

Table 3. Reporting Extended Spectrum β -Lactam Resistance Molecular Results in *Enterobacteriaceae*

Indication	Target(s)	Method	Specimen Type	Result		Suggestions for Resolution	Report as:	Footnotes*
				Molecular Target Result	Observed Phenotype (if tested)			
Detection of Extended Spectrum β-Lactam resistance in <i>Enterobacteriaceae</i> (in an isolate susceptible to all carbapenems)	ESBL Type CTX-M, SHV, TEM	NAAT, Microarray	Colony, blood culture	Detection of any ESBL target	R to all 3 rd and 4 th generation cephalosporins tested, e.g. ceftriaxone R cefotaxime R ceftazidime R cefepime R	N/A	Report phenotypic results as found (if available); consider reporting presence of molecular target per institutional protocol	1-12
				Detection of any ESBL target	S to all 3 rd and 4 th generation cephalosporins tested, e.g. ceftriaxone S cefotaxime S ceftazidime S cefepime S	Repeat molecular and phenotypic tests; If blood culture, check for mixed culture; If mixed, test isolates individually and report phenotypic results as found	If discrepancy is not resolved, repeat susceptibility testing should be performed using a reference method and the conflicting genotypic and phenotypic testing results should both be reported	1-12
				Detection of CTX-M ESBL target	Variable resistance to 3 rd and 4 th generation cephalosporins e.g. ceftriaxone R cefotaxime R ceftazidime R or S cefepime R or S	Expected phenotype for some CTX-M strains; Check cefepime using a reference method if S	Report phenotypic results as found, including reference cefepime result; consider reporting presence of molecular target per institutional protocol	1-12
				Detection of TEM or SHV ESBL target	Variable resistance to 3 rd and 4 th generation cephalosporins, e.g. ceftriaxone R or S cefotaxime R or S ceftazidime R or S cefepime R or S	Expected phenotype for some TEM/SHV strains; Check cefepime using a reference method if S	Report phenotypic results as found, including reference cefepime result; consider reporting presence of molecular target per institutional protocol	1-12
				No detection of ESBL targets	Resistance to 3 rd generation cephalosporins and variable resistance to 4 th generation cephalosporins e.g. ceftriaxone R cefotaxime R ceftazidime R cefepime R or S	Likely non-tested broad spectrum β -lactamase (e.g. AmpC, carbapenemase or other ESBL); consider repeating molecular tests and checking cefepime using reference method if S	Report phenotypic results as found, including reference cefepime result if tested	1-12

Detection of Carbapenem resistance in <i>Enterobacteriaceae</i>	KPC, OXA-48-like, VIM, NDM or IMP	NAAT, microarray	Colony, blood culture	Detection of any tested carbapenemase target	Resistance to all carbapenems, e.g. meropenem R imipenem R doripenem R ertapenem R	N/A	Report phenotypic results as found (if available); consider reporting presence of molecular target per institutional protocol	1-4, 12-14
				Detection of any tested carbapenemase target	Susceptible to all carbapenems except ertapenem (variable), e.g. meropenem S imipenem S doripenem S ertapenem R or S	Repeat molecular and phenotypic tests; if blood culture, check for mixed culture; if mixed, test isolates individually and report phenotypic results as found; consider a phenotypic test for carbapenemase activity (such as Carba NP or mCIM)	If discrepancy is not resolved, repeat susceptibility testing should be performed using a reference method and the conflicting genotypic and phenotypic testing results should both be reported along with a comment advising caution; current clinical and laboratory evidence is insufficient to conclude whether carbapenem monotherapy of carbapenemase-carrying strains with an MIC in the susceptible range will be effective, or whether the molecular assays are completely accurate.	1-4, 12-15
				No detection of tested carbapenemase targets	Susceptible to all carbapenems except ertapenem, e.g. meropenem S imipenem S doripenem S ertapenem R	Likely ESBL/AmpC and porin alteration, especially for <i>Enterobacter</i> ; consider a phenotypic test for carbapenemase activity (such as Carba NP or mCIM); carbapenemase unlikely if negative although rare carbapenemases, e.g. GES-types, are still possible	If carbapenemase activity is detected, repeat susceptibility testing should be performed using a reference method and the conflicting genotypic and phenotypic testing results should both be reported along with a comment advising caution; current clinical and laboratory evidence is insufficient to conclude whether carbapenem monotherapy of carbapenemase-carrying strains with an MIC in the susceptible range will be effective, or whether the molecular assays are completely accurate. Otherwise report phenotypic results as found.	1-4, 12-15
				No detection of tested carbapenemase targets	Resistance to any carbapenems except ertapenem, e.g. meropenem R imipenem R doripenem R ertapenem R or S	Possible other carbapenemase; if blood culture, check for mixed culture; if mixed, test isolates individually and report as found; consider repeating molecular and susceptibility tests and performing a phenotypic test for carbapenemase activity (such as Carba NP or mCIM)	If carbapenemase activity is detected, repeat susceptibility testing should be performed using a reference method and the conflicting genotypic and phenotypic testing results should both be reported along with a comment advising caution; current clinical and laboratory evidence is insufficient to conclude whether carbapenem monotherapy of carbapenemase-carrying strains with an MIC in the susceptible range will be effective, or whether the molecular assays are completely accurate. Otherwise report phenotypic results as found.	1-4, 12-16

*In addition the specific possibilities listed, genotype/phenotype discrepancies could arise as a consequence of mixed cultures, emergence of new genotypes, or mutations and/or wild-type reversions of resistance targets.

Footnotes

1. Multiple β -lactamases may be carried by individual bacterial isolates. Most carbapenemase-producing bacteria are resistant to 3rd and 4th gen cephalosporins, although bacteria with OXA-48 enzymes may not be unless they co-produce an ESBL or AmpC enzyme.
2. Molecular assays can detect the presence of specific β -lactamase genes but cannot exclude the presence of other beta-lactamase genes or resistance mechanisms, or novel variants with changes in primer / probe annealing sites. Therefore, phenotypic resistance should always be reported.
3. Isolates with phenotypic susceptibility despite the presence of a resistance determinant may indicate the potential for resistance to emerge during therapy.
4. These are provisional guidelines based on general principles; however, the performance characteristics of many individual RUO assays are presently unknown.
5. Susceptibility of TEM/SHV-carrying strains to β -lactam/inhibitor combinations is variable.
6. Susceptibility of ESBL-carrying strains to cefepime is variable.
7. Susceptibility of ESBL-carrying strains to β -lactam/inhibitor combinations is variable.
8. Some strains carrying CTX-M ESBLs remain susceptible to ceftazidime.
9. Some strains carrying TEM/SHV-derived ESBLs remain susceptible to cefotaxime/ceftriaxone.
10. Some molecular assays for *ampC* may not reliably distinguish between chromosomal and plasmid-encoded genes in some bacterial species.
11. Most strains with de-repressed AmpC expression remain susceptible to cefepime.
12. These recommendations are based on cephalosporin and carbapenem breakpoints in M100S, 26th edition.
13. The susceptibility to other carbapenems of ertapenem-resistant strains with ESBL or AmpC enzymes and reduced porin expression that do not contain carbapenemase genes or express carbapenemase activity may be reported as measured in phenotypic susceptibility assays.
14. Rapid tests for carbapenemase activity (e.g., CarbaNP) may not detect OXA-48-like and some other carbapenemases.
15. Caution is advised. Current clinical evidence is insufficient to conclude whether carbapenem monotherapy of carbapenemase-carrying strains with an MIC in the susceptible range will be effective.
16. Some isolates of Enterobacteriaceae, in particular but not exclusively *Morganella*, *Proteus* spp. and *Providencia* spp., may exhibit intrinsic low-level resistance to imipenem on a non-carbapenemase-mediated basis.