observed on Citrobacter koseri, Proteus mirabilis,
	Proteus vulgaris and Serratia liquefacians, send isolate to MDH.
Cefotaxime	Perform alternate method on <i>Proteus vulgaris</i> with MIC = 1-4 if requested.
Imipenem	Perform alternate method on Proteus spp., Providencia spp.,
	Morganella spp., Serratia spp.
Imipenem/ Relebactam	Perform alternate method on Morganella spp., Proteus spp.,
	Providencia spp., Serratia spp.
Tobramycin	Perform alternate method on <i>Providencia stuartii</i> if requested.

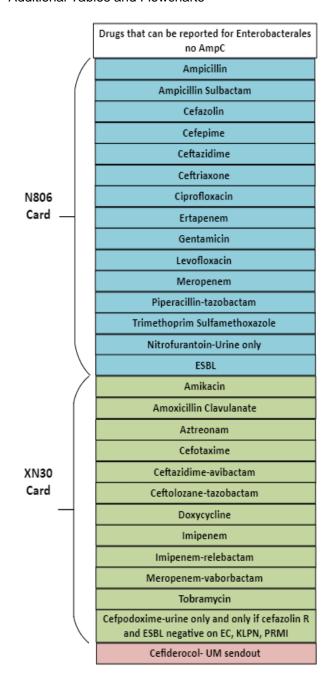


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Appendix

Additional Tables and Flowcharts

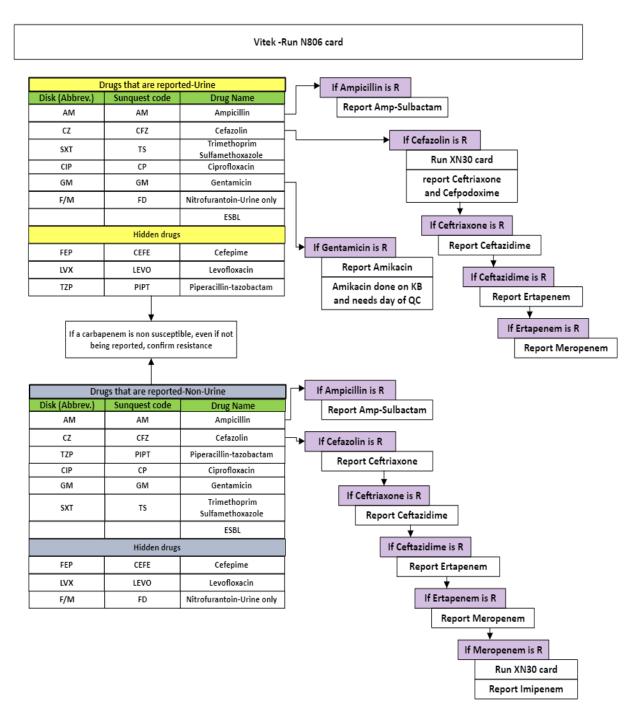


Enterobacterales with no concern for AmpC
Budvicia sp.
Buttiauxella sp.
Cedecea sp.
Citrobacter amalonaticus
Citrobacter farmeri
Citrobacter gilleni
Citrobacter koseri
Citrobacter sedlakii
Cronobacter sp.
Edwardsiella sp.
Escherichia sp.
Ewingella sp.
Klebsiella sp.
Kluyvera sp.
Leclercia sp.
Moellerella sp.
Morganella sp.
Plesiomonas sp.
Providencia sp.
Proteus sp.
Rahenella sp.
Raoultella sp.
Shewanella sp
Pantoea sp.
Serratia sp.
Tatumella sp.
Yersinia sp.
Yokenella sp.



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Microscan-

Pip/Taz is the only drug that is different for reporting with Urine vs Non-Urine Results will appear hidden until they are accepted in Sunquest

	Drugs that are rep	orted	│ ┌ ▶	If Ampi	cillin is R				
icroscan	Sunquest code	Drug Name					٦		
m	AM	Ampicillin	\vdash	Rep	ort Amp-Si	ulbactam			
Cfz	CFZ	Cefazolin	Ь						
Р/Т	PIPT	Piperacillin-tazobactam - Reported for Non-urine Hidden for urine		If Cefaz	olin is R		_		
	СР	Ciprofloxacin		R	eport Ceftr	iaxone			
n	GM	Gentamicin			<u> </u>				
/s	TS	Trimethoprim Sulfamethoxazole			If Ceftriax	one is R			
		ESBL			Repo	rt Ceftazid	ime		
Drugs that are hidden unless cascaded						<u> </u>			
A/S	AS	Amp/sulb				If Ceftazio	lime is R		,
Caz	CAZ	Ceftazidime				Rep	ort Ertape	nem	
Cax	CAX	Ceftriaxone					<u> </u>		
Etp ETP Ertapenem		Ertapenem					If Ertapen	em is R	
Mer MERO Meropene		Meropenem					Repo	rt Merop	en
	Hidden drugs								
Сре	CEFE	Cefepime							
Lvx	LEVO	Levofloxacin]						
То	то	Tobramycin	1						
Azt	AZTR	Aztreonam	1						
Min	MINO	Minocycline	1						

Ceftazidime-Avibactam

Meropenem-Vabrobactam

Cza

Mev

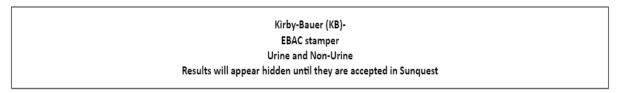
CZA

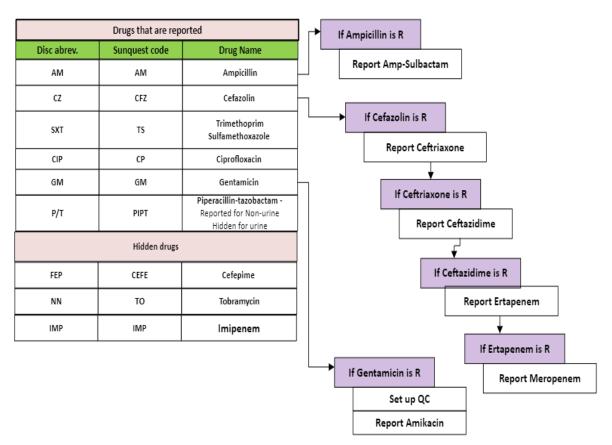
Mev



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References

- 1. bioMerieux Vitek 2 AST-N806 Gram Negative Susceptibility Card 424709 2023-07
- 2. bioMerieux Vitek 2 AST-XN30 Gram Negative Susceptibility Card 424639 20235-04
- 3. Beckman Coulter Diagnostics. 250 South Kraemer Boulevard. Brea, CA 92821-6232 USA,



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MicroScan® Dried Gram Negative (8/2022).

4. CLSI M100 edition 34 Performance Standards for Antimicrobial Susceptibility Testing 2024

Training Plan/ Competency Assessment

Tra	aining Plan	Initial Competency Assessment		
1. 2.	Employee must read the procedure. Employee will observe trainer performing the procedure.	1.	Direct observation.	
3.	Employee will demonstrate the ability to perform procedure, record results and document corrective action after instruction by the trainer.			

Historical Record

Version	Version Written/Revised by:		Summary of Revisions		
1	Susan DeMeyere	11/12/2024	Initial version		