Appendix B. Intrinsic Resistance

Intrinsic resistance is defined as inherent or innate (not acquired) antimicrobial resistance, which is reflected in wild-type antimicrobial patterns of all or almost all representatives of a species. Intrinsic resistance is so common that susceptibility testing is unnecessary. For example, *Citrobacter* spp. are intrinsically resistant to ampicillin.

These tables can be helpful in at least 3 ways: 1) they provide a way to evaluate the accuracy of testing methods; 2) they aid in the recognition of common phenotypes; and 3) they can assist with verification of cumulative antimicrobial susceptibility test data. In the tables, an "R" occurring with an antimicrobial agent–organism combination means that strains should test resistant. A small percentage (1% to 3%) may appear susceptible due to method variation, mutation, or low levels of resistance expression.

Each laboratory should decide which agents to test and report in consultation with the antimicrobial stewardship team and other relevant institutional stakeholders. If tested, the result for an antimicrobial agent–organism combination listed as having intrinsic resistance should be reported as resistant. Consideration may be given to adding comments regarding intrinsic resistance of agents not tested. See Appendix A, footnote a.

Refer to Glossary I and II for individual agents within the drug classes listed below.

B1. Enterobacterales

Antimicrobial Agent → / Organism ↓	Ampicillin	Amoxicillin-clavulanate	Ampicillin-sulbactam	Ticarcillin	Cephalosporins I	Cephamycins	Cephalosporins II	Imipenem	Tetracyclines	Tigecycline	Nitrofurantoin	Colistin Polymyxin B	Aminoglycosides
Citrobacter freundii	R	R	R		R	R	R						
Citrobacter koseri, Citrobacter amalonaticus group[a]	R			R									
Enterobacter cloacae complex[b]	R	R	R		R	R							
Escherichia coli	There is no intrinsic resistance to β-lactams in this organism.												
Escherichia hermannii	R			R									
Hafnia alvei	R	R	R		R	R						R[c]	
Klebsiella (formerly *Enterobacter*) *aerogenes*	R	R	R		R	R							
Klebsiella pneumoniae, Klebsiella oxytoca, Klebsiella variicola	R			R									
Morganella morganii	R	R			R		R	[d]		R	R	R	
Proteus mirabilis	There is no intrinsic resistance to penicillins and cephalosporins in this organism.							[d]	R	R	R	R	

Appendix B. (Continued)

B1. Enterobacterales (Continued)

Antimicrobial Agent → / Organism ↓	Ampicillin	Amoxicillin-clavulanate	Ampicillin-sulbactam	Ticarcillin	Cephalosporins I	Cephamycins	Cephalosporins II	Imipenem	Tetracyclines	Tigecycline	Nitrofurantoin	Colistin Polymyxin B	Aminoglycosides
Proteus penneri	R				R		R	[d]	R	R	R	R	
Proteus vulgaris	R				R		R	[d]	R	R	R	R	
Providencia rettgeri	R	R			R			[d]	R	R	R	R	
Providencia stuartii	R	R			R			[d]	R	R	R	R	[e]
Raoultella spp.[f]	R			R									
Salmonella and *Shigella* spp.	There is no intrinsic resistance to β-lactams in these organisms; refer to **WARNING** below for reporting.												
Serratia marcescens	R	R	R		R	R	R				R	R	
Yersinia enterocolitica	R	R		R	R								

Abbreviations: AST, antimicrobial susceptibility testing; MIC, minimal inhibitory concentration; R, resistant.

WARNING: For *Salmonella* and *Shigella* spp., aminoglycosides, first- and second-generation cephalosporins, and cephamycins may appear active *in vitro* but are not effective clinically and should not be reported as susceptible.

Footnotes

a. *C. amalonaticus* group includes *C. amalonaticus, Citrobacter farmeri, a*nd *Citrobacter sedlakii*.

b. *E. cloacae* complex includes *Enterobacter asburiae, E. cloacae,* and *Enterobacter hormaechei*. Other members of the complex include *Enterobacter kobei* and *Enterobacter ludwigii*, for which AST data are not available.

c. Colistin and polymyxin B resistance also applies to *Hafnia paralvei*.

d. *Proteus*, *Providencia*, and *Morganella* spp. may have elevated MICs to imipenem by mechanisms other than by production of carbapenemases. Isolates that test as susceptible should be reported as susceptible.

e. *P. stuartii* should be considered resistant to gentamicin, netilmicin, and tobramycin but not intrinsically resistant to amikacin.

Appendix B. (Continued)

f. *Raoultella* spp. include *Raoultella ornithinolytica, Raoultella terrigena,* and *Raoultella planticola*.

NOTE 1: Cephalosporins III, cefepime, cefiderocol, aztreonam, ticarcillin-clavulanate, piperacillin-tazobactam, imipenem-relebactam, ceftazidime-avibactam, meropenem-vaborbactam, and carbapenems are not listed because there is no intrinsic resistance in Enterobacterales.

NOTE 2: Enterobacterales are also intrinsically resistant to clindamycin, daptomycin, fusidic acid, glycopeptides (vancomycin), lipoglycopeptides (oritavancin, teicoplanin, telavancin), linezolid, tedizolid, quinupristin-dalfopristin, rifampin, and macrolides (erythromycin, clarithromycin, and azithromycin). However, there are some exceptions with macrolides (eg, *Salmonella* and *Shigella* spp. with azithromycin).

B2. Non-Enterobacterales

Antimicrobial Agent → / Organism ↓	Ampicillin, amoxicillin	Piperacillin	Ticarcillin	Ampicillin-sulbactam	Amoxicillin-clavulanate	Piperacillin-tazobactam	Cefotaxime	Ceftriaxone	Ceftazidime	Cefepime	Aztreonam	Imipenem	Meropenem	Ertapenem	Polymyxin B Colistin	Aminoglycosides	Tetracyclines Tigecycline	Trimethoprim	Trimethoprim-sulfamethoxazole	Chloramphenicol	Fosfomycin
Acinetobacter baumannii/ Acinetobacter calcoaceticus complex	R				R						R			R				R		R	R
Burkholderia cepacia complex[a]	R	R	R	R	R	[a]	[a]	[a]		[a]	[a]	[a]		R	R	[a]		[a]			R
Pseudomonas aeruginosa	R			R	R		R	R						R			R	R	R	R	
Stenotrophomonas maltophilia	R	R	R	R	R	R	R	R			R	R	R	R		R	[b]	R			R

Abbreviations: MIC, minimal inhibitory concentration; R, resistant.

Footnotes

a. *B. cepacia* complex isolates have chromosomal genes that must undergo mutational changes before expressing resistance. It is not known how often these mutations occur during growth. Intrinsic resistance implies the presence of resistance mechanisms in natural or wild-type strains that result in phenotypic resistance for all or nearly all strains. Environmental *B. cepacia* complex strains lacking mutations do not express resistance mechanisms, resulting in low MICs to many antimicrobial agents, whereas clinical strains that express resistance genes, such as those from cystic fibrosis patients, have high MIC values to these same antimicrobial agents. There is insufficient clinical evidence to confirm whether strains that have low MICS, despite the presence of resistance mechanisms, will respond *in vivo*. Therefore, intrinsic resistance to the footnoted antibiotics (listed as resistant in previous editions of CLSI M100) cannot be confirmed.

b. *S. maltophilia* is intrinsically resistant to tetracycline but not to doxycycline, minocycline, or tigecycline.

Appendix B. (Continued)

NOTE: These nonfermentative gram-negative bacteria are also intrinsically resistant to penicillin (ie, benzylpenicillin), cephalosporins I (cephalothin, cefazolin), cephalosporin II (cefuroxime), cephamycins (cefoxitin, cefotetan), clindamycin, daptomycin, fusidic acid, glycopeptides (vancomycin), linezolid, macrolides (erythromycin, azithromycin, clarithromycin), quinupristin-dalfopristin, and rifampin.

B3. *Staphylococcus* spp.

Antimicrobial Agent → / Organism ↓	Novobiocin	Fosfomycin	Fusidic acid
S. aureus *S. lugdunensis*	There is no intrinsic resistance in these species.		
S. epidermidis			
S. haemolyticus			
S. saprophyticus	R	R	R
S. capitis		R	
S. cohnii	R		
S. xylosus	R		

Abbreviations: MRS, methicillin (oxacillin)-resistant staphylococci; R, resistant.

NOTE 1: These gram-positive bacteria are also intrinsically resistant to aztreonam, polymyxin B/colistin, and nalidixic acid.

NOTE 2: MRS, as defined by cefoxitin or oxacillin testing, as appropriate to the species, are considered resistant to other β-lactam agents, ie, penicillins, β-lactam combination agents, cephems with the exception of ceftaroline, and carbapenems. This is because most cases of documented MRS infections have responded poorly to β-lactam therapy, or because convincing clinical data that document clinical efficacy for those agents have not been presented.

Appendix B. (Continued)

B4. *Enterococcus* spp.

Antimicrobial Agent → / Organism ↓	Cephalosporins	Vancomycin	Teicoplanin	Aminoglycosides	Clindamycin	Quinupristin-dalfopristin	Trimethoprim	Trimethoprim-sulfamethoxazole	Fusidic acid
E. faecalis	R[a]			R[a]	R[a]	R	R	R[a]	R
E. faecium	R[a]			R[a]	R[a]		R	R[a]	R
E. gallinarum/E. casseliflavus	R[a]	R		R[a]	R[a]	R	R	R[a]	R

Abbreviation: R, resistant.

Footnote

a. **WARNING:** For *Enterococcus* spp., cephalosporins, aminoglycosides (except for high-level resistance testing), clindamycin, and trimethoprim-sulfamethoxazole may appear active *in vitro* but are not effective clinically and should not be reported as susceptible.

NOTE: These gram-positive bacteria are also intrinsically resistant to aztreonam, polymyxin B/colistin, and nalidixic acid.

B5. Anaerobic Gram-Positive Bacilli

Antimicrobial Agent → / Organism ↓	Vancomycin	Aminoglycosides
Clostridium and *Clostridioides* spp.		R
Clostridium innocuum	R	R

Abbreviation: R, resistant.

Appendix B. (Continued)

B6. Anaerobic Gram-Negative Bacilli

Antimicrobial Agent → / Organism ↓	Aminoglycosides	Penicillin	Ampicillin	Quinolones
Bacteroides spp.	R	R	R	
Fusobacterium canifelinum	R			R

Abbreviation: R, resistant.

NOTE: Information in boldface type is new or modified since the previous edition.