

## 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 three 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 institutional leaders representing infectious diseases practitioners, the pharmacy and therapeutics and infection prevention committees of the medical staff, and the antimicrobial stewardship team. 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.”

## Appendix B. (Continued)

## B1. Enterobacterales

Antimicrobial Agent Organism	Ampicillin	Amoxicillin-clavulanate	Ampicillin-sulbactam	Ticarcillin	Cephalosporins I: Cefazolin, Cephalothin	Cephamycins: Cefoxitin, Cefotetan	Cephalosporin II: Cefuroxime	Imipenem	Tetracyclines	Tigecycline	Nitrofurantoin	Polymyxin B Colistin	Aminoglycosides
<i>Citrobacter freundii</i>	R	R	R		R	R	R						
<i>Citrobacter koseri</i> , <i>Citrobacter amalonaticus</i> group <sup>a</sup>	R			R									
<i>Enterobacter cloacae</i> complex <sup>b</sup>	R	R	R		R	R							
<i>Escherichia coli</i>	There is no intrinsic resistance to $\beta$ -lactams in this organism.												
<i>Escherichia hermannii</i>	R			R									
<i>Hafnia alvei</i>	R	R	R		R	R							
<i>Klebsiella</i> (formerly <i>Enterobacter) aerogenes</i>	R	R	R		R	R							
<i>Klebsiella pneumoniae</i> , <i>Klebsiella oxytoca</i> , <i>Klebsiella</i> <i>variicola</i>	R			R									
<i>Morganella morganii</i>	R	R			R		R	<sup>c</sup>		R	R	R	
<i>Proteus mirabilis</i>	There is no intrinsic resistance to penicillins and cephalosporins in this organism.							<sup>c</sup>	R	R	R	R	
<i>Proteus penneri</i>	R				R		R	<sup>c</sup>	R	R	R	R	
<i>Proteus vulgaris</i>	R				R		R	<sup>c</sup>	R	R	R	R	
<i>Providencia rettgeri</i>	R	R			R			<sup>c</sup>	R	R	R	R	
<i>Providencia stuartii</i>	R	R			R			<sup>c</sup>	R	R	R	R	<sup>d</sup>
<i>Raoultella</i> spp. <sup>e</sup>	R			R									

## Appendix B. (Continued)

### B1. Enterobacterales (Continued)

Antimicrobial Agent \ Organism	Ampicillin	Amoxicillin-clavulanate	Ampicillin-sulbactam	Ticarcillin	Cephalosporins I: Cefazolin, Cephalothin	Cephamycins: Cefoxitin, Cefotetan	Cephalosporin II: Cefuroxime	Imipenem	Tetracyclines	Tigecycline	Nitrofurantoin	Polymyxin B Colistin	Aminoglycosides
<i>Salmonella</i> and <i>Shigella</i> spp.	There is no intrinsic resistance to $\beta$ -lactams in these organisms; refer to <b>WARNING</b> below for reporting.												
<i>Serratia marcescens</i>	R	R	R		R	R	R				R	R	
<i>Yersinia enterocolitica</i>	R	R		R	R								

Abbreviation: R, resistant.

**WARNING:** For *Salmonella* spp. 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

- Citrobacter amalonaticus* group includes *C. amalonaticus*, *C. farmeri*, and *C. sedlakii*.
- E. cloacae* complex includes *Enterobacter asburiae*, *Enterobacter cloacae*, and *Enterobacter hormaechei*. Other members of the complex include *Enterobacter kobei* and *Enterobacter ludwigii*, for which antimicrobial susceptibility testing data are not available.
- Proteus* spp., *Providencia* spp., and *Morganella* spp. may have elevated minimal inhibitory concentrations to imipenem by mechanisms other than by production of carbapenemases. Isolates that test as susceptible should be reported as susceptible.
- P. stuartii* should be considered resistant to gentamicin, netilmicin, and tobramycin but not intrinsically resistant to amikacin.
- Raoultella* spp. includes *R. ornithinolytica*, *R. terrigena*, and *R. planticola*.

**NOTE 1:** Cephalosporins III, cefepime, aztreonam, ticarcillin-clavulanate, piperacillin-tazobactam, and the 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).

**NOTE 3:** Information in boldface type is new or modified since the previous edition.

## Appendix B. (Continued)

### 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	
<i>Acinetobacter baumannii</i> / <i>Acinetobacter calcoaceticus</i> complex	R				R						R			R				R		R	R	
<i>Burkholderia cepacia</i> complex <sup>a</sup>	R	R	R	R	R	a	a	a	a	a	a	a		R	R	a		a				R
<i>Pseudomonas aeruginosa</i>	R			R	R		R	R						R			R	R	R	R		
<i>Stenotrophomonas maltophilia</i>	R	R	R	R	R	R	R	R			R	R	R	R		R	<sup>b</sup>	R				R

Abbreviation: 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 test susceptible *in vitro*, despite the presence of resistance mechanisms, will respond *in vivo*. Therefore, intrinsic resistance to the footnoted antibiotics (listed as resistant in previous editions of M100) cannot be confirmed.
- b. *S. maltophilia* is intrinsically resistant to tetracycline but not to doxycycline, minocycline, or tigecycline.

**NOTE 1:** 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.

**NOTE 2:** Information in boldface type is new or modified since the previous edition.

## Appendix B. (Continued)

### B3. Staphylococci

Antimicrobial Agent	Novobiocin	Fosfomycin	Fusidic Acid
Organism			
<i>S. aureus</i>	There is no intrinsic resistance in these species.		
<i>S. lugdunensis</i>			
<i>S. epidermidis</i>			
<i>S. haemolyticus</i>			
<i>S. saprophyticus</i>	R	R	R
<i>S. capitis</i>		R	
<i>S. cohnii</i>	R		
<i>S. xylosus</i>	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 ceftaxime or oxacillin testing, as appropriate to the species, are considered resistant to other  $\beta$ -lactam agents, ie, penicillins,  $\beta$ -lactam combination agents, cephalosporins with the exception of ceftazidime, and carbapenems. This is because most cases of documented MRS infections have responded poorly to  $\beta$ -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	Cephalosporins	Vancomycin	Teicoplanin	Aminoglycosides	Clindamycin	Quinupristin-dalfopristin	Trimethoprim	Trimethoprim-sulfamethoxazole	Fusidic Acid
Organism									
<i>E. faecalis</i>	R <sup>a</sup>			R <sup>a</sup>	R <sup>a</sup>	R	R	R <sup>a</sup>	R
<i>E. faecium</i>	R <sup>a</sup>			R <sup>a</sup>	R <sup>a</sup>		R	R <sup>a</sup>	R
<i>E. gallinarum</i> / <i>E. casseliflavus</i>	R <sup>a</sup>	R		R <sup>a</sup>	R <sup>a</sup>	R	R	R <sup>a</sup>	R

Abbreviation: R, resistant.

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.

## Appendix B. (Continued)

### B5. Anaerobic Gram-Positive Bacilli

Antimicrobial Agent	Vancomycin	Aminoglycosides
Organism		
<i>Clostridium</i> and <i>Clostridioides</i> spp.		R
<i>Clostridium innocuum</i>	R	R

Abbreviation: R, resistant.

### B6. Anaerobic Gram-Negative Bacilli

Antimicrobial Agent	Aminoglycosides	Penicillin	Ampicillin	Quinolones
Organism				
<i>Bacteroides</i> spp.	R	R	R	
<i>Fusobacterium canifelinum</i>	R			R

Abbreviation: R, resistant.