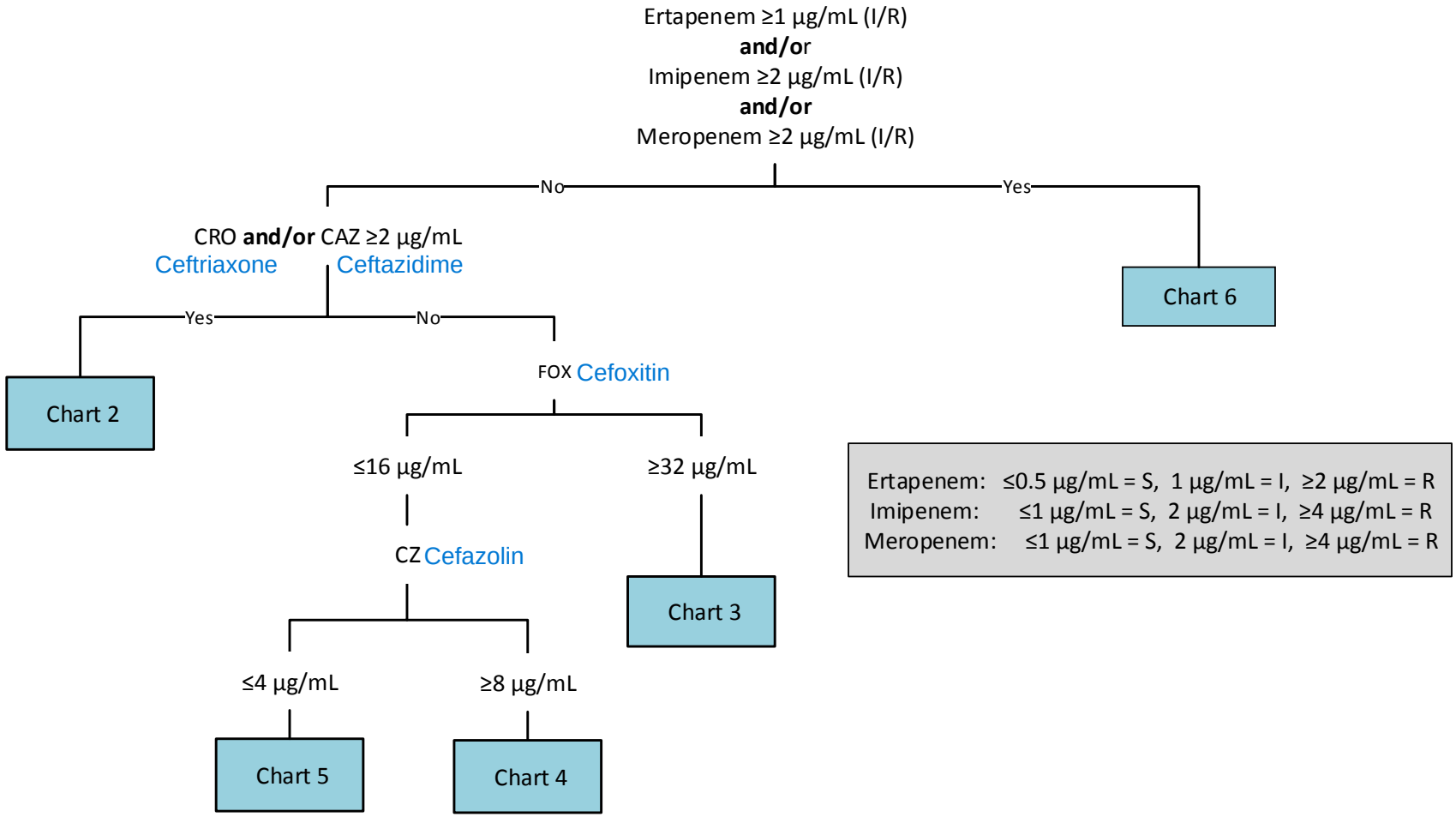
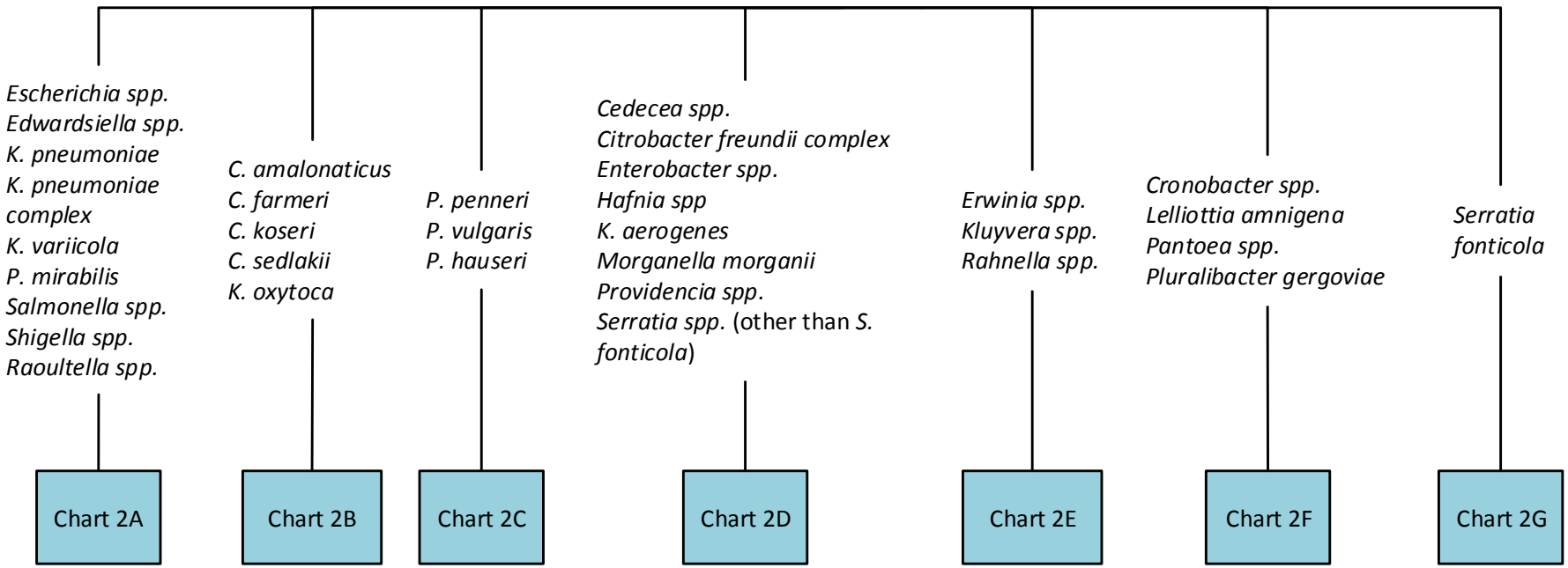
Detection of Beta Lactam Resistance Based on Ertapenem, Imipenem and Meropenem Susceptibility

Chart 1



Ceftriaxone and/or Ceftazidime ≥ 2 µg/mL

Chart 2



Ceftriaxone **and/or** Ceftazidime ≥ 2µg/mL

Chart 2A

Escherichia spp.
Edwardsiella spp.
Klebsiella pneumoniae
Klebsiella pneumoniae complex
Klebsiella variicola
Proteus mirabilis
Raoultella spp.
Salmonella spp.
Shigella spp.

MAST AmpC and ESBL discs (D68C)

Interpret:

Amox/clav	AMC oral - R
Amox/clav IV	AMC IV - R - Do not report
Ampicillin	AM - R
Cephalexin	CEX - R (Urine Only) Note 1
Cefazolin	CZ - R
Cefixime	CFM - R (Urine Only)
Ceftriaxone	CRO - R
Pip/taz	TZP - Do not report

Note 1: Report for *E. coli, K. pneumo* and *P. mirabilis* only

- ESBL → **Comment** &1744
- AmpC → **Comment** &1746
- ESBL + AmpC → **Comment** &1744
- Negative or Undetermined Mechanism → Cefepime ESBL discs
  - ESBL positive → **Comment** &1744
  - ESBL Negative → **Consult** Supervisor

NOTES:

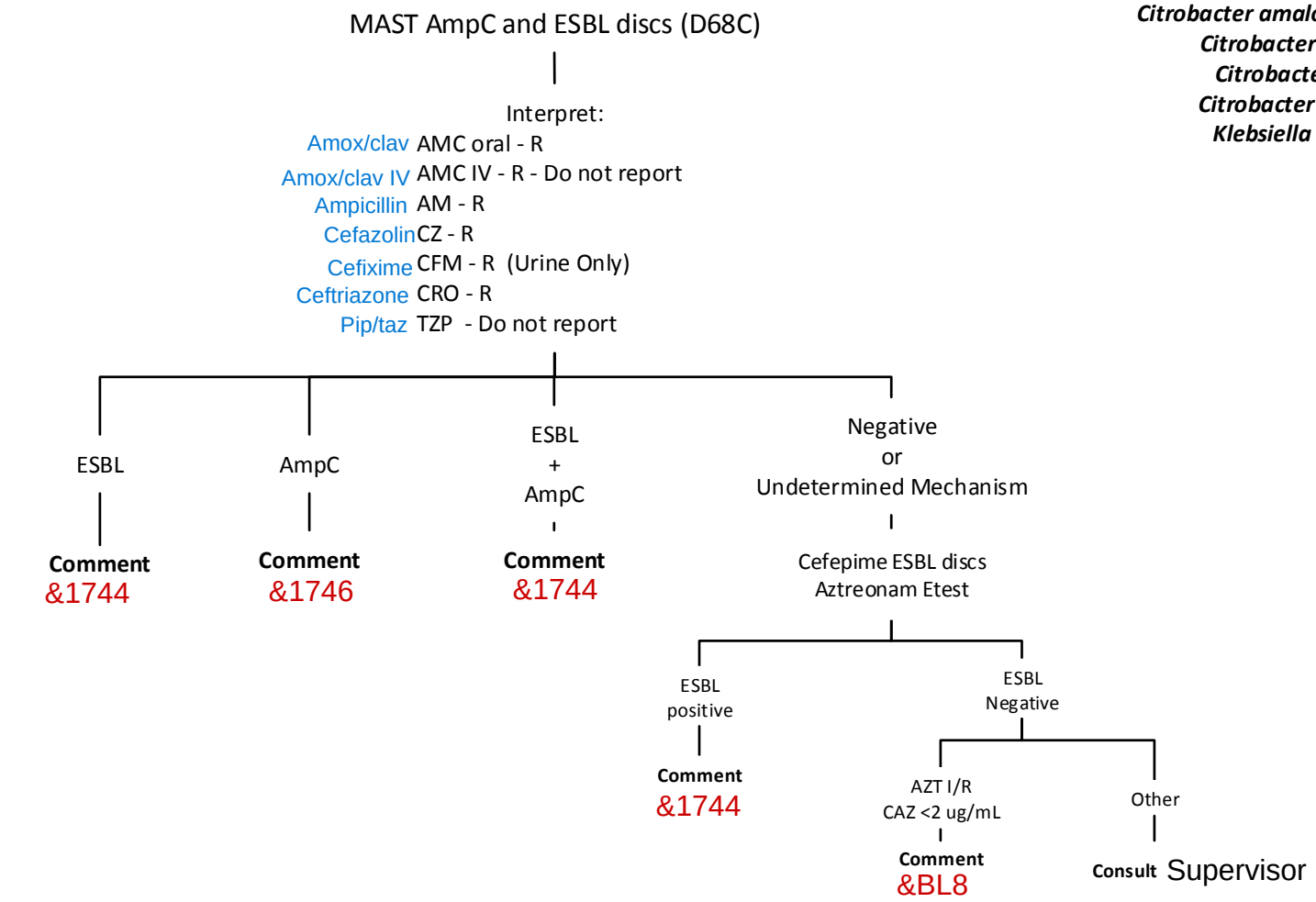
For *E. coli* and *Shigella* spp., it is not possible, with current phenotypic methods to differentiate between plasmid mediated AmpC cephalosporinase and hyperproduction of intrinsic chromosomal AmpC enzyme.

Edwardsiella spp., *Klebsiella* spp., *Proteus mirabilis* and *Salmonella* spp. do not produce chromosomal beta-lactamases. Hence, all beta-lactamase detection implies acquisition of a transmissible beta-lactamase.

Ceftriaxone **and/or** Ceftazidime ≥ 2µg/mL

Chart 2B

Citrobacter amalonaticus
Citrobacter farmeri
Citrobacter koseri
Citrobacter sedlakii
Klebsiella oxytoca

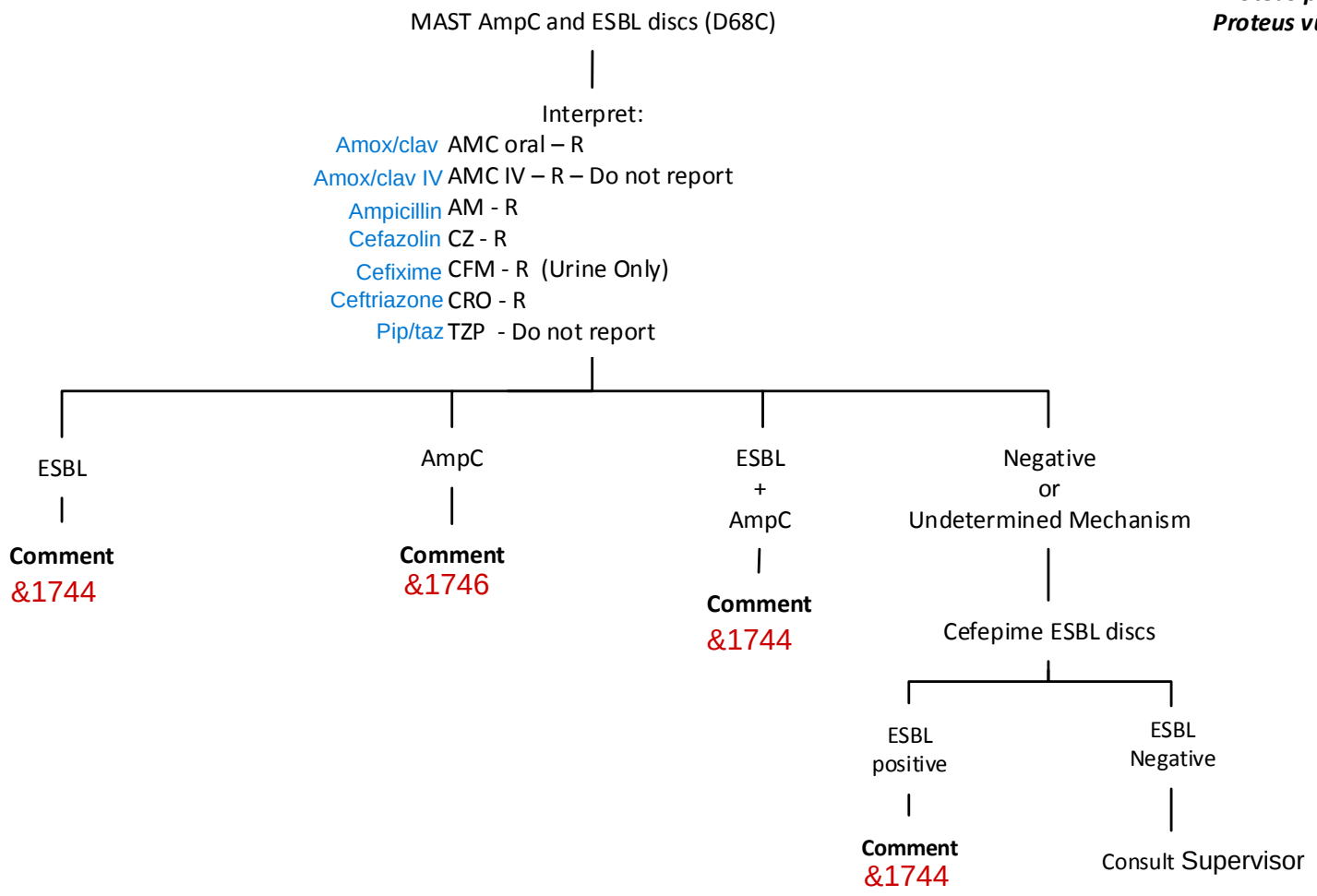


NOTE: Hyperproduction of the class A enzymes (K1 in *K. oxytoca*, Cko in *Citrobacter koseri* and CdiA *Citrobacter amalonaticus*) typically results in resistance to aztreonam, ceftriaxone (cefotaxime less affected than ceftriaxone) and cefepime. Although ceftazidime usually tests susceptible its use is not recommended as it may select resistant mutants.

Ceftriaxone **and/or** Ceftazidime ≥ 2 µg/mL

Chart 2C

Proteus hauseri
Proteus penneri
Proteus vulgaris



These organisms produce an inducible class A cephalosporinase (cefuroximase) that results in resistance to penicillins, and 1st/2nd generation cephalosporins. They remain susceptible to beta-lactamase inhibitor combination drugs. Hyperproduction/derepression of this enzyme typically results in cefotaxime/ceftriaxone resistance (ceftazidime remains susceptible).

Ceftriaxone **and/or** Ceftazidime ≥ 2µg/mL

Chart 2D

Cedecea spp.
Citrobacter freundii complex
Enterobacter spp.
Hafnia spp.
Klebsiella aerogenes
Morganella morganii
Providencia spp.
***Serratia spp.* (other than *S. fonticola*)**

Interpret:

Ampicillin AM - R
Cefazolin CZ - R
Cefixime CFM - R (Urine Only)
Ceftriazone CRO - R
Pip/taz TZP - Do not report

Comment
&1746

These organisms produce an inducible chromosomal Amp C cephalosporinase that typically results in resistance to penicillins and 1st/2nd generation cephalosporins, including cefoxitin (exceptions: *Serratia* spp, cefuroxime may test more resistant than cefoxitin; *Hafnia* and *Providencia* species, both may still test susceptible to cefoxitin and cefuroxime). Induction and/or derepression of the Amp C enzyme results in broad resistance including 3rd generation cephalosporins, especially cefotaxime and ceftriaxone. Cefepime, a 4th generation cephalosporin, is poorly hydrolyzed by the Amp C enzyme (typical MICs ≤ 1µg/mL).

NOTE: Resistance to cefepime implies either acquisition of an extended spectrum beta lactamase (ESBL) or an extended spectrum Amp C cephalosporinases (ESAC) resulting from further derepression of the chromosomal enzyme. Acquisition of an ESBL is common but difficult to detect by standard ESBL confirmatory tests due to interference from the chromosomal Amp C enzyme that is not inhibited by clavulanate. Cefepime ESBL discs may be useful in detecting ESBL production in the presence of an Amp C cephalosporinase.

It is not possible to detect an ESBL in the presence of an ESAC as the higher level of Amp C cephalosporinase interferes with the cefepime ESBL test. Nosocomial outbreaks of cefepime resistant organisms warrant molecular confirmation of resistance mechanism(s) (ESBL or ESAC).

Ceftriaxone **and/or** Ceftazidime ≥ 2µg/mL

Chart 2E

Erwinia spp.
Kluyvera spp.
Rahnella spp.

Interpret:

Ampicillin AM - R
Cefazolin CZ - R
Cefixime CFM - R (Urine Only)
Ceftriaxone CRO - R

Comment

&1744

These organisms produce a low level chromosomal Class A extended spectrum beta-lactamase (ESBL) conferring resistance to penicillins, and 1st/ 2nd generation cephalosporins, but not cefoxitin. Like other ESBLs, resistance to 3rd generation cephalosporins may not be apparent in vitro, but should be implied. ESBL testing is not useful as all should test positive due to the chromosomal ESBL.

Ceftriaxone **and/or** Ceftazidime ≥ 2µg/mL

Chart 2F

Cronobacter spp.
Lelliottia amnigena
Pluralibacter gergoviae
Pantoea spp.

Interpret:

Ampicillin	AM - R
Cefazolin	CZ - R
Cefixime	CFM - R (Urine Only)
Ceftriaxone	CRO - R

Comment
&1746

These organisms differ from *E. cloacae* and *K. aerogenes* in that the chromosomal Amp C cephalosporinase is produced at very low levels. Ampicillin, 1st generation cephalosporins and cefoxitin often test susceptible but still should be reported as resistant. For these organisms, the Amp C cephalosporinase may or may not be inducible. Third generation cephalosporins and/or aztreonam resistance implies acquisition of ESBL or hyperproduction of Amp C cephalosporinase.

Ceftriaxone **and/or** Ceftazidime ≥ 2µg/mL

Chart 2G

Serratia fonticola

Multiple
Beta - lactamases

Interpret:

Ampicillin	AM - R
Cefazolin	CZ - R
Cefixime	CFM - R (Urine Only)
Ceftriaxone	CRO - R

Comment

&BL11

Serratia fonticola produces both an inducible chromosomal cephalosporinase (Amp C) and an inducible, extended spectrum Class A enzyme conferring resistance to penicillins, amoxicillin/clavulanate and 1st generation cephalosporins.

If 3rd generation cephalosporins are resistant, all penicillins, 1st/2nd/3rd generation cephalosporins and beta-lactamase inhibitor combinations should be considered resistant. Acquisition of ESBL enzymes may occur, but would be difficult to detect.

Ceftriaxone and Ceftazidime < 2 µg/mL **and** Cefoxitin ≥ 32 µg/mL

Chart 3

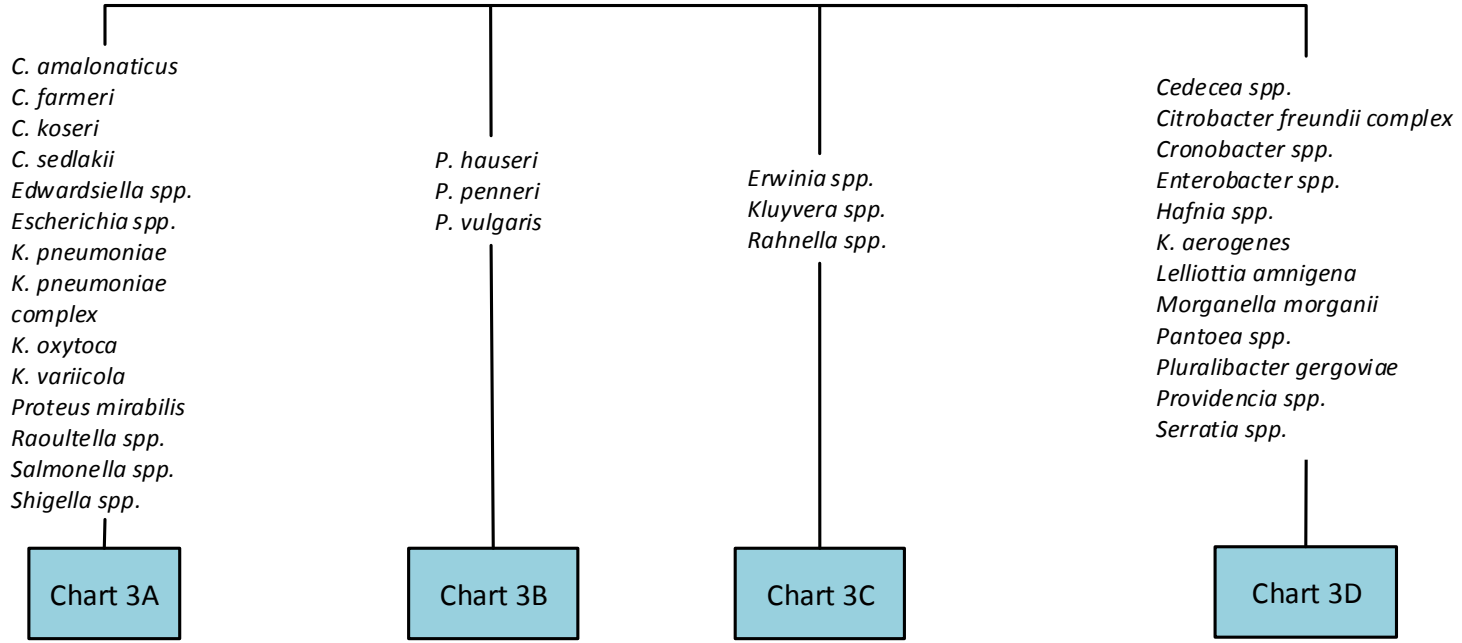


Chart 3A

Ceftriaxone and/or Ceftazidime < 2 µg/mL
and
Cefoxitin ≥ 32 µg/mL

Citrobacter amalonaticus
Citrobacter farmeri
Citrobacter koseri
Citrobacter sedlakii
Edwardsiella spp.
Escherichia spp.
Klebsiella oxytoca
Klebsiella pneumoniae
Klebsiella pneumoniae complex
Klebsiella variicola
Proteus mirabilis
Raoultella spp.
Salmonella spp.
Shigella spp.

Interpret:

Ampicillin	AM - R
Cephalexin	CEX - R (Urine Only) [Note 1]
Cefazolin	CZ - R
Cefixime	CFM - As Tested (Urine Only)
Ceftriaxone	CRO - S
Amox/clav	AMC oral - R
Amox/clav IV	AMC IV - R
Pip/taz	TZP - As Tested

Note 1: Report for *E. coli, K. pneumo* and *P. mirabilis* only

E. coli and *Shigella* spp. produce a noninducible Amp C cephalosporinase in minute amount, not resulting in any significant beta-lactam resistance (although the MICs of cephalothin/cephalexin and occasionally amoxicillin/clavulanate may be slightly elevated). Cefoxitin resistance is due to either a permeability mutation or expression of Amp C cephalosporinase (hyperproduction of chromosomal Amp C or acquisition of plasmid Amp C cephalosporinase enzyme.
Hyperproduction of the chromosomal enzymes of *Klebsiella* spp., *Citrobacter koseri*, *Citrobacter amalonaticus* does not affect cefoxitin.
Cefoxitin resistance indicates a permeability mutation or acquisition of AmpC cephalosporinase.

Note: Cefazolin and amoxicillin/clavulanate should be reported as R if either permeability mutation or cephalosporinase suspected.

Ceftriaxone and/or Ceftazidime < 2 µg/mL
and
Cefoxitin ≥ 32 µg/mL

Chart 3B

Proteus hauseri
Proteus penneri
Proteus vulgaris

Interpret:

Ampicillin	AM - R
Cefazolin	CZ - R
Cefixime	CFM - R (Urine Only)
Ceftriaxone	CRO – Do Not Report
Amox/clav	AMC oral - R
Amox/clav IV	AMC IV - R
Pip/taz	TZP - As Tested

These organisms produce an inducible chromosomal cephalosporinase (Class A cefuroximase). Hyperproduction of this enzyme should not affect cefoxitin. Cefoxitin resistance indicates a permeability mutation or acquisition of AmpC cephalosporinase.

Note: Cefazolin and amoxicillin/clavulanate should be reported as R if either permeability mutation or cephalosporinase suspected.

Ceftriaxone and/or Ceftazidime < 2 µg/mL
and
Cefoxitin ≥ 32 µg/mL

Chart 3C

Erwinia spp.
Kluyvera spp.
Rahnella spp.

Interpret:

Ampicillin AM - R
Cefazolin CZ - R
Cefixime CFM - R (Urine Only)
Ceftriaxone CRO - R

Comment

&1744

These organisms produce a low level chromosomal Class A extended spectrum beta-lactamase (ESBL) conferring resistance to penicillins, and 1st/ 2nd generation cephalosporins, but not cefoxitin. Even hyperproduction of this enzyme does not affect cefoxitin. Cefoxitin resistance indicates a permeability mutation (porin mutation/upregulated efflux). Typically, acquisition of a plasmid-mediated Amp C cephalosporinase enzyme results in elevated MIC (≥ 2 µg/mL) to one or more 3rd generation cephalosporins. Like other ESBLs, resistance to 3rd generation cephalosporins may not be apparent in vitro, but should be implied. ESBL testing is not useful as all should test positive due to the chromosomal ESBL enzyme.

Ceftriaxone and/or Ceftazidime < 2µg/mL
and
Cefoxitin ≥ 32 µg/mL

Chart 3D

Cedecea spp.
Citrobacter freundii complex
Cronobacter spp.
Enterobacter spp.
Hafnia spp.
Klebsiella aerogenes
Lelliottia amnigena
Morganella morganii
Pantoeae spp.
Pluralibacter gergoviae
Providencia spp.
Serratia spp.

Interpret:

Ampicillin AM - R
Cefazolin CZ - R
Cefixime CFM - R (Urine Only)
Ceftriaxone CRO - R for CSF/Brain, Blood/Sterile body site/ Endovascular catheter sites
- Do not report for other sites
Pip/taz TZP - R Exception: *Morganella morganii* - As Tested*

All of these organisms produce a chromosomal Amp C cephalosporinase. In many, it is inducible, and in some it is constitutively expressed at low or high levels. The use of 3rd generation cephalosporins, even if susceptible (< 2 µg/mL), should be avoided to prevent selection of derepressed mutants. Selection of derepressed mutants is more common in certain clinical settings, such as pneumonia, bacteremia and abscesses. For these infections, 3rd generation cephalosporins should not be reported. For urine isolates, where therapeutic options are limited, cefotaxime or ceftriaxone may be reported if the MIC is < 2 µg/mL, as the risk of selecting derepressed mutants is low, given the high drug concentration of these agents in urine. Ceftazidime is a strong selector of derepressed mutants and should not be reported on any of these isolates (regardless of MIC). Permeability mutations in association with Amp C cephalosporinase may result in carbapenem resistance.

***As the AmpC cephalosporinase is poorly inhibited by beta-lactamase inhibitors, amoxicillin/clavulanate and piperacillin/tazobactam should be reported as resistant. **Exception:** The cephalosporinase of *Morganella morganii* is inhibited by tazobactam (but not clavulanate). Therefore piperacillin/tazobactam can be reported as tested.

Ceftriaxone and Ceftazidime < 2 µg/mL
and
Cefoxitin ≤ 16 µg/mL
and
Cefazolin ≥ 8 µg/mL

Chart 4

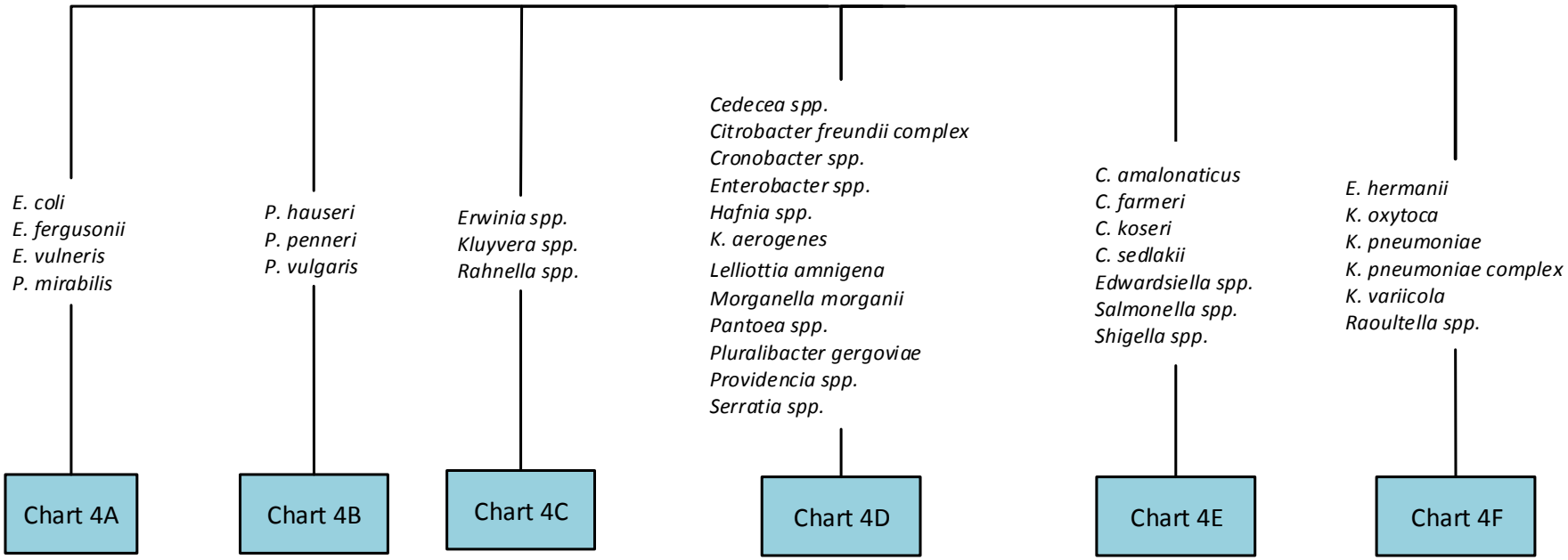
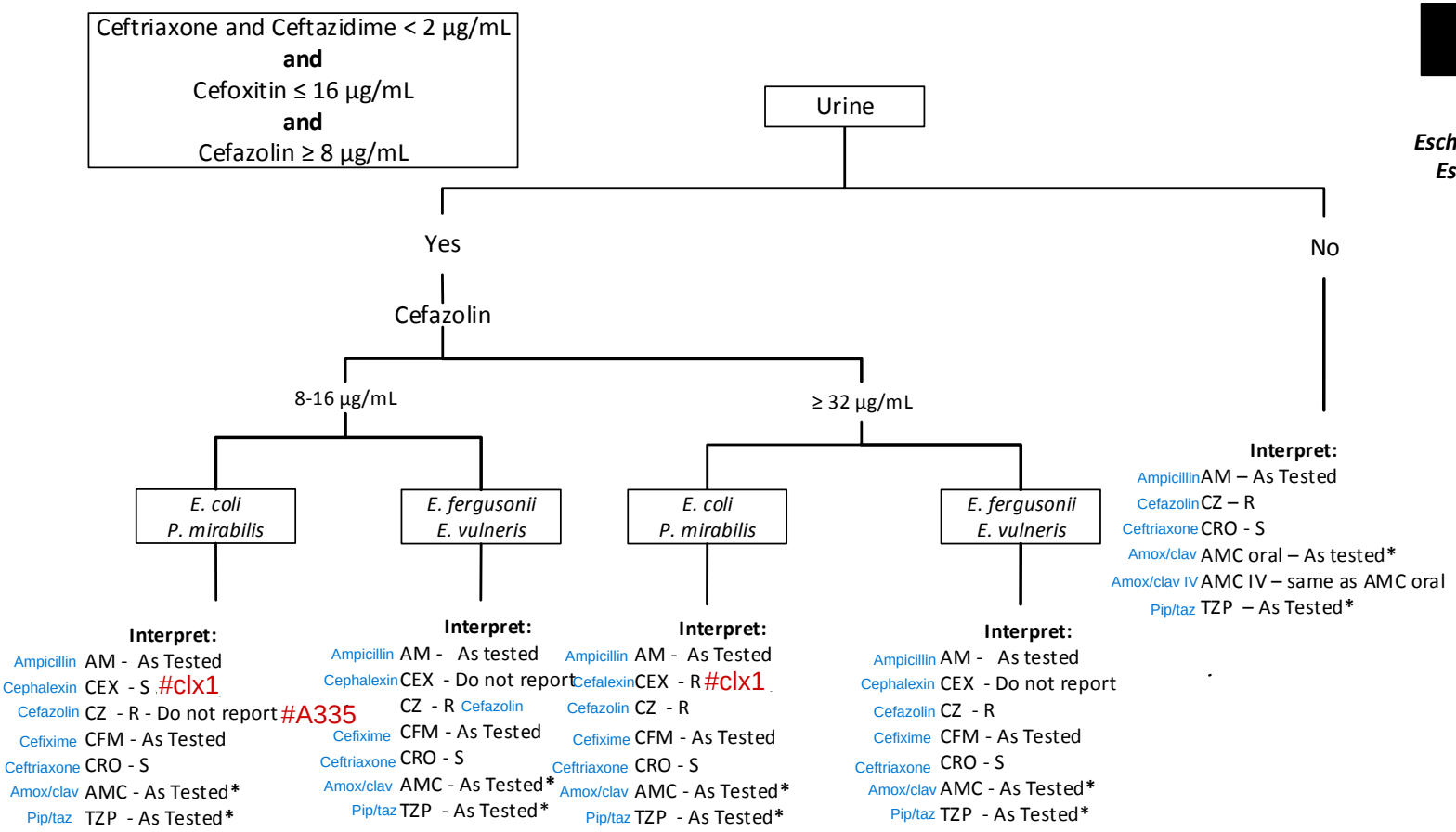


Chart 4A

Escherichia coli
Escherichia fergusonii
Escherichia vulneris
Proteus mirabilis



***Confirm results if piperacillin/tazobactam I/R and amoxicillin/clavulanate oral S. If TZP confirms as I/R report AMC oral as R.**

For *E. coli* and *P. mirabilis*, a cefazolin MIC ≥ 8µg/mL implies a high level production of penicillinase, rather than a cephalosporinase or a low level penicillinase. Low level penicillinase would affect only ampicillin and cephalothin/cephalexin, but not cefazolin, while a cephalosporinase should result in elevated cefoxitin MIC.

Comment #clx1 For uncomplicated lower UTI only. (auto adds to cephalexin) Add to cephalexin
Comment #A335 Cefazolin susceptibility result is available upon request. (auto adds to organism for *E. coli, K. pneumoniae, P. mirabilis*) Add to cephalexin

Ceftriaxone and Ceftazidime < 2 µg/mL
and
Cefoxitin ≤ 16 µg/mL
and
Cefazolin ≥ 8 µg/mL

Chart 4B

Proteus hauseri
Proteus penneri
Proteus vulgaris

Urine

Yes

Interpret

Ampicillin	AM – R
Cefazolin	CZ – R
Cefixime	CFM – R
Ceftriaxone	CRO – Do Not Report
Amox/clav	AMC oral – As Tested *

No

Interpret:

Ampicillin	AM - R
Cefazolin	CZ - R
Ceftriaxone	CRO - Do Not Report
Amox/clav	AMC oral - As Tested*
Amox/clav IV	AMC IV - same as AMC oral
Pip/taz	TZP - As Tested*

***Confirm results if piperacillin/tazobactam I/R and amoxicillin/clavulanate oral S. If TZP confirms as I/R report AMC oral as R.**

These organisms all have an inducible chromosomal cephalosporinase (Class A cefuroximase) that typically results in resistance to ampicillin and 1st/2nd generation cephalosporins, but not cefoxitin. Amoxicillin/clavulanate and piperacillin/tazobactam typically remain susceptible.

Ceftriaxone and Ceftazidime < 2 µg/mL
and
Cefoxitin ≤ 16 µg/mL
and
Cefazolin ≥ 8 µg/mL

Chart 4C

Erwinia spp.
Kluyvera spp.
Rahnella spp.

Interpret

Ampicillin AM – R
Cefazolin CZ - R
Cefixime CFM - R (Urine Only)
Ceftriaxone CRO – R

Comment
&1744

These organisms have a chromosomal ESBL that typically results in cefazolin resistance. Beta lactamase inhibitor combination drugs may test susceptible, but should be used with caution as the level of beta-lactamase inhibitor may not be sufficient to inhibit the ESBL enzyme produced. It is safest not to report these agents at all.

Ceftriaxone and Ceftazidime < 2 µg/mL
and
Cefoxitin ≤ 16 µg/mL
and
Cefazolin ≥ 8 µg/mL

Chart 4D

Cedeceae spp.
Citrobacter freundii complex
Cronobacter spp.
Enterobacter spp.
Hafnia spp.
Klebsiella aerogenes
Lelliottia amnigena
Morganella spp.
Pantoea spp.
Pluralibacter gergoviae
Providencia spp.
Serratia spp.

Interpret

Ampicillin AM - R
Cefazolin CZ - R
Cefixime CFM - R (Urine Only)
Ceftriaxone CRO - R for CSF/Brain, Blood/Sterile body site/Endovascular catheter sites
- Do Not Report for other sites
Pip/taz TZP - R Exception: *Morganella morganii* - As Tested*****

All of these organisms produce a chromosomal Amp C cephalosporinase. In most, it is inducible, and in some it is constitutively expressed at low or high levels. The use of 3rd generation cephalosporins, even if susceptible (< 2 µg/mL), should be avoided to prevent selection of derepressed mutants. Selection of derepressed mutants is common in certain clinical settings, such as pneumonia, bacteremia and abscesses. For these infections, 3rd generation cephalosporins should not be reported. For urine isolates, where therapeutic options are limited, cefotaxime or ceftriaxone may be reported if the MIC is < 2 µg/mL, as the risk of selecting derepressed mutants is low, given the high drug concentration of these agents in urine. Ceftazidime is a strong selector of derepressed mutants and should never be reported on any of these isolates (regardless of MIC). Permeability mutations in association with Amp C cephalosporinase may result in carbapenem resistance.

*****As this cephalosporinase is poorly inhibited by beta-lactamase inhibitors, amoxicillin/clavulanate and piperacillin/tazobactam should be reported as resistant. **Exception:** The cephalosporinase of *Morganella morganii* is inhibited by tazobactam (but not clavulanate). Therefore, piperacillin/tazobactam can be reported as tested.

Ceftriaxone and Ceftazidime < 2 µg/mL
and
Cefoxitin ≤ 16 µg/mL
and
Cefazolin ≥ 8 µg/mL

Chart 4E

Citrobacter amalonaticus
Citrobacter farmeri
Citrobacter koseri
Citrobacter sedlakii
Edwardsiella spp.
Salmonella spp.
Shigella spp.

Organism

Edwardsiella spp.
Salmonella spp.
Shigella spp.

Interpret:

Ampicillin AM – As Tested
Cefazolin CZ - R
Cefixime CFM - As Tested (Urine and stool only)
Ceftriaxone CRO – S

C. amalonaticus
C. farmeri
C. koseri
C. sedlakii

Urine

Yes

Interpret:

Ampicillin AM - R
Cefazolin CZ - R
Cefixime CFM - As Tested
Ceftriaxone CRO – S
Amox/clav AMC oral – As Tested *

No

Interpret:

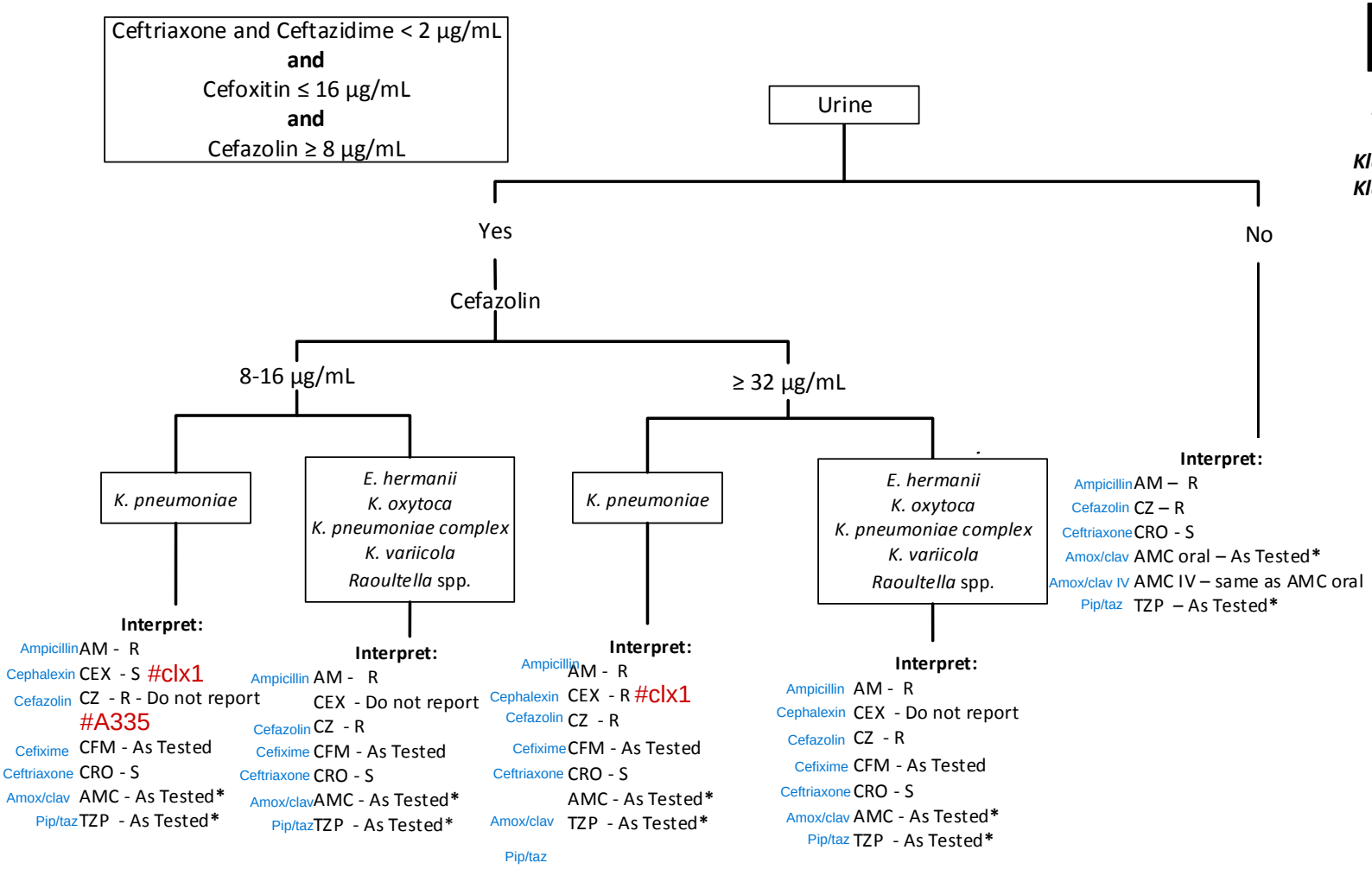
Ampicillin AM – R
Cefazolin CZ – R
Ceftriaxone CRO - S
Amox/clav AMC oral- As Tested*
Amox/clav IV AMC IV – same as AMC oral
Pip/taz TZP - As Tested*

***Confirm results if piperacillin/tazobactam I/R and amoxicillin/clavulanate oral S. If TZP confirms as I/R report AMC oral as R.**

C. koseri and *C. amalonaticus* produce a chromosomal class A penicillinase which confers resistance to penicillins (amoxicillin, piperacillin) and, to a lesser degree, to cephalothin/cephalexin. Cefazolin MIC ≥ 8µg/mL implies high level penicillinase production.

Chart 4F

Escherichia hermanii
Klebsiella oxytoca
Klebsiella pneumoniae
Klebsiella pneumoniae complex
Klebsiella variicola
***Raoultella* spp.**



***Confirm results if piperacillin/tazobactam I/R and amoxicillin/clavulanate oral S. If TZP confirms as I/R report AMC oral as R.**

K. pneumoniae and *K. oxytoca* produce a chromosomal class A penicillinase which confers resistance to penicillins (amoxicillin, piperacillin) and, to a lesser degree, to cephalothin/cephalexin. Cefazolin MIC ≥ 8µg/mL implies high level penicillinase production.

Comment #clx1 For uncomplicated lower UTI only Add to cephalexin
Comment #A335 Cefazolin susceptibility result is available upon request Add to cephalexin

Chart 5

Ceftriaxone and Ceftazidime < 2 µg/mL
and
Cefoxitin ≤ 16 µg/mL
and
Cefazolin ≤ 4 µg/mL

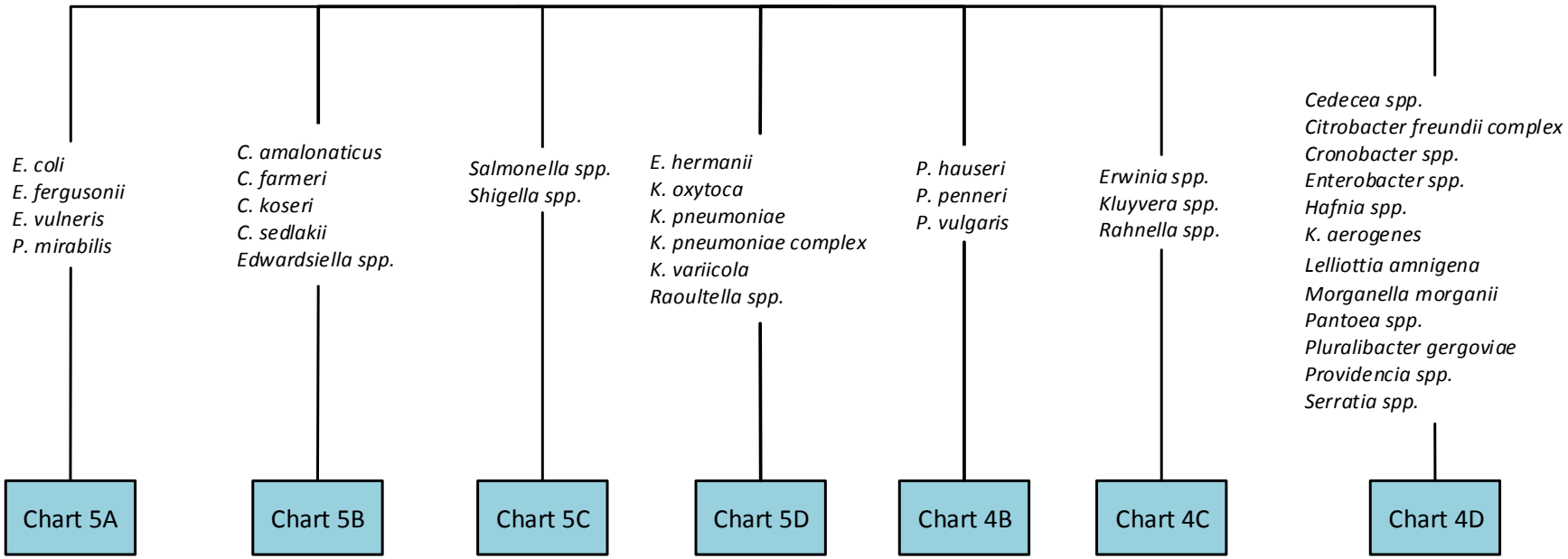
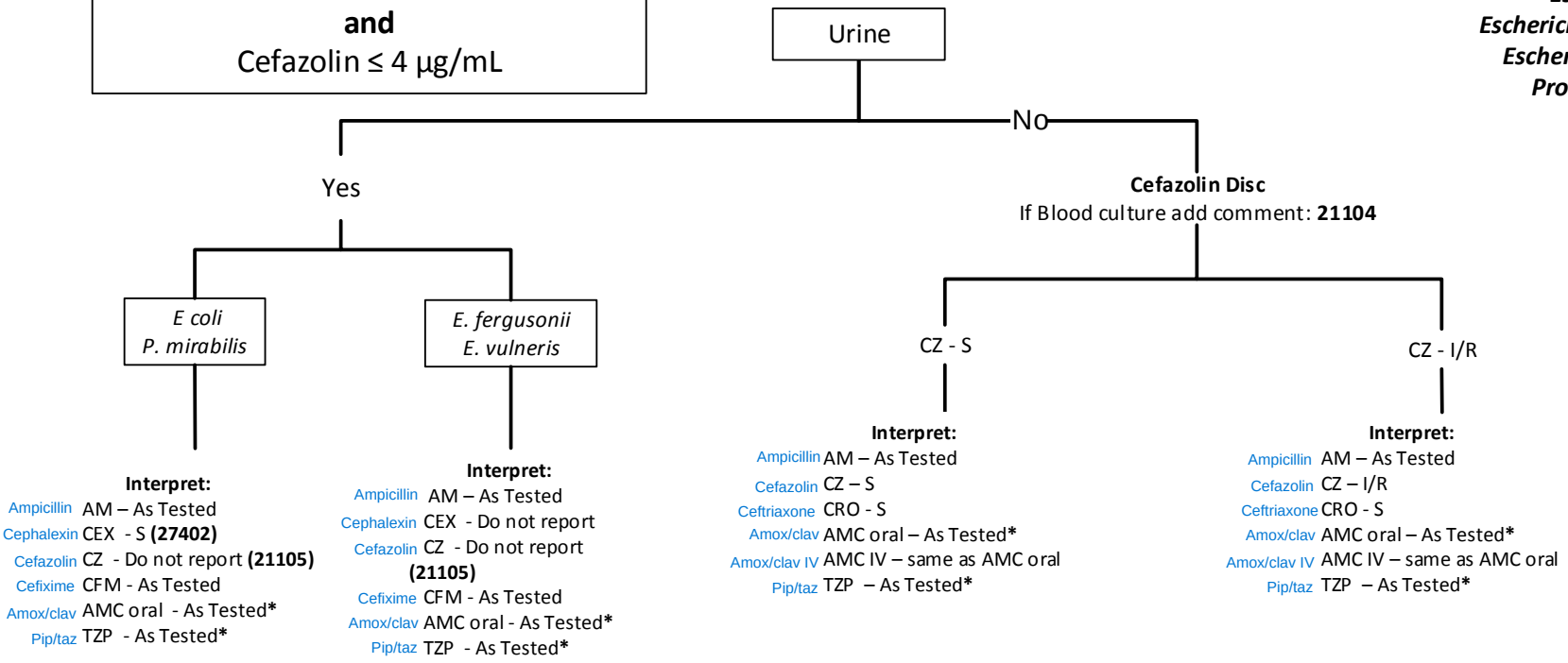


Chart 5A

Escherichia coli
Escherichia fergusonii
Escherichia vulneris
Proteus mirabilis

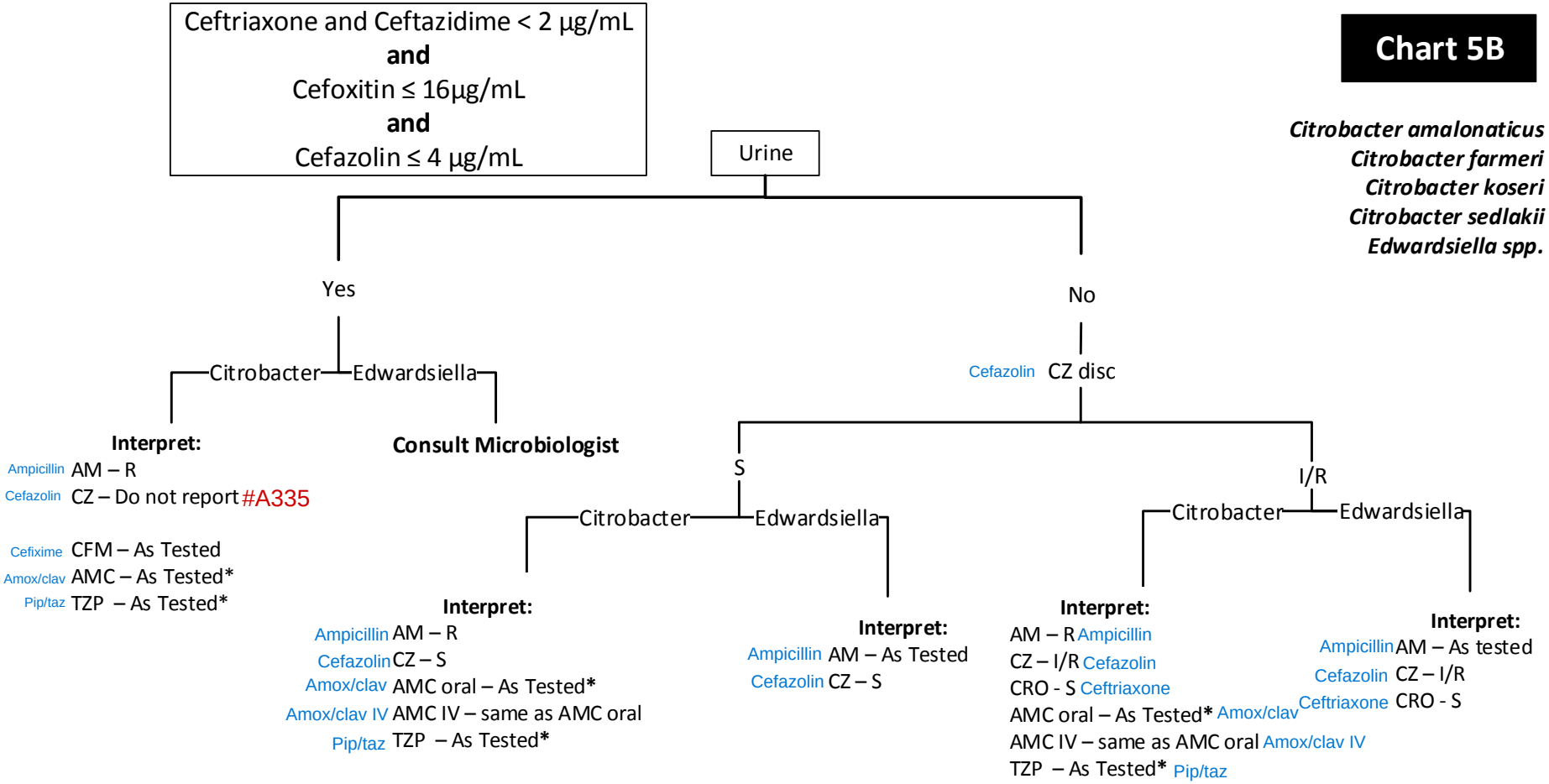
Ceftriaxone and Ceftazidime < 2 µg/mL
and
Cefoxitin ≤ 16µg/mL
and
Cefazolin ≤ 4 µg/mL



***Confirm results if piperacillin/tazobactam I/R and amoxicillin/clavulanate oral S. If TZP confirms as I/R report AMC oral as R.**

E. coli produce a non-inducible basal Amp C cephalosporinase that typically does not result in significant beta-lactam resistance (although in vitro the MICs of cephalothin/cephalexin and occasionally amoxicillin/clavulanate may be slightly elevated).

Comment #clx1 For uncomplicated lower UTI only. Add to cephalexin
Comment #A335 Cefazolin susceptibility result is available upon request. Add to cephalexin
Comment 21104: Cefazolin result to follow. If susceptible, this would be the preferred (or most narrow spectrum) parenteral cephalosporin.



***Confirm results if piperacillin/tazobactam I/R and amoxicillin/clavulanate oral S. If TZP confirms as I/R report AMC oral as R.**

The chromosomal penicillinase of these organisms has variable activity against oral/narrow spectrum cephalosporins (cephalexin). It is safest to report them all as I/R but not S.

Comment #A335 Cefazolin susceptibility result is available upon request.

Ceftriaxone and Ceftazidime < 2 µg/mL
and
Cefoxitin ≤ 16 µg/mL
and
Cefazolin ≤4 µg/mL

Chart 5C

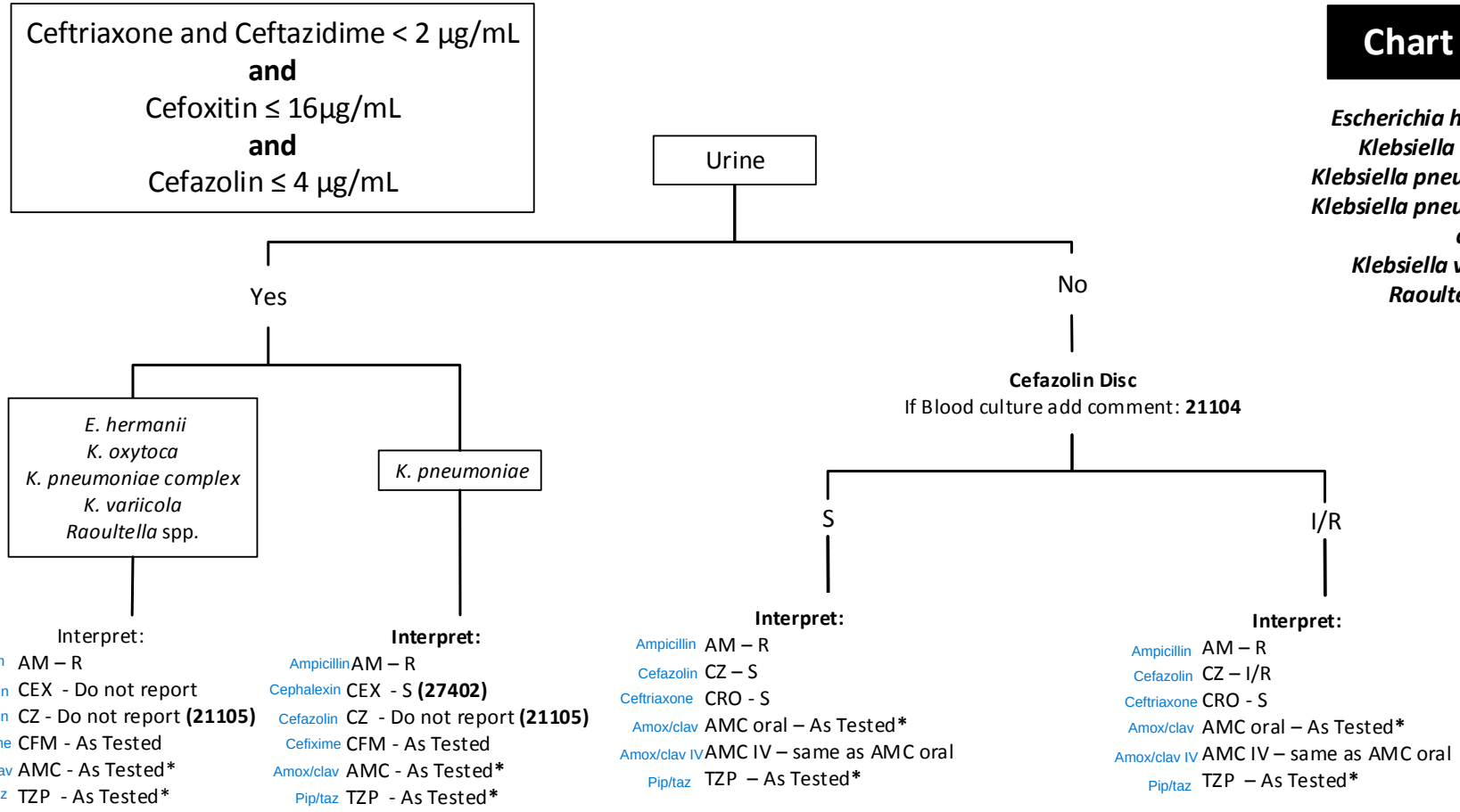
Salmonella spp
Shigella spp

Interpret:

Ampicillin AMP - As Tested
Cefixime CFM - As Tested
Ceftriaxone CRO - S

Chart 5D

Escherichia hermanii
Klebsiella oxytoca
Klebsiella pneumoniae
Klebsiella pneumoniae complex
Klebsiella variicola
***Raoultella* spp.**

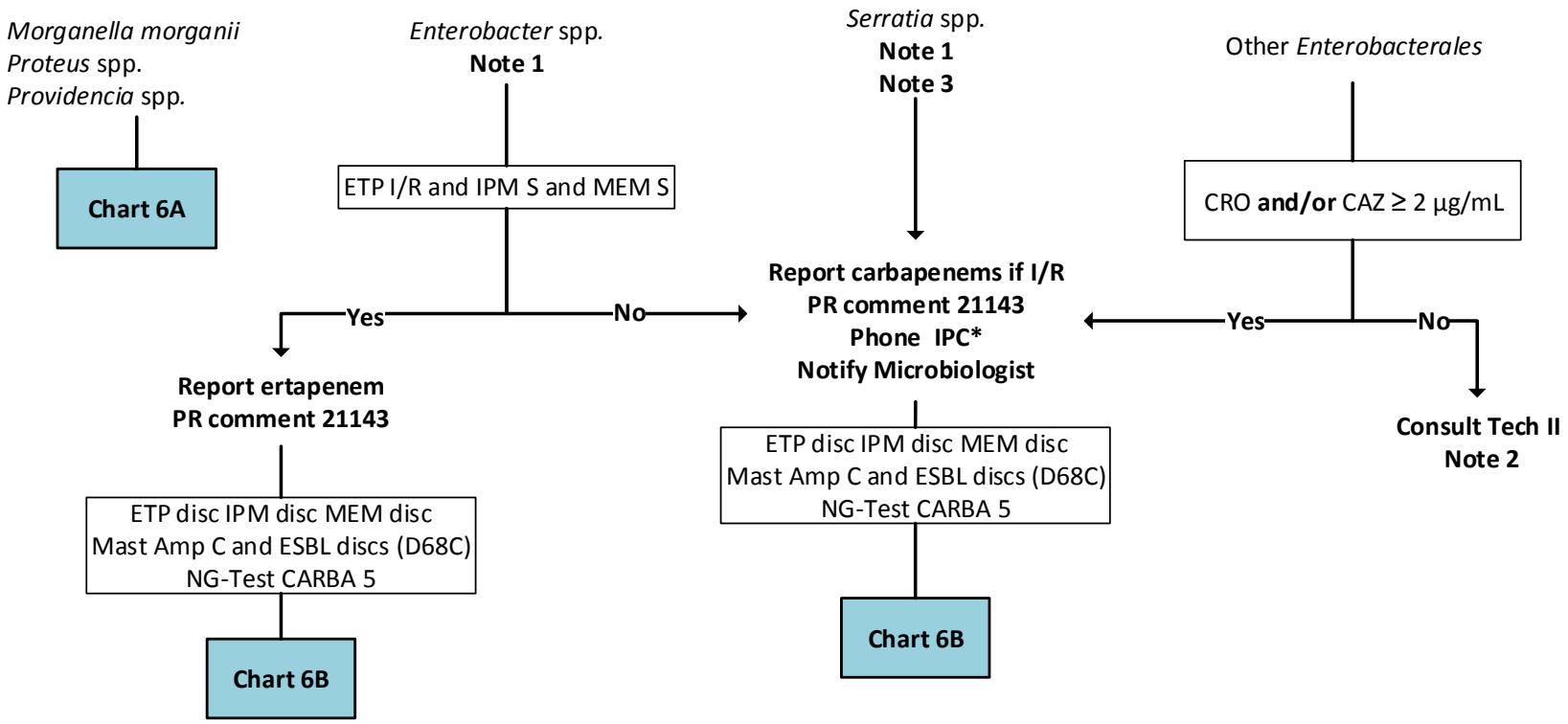


***Confirm results if piperacillin/tazobactam I/R and amoxicillin/clavulanate oral S. If TZP confirms as I/R report AMC oral as R.**

Comment#clx1: For uncomplicated lower UTI only. Add to cephalexin
Comment#A335: Cefazolin susceptibility result is available upon request. (Add to cephalexin)
Comment: Cefazolin result to follow. If susceptible, this would be the preferred (or most narrow spectrum) parenteral cephalosporin.

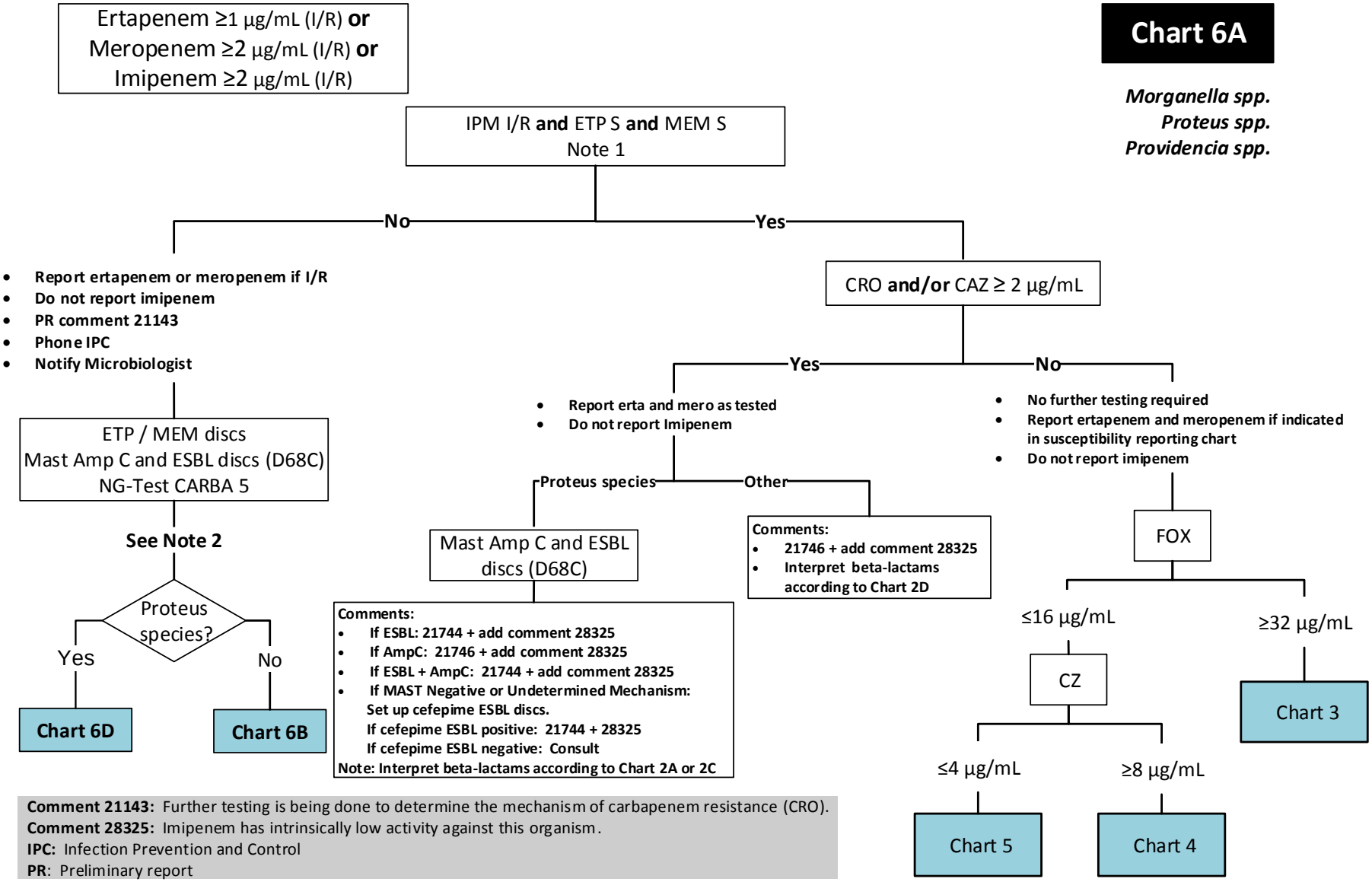
Ertapenem ≥1 µg/mL (I/R) **or** Meropenem ≥2 µg/mL (I/R) **or** Imipenem ≥2 µg/mL (I/R)

Chart 6



Comment 21143: Further testing is being done to determine the mechanism of carbapenem resistance (CRO).
IPC: Infection Prevention and Control
PR: Preliminary report
*: Phone call to IPC not required if only I/R to ertapenem.

Note 1: Chromosomal Class A carbapenemases have been found in *Enterobacter* spp. (NMC, IMI), *Serratia marcescens* (SME) and *Serratia fonticola* (SFC). These genes have also been found on transmissible elements. It is necessary to perform molecular testing to definitely determine the type of carbapenemase.
Note 2: Certain OXA enzymes (eg. OXA-48) hydrolyze carbapenems but not cephalosporins.
Note 3: Vitek N390 card has a card limitation for Serratia marcescens and imipenem. Test imipenem by disc diffusion before reporting imipenem result.

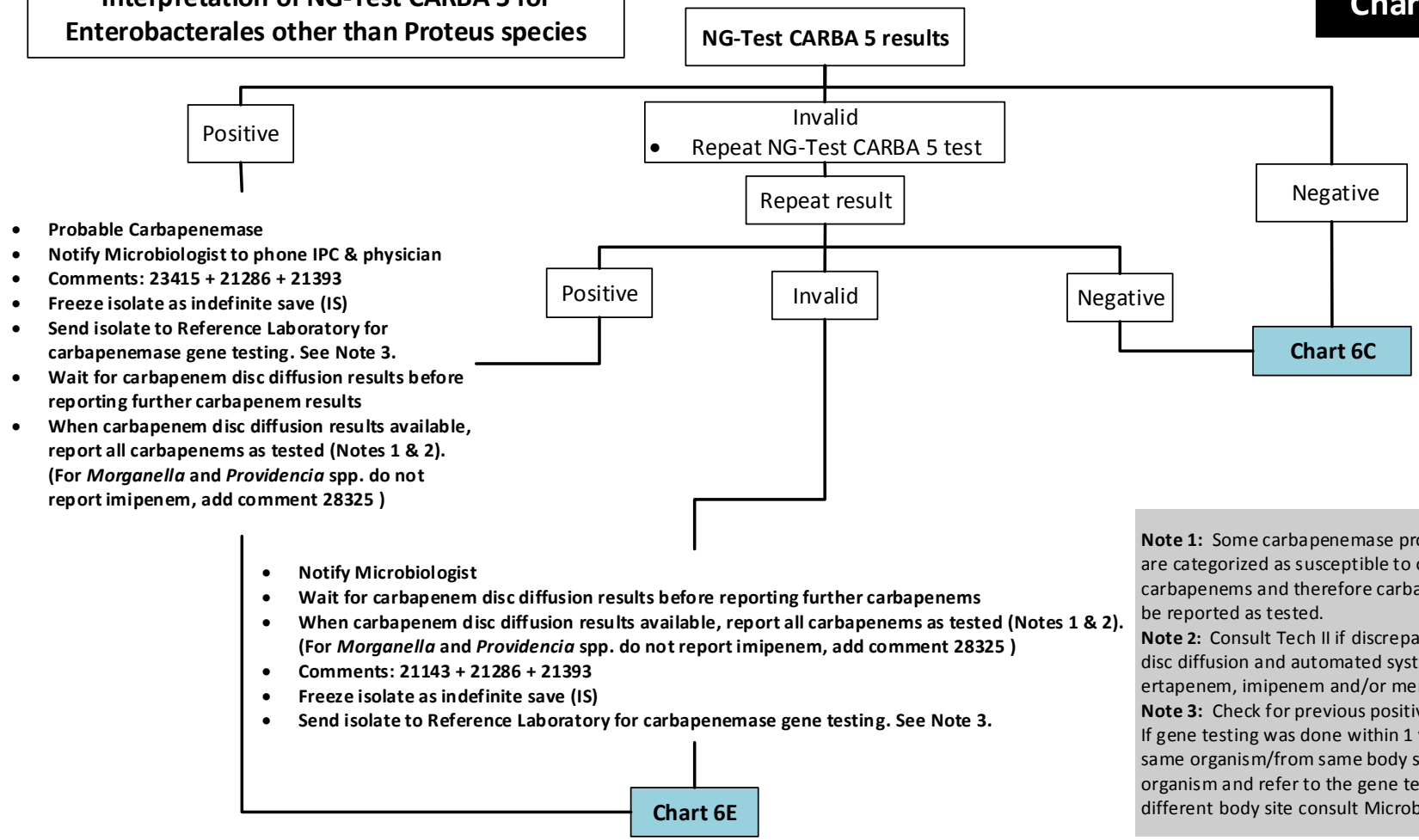


Comment 21143: Further testing is being done to determine the mechanism of carbapenem resistance (CRO).
Comment 28325: Imipenem has intrinsically low activity against this organism.
IPC: Infection Prevention and Control
PR: Preliminary report

Note 1: *Proteus, Providencia* and *Morganella* spp. may have low-level imipenem resistance (2-8 µg/mL) due to altered penicillin binding protein (PBP2).
Note 2: Consult Tech II if discrepancy between disc diffusion and automated system for ertapenem or meropenem.

Interpretation of NG-Test CARBA 5 for Enterobacterales other than Proteus species

Chart 6B

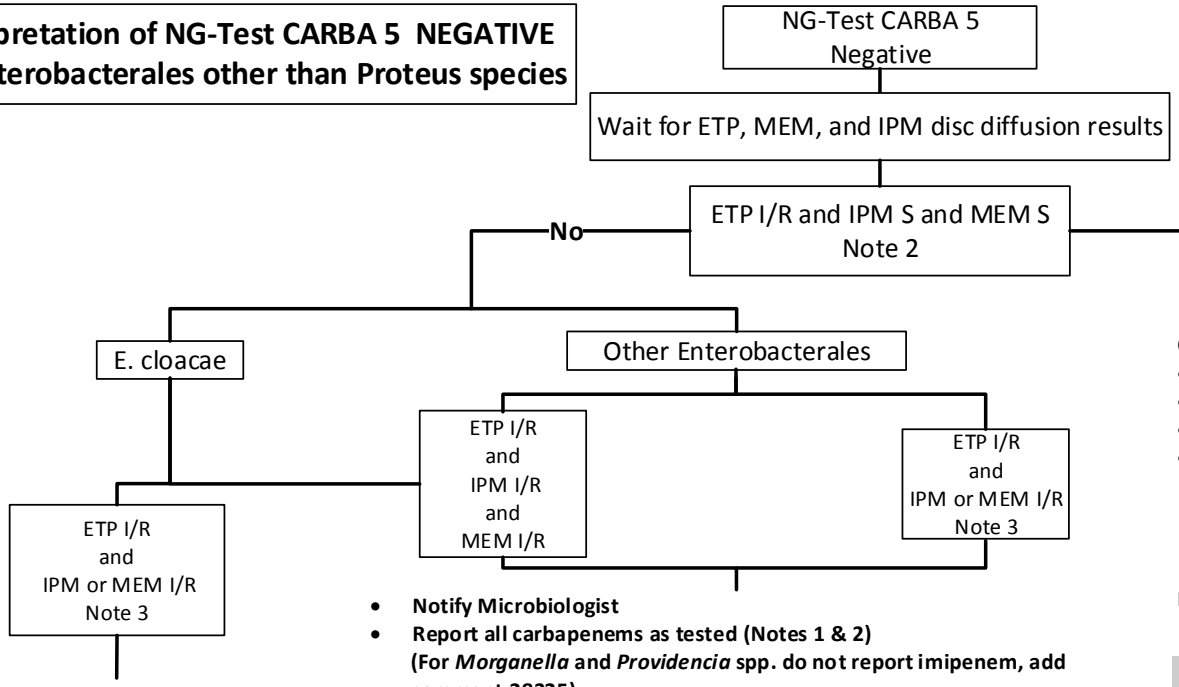


Note 1: Some carbapenemase producing isolates are categorized as susceptible to one or more carbapenems and therefore carbapenems should be reported as tested.
Note 2: Consult Tech II if discrepancy between disc diffusion and automated system for ertapenem, imipenem and/or meropenem.
Note 3: Check for previous positive gene testing. If gene testing was done within 1 year on the same organism/from same body site, report the organism and refer to the gene testing results. If different body site consult Microbiologist.

Comment 23415: Phenotypic testing suggests probable CARBAPENEMASE.
Comment 21143: Further testing is being done to determine the mechanism of carbapenem resistance (CRO).
Comment 21286: Sent for carbapenemase gene testing to National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2.
Comment 21393: Treatment of this organism is complex and may require high dose combination antibiotic therapy. Infectious Diseases consultation (by phone consultation if on site specialty services don't exist) is advisable.
Comment 28325: Imipenem has intrinsically low activity against this organism.
IPC: Infection Prevention and Control

Interpretation of NG-Test CARBA 5 NEGATIVE for Enterobacterales other than Proteus species

Chart 6C



Comments:

- **If ESBL: 21744 + 23340 + ***
- **If AmpC: 21746 + 23340 + ***
- **If ESBL + AmpC: 21744 + 23340 + ***
- **If MAST Negative or Undetermined Mechanism: Set up cefepime ESBL discs.**
  If cefepime ESBL positive: 21744 + 23340 + *
  If cefepime ESBL negative: Consult

Note: Interpret beta-lactams according to Chart 2

- **Notify Microbiologist**
- **Report all carbapenems as tested (Notes 1 & 2)**
  (For *Morganella* and *Providencia* spp. do not report imipenem, add comment 28325)
- **Comments: 21143 + 21286 + 21393**
- **Freeze isolate as indefinite save (IS)**
- **Phone IPC if not previously phoned**
- **Send isolate to Reference Laboratory for carbapenemase gene testing**

Note: Check for previous positive gene testing. If gene testing was done within 1 year on the same organism/from same body site, report the organism and refer to the gene testing results. If different body site consult Microbiologist.

Chart 6E

Comments:

- **If ESBL: 21744 + 23339**
- **If AmpC: 21746 + 23339**
- **If ESBL + AmpC: 21744 + 23339**
- **If MAST Negative or Undetermined Mechanism:**
  Set up cefepime ESBL discs.
  If cefepime ESBL positive: 21744 + 23339
  If cefepime ESBL negative: Consult

Note: Interpret beta-lactams according to Chart 2

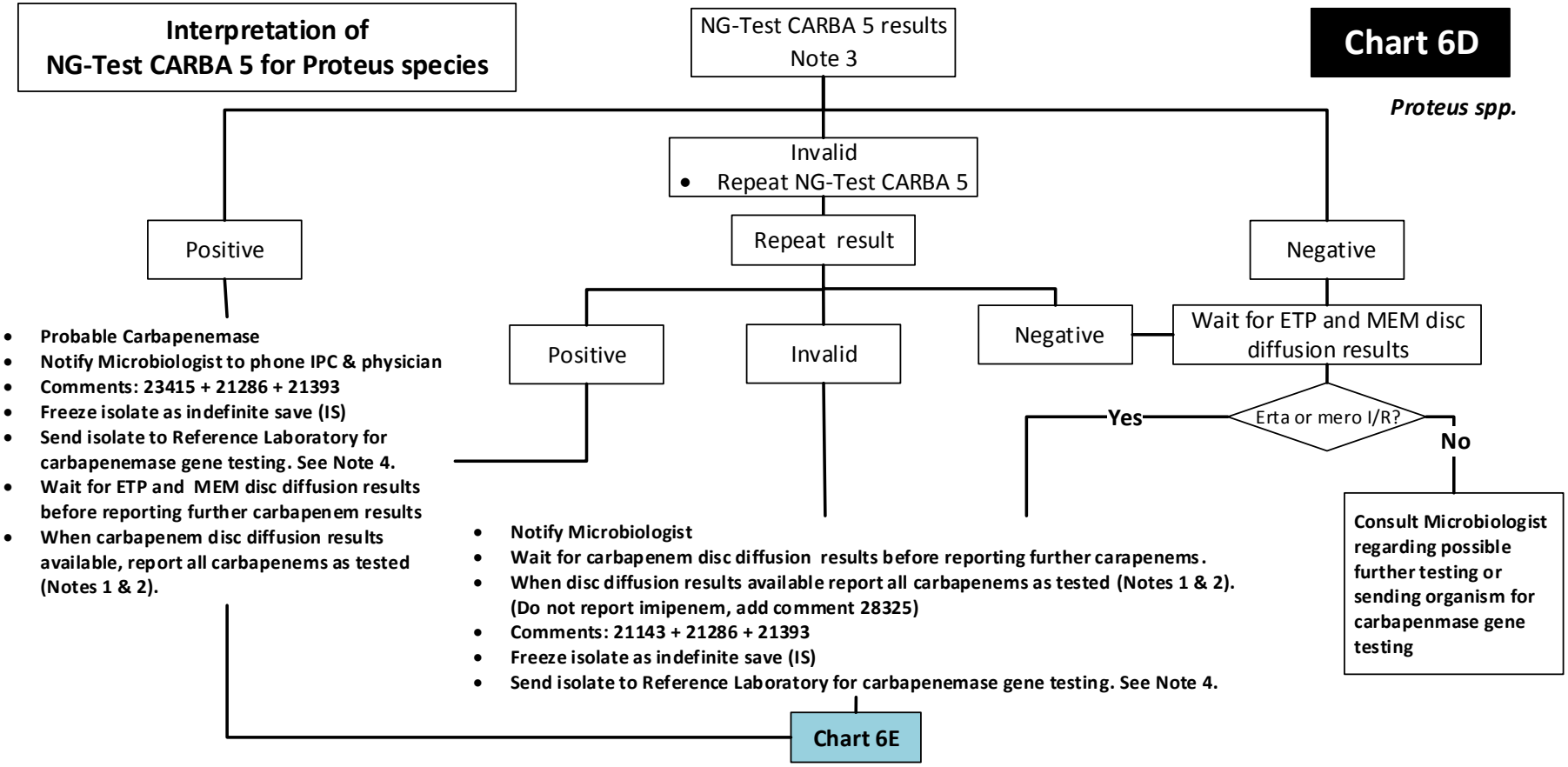
Note 1: Some carbapenemase producing isolates are categorized as susceptible to one or more carbapenems and therefore carbapenems should be reported as tested.
Note 2: Consult Tech II if discrepancy between disc diffusion and automated system for ertapenem, imipenem and/or meropenem.
Note 3: Consult MOC for any other combination of results.

Comment 21143: Further testing is being done to determine the mechanism of carbapenem resistance (CRO).
Comment 21286: Sent for carbapenemase gene testing to National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2.
Comment 21393: Treatment of this organism is complex and may require high dose combination antibiotic therapy. Infectious Diseases consultation (by phone consultation if on site specialty services don't exist) is advisable.
Comment 23339: This organism exhibits resistance to ertapenem (CRO) likely mediated by impermeability. Susceptible carbapenems should be used with caution.
Comment 23340: This organism exhibits resistance to carbapenems (CRO) likely mediated by impermeability.
Comment 28325: Imipenem has intrinsically low activity against this organism.
*** add:** Susceptible carbapenems should be used with caution.
IPC: Infection Prevention and Control

Interpretation of NG-Test CARBA 5 for Proteus species

Chart 6D

Proteus spp.

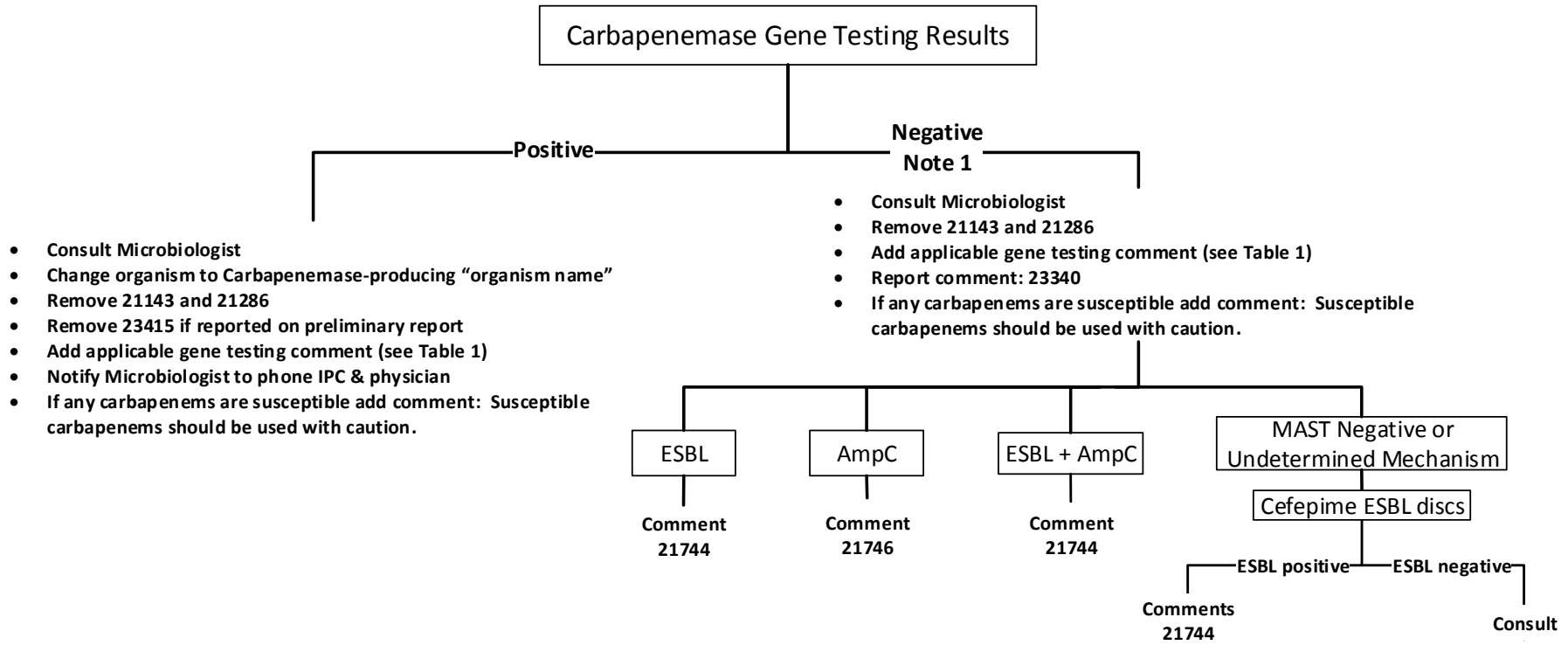


Comment 23415: Phenotypic testing suggests probable CARBAPENEMASE.
Comment 21143: Further testing is being done to determine the mechanism of carbapenem resistance (CRO).
Comment 21286: Sent for carbapenemase gene testing to National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2.
Comment 21393: Treatment of this organism is complex and may require high dose combination antibiotic therapy. Infectious Diseases consultation (by phone consultation if on site specialty services don't exist) is advisable.
Comment 28325: Imipenem has intrinsically low activity against this organism.
IPC: Infection Prevention and Control

Note 1: Some carbapenemase producing isolates are categorized as susceptible to one or more carbapenems and therefore carbapenems should be reported as tested.
Note 2: Consult Tech II if discrepancy between disc diffusion and automated system for ertapenem and/or meropenem.
Note 3: False negative NG-Test CARBA 5 results may occur with Proteus species.
Note 4: Check for previous positive gene testing. If gene testing was done within 1 year on the same organism/from same body site, report the organism and refer to the gene testing results. If different body site consult Microbiologist.

Interpretation of Carbapenemase Gene Testing Results

Chart 6E



Comment 23340: This organism exhibits resistance to carbapenems (CRO) likely mediated by impermeability.
IPC: Infection Prevention and control

Note 1: Most likely a permeability mutation. Permeability mutations are most common in *Klebsiella* and *Enterobacter* spp. Although they typically affect only ertapenem, they can also affect other carbapenems especially if concurrent ESBL or AmpC present. In addition to ertapenem, permeability mutations may preferentially affect meropenem (*Klebsiella* spp.) or imipenem (*Enterobacter* spp.).

Table 1
Carbapenemase Gene Testing Result Codes

CODE	COMMENT
21252+21314	Positive for KPC gene. Testing performed by the National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2.
21251+21314	Positive for IMP gene. Testing performed by the National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2.
21266+21314	Positive for VIM gene. Testing performed by the National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2.
21255+21314	Positive for NDM gene. Testing performed by the National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2.
21249+21314	Positive for GES gene. Testing performed by the National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2.
21261+21314	Positive for OXA-48 gene. Testing performed by the National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2.
21265+21314	Positive for SME gene. Testing performed by the National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2.
21256+21314	Positive for NMC gene. Testing performed by the National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2.
21201+21314	Negative for carbapenemase genes (GES, IMP, KPC, NDM, NMC, OXA and VIM). Testing performed by the National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2. **Note: add "-48" to OXA.**
21209+21314 (For *Serratia* spp.)	Negative for carbapenemase genes (GES, IMP, KPC, NDM, NMC, OXA, SME and VIM). Testing performed by the National Microbiology Laboratory (NML), 1015 Arlington Street, Winnipeg, MB, Canada, R3E 3R2. **Note: add "-48" to OXA.**

BETA-LACTAM RESISTANCE INTERPRETATION CHART

LIS Code	Comment	Ampicillin	Cephalexin	Cefazolin	Cefotaxime	Ceftriaxone	Ceftazidime	Cefixime	Cefepime	Aztreonam	Piperacillin/ Tazobactam	Amoxicillin/ Clavulanate	Ertapenem	Imipenem	Meropenem	Probable mechanism of resistance	Phone Infection Prevention and Control?
&1744	This organism is considered resistant to penicillins and cephalosporins. Amoxicillin-clavulanate and piperacillin-tazobactam are generally NOT recommended.	R	R	R	R	R	R	R	R	R	Do Not Report	R	S	S	S	ESBL	No
&1746	This organism is considered resistant to penicillins and cephalosporins (not including cefepime). Amoxicillin-clavulanate and piperacillin-tazobactam are generally NOT recommended.	R	R	R	R	R	R	R	Use With Caution	R	R Do Not Report	R	S	S	S	AmpC cephalosporinase	No
&1744	This organism is considered resistant to penicillins and cephalosporins. Amoxicillin-clavulanate and piperacillin-tazobactam are generally NOT recommended.	R	R	R	R	R	R	R	R	R	R Do Not Report	R	S	S	S	ESBL + AmpC cephalosporinase	No
&BL07	Beta-lactam resistance of this organism is mediatedby an undetermined mechanism of resistance. All penicillins, cephalosporins and aztreonam should be considered resistant.	R	R	R	R	R	R	R	Do Not Report	R	R Do Not Report	R	S	S	S	Indeterminate	No

BETA-LACTAM RESISTANCE INTERPRETATION CHART

LIS Code	Comment	Ampicillin	Cephalexin	Cefazolin	Cefotaxime	Ceftriaxone	Ceftazidime	Cefixime	Cefepime	Aztreonam	Piperacillin/ Tazobactam	Amoxicillin/ Clavulanate	Ertapenem	Imipenem	Meropenem	Probable mechanism of resistance	Phone Infection Prevention and Control?
&BL19	Beta-lactam resistance of this organism is likely mediated by hyperproduction of its chromosomal beta-lactamase conferring resistance to all penicillins and cephalosporins, aztreonam and beta-lactamase inhibitor combination drugs.	R	R	R	R	R	Do Not Report	R	R	R	R Do Not Report	R	S	S	S	Hyper-production of chromosomal enzymes	No
&BL11	Beta-lactam resistance of this organism is likely mediated by multiple beta-lactamases conferring resistance to all penicillins and cephalosporins, aztreonam and beta-lactamase inhibitor combination drugs.	R	R	R	R	R	R	R	R	R	R Do Not Report	R	S	S	S	Multiple beta-lactamases	No

CODE	COMMENT
&BL11	Beta-lactam resistance of this organism is likely mediated by multiple beta-lactamases conferring resistance to all penicillins and cephalosporins, aztreonam and beta-lactamase inhibitor combination drugs.
&BL07	Beta-lactam resistance of this organism is mediated by an undetermined mechanism of resistance. All penicillins, cephalosporins and aztreonam should be considered resistant.
#cz1	Cefazolin result to follow. If susceptible, this would be the preferred (or most narrow spectrum) parenteral cephalosporin.
#A335	Cefazolin susceptibility result is available upon request.
&2143	Further testing is being done to determine the mechanism of carbapenem resistance (CRO).
&2130	Susceptibility testing for this organism was performed by a non-reference method and/or required modifications to the standard test conditions.
&1744	This organism is considered resistant to penicillins and cephalosporins. Amoxicillin-clavulanate and piperacillin-tazobactam are generally NOT recommended.
&1746	This organism is considered resistant to penicillins and cephalosporins (not including cefepime). Amoxicillin-clavulanate and piperacillin-tazobactam are generally NOT recommended.
&BL19	Beta-lactam resistance of this organism is likely mediated by hyperproduction of its chromosomal beta-lactamase conferring resistance to all penicillins and cephalosporins, aztreonam and beta-lactamase inhibitor combination drugs.

DRUG NAME	CODE
Amoxicillin/Clavulanate	AMC
Ampicillin	AM
Aztreonam	ATM
Cefazolin	CZ
Cefepime	FEP
Cefixime	CFM
Cefotaxime	CTX
Cefoxitin	FOX
Ceftazidime	CAZ
Ceftriaxone	CRO
Cephalexin	CEX
Ertapenem	ETP
Imipenem	IPM
Meropenem	MEM
Piperacillin-tazobactam	TZP