EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases

Expected Resistant Phenotypes

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This document is based on previous document “Intrinsic Resistance and Unusual Phenotypes” version 3.3, October 2021. Since then EUCAST has decided to abandon the term “intrinsic resistance” because of the difficulties identified when discussing the term “intrinsic”. The document has been divided into “Expected resistant phenotypes” and “Expected susceptible phenotypes” organised by species, and together with “Expert rules” they are available on https://www.eucast.org/expert_rules_and_intrinsic_resistance/.

Definitions of “Expected Phenotypes”

Expected Phenotypes

The purpose of the Expected phenotypes tables is to serve as a tool for the validation of species identification, to aid in the validation of susceptibility test results and to prevent unnecessary susceptibility testing. The presence of an unexpected phenotype indicates that the laboratory should check the species identification, the susceptibility test results or both.

A microorganism is listed as an “expected phenotype” for an agent (or group of agents) because the vast majority of isolates are resistant (expected resistant phenotype) or in another case, susceptible (expected susceptible phenotype).

Expected Resistant phenotype (previously categorized as “intrinsic resistance”). When isolates of a species (or group of species) are generally and universally resistant (>90% of all isolates irrespective of origin exhibit a characteristic resistance mechanism or MIC values above the PK/PD breakpoint listed in the EUCAST tables), a susceptible result should be viewed with suspicion (Tables below). Testing should normally be avoided, and laboratories are expected to either not report a result at all, or if a result is desired, to report the isolate as resistant without testing. Clinical colleagues should be advised against using the agent for the species in question. In the tables, where there is an “R”, any other result is unexpected.

Expected Susceptible phenotype. When isolates of a species (or group of species) are generally and universally expected to be susceptible (>99% of all isolates susceptible to the agent irrespective of origin because resistance mechanisms of clinical significance have not been reported and/or because MIC-values are consistently below the PK/PD breakpoint listed in EUCAST tables), a resistant result should be viewed with suspicion. If testing is performed, unexpected test results indicate a problem with species identification and/or susceptibility testing and results should be confirmed with alternative methods. When the resistant result is thought to reflect an acquired resistance mechanism this must be confirmed by reference methodology and preferably also by sequencing of the genome.

Table 1 **Expected resistant phenotype (susceptibility not expected) in *Enterobacterales* and *Aeromonas* spp. *Enterobacterales* and *Aeromonas* spp. are also expected to be resistant to benzylpenicillin, glycopeptides, lipoglycopeptides, fusidic acid, macrolides (with some exceptions[1]), lincosamides, streptogramins, rifampicin, and oxazolidinones**

Rule	Organisms	Ampicillin/Amoxicillin	Amoxicilin-clavulanic acid	Ampicillin-sulbactam	Ticarcillin	Cefazolin, Cephalothin Cefalexin, Cefadroxil	Cefoxitin[2]	Cefuroxime	Tetracyclines	Tigecycline	Polymyxin B, Colistin	Fosfomycin	Nitrofurantoin
1.1	*Citrobacter koseri, Citrobacter amalonaticus*[3]	R			R								
1.2	*Citrobacter freundii*[4]	R	R	R		R	R						
1.3	*Enterobacter cloacae* complex	R	R	R		R	R						
1.4	*Escherichia hermannii*	R			R								
1.5	*Hafnia alvei*	R	R								R		
1.6	*Klebsiella aerogenes*	R	R	R		R	R						
1.7	*Klebsiella pneumoniae* complex	R			R								
1.8	*Klebsiella oxytoca*	R			R								
1.9	*Leclercia adecarboxylata*											R	
1.10	*Morganella morganii*	R	R	R		R			R		R		R
1.11	*Plesiomonas shigelloides*	R	R	R									
1.12	*Proteus mirabilis*								R		R		R
1.13	*Proteus penneri*	R				R		R	R		R		R
1.14	*Proteus vulgaris*	R				R		R	R		R		R
1.15	*Providencia rettgeri*	R	R	R		R			R		R		R

Rule	Organisms	Ampicillin/Amoxicillin	Amoxicilin-clavulanic acid	Ampicillin-sulbactam	Ticarcillin	Cefazolin, Cephalothin Cefalexin, Cefadroxil	Cefoxitin[2]	Cefuroxime	Tetracyclines	Tigecycline	Polymyxin B, Colistin	Fosfomycin	Nitrofurantoin
1.16	*Providencia stuartii*	R	R	R		R			R		R		R
1.17	*Raoultella* spp.	R			R								
1.18	*Serratia marcescens*	R	R	R		R	R	R			R		R
1.19	*Yersinia enterocolitica*	R	R	R	R	R	R						
1.20	*Yersinia pseudotuberculosis*										R		
1.21	*Aeromonas hydrophila*	R		R									
1.22	*Aeromonas veronii*	R		R	R								
1.23	*Aeromonas dhakensis*	R		R			R						
1.24	*Aeromonas caviae*	R		R									
1.25	*Aeromonas jandaei*	R		R	R								

[1] Azithromycin is effective *in vivo* for the treatment of typhoid/paratyphoid fever and erythromycin may be used to treat travellers' diarrhoea.

[2] Clinical breakpoints for cefoxitin have not been defined. *Enterobacterales* species expected to be resistant to this antibiotic produce a chromosomal inducible AmpC β-lactamase (AmpC) that is responsible for higher cefoxitin MIC values when compared with those from *Enterobacterales* species lacking production of this beta-lactamase.

[3] Also includes *Citrobacter sedlakii, Citrobacter farmeri* and *Citrobacter rodentium.*

[4] Also includes *Citrobacter braakii*, *Citrobacter murliniae*, *Citrobacter werkmanii* and *Citrobacter youngae.*

Table 2 Expected resistant phenotype (susceptibility not expected) in non-fermentative gram-negative bacteria. Non-fermentative gram-negative bacteria are also generally intrinsically resistant to benzylpenicillin, first- and second-generation cephalosporins, glycopeptides, lipoglycopeptides, fusidic acid, macrolides, lincosamides, streptogramins, rifampicin and oxazolidinones

Rule	Organisms	Ampicillin/Amoxicillin	Amoxicillin-clavulanic	Ampicillin-sulbactam	Ticarcillin	Ticarcillin-clavulanic acid	Piperacillin	Piperacillin-tazobactam	Cefotaxime/Ceftriaxone	Ceftazidime	Cefepime	Aztreonam	Ertapenem	Imipenem	Meropenem	Ciprofloxacin	Chloramphenicol	Aminoglycosides	Trimethoprim	Fosfomycin	Tetracyclines	Tigecycline	Polymyxin B/Colistin
2.1	*Acinetobacter baumannii*, *Acinetobacter pittii*, *Acinetobacter nosocomialis*	R	R	Note[1]					R			R	R						R	R	R[2]	Note[2]	
2.2	*Achromobacter xylosoxidans*	R							R			R	R										
2.3	*Burkholderia cepacia* complex[3]	R	R	R	R	R	R	R	R			R	R			R	R	R[4]	R	R			R
2.4	*Elizabethkingia meningoseptica*	R	R	R	R	R			R	R	R	R	R	R	R								R
2.5	*Elizabethkingia anophelis*	R	R	R	R	R			R	R	R	R	R	R	R								
2.6	*Ochrobactrum anthropi*	R	R	R	R	R	R	R	R	R	R	R	R										
2.7	*Pseudomonas aeruginosa*	R	R	R					R				R				R	Note[5]	R		R	R	
2.8	*Stenotrophomonas maltophilia*	R	R	R	R		R	R	R			R	R	R	R			R[4]	R[6]	R	R[7]		
2.9	*Chryseobacterium spp.*	R	R	R	R	R			R	R		R	R	R	R			R					R

[1] *Acinetobacter baumannii* may appear to be susceptible to ampicillin-sulbactam due to activity of sulbactam with this species.

[2] *Acinetobacter* is resistant to tetracycline and doxycycline but to a lesser degree to minocycline and tigecycline. Clinical results have varied.

[3] *Burkholderia cepacia* complex includes different species. Some strains may appear susceptible to some beta-lactams *in vitro* but they are clinically resistant.

[4] *Burkholderia cepacia* and *Stenotrophomonas maltophilia* are expected to be resistant to all aminoglycosides. Resistance is attributed to poor permeability and putative efflux. In addition, most *Stenotrophomonas maltophilia* produce the AAC(6')Iz enzyme.

[5] *Pseudomonas aeruginosa* is resistant to kanamycin and neomycin due to low level APH(3')-IIb activity.

[6] *Stenotrophomonas maltophilia* is typically susceptible to trimethoprim-sulfamethoxazole, but resistant to trimethoprim alone.

[7] *Stenotrophomonas maltophilia* is always resistant to tetracycline whereas susceptibility to doxycycline, minocycline and tigecycline vary. Clinical results have varied.

Table 3 **Expected resistant phenotype (susceptibility not expected) in gram-negative bacteria other than *Enterobacterales* and non-fermentative gram-negative bacteria. Gram-negative bacteria other than *Enterobacterales* and non-fermentative gram-negative bacteria listed are also expected to be resistant to glycopeptides, lipoglycopeptides, lincosamides, and oxazolidinones.**

Rule	Organisms	Fusidic acid	Streptogramins	Trimethoprim	Nalidixic acid
3.1	*Haemophilus influenzae*	R	R		
3.2	*Moraxella catarrhalis*			R	
3.3	*Neisseria* spp.			R	
3.4	*Campylobacter fetus*	R	R	R	R
3.5	*Campylobacter jejuni, Campylobacter coli*	R	R	R	

Table 4 Expected resistant phenotype (susceptibility not expected) in gram-positive bacteria. Gram-positive bacteria are expected to be resistant to aztreonam, temocillin, polymyxin B/colistin and nalidixic acid.

Rule	Organisms	Fusidic acid	Ceftazidime	Cephalosporins (except ceftazidime)	Aminoglycosides	Macrolides	Clindamycin	Quinupristin-dalfopristin	Vancomycin	Teicoplanin	Fosfomycin	Novobiocin	Sulfonamides
4.1	*Staphylococcus saprophyticus*	R	R								R	R	
4.2	*Staphylococcus cohnii*		R									R	
4.3	*Staphylococcus xylosus*		R									R	
4.4	*Staphylococcus capitis*		R								R		
4.5	Other coagulase-negative staphylococci and *S. aureus*		R										
4.6	*Streptococcus* spp.	R	R		R[1]								
4.7	*Enterococcus faecalis*	R	R	R	R[1]	R	R	R					R
4.8	*Enterococcus gallinarum, Enterococcus casseliflavus*	R	R	R	R[1]	R	R	R	R				R
4.9	*Enterococcus faecium*	R	R	R	R[1,2]	R							R
4.10	*Corynebacterium* spp.										R		
4.11	*Listeria monocytogenes*		R	R									
4.12	*Leuconostoc* spp., *Pediococcus* spp.								R	R			
4.13	*Lactobacillus* spp. (*L. casei, L. casei* var. *rhamnosus*)								R	R			

[1] Low-level resistance (LLR) to aminoglycosides. Combinations of aminoglycosides with cell wall inhibitors (penicillins and glycopeptides) are synergistic and bactericidal against isolates that are susceptible to cell wall inhibitors and do not display high-level resistance to aminoglycosides

[2] In addition to LLR to aminoglycosides, *Enterococcus faecium* produces a chromosomal AAC(6')-I enzyme that is responsible for the loss of synergism between aminoglycosides (except gentamicin, amikacin and streptomycin) and penicillins or glycopeptides

Table 5 **Expected resistant phenotype (susceptibility not expected) in anaerobes. Anaerobes are usually resistant to aztreonam, aminoglycosides, polymyxin B/colistin and nalidixic acid.**

Rule	Organisms	Vancomycin
5.1	*Clostridium ramosum*, *Clostridium innocuum*	R