MC 6.015 Enterobacterales with concern for AmpC Susceptibility Reporting

Purpose

This procedure provides instruction and guidance for routine testing and selective and cascade susceptibility reporting on Enterobacterales, with 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.

Some Enterobacterales may develop resistance during therapy with third generation cephalosporins as a result of derepression on AmpC β-lactamase. This derepression is most commonly seen with *Citrobacter freundii* complex, *Enterobacter cloacae* complex and *Klebsiella aerogenes*. Isolates that are initially susceptible may become resistant within a few days after initiation of therapy. The decision to restrict reporting of Ampicillin, Ampicillin Sulbactam, Cephalosporins I, II, III and Piperacillin Tazobactam was made by the Antimicrobial Stewardship Committee for the organisms listed below.

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 concern for derepression of AmpC β-lactamase include:
    - *Citrobacter braakii*
    - *Citrobacter freundii*
    - *Citrobacter freundii* complex
    - *Citrobacter* species not listed in MC 6.014 without concern for AmpC
    - *Citrobacter werkmanii*
    - *Citrobacter youngae*
    - *Enterobacter* species
    - *Hafnia* species
    - *Klebsiella aerogenes*
    - *Kluyvera intermedia*
    - *Lelliottia* species
    - *Pantoea agglomerans*
    - *Pluralibacter* species

2. Antibiotics appropriate for routine testing and reporting for Enterobacterales with concern for derepression of AmpC β-lactamase include:
    - Cefepime
    - Gentamicin
    - Tobramycin
    - Ciprofloxacin
    - Levofloxacin
    - Trimethoprim Sulfamethoxazole

- Ertapenem
- Imipenem
- Meropenem
- Cefiderocol
- Ceftazidime-avibactam
- Ceftolozane-tazobactam
- Imipenem-relebactam
- Meropenem-vaborbactam
- Aztreonam
- Amikacin
- Nitrofurantoin-Urine only

3. 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 respiratory cultures/CF patients for Tobramycin.**
    - 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.

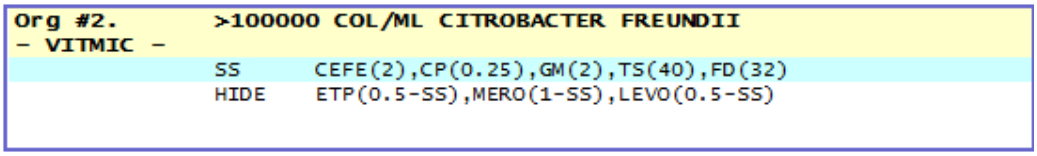
6. MicroScan and Kirby Bauer results will be entered manually under the **MMIC** and **KB** keyboards respectively under the Susceptibility tab.

Selective Reporting

1. Antibiotics will be reported in a specific order indicating the first and subsequent preferences of the Antimicrobial Stewardship Committee and Infectious Disease physicians.
2. Antibiotics will be reported depending on the source, if the sample is a urine or non-urine source.
3. There will be exceptions based on the method used for testing, type of culture and diagnosis of the patient.

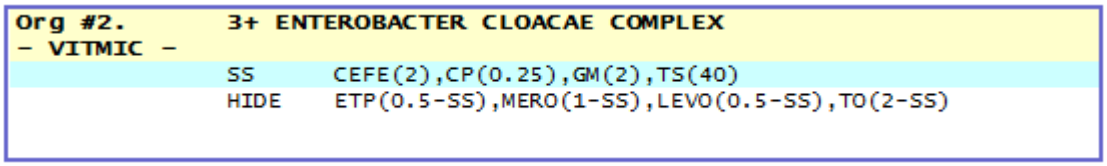
4. For **urine sources**, these 5 antibiotics will be reported routinely, in this order.
    1. Cefepime
    2. Ciprofloxacin
    3. Gentamicin
    4. Trimethoprim-Sulfa
    5. Nitrofurantoin

Figure 1 -Only CEFE, CP, GM, TS, FD are reported. All other antibiotics are in HIDE.



5. For **non-urine sources**, these 4-5 antibiotics will be reported routinely, in this order.
    1. Cefepime
    2. Ciprofloxacin
    3. Gentamicin
    4. Trimethoprim-Sulfa
    5. Tobramycin-respiratory cultures/CF patients

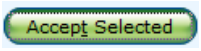
Figure 2-Only CEFE, CP, GENT, TS are reported. All other antibiotics are in HIDE.

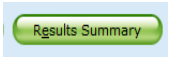


6. If any carbapenem is resistant, confirm result by alternate method. Report in Sunquest if confirmed resistant and submit isolate to MDH. See Carbapenemase Detection section of procedure for further instructions. Resistant carbapenems will be reported regardless of selective or cascade reporting.

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. 

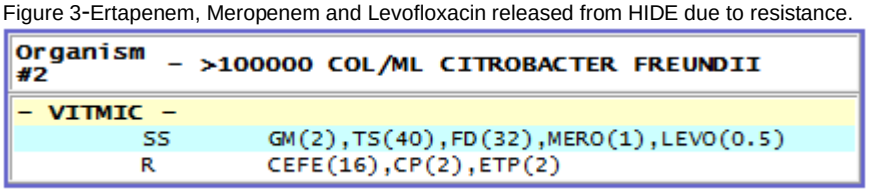
The released results will be visible in Results Summary. 

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

Method: **Vitek** -urine source

- If Cefepime is R → report Ertapenem
    - If Ertapenem is R→ report Meropenem
        - If Ciprofloxacin is R → report Levofloxacin

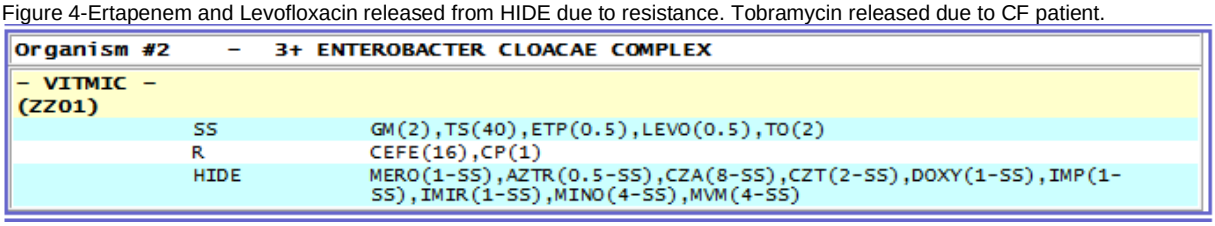
Figure 3-Ertapenem, Meropenem and Levofloxacin released from HIDE due to resistance.



Method: **Vitek:** -non-urine sources

- If culture type is respiratory → report Tobramycin
- If CF patient→ report Tobramycin
    - If Cefepime is R → report Ertapenem
        - If Ertapenem is R → report Meropenem
            - If Ciprofloxacin is R → report Levofloxacin

Figure 4-Ertapenem and Levofloxacin released from HIDE due to resistance. Tobramycin released due to CF patient.

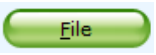


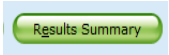
3. All other antibiotics on the XN30 panel that are not part of the cascade are hidden. Do not release and report. Hidden antibiotics include:
    - Aztreonam
    - Imipenem
    - Ceftazidime-avibactam
    - Ceftolozane-tazobactam
    - Imipenem-relebactam
    - Meropenem-vaborbactam
    - Doxycycline
    - Minocycline

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

Cascade Reporting-MicroScan Method

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

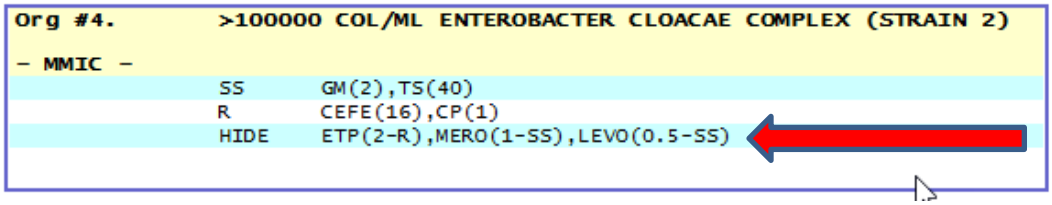
1. Enter **all** results manually under the **MMIC** keyboard. Antibiotics will be released following the cascade rules.
2. For MicroScan method, hidden antibiotics will be released when File 

is clicked. Results will be visible in Results Summary. 

Method: **MicroScan** – urine source

- If Cefepime is R → report Ertapenem
    - If Ertapenem is R→ report Meropenem
        - If Ciprofloxacin is R → report Levofloxacin

Figure 5- Ertapenem, Meropenem and Levofloxacin still in HIDE



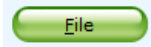
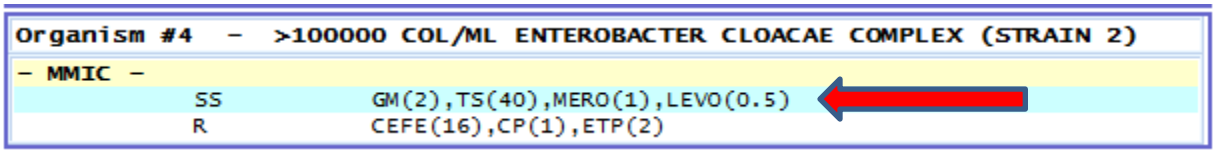
3. It will appear as the results are hidden but Sunquest will release from HIDE automatically after results are filed. 

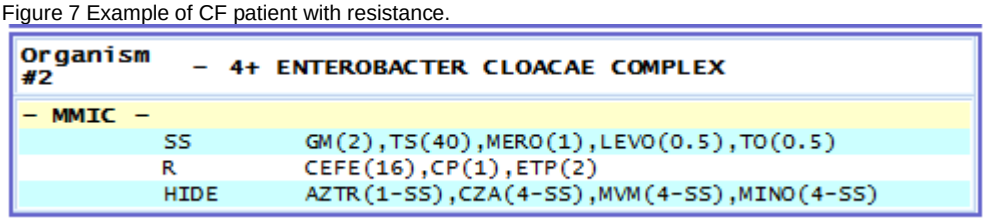
Figure 6- Ertapenem, Meropenem and Levofloxacin released from HIDE due to resistance



Method**: MicroScan** – non-urine sources

- If culture type is respiratory → report Tobramycin
- If CF patient→ report Tobramycin
  - If Cefepime is R → report Ertapenem
    - If Ertapenem is R → report Meropenem
      - If Ciprofloxacin is R → report Levofloxacin

Figure 7 Example of CF patient with resistance.

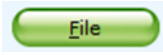


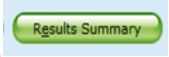
4. All other antibiotics on the panel that are not part of the cascade are hidden. Do not release and report. Hidden antibiotics include:
   - Aztreonam
   - Minocycline
   - Ceftazidime-avibactam
   - Meropenem-vaborbactam

5. Additional antibiotics may be released with a provider request.

Cascade Reporting- Kirby Bauer Method

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

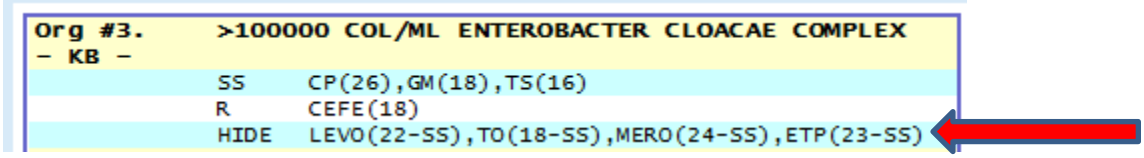
1. Enter **all** results manually under the **KB** keyboard. Antibiotics will be released following the cascade rules.
2. For Kirby Bauer method, hidden antibiotics will be released when File 

is clicked. The released Results will be visible in Results Summary. 

Method: **Kirby Bauer** – urine source

- If Cefepime is R → report Ertapenem
  - If Ertapenem is R→ report Meropenem
    - If Ciprofloxacin is R → report Levofloxacin

Figure 8 -Cefepime resistance



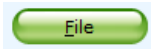
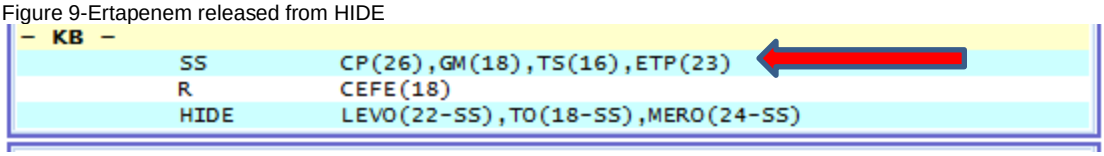
3. It will appear as the results are hidden but Sunquest will release from HIDE automatically after results are filed. 

Figure 9-Ertapenem released from HIDE



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

- If culture type is respiratory → report Tobramycin
- If CF patient→ report Tobramycin
  - If Cefepime is R → report Ertapenem
    - If Ertapenem is R → report Meropenem
      - If Ciprofloxacin is R → report Levofloxacin

Figure 10 -Cefepime and Ciprofloxacin resistance and CF patient

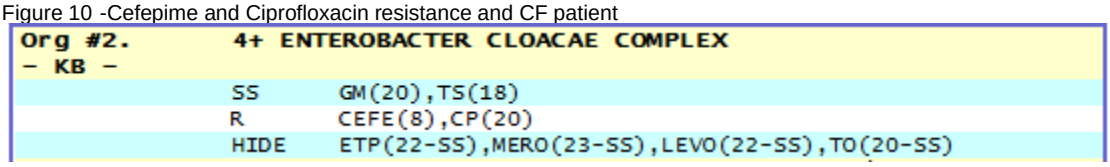
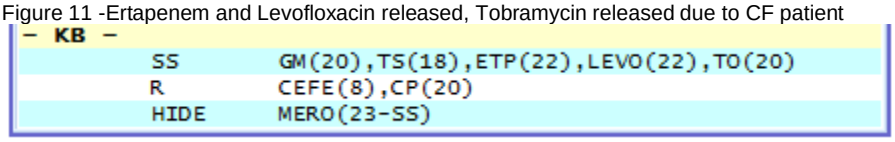


Figure 11 -Ertapenem and Levofloxacin released, Tobramycin released due to CF patient



4. All other antibiotics on the panel that are not part of the cascade are hidden. Do not release and report.

5. 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 concern for AmpC.
2. Report Tobramycin on respiratory cultures and CF patients
   - Set up the XN30 to obtain result for Tobramycin and release only the Tobramycin. Refer to MC 6.02 AST-XN30 for further reporting instructions.
3. Mucoid isolate susceptibility testing should be performed with the Kirby Bauer method.

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:
   - Report MIC results as tested. Do not change interpretations.
   - Label as **MDRO**
   - Notify provider
   - Send isolate to MDH Project 1380

- Add MDHADD comment
- 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-ENCL-MDRO-NCPO
2. Result Enterobacterales with resistance to a carbapenem and positive mCIM result as: example-ENCL-MDRO-OXA
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.

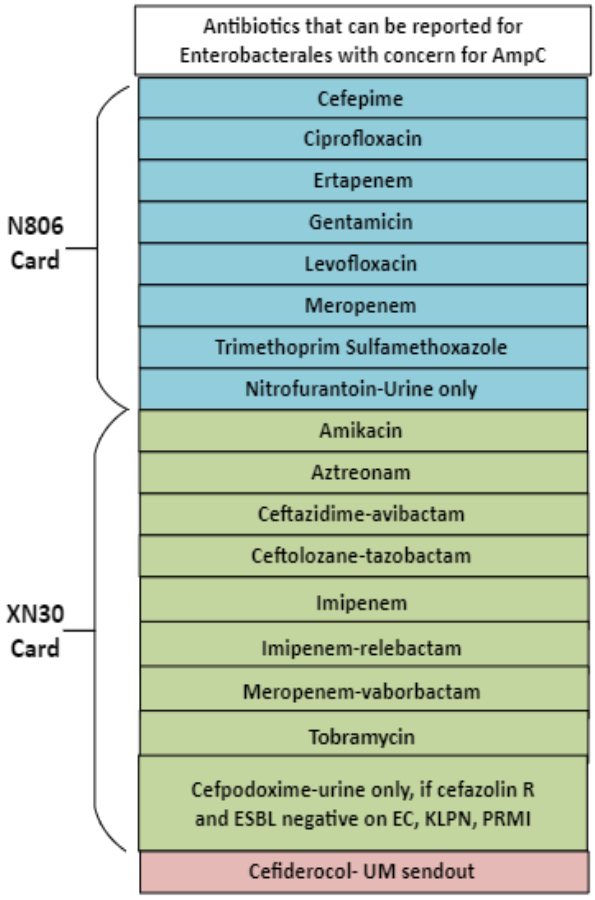
AST-N806 card for Enterobacterales with concern for AmpC

Antibiotic	Product Limitations
Cefepime	Perform KB on *Hafnia alvei*
Ertapenem	Perform alternate method with MIC of 0.25-0.5 Perform alternate method on *Hafnia alvei*
Gentamicin	If resistance is observed on *Klebsiella aerogenes, Enterobacter cloacae.* Send isolate to MDH.
Meropenem	Perform alternate method on *Enterobacter cloacae* with MIC>=16

AST-XN30 card for Enterobacterales with concern for AmpC

Antibiotic	Product Limitations
Amikacin	Not validated. Perform KB and day of use QC
Imipenem	Perform alternate method on *Klebsiella aerogenes*

Appendix Additional Tables and Flowcharts



Vitek -Run N806 card (Add XN30 for respiratory source or CF patient)

Antibioticss that are reported-Urine		
Disk (Abbrev.)	Sunquest code	Drug Name
FEP	CEFE	Cefepime
CIP	CP	Ciprofloxacin
GM	GM	Gentamicin
SXT	TS	Trimethoprim Sulfamethoxazole
F/M	FD	Nitrofurantoin-Urine only
Antibiotics that are hidden unless cascaded		
LVX	LEVO	Levofloxacin
MER	MERO	Meropenem
ETP	ETP	Ertapenem

If Cefepime is R → Report Ertapenem → If Ertapenem is R → Report Meropenem

If Ciprofloxacin is R → Report Levofloxacin

If a carbapenem is non susceptible, even if not being reported, confirm resistance

Drugs that are reported-Non Urine		
Disk (Abbrev.)	Sunquest code	Drug Name
FEP	CEFE	Cefepime
CIP	CP	Ciprofloxacin
GM	GM	Gentamicin
SXT	TS	Trimethoprim Sulfamethoxazole
NN	TO	Tobramycin- for respiratory sources and CF patients
Drugs that are hidden unless cascaded		
Etp	ETP	Ertapenem
LVX	LEVO	Levofloxacin
MER	MERO	Meropenem
Hidden drugs		
AZT	AZTR	Aztreonam
CZA	CZA	Ceftazidime-avibactam
	CZT	Ceftolozane-tazobactam
	DOXY	Doxycycline
IMP	IMP	Imipenem
	IMIR	Imipenem-relebactam
MIN	MINO	Minocycline
MEV	MVM	Meropenem-vaborbactam

If Respiratory source / If CF Patient (any non-urine source) → Set up XN30 card → Report Tobramycin

If Cefepime is R → Report Ertapenem → If Ertapenem is R → Report Meropenem

If Ciprofloxacin is R → Report Levofloxacin

Microscan-
Urine and Non-urine
Results will appear hidden until they are accepted in Sunquest

Drugs that are reported		
Microscan	**Sunquest code**	**Drug Name**
Cpe	CEFE	Cefepime
Cp	CP	Ciprofloxacin
Gm	GM	Gentamicin
T/S	TS	Trimethoprim Sulfamethoxazole
To	TO	Tobramycin- for respiratory sources and non-urine CF patients

Drugs that are hidden unless cascaded		
Etp	ETP	Ertapenem
Lvx	LEVO	Levofloxacin
Mer	MERO	Meropenem
Hidden drugs		
Azt	AZTR	Aztreonam
Min	MINO	Minocycline
Cza	CZA	Ceftazidime-Avibactam
Mev	Mev	Meropenem-Vabrobactam

If Respiratory source
If CF Patient (any non-urine source)
Report Tobramycin

If Cefepime is R
Report Ertapenem

If Ertapenem is R
Report Meropenem

If Ciprofloxacin is R
Report Levofloxacin

Kirby-Bauer (KB)-
EBAC stamper
Urine and Non-Urine
Results will appear hidden until they are accepted in Sunquest

Drugs that are reported		
Disc abrev.	**Sunquest code**	**Drug Name**
FEP	CEFE	Cefepime
CIP	CP	Ciprofloxacin
GM	GM	Gentamicin
TS	SXT	Trimethoprim Sulfamethoxazole
To	TO	Tobramycin- for respiratory sources and non-urine CF patients
Hidden drugs		
IMP	IMP	Imipenem

If Respiratory source
If CF Patient (any non-urine source)
Report Tobramycin

If Cefepime is R
Report Ertapenem

If Ertapenem is R
Report Meropenem

If Ciprofloxacin is R
Report Levofloxacin

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, MicroScan® Dried Gram Negative (8/2022).
4. CLSI M100 edition 34 Performance Standards for Antimicrobial Susceptibility Testing 2024

Training Plan/ Competency Assessment

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

Historical Record

Version	Written/Revised by:	Effective Date:	Summary of Revisions
1	Susan DeMeyere	11/12/2024	Initial version
2			