COMITE DE L'ANTIBIOGRAMME DE LA SOCIETE FRANCAISE DE MICROBIOLOGIE

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Following the recommendations of the WHO Experts Committee of biological Standardization (technical reports N°610, 1977), the French Society for Microbiology has created an Antibiogramme Committee (CA-SFM), with the aim of proposing the standards which define the clinical categories (former therapeutic categories). The MIC and zone diameter interpretive standards, as well as the specific recommendations for certain species or certain antibiotic groups, are published in a yearly report.

INTERPRETIVE STANDARDS FOR THE ANTIBIOGRAMME

The interpretive standards which define the categories result from the integration of several data: distribution of minimum inhibitory concentrations (MIC) for the populations of resistant and susceptible strains belonging to different species, humors and tissues concentrations obtained with the dosages recommended in the therapeutic indications written by the *agence française de sécurité sanitaire des produits de santé* (AFSSAPS, French agency of sanitary safety of health products), confrontation of the *in vitro* results and clinical results, statistical variability of the methods used.

DEFINITION OF THE CLINICAL CATEGORIES

Three clinical categories were chosen for the interpretation of the *in vitro* susceptibility tests:
Susceptible (S), Resistant (R) and Intermediate (I).

Susceptible

The **S** strains are those for which there is a strong likelihood of therapeutic success in the case of a treatment by the systemic route with the recommended dosage.

Resistant

The **R** strains are those for which there is a strong likelihood of therapeutic failure, whatever the treatment.

Intermediate

The **I** strains are those for which therapeutic success cannot be predicted.
These strains constitute a heterogeneous group for which the sole value of the MIC cannot predict the therapeutic success:

- their resistance mechanism, with a weak *in vitro* expression can lead to a classification in the S category. Therefore, *in vivo*, a part of these strains seems resistant to the therapeutics;
- their resistance mechanism has an insufficient expression to justify a classification in the R category but allows the emergence of *in vivo* resistance during the treatment;
- their resistance mechanism has an insufficient expression to justify a classification in the R category but allows to hope a therapeutic effect under certain conditions (high level local concentrations or increased dosages);
- the intermediate category is also a buffer zone which takes into account the technical and biological uncertainties (the strains for which the MICs are close to the critical concentrations can be, on the account of these uncertainties, accidentally categorized I).

CATEGORIZATION PROCEDURE

According to interpretive standards

For the main antimicrobial agents, interpretive standards of low (c) and high (C) concentrations and equivalent zone diameters allow the categorization according to criteria shown in table I. MIC and zone diameter interpretive standards for various antimicrobial agent classes and agar dilution test or disk diffusion test are shown in table III. For certain species or certain bacterial groups, specific criteria have been chosen.

Table I - Categorization criteria according to interpretive standards

Categorie	MIC (mg/L)	Diameter (∅) (mm)
S	MIC ≤ c	∅ ≥ D
R	MIC > C	∅ < d
I	c < MIC ≤ C	d ≤ ∅ < D

Interpretive reading of the antibiogramme

The interpretive reading of the antibiogramme, based on the knowledge of the resistance phenotypes aims at transforming a result, originally S categorized, according to interpretive standards, into I or R result, due to a risk of therapeutic failure. First of all, it requires the correct identification of the bacterial strain and a standardized antibiogramme method. It does not aim at the formal identification of the implied resistance mechanism(s), a procedure that imposes the implementation of specific techniques.
The interpretive reading rules are mentioned for certain species or certain bacterial groups in the additional notes of tables VII to XIX.

GENERAL TECHNICAL CONDITIONS FOR THE AGAR DILUTION AND DISK DIFFUSION TESTS.

(Bull. Soc. Fr. Microbiol., 1993, 8, 156-66 ; Clin. Microbiol. Infect. 1996, 2, Suppl. 1)

***Enterobacteriaceae*, gram-negative nonfermenters (*Pseudomonas aeruginosa*, *Acinetobacter* spp., *Stenotrophomonas maltophilia*, *Burkholderia cepacia* ...), *Staphylococcus* spp., *Enterococcus* spp.**
(Tables VII to XI)

- Inoculum

From an overnight non-selective agar medium culture plate, prepare a suspension in Mueller-Hinton broth or 0.9% saline equivalent to the 0.5 McFarland standard (~ 10^8 CFU/mL). This suspension can also be prepared from a Mueller-Hinton broth culture obtained after incubation at 37°C in a water bath stirred for 3 to 5 hours, with a density adjusted to the 0.5 McFarland standard.

- Agar medium

Mueller-Hinton agar

- Inoculation

• agar dilution test: dilute the inoculum suspension to 1/10 and put 1 to 2 µl, i e ~10^4 CFU per spot.

• disk diffusion test: dilute the inoculum suspension to 1/100 (~10^6 CFU/mL) and seed by swabbing or by flooding while respecting the necessary safety measures.

- Reading

After 18-24 hours of incubation at 35-37° C.

***Streptococcus pneumoniae*, *Streptococcus* spp.**
(Tables XII and XIII)

- Inoculum

From an overnight sheep blood agar culture plate, prepare a suspension in Mueller-Hinton broth or 0.9% saline equivalent to the 0.5 McFarland standard (~ 10^8 CFU/mL).

- Agar media

Mueller Hinton agar supplemented with 5% defibrinated sheep blood.
For cotrimoxazole: Mueller Hinton agar supplemented with 5% hemolysed horse blood.

- Inoculation

• agar dilution test: dilute the inoculum suspension to 1/10 and put 1 to 2 µl, i e ~10^4 CFU per spot.

• disk diffusion test: dilute the inoculum suspension to 1/10 (~10^7 CFU/mL) and seed by swabbing or by flooding while respecting the necessary safety measures.

- Reading

After 18-24 hours of incubation at 35-37° C in an atmosphere of 5% CO_2.

Haemophilus influenzae
(Table XIV)

- Inoculum

From an overnight chocolate PolyViteX® agar culture plate, prepare a suspension in Mueller-Hinton broth or 0.9% saline equivalent to the 0.5 McFarland standard (~ 10^7 CFU/mL).

- Agar media

Chocolate PolyViteX® agar or HTM agar (Mueller Hinton + NAD 15 mg/L + hematin 15 mg/L + yeast extract 5 g/L).

- Inoculation

- agar dilution test: put 1 to 2 µl of the inoculum suspension, i e ~10^4 CFU per spot.
- disk diffusion test: dilute the inoculum suspension to 1/10 (~10^6 CFU/mL) and seed by swabbing or by flooding while respecting the necessary safety measures.

- Reading

After 18-24 hours of incubation at 35-37° C.

Neisseria meningitidis
(table XV)

- Inoculum

From an overnight chocolate PolyViteX® agar culture plate, prepare a suspension in M/15 PBS (pH 7.2) equivalent to the 0.5 McFarland standard (~ 10^6 CFU/mL).

- Agar medium

Mueller-Hinton agar

- Inoculation

- agar dilution test: put 10 µl of the inoculum suspension, i e ~10^4 CFU per spot.
- disk diffusion test: seed the inoculum suspension by swabbing or by flooding while respecting the necessary safety measures. Lay out the disks 60 mm apart from center to center, in order to avoid the overlapping of the inhibition zones.

- Reading

After 18-24 hours of incubation at 35-37° C in an atmosphere of 5% CO_2.

Neisseria gonorrhoeae
(table XVI)

- Inoculum

From an overnight chocolate PolyViteX® agar culture plate, prepare a suspension in M/15 PBS (pH 7.2) equivalent to the 1 McFarland standard (~ 10^8 CFU/mL).

- Agar medium

Chocolate PolyViteX® agar

- Inoculation

- agar dilution test: put 10 µl of the inoculum suspension, i e ~10^6 CFU per spot.
- disk diffusion test: seed the inoculum suspension by swabbing or by flooding while respecting the necessary safety measures. Lay out the disks 60 mm apart from center to center, in order to avoid the overlapping of the inhibition zones.

- Reading

After 18-24 hours of incubation at 35-37° C in an atmosphere of 5% CO_2 or after 36-40 hours if the growth is insufficient.

***Campylobacter* spp.**
(table XVII)

- Inoculum

From an overnight isolation agar culture plate, prepare a suspension in Brucella broth or 0.9% saline equivalent to the 0.5 McFarland standard (~ 10^8 CFU/mL).

- Agar medium

Mueller Hinton agar supplemented with 5% defibrinated sheep or horse blood.

- Inoculation

- agar dilution test: put 2 to 5 µl of the inoculum suspension, i e ~10^5 CFU per spot.
- disk diffusion test: dilute the inoculum suspension to 1/100 and seed the inoculum suspension by swabbing or by flooding while respecting the necessary safety measures. Dry the surface of the agar plates in order to eliminate any moisture traces, which enhance spreading.

- Reading

After 18-24 hours of incubation at 35-37° C in a microaerophilic or anaerobic atmosphere according to the needs of the strain.

Helicobacter pylori
(table XVIII)

- Inoculum

Prepare a suspension in Mueller-Hinton broth or 0.9% saline equivalent to the 3 McFarland standard (~ 10^9 CFU/mL). Check the absence of coccoid shaped cells (<10%).

- Agar medium

Mueller Hinton agar supplemented with 10% defibrinated horse blood.

- Inoculation

- disk diffusion test: seed the inoculum suspension by swabbing or by flooding while respecting the necessary safety measures.

- Reading

After 72 hours of incubation at 35-37° C in a microaerophilic atmosphere and after 4 days to detect the double populations.

Anaerobes
(table XIX)

- Inoculum

From an overnight Columbia supplemented with 5% sheep blood agar culture plate or Brucella supplemented with K1 vitamin (1 mg/L) and 5% hemolysed sheep blood agar culture plate, prepare a suspension in Brucella or Schaedler broth equivalent to the 0.5 McFarland standard (~ 10^7 CFU/mL) for the dilution test or the 1 McFarland standard (~ 10^8 CFU/mL) for the disk diffusion test.
For slow growing strains (> 72 hours), prepare a suspension in Brucella or Schaedler broth (~ 10^7 CFU/mL) to the 0.5 McFarland standard from a Brucella or Schaedler broth culture.

- Agar media

Wilkins Chalgren agar supplemented with 5% defibrinated sheep blood or Brucella agar + K1 vitamin (1 mg/L) supplemented with 5% hemolysed sheep blood. For certain species, other supplements (sodium bicarbonate 1 mg/L, hemin 5 mg/L) are used.

- Inoculation

- agar dilution test: put 2 to 3 µl of the inoculum suspension (0.5 McFarland), i e ~10^5 CFU per spot.
- disk diffusion test: seed the inoculum suspension (1 McFarland) by swabbing.

- Reading

After 48 hours of incubation at 35-37° C in an anaerobic atmosphere if the growth is sufficient. For clindamycin, the reading must be absolutely performed after 48 hours.

INTERNAL QUALITY CONTROL (Revision 2000)

An internal quality control must be carried out to be sure of the validity of the results obtained. The recommended reference strains are:
- *Escherichia coli* ATCC 25922 (CIP 7624),
- *Pseudomonas aeruginosa* ATCC 27853 (CIP 76110),
- *Staphylococcus aureus* ATCC 25923 (CIP 7625),

The control frequency and the measures to be taken in case of a difference with the expected result must be determined according to the method used and the number of tests carried out. As an example, table II shows the acceptable limits (mean ± 1 standard deviation obtained with 400 tests) of the inhibition diameters obtained by disk diffusion test, for these reference strains.

Table II – Acceptable zone diameter quality control limits for the reference strains.

Antimicrobial Agent	Disk Content	*Escherichia coli* ATCC 25922	*Pseudomonas aeruginosa* ATCC 27853	*Staphylococcus aureus* ATCC 25923
Penicillin G	6 µg (10 IU)	-	-	31.0 – 38.5
Oxacillin	5 µg	-	-	27.0 – 34.0
Amoxicillin	25 µg	22.0 – 26.5	-	-
Amoxicillin/clavulanic acid	20/10 µg	22.0 – 27.0	-	-
Ticarcillin	75 µg	-	25.0 – 30.5	-
Piperacillin	75 µg	-	27.5 – 32.5	-
Cephalotin	30 µg	18.0 – 23.0	-	-
Cefotaxime	30 µg	32.5 – 37.5	-	-
Ceftazidime	30 µg	-	25.5 – 31.5	-
Imipenem	10 µg	-	24.5 – 29.5	-
Gentamicin	15 µg (10 IU)	22.0 – 26.5	15.5 – 22.5	24.0 – 28.5
Tobramycin	10 µg	-	20.5 – 26.5	-
Amikacin	30 µg	21.5 – 26.0	20.0 – 26.0	-
Nalidixic acid	30 µg	25.5 – 30.5	-	-
Pefloxacin	5 µg	29.0 – 35.5	-	25.5 – 29.5
Ciprofloxacin	5 µg	31.0 – 38.0	29.0 – 36.5	-
Trimethoprim/sulfamethoxazole	1.25/23.75µg	25.5 – 30.5	-	28.0 – 32.5
Erythromycin	15 IU	-	-	26.5 – 31.5
Lincomycin	15 µg	-	-	24.5 – 29.5
Pristinamycin	15 µg	-	-	26.5 – 32.0
Rifampin	30 µg	-	-	34.0 – 39.0
Fusidic acid	10 µg	-	-	28.5 – 34.5
Fosfomycin	50 µg	-	-	24.0 – 35.0
Colistin	50 µg	-	17.0 – 22.0	-
Vancomycin	30 µg	-	-	17.5 – 20.5
Teicoplanin	30 µg	-	-	17.0 – 20.0

Table III – MIC and zone diameter interpretive standards for various antimicrobial agent classes and agar dilution test or disk diffusion test (see specific rules for certain species or bacterial groups, tables VII to XVIII – Information in italic type is considered tentative for one year).

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)	
		S	R	S	R
PENICILLINS					
Penicillin G	6 µg (10 IU)	≤ 0.25	> 16	≥ 29	< 8
Oxacillin (when testing staphylococci)	5 µg	≤ 2	> 2	≥ 20	< 20
Ampicillin	10 µg	≤ 4	> 16	≥ 19	< 14
Ampicillin/sulbactam	10/10 µg	≤ 4/8	> 16/8	≥ 19	< 14
Amoxicillin	25 µg	≤ 4	> 16	≥ 21	< 14
Amoxicillin/clavulanic acid	20/10 µg	≤ 4/2	> 16/2	≥ 21	< 14
Mecillinam	10 µg	≤ 2	> 8	≥ 22	< 18
Ticarcillin	75 µg	≤16	> 64	≥ 22	< 18
Ticarcillin/clavulanic acid	75/10 µg	≤ 16/2	> 64/2	≥ 22	< 18
Mezlocillin	75 µg	≤ 8	> 32	≥ 21	< 16
Azlocillin	75 µg	≤ 16	> 64	≥ 19	< 13
Piperacillin					
- when testing Enterobacteriaceae	75 µg	≤ 8	> 64	≥ 20	< 12
- when testing other gram-negative rods	75 µg	≤ 16	> 64	≥ 18	< 12
Piperacillin/tazobactam					
- when testing Enterobacteriaceae	75/10 µg	≤ 8/4	> 64/4	≥ 21	< 14
- when testing other gram-negative rods	75/10 µg	≤ 16/4	> 64/4	≥ 19	< 14
Sulbactam					
CARBAPENEMS					
Imipenem	10 µg	≤ 4	> 8	≥ 22	< 17
Meropenem	10 µg	≤ 4	> 8	≥ 20	< 15
MONOBACTAMS					
Aztreonam	30 µg	≤ 4	> 32	≥ 23	< 17

Table III (continued) – MIC and zone diameter interpretive standards for various antimicrobial agent classes and agar dilution test or disk diffusion test (see specific rules for certain species or bacterial groups, tables VII to XVIII – Information in italic type is considered tentative for one year).

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)	
		S	R	S	R
CEPHALOSPORINS (parenteral)					
Cephalothin	30 µg	≤ 8	> 32	≥ 18	< 12
Cefamandole	30 µg	≤ 8	> 32	≥ 22	< 15
Cefuroxime	30 µg	≤ 8	> 32	≥ 22	< 15
Cefoxitin	30 µg	≤ 8	> 32	≥ 22	< 15
Cefotetan	30 µg	≤ 4	> 32	≥ 23	< 17
Cefotiam	30 µg	≤ 4	> 32	≥ 22	< 15
Cefoperazone	30 µg	≤ 4	> 32	≥ 21	< 14
Cefotaxime	30 µg	≤ 4	> 32	≥ 21	< 15
Ceftizoxime	30 µg	≤ 4	> 32	≥ 21	< 15
Ceftriaxone	30 µg	≤ 4	> 32	≥ 21	< 15
Ceftazidime	30 µg	≤ 4	> 32	≥ 21	< 15
Cefepime	30 µg	≤ 4	> 32	≥ 21	< 15
Cefpirome	30 µg	≤ 4	> 32	≥ 21	< 15
Latamoxef	30 µg	≤ 4	> 32	≥ 23	< 17
Cefsulodin	30 µg	≤ 8	> 32	≥ 22	< 14
CEPHALOSPORINS (oral)					
Cefadroxil	30 µg	≤ 8	> 32	≥ 18	< 12
Cephalexin	30 µg	≤ 8	> 32	≥ 18	< 12
Cephradine	30 µg	≤ 8	> 32	≥ 18	< 12
Cefaclor	10 µg	≤ 2	> 8	≥ 22	< 16
Cefatrizin	10 µg	≤ 2	> 8	≥ 22	< 15
Loracarbef	10 µg	≤ 2	> 8	≥ 23	< 15
Cefuroxime (axetil)	10 µg	≤ 1	> 4	≥ 26	< 20
Cefotiam (hexetil)	10 µg	≤ 1	> 2	≥ 22	< 19
Cefixime	10 µg	≤ 1	> 2	≥ 25	< 22
Cefpodoxime (proxetil)	10 µg	≤ 1	> 2	≥ 24	< 21

Table III (continued) – MIC and zone diameter interpretive standards for various antimicrobial agent classes and agar dilution test or disk diffusion test (see specific rules for certain species or bacterial groups, tables VII to XVIII – Information in italic type is considered tentative for one year).

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)	
		S	R	S	R
AMINOGLYCOSIDES					
Streptomycin					
- when testing streptococci and enterococci	500 µg	≤ 250	> 500	≥ 14	< 12
- when testing other bacteria	10 IU	≤ 8	> 16	≥ 15	< 13
Gentamicin					
- when testing streptococci and enterococci	500 µg	≤ 250	> 500	≥ 17	< 11
- when testing other bacteria	15 µg (10 IU)	≤ 4	> 8	≥ 16	< 14
Sisomicin	10 µg	≤ 4	> 8	≥ 16	< 14
Netilmicin	30 µg	≤ 4	> 8	≥ 19	< 17
Kanamycin					
- when testing streptococci and enterococci	1000 µg	≤ 250	> 500	≥ 14	< 10
- when testing other bacteria	30 IU	≤ 8	> 16	≥ 17	< 15
Tobramycin	10 µg	≤ 4	> 8	≥ 16	< 14
Dibekacin	10 µg	≤ 4	> 8	≥ 16	14
Amikacin	30 µg	≤ 8	> 16	≥ 17	15
Isepamicin	30 µg	8	> 16	≥ 17	15
Spectinomycin (when testing *Neisseria gonorrhoeae*)	100 µg	≤ 64	> 64	≥ 20	< 20
PHENICOLS					
Chloramphenicol	30 µg	≤ 8	> 16	≥ 23	< 19
TETRACYCLINES					
Tetracycline	30 IU	≤ 4	> 8	≥ 19	< 17
Oxytetracycline	30 IU	≤ 4	> 8	≥ 19	< 17
Doxycycline	30 IU	≤ 4	> 8	≥ 19	< 17
Minocycline	30 IU	≤ 4	> 8	≥ 19	< 17

Table III (continued) – MIC and zone diameter interpretive standards for various antimicrobial agent classes and agar dilution test or disk diffusion test (see specific rules for certain species or bacterial groups, tables VII to XVIII – Information in italic type is considered tentative for one year).

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)	
		S	R	S	R
MACROLIDES					
Erythromycin	15 IU	≤ 1	> 4	≥ 22	< 17
Dirithromycin	15 µg	≤ 0.12	> 4	≥ 28	< 16
Telithromycin	*15 µg*	*≤ 0.5*	*> 2*	*≥ 21*	*< 17*
Azithromycin	15 µg	≤ 0.5	> 4	≥ 22	< 17
Spiramycin	100 µg	≤ 1	> 4	≥ 24	< 19
LINCOSAMIDES					
Lincomycin	15 µg	≤ 2	> 8	≥ 21	< 17
Clindamycin	2 IU	≤ 2	> 2	≥ 15	< 15
STREPTOGRAMINS					
Pristinamycin	15 µg	≤ 1	> 2	≥ 22	< 19
Virginiamycin	15 µg	≤ 1	> 2	≥ 22	< 19
Quinupristin/dalfopristin	15 µg	≤ 0.5	> 2	≥ 25	< 19
GLYCOPEPTIDES					
Teicoplanin	30 µg	≤ 4	> 16	≥ 17	-
Vancomycin	30 µg	≤ 4	> 16	≥ 17	-
POLYPEPTIDES					
Bacitracin	130 µg	≤ 2	> 2	≥ 15	< 15
Colistin	50 µg	≤ 2	> 2	≥ 15	< 15
SULFONAMIDES - TRIMETHOPRIM					
Sulfonamides	200 µg	≤ 64	> 256	≥ 17	< 12
Trimethoprim	5 µg	≤ 4	> 8	≥ 16	< 12
Trimethoprim/sulfamethoxazole	1.25/23.75µg	≤ 2/38	> 8/152	≥ 16	< 10
NITROFURANTOIN	300 µg	≤ 32	> 128	≥ 17	< 14

Table III (continued) – MIC and zone diameter interpretive standards for various antimicrobial agent classes and agar dilution test or disk diffusion test (see specific rules for certain species or bacterial groups, tables VII to XVIII – Information in italic type is considered tentative for one year).

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)	
		S	R	S	R
QUINOLONES					
Oxolinic acid	10 µg	≤ 2	> 4	≥ 20	< 17
Flumequine	30 µg	≤ 4	> 8	≥ 25	< 21
Nalidixic acid	30 µg	≤ 8	> 16	≥ 20	< 15
Pipemidic acid	20 µg	≤ 8	> 16	≥ 19	< 14
Piromidic acid	25 µg	≤ 16	> 32	≥ 20	< 16
Rosoxacin (when testing *Neisseria gonorrhoeae*)	5 µg	≤ 1	> 1	-	-
FLUOROQUINOLONES					
Norfloxacin	5 µg	≤ 1	> 2	≥ 22	< 19
Lomefloxacin	5 µg	≤ 1	> 2	≥ 22	< 19
Enoxacin	5 µg	≤ 1	> 2	≥ 22	< 19
Pefloxacin	5 µg	≤ 1	> 4	≥ 22	< 16
Ofloxacin	5 µg	≤ 1	> 4	≥ 22	< 16
Ciprofloxacin	5 µg	≤ 1	> 2	≥ 22	< 19
Sparfloxacin	5 µg	≤ 1	> 2	≥ 20	< 16
Trovafloxacin	10 µg	≤ 1	> 2	≥ 20	< 17
Levofloxacin					
- when testing *Streptococcus pneumoniae*	5 µg	≤ 2	> 4	≥ 17	< 15
- when testing other bacteria	5 µg	≤ 1	> 4	≥ 20	< 15
Moxifloxacin	*5 µg*	*≤ 1*	*> 2*	*≥ 21*	*< 18*

Table III (continued) – MIC and zone diameter interpretive standards for various antimicrobial agent classes and agar dilution test or disk diffusion test (see specific rules for certain species or bacterial groups, tables VII to XVIII – Information in italic type is considered tentative for one year).

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)	
		S	R	S	R
MISCELLANEOUS					
Fosfomycin	50 µg	≤ 32	> 32	≥ 14	< 14
Fusidic acid	10 µg	≤ 2	> 16	≥ 22	< 15
Linezolid	-	≤ 2	> 4	-	-
Metronidazole	Tabs 16 µg	≤ 4	> 16	-	< 21
Nitroxolin	20 µg	≤ 1	> 32	≥ 30	< 12
Rifampin					
- when testing staphylococci	30 µg	≤ 0.5	> 16	≥ 29	< 14
- when testing other bacteria	30 µg	≤ 4	> 16	≥ 19	< 14

INTRINSIC RESISTANCES TO ANTIMICROBIAL AGENTS OF THE MAIN BACTERIAL SPECIES OF MEDICAL INTEREST

Intrinsic resistance is characteristic of a bacterial species. It delimits the natural spectrum of the antibiotic and helps identification. The intrinsic resistance is expressed by MICs higher than the low concentration interpretive standard (c) of the antibiotic concerned. For certain genera or certain species, the intrinsic resistance (indicated by an asterisk) can have a weak expression and led to MICs close to this low concentration standard. This intrinsic resistance must also be taken into account for the interpretive reading.

Nonfastidious gram-negative rods

Penicillin G, oxacillin, macrolides, lincosamides, streptogramins, fusidic acid, vancomycin, teicoplanin.

Enterobacteriaceae

Table IV – Intrinsic resistance of some species of *Enterobacteriaceae*.

Species	AM	AMC	TIC	C1G	FOX	CTT	MA	CXM	GM	TET	COL	FT
Klebsiella spp.	R		R									
C. diversus	R		R									
C. freundii	R	R		R	R	R						
E. cloacae	R	R		R	R	R						
E. aerogenes	R	R		R	R	R						
S. marcescens	R	R		R			R	R			R	
P. mirabilis										R	R	R
P. vulgaris	R			R			R	R			R	R
M. morganii	R	R		R				R			R	R
P. stuartii	R	R		R					R*		R	R
Y. enterocolitica	R	R	R	R	R		R	R				

R: intrinsic resistance
R*: intrinsic resistance with a weak expression
AM: aminopenicillins; AMC: amoxicillin + clavulanic acid; TIC: ticarcillin;
C1G. first-generation cephalosporins; FOX: cefoxitin; CTT: cefotetan; MA: cefamandole; CXM: cefuroxime;
GM: gentamicin; TET: tetracyclines; COL: colistin, polymyxin B; FT: nitrofurantoin.

Nonfermenter gram-negative rods

Pseudomonas aeruginosa: aminopenicillins, first- second-generation cephalosporins, cefotaxime, ceftriaxone, ceftizoxime, kanamycin, tetracyclines, chloramphenicol, trimethoprim, quinolones.
Acinetobacter baumannii, Acinetobacter calcoaceticus: aminopenicillins, first- second-generation cephalosporins, fosfomycin, trimethoprim, nitrofurantoin.

Other nonfermenter gram-negative rods: aminopenicillins, first- second-generation cephalosporins. See also table V.

Tableau V – **Intrinsic resistance of some species of nonfermenter gram-negative rods.**

Species	TIC	TCC	PIP	CTX	CAZ	IPM	QUI	C	TMP	FOS	COL
S. maltophilia	R		R	R		R			R	R	
B. cepacia	R	R				R	R	R	R	R	R
A. denitrificans				R							
C. meningosepticum	R	R	R	R	R	R	R				R
O. anthropi	R	R	R	R	R						

R: intrinsic resistance
TIC: ticarcillin; TCC: ticarcillin + clavulanic ac.; PIP: piperacillin; CTX: cefotaxime; CAZ: ceftazidime;
IPM: imipenem; QUI: quinolones; C: chloramphenicol; TMP: trimethoprim; FOS: fosfomycin;
COL: colistin, polymyxin B.

Aeromonas

aminopenicillins (except *Aeromonas rota*), first- second-generation cephalosporins (except *Aeromonas veronii*).

Fastidious gram-negative rods

Haemophilus: macrolides (macrocyclic ring of 16 atoms: spiramycin, josamycin, midecamycin), lincosamides.
Campylobacter: aztreonam, novobiocin, streptogramins, trimethoprim, vancomycin, teicoplanin.
Campylobacter jejuni, Campylobacter coli and *Campylobacter lari*: first-generation cephalosporins.
Campylobacter fetus and *Campylobacter lari* : quinolones.

Gram-positive cocci

mecillinam, aztreonam, quinolones, colistin.

Staphylococcus saprophyticus: fosfomycin, novobiocin.
Staphylococcus cohnii and *Staphylococcus xylosus*: novobiocin, lincomycin.
Micrococcus: furantoin.
Streptococcus (included *Streptococcus pneumoniae*): aminoglycosides (low level), pefloxacin.
Enterococcus: oxacillin, cephalosporins, aminoglycosides (low level), pefloxacin, fosfomycin (low level), sulfamides.
Enterococcus faecalis: lincosamides.
Enterococcus gallinarum - Enterococcus casseliflavus: glycopeptides *.
Pediococcus – Leuconostoc: vancomycin, teicoplanin.

Gram-positive rods

mecillinam, aztreonam, colistin, polymyxin B, quinolones.

Listeria monocytogenes: oxacillin, cephalosporins, lincosamides, fosfomycin, fluoroquinolones (low level).
Erysipelothrix rhusiopathiae: vancomycin, teicoplanin.
Corynebacterium urealyticum - Corynebacterium jeikeium. β-lactams, aminoglycosides, macrolides, lincosamides, sulfonamides.
Rhodococcus equi : streptogramins, lincosamides.
Bacillus cereus: penicillin G, amino- carboxypenicillins, cephalosporins.
Nocardia asteroides – Nocardia farcinica: trimethoprim, vancomycin, rifampin, fluoroquinolones.
Lactobacillus: sulfamides.
Lactobacillus (heterofermenter): vancomycin, teicoplanin.

Gram-negative cocci

Neisseria: trimethoprim, vancomycin, teicoplanin,
Neisseria meningitidis - Neisseria gonorrhoeae . lincosamides, colistin, polymyxin B.
Branhamella catarrhalis: lincosamides, trimethoprim.
Moraxella: trimethoprim.

Anaerobes

aminoglycosides, aztreonam (except *Fusobacterium*), trimethoprim, quinolones.

Bacteroides group *fragilis*: aminopenicillins, first-generation cephalosporins, cefamandole, cefuroxime, colistin, polymyxin B, vancomycin, teicoplanin, fosfomycin.
Prevotella: vancomycin, teicoplanin, fosfomycin.
Porphyromonas: fosfomycin, colistin, polymyxin B.
Fusobacterium: macrolides (low level) .
Fusobacterium varium - Fusobacterium mortiferum: rifampin.
Clostridium - Eubacterium – Peptostreptococcus: colistin, polymyxin B, fosfomycin
Clostridium difficile : cephalosporins.
Clostridium innocuum: vancomycin (low level).
Actinomyces – Propionibacterium: first-generation cephalosporins, metronidazole, ornidazole.
Mobiluncus: metronidazole.
Veillonella: macrolides (low level), glycopeptides.

ANTIMICROBIAL AGENTS TO BE TESTED

The antimicrobial agents to be tested by species or bacterial group are listed in table VI. Each antimicrobial agent (or its equivalent) is representative of a class of antimicrobial agents. Two distinct lists are presented:

Standard list

This list includes the antimicrobial agents necessary for the therapeutic orientation, according to the clinical indications and the prevalence of the acquired resistance.

Supplemental list

This list includes the antimicrobial agents more specifically used for the study of multi-resistant strains, the epidemiological monitoring of the resistance or the help to interpretation of the test results.

It is of no use to routinely test other drugs than those mentioned in the standard and supplemental list. The choice of the antimicrobial agents of the standard list can be adapted locally according to the therapeutic guidelines, or according to epidemiological data.

Table VI — Antimicrobial agents to be tested.

Standard list	
Enterobacteriaceae [1]	***Pseudomonas aeruginosa*** [2]
Amoxicillin or ampicillin	Ticarcillin (H)
Amoxicillin/clavulanic ac. or ampicillin/sulbactam	Piperacillin (H)
Mecillinam	Ceftazidime (H)
Cephalotin (H)	Imipenem (H)
Ceftriaxone or cefotaxime (H) or ceftizoxime (H)	Gentamicin Tobramycin Amikacin (H)
Cefixime	Ciprofloxacin
Gentamicin Amikacin (H)	Colistin
Nalidixic ac. Norfloxacin Ciprofloxacin	
Trimethoprim/sulfamethoxazole	
Nitrofurantoin	

(H) – Antimicrobial agent for hospital use
1 – See table VII for specific recommendations.
2 – See table VIII for specific recommendations.

Supplemental list	
Enterobacteriaceae [1]	***Pseudomonas aeruginosa*** [2]
Ticarcillin (H) Ticarcillin/clavulanic ac. (H)	Ticarcillin/clavulanic ac. (H)
Mezlocillin (H) or piperacillin (H) Piperacillin/tazobactam (H)	Piperacillin/tazobactam (H)
Cefamandole	Cefepime (H) or cefpirome (H)
Cefuroxime (H) Cefoxitin (H)	Cefsulodin (H)
Cefotetan (H) Latamoxef	Aztreonam (H)
Ceftazidime (H) Cefepime (H) or cefpirome (H)	Netilmicin Isepamicin (H)
Aztreonam (H)	Pefloxacin or ofloxacin
Imipenem (H)	
Kanamycin Tobramycin Netilmicin Isepamicin (H)	Sulfonamides
Chloramphenicol	Fosfomycin (H)
Tetracycline Minocycline	
Pefloxacin or ofloxacin	
Sulfonamides Trimethoprim	
Colistin	
Fosfomycin (H)	

Table VI (continued) — Antimicrobial agents to be tested.

Other nonfermenter gram-negative rods [3]			
Standard list for the 3 species	Standard list selectively		
	***Acinetobacter* spp.**	***Stenotrophomonas maltophilia***	***Burkholderia cepacia***
Ticarcillin (H) Ticarcillin/clavulanic ac. (H) Piperacillin (H) Piperacillin/tazobactam (H) Ceftazidime (H) Imipenem (H) Gentamicin Tobramycin Amikacin (H) Trimethoprim/sulfamethoxazole Ciprofloxacin	Ticarcillin (H) or ticarcillin/clavulanic ac. (H) Piperacillin (H) or piperacillin/tazobactam (H) Ceftazidime (H) Imipenem (H) Gentamicin Tobramycin Amikacin (H) Pefloxacin or ofloxacin or ciprofloxacin	Ticarcillin/clavulanic ac. (H) Trimethoprim/sulfamethoxazole Ciprofloxacin	Piperacillin (H) Ceftazidime (H) Imipenem (H) Trimethoprim/sulfamethoxazole Ciprofloxacin

Other nonfermenter gram-negative rods [3]			
Supplemental list for the 3 species	Supplemental list selectively		
	***Acinetobacter* spp.**	***Stenotrophomonas maltophilia***	***Burkholderia cepacia***
Sulbactam (H) Cefepime (H) Cefpirome (H) Sulbactam (H) + ceftazidime (H) or sulbactam (H) + cefepime (H) or sulbactam (H) + cefpirome (H) Meropenem (H) Netilmicin Isepamicin (H) Chloramphenicol Tetracycline Colistin Rifampin	Sulbactam (H) Cefepime (H) Cefpirome (H) Sulbactam (H) + ceftazidime (H) or sulbactam (H) + cefepime (H) or sulbactam (H) + cefpirome (H) Netilmicin Isepamicin (H) Trimethoprim/sulfamethoxazole Rifampin	Ceftazidime (H) Imipenem (H) Chloramphenicol Tetracycline Rifampin	Sulbactam (H) Chloramphenicol Tetracycline Colistin[4]

(H) – Antimicrobial agent for hospital use
3 – See table IX for specific recommendations.
4 – Aid to identification (intrinsic resistance).

Table VI (continued) — Antimicrobial agents to be tested.

Standard list	
***Staphylococcus* spp.** [5]	***Enterococcus* spp.** [6]
Penicillin G	Ampicillin
Oxacillin	Gentamicin
Gentamicin	Nitrofurantoin
Erythromycin Lincomycin	
Pristinamycin	
Pefloxacin or ofloxacin or ciprofloxacin	
Fusidic acid	
Trimethoprim/sulfamethoxazole	
Rifampin	
Fosfomycin (H)	
Vancomycin (H) Teicoplanin (H)	

Supplemental list	
***Staphylococcus* spp.** [5]	***Enterococcus* spp.** [6]
Streptomycin Kanamycin Tobramycin	Oxacillin
Sulfonamides Trimethoprim	Streptomycin Kanamycin
Chloramphenicol	Chloramphenicol
Tetracycline Minocycline	Tetracycline
Nitrofurantoin	Erythromycin Lincomycin [9] or clindamycin [9]
Novobiocin [7] O/129 [8]	Pristinamycin
	Trimethoprim/sulfamethoxazole
	Rifampin
	Fluoroquinolones [6]
	Vancomycin (H) Teicoplanin (H)

(H) – Antimicrobial agent for hospital use

5 – See table X for specific recommendations.
6 – See table XI for specific recommendations.

7 – Aid to identification of *S. saprophyticus*, *S. xylosus* and *S cohnii* (intrinsic resistance).
8 - For the differentiation between staphylococci (R) and micrococci (S).
9 – Aid to identification of *E. faecalis* (intrinsic resistance).

Table VI (continued) — Antimicrobial agents to be tested.

Standard list	
Streptococcus pneumoniae [10]	***Streptococcus* spp.** [11] **(other than *S. pneumoniae*)**
Penicillin G	Penicillin G
Ampicillin or amoxicillin	Ampicillin or amoxicillin
Oxacillin	Tetracycline
Cefotaxime (H) or ceftriaxone	Erythromycin Lincomycin or clindamycin
Tetracycline	Pristinamycin
Erythromycin Lincomycin or clindamycin	
Pristinamycin	

(H) – Antimicrobial agent for hospital use

10 – See table XII for specific recommendations.
11 – See table XIII for specific recommendations.

Supplemental list	
Streptococcus pneumoniae [10]	***Streptococcus* spp.** [11] **(other than *S. pneumoniae*)**
Imipenem (H)	Streptomycin Kanamycin Gentamicin
Streptomycin Kanamycin Gentamicin	Chloramphenicol
Chloramphenicol	Spiramycin
Trimethoprim/sulfamethoxazole [12]	Trimethoprim/sulfamethoxazole [12]
Fluoroquinolones [10]	Fluoroquinolones [11]
Fosfomycin (H)	Rifampin
Vancomycin (H) Teicoplanin (H)	Vancomycin (H) Teicoplanin (H)

12 – Use Mueller-Hinton agar supplemented with 5% hemolysed horse blood.

Table VI (continued) — Antimicrobial agents to be tested.

Standard list		
***Haemophilus* spp.** [13]	***Neisseria meningitidis*** [14]	***Neisseria gonorrhoeae*** [15]
Ampicillin [16] Amoxicillin/clavulanic ac. Cephalotin Tetracycline Trimethoprim/sulfamethoxazole	Penicillin G (oxacillin) or amoxicillin Chloramphenicol Rifampin	Penicillin G [16] (oxacillin) or amoxicillin Spectinomycin Tetracycline Nalidixic ac.

Supplemental list		
***Haemophilus* spp.** [13]	***Neisseria meningitidis*** [14]	***Neisseria gonorrhoeae*** [15]
Chloramphenicol Rifampin Kanamycin Gentamicin Fluoroquinolones	Cefotaxime (H) or ceftriaxone	Ceftriaxone Chloramphenicol Erythromycin Ciprofloxacin or ofloxacin

(H) – Antimicrobial agent for hospital use

13 – See table XIV for specific recommendations.
14 – See table XV for specific recommendations.
15 – See table XVI for specific recommendations.
16 – Test β-lactamase production to detect β by using a nitrocefin-based test and colonies taken directly from an overnight agar culture plate.

Table VI (continued) — Antimicrobial agents to be tested.

Standard list	
***Campylobacter* spp.** [17]	***Helicobacter pylori*** [18]
Ampicillin Amoxicillin/clavulanic ac. Imipenem (H) Gentamicin Erythromycin Ciprofloxacin Tetracycline	Erythromycin

Supplemental list	
***Campylobacter* spp.** [17]	***Helicobacter pylori*** [18]
Cephalotin (H) Cefotaxime (H) Streptomycin Kanamycin Tobramycin Nalidixic ac.[19] Chloramphenicol	

(H) – Antimicrobial agent for hospital use

17 – See table XVII for specific recommendations.
18 – See table XVIII for specific recommendations.
19 – Aid to identification.

Table VI (continued) — Antimicrobial agents to be tested.

Standard list
Anaerobes [20]
Amoxicillin Amoxicillin/clavulanic ac.
Imipenem (H)
Clindamycin
Metronidazole
Vancomycin (H)
Chloramphenicol

Supplemental list
Anaerobes [20]
Ticarcillin (H) or piperacillin (H)
Ticarcillin/clavulanic ac. (H) or piperacilline/tazobactam (H)
Cefoxitine (H) Cefotetan (H) Cefotaxime (H)
Pristinamycin
Spiramycin [21]
Colistin [22]
Ofloxacin [23]
Rifampin

(H) – Antimicrobial agent for hospital use

20 – See table XIX for specific recommendations.
21 – For dental infection.
22 – Aid to identification of gram-negative rods.
23 - Against *Propionibacterium* spp. and some isolates of *Peptostreptococcus* spp. from brain or bone infections.

Table VII – Minimum inhibitory concentration and zone diameter interpretive standards for *Enterobacteriaceae.*

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Ampicillin	10 µg	≤ 4	> 16	≥ 19	< 14	Interpretation valid for bacampicillin, metampicillin, pivampicillin. See rules (1) and (2).
Amoxicillin	25 µg	< 4	> 16	≥ 21	< 14	See rules (1) and (2).
Ampicillin/sulbactam	10/10 µg	≤ 4/8	> 16/8	≥ 19	< 14	See rule (1b).
Amoxicillin/clavulanic ac.	20/10 µg	≤ 4/2	> 16/2	≥ 21	< 14	See rule (1b).
Ticarcillin (H)	75 µg	≤ 16	64	≥ 22	< 18	Interpretation valid for an intravenous route. See rules (1), (2) and (3).
Ticarcillin/clavulanic ac. (H)	75/10 µg	≤ 16/2	> 64/2	≥ 22	< 18	
Mezlocillin (H)	75 µg	≤ 8	> 32	≥ 21	< 16	See rules (1), (2) and (3).
Piperacillin (H)	75 µg	≤ 8	> 64	≥ 20	< 12	Interpretation valid for an intravenous route. See rules (1), (2) and (3).
Piperacillin/tazobactam (H)	75/10 µg	≤ 8/4	> 64/4	≥ 21	< 14	
Mecillinam	10 µg	≤ 2	> 8	≥ 22	< 18	Interpretation valid for isolates from urinary tract only.
Imipenem (H)	10 µg	≤ 4	> 8	≥ 22	< 17	
Aztreonam (H)	30 µg	≤ 4	> 32	≥ 23	< 17	See rules (4) and (5).

(H) – Antimicrobial agent for hospital use

Rules for interpretive reading

(1) Interpret I, the S test results (weak expression of intrinsic resistance) as follows:
a – *Klebsiella pneumoniae, Klebsiella oxytoca, Citrobacter diversus* and *Escherichia hermannii*, S to amino- and/or carboxy- and/or ureidopenicillins
b – *Enterobacter cloacae, Enterobacter aerogenes, Citrobacter freundii, Serratia marcescens, Morganella morganii, Providencia rettgeri, Providencia stuartii* and *Hafnia alvei*, S to amino-penicillins and/or first generation cephalosporins and/or to amoxicillin + clavulanic acid and ampicillin + sulbactam
c – *Proteus vulgaris* and *Proteus penneri*, S to aminopenicillins and/or to first-generation cephalosporins.

(2) Interpret I, a S test result to carboxy- and/or ureidopenicillins for *Proteus mirabilis* R to aminopenicillins.

(3) Interpret I, a S test result to ureidopenicillins for Enterobacteriaceae I or R to carboxypenicillins.

Table VII (continued) – Minimum inhibitory concentration and zone diameter interpretive standards for *Enterobacteriaceae*.

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Cephalotin (H)	30 µg	≤ 8	> 32	≥ 18	< 12	Interpretation valid for first generation parenteral cephalosporins (cephapirin, cefazolin). Interpretation also valid for first generation oral cephalosporins (cefadroxil, cephalexin, cephradin, cefaclor, cefatrizin, loracarbef) but for isolates from urinary tract only.
Cefuroxime (H)	30 µg	≤ 8	> 32	≥ 22	< 15	
Cefamandole	30 µg	≤ 8	> 32	≥ 22	< 15	
Cefoxitin (H)	30 µg	≤ 8	> 32	≥ 22	< 15	
Cefotetan (H)	30 µg	≤ 4	> 32	≥ 23	< 17	
Latamoxef	30 µg	≤ 4	> 32	≥ 23	< 17	Unavailable in France.
Cefotaxime (H)	30 µg	≤ 4	> 32	≥ 21	< 15	
Ceftizoxime (H)	30 µg	≤ 4	> 32	≥ 21	< 15	
Ceftriaxone	30 µg	≤ 4	> 32	≥ 21	< 15	For this antimicrobial subclass, see rules (4) and (5)
Ceftazidime (H)	30 µg	≤ 4	> 32	≥ 21	< 15	
Cefepime (H)	30 µg	≤ 4	> 32	≥ 21	< 15	
Cefpirome (H)	30 µg	≤ 4	> 32	≥ 21	< 15	
Cefixime	10 µg	≤ 1	> 2	≥ 25	< 22	Interpretation valid for isolates from urinary tract only.

(H) – Antimicrobial agent for hospital use

Rules for interpretive reading (continued)

(4) For species producing intrinsic inducible cephalosporinase (*Enterobacter cloacae, Citrobacter freundii, ...*), interpret I every S test result obtained for the following antimicrobial agents cefotaxime, ceftriaxone, ceftazidime, azteonam.

(5) The recognition of a synergy between a β-lactamase inhibitor and third generation cephalosporin and/or aztreonam enables the detection of resistance mechanisms, which cannot be detected by the usual tests In practice, the synergy test is carried out by placing β-lactam disks to study 30 mm apart (center to center) of a disk of amoxicillin+ clavulanic acid (AMC).

a) A synergy between AMC and ceftazidime and/or aztreonam (the most sensitive broad indicators) and/or cefotaxime and/or ceftriaxone enables the detection of an extended broad spectrum β-lactamase (ESBL) The ESBL detection among the strains which are also hyperproductive of cephalosporinase (*Enterobacter*, for example) is facilitated by the research of a synergy between AMC and cefepime or cefpirome Among *P mirabilis, P vulgaris, P penneri, M morganii, P stuartii and P. rettgeri*, the ESBL are expressed at a low level. In this case, the synergy test is optimized by placing the disks 40-45 mm apart instead of 30 mm.
In case of synergy, interpret I any S test result obtained for cefotaxime, ceftriaxone, ceftizoxime, ceftazidime, cefepime, cefpirome, cefixime and for aztreonam
Given the present epidemiology, when an enterobacteriaceae is R to tobramycin, netilmicin and amikacin, but S to gentamicin, it is advised to research the presence of an associated ESBL, mainly among the species where this type of enzyme is weakly expressed (*Proteus spp , Providencia spp)*

b) Among *K oxytoca*, a positive synergy test with aztreonam and/or ceftriaxone, but negative with ceftazidime whose activity is maintained, evokes a hyperproduction of chromosomal intrinsic β-lactamase Interpret I the only S results associated with a synergy.

c) Among *P vulgaris, P penneri* and *C diversus*, a positive synergy test with cefotaxime and/or aztreonam evokes a hyperproduction of chromosomal intrinsic β-lactamase and much more rarely the presence of a plasmidic ESBL

Table VII (continued) – Minimum inhibitory concentration and zone diameter interpretive standards for *Enterobacteriaceae*.

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Kanamycin	30 IU	≤ 8	16	≥ 17	< 15	Interpretation valid for neomycin, framycetin, paromomycin.
Tobramycin	10 µg	≤ 4	> 8	≥ 16	< 14	See rules (6), (9) and (11).
Amikacin (H)	30 µg	≤ 8	> 16	≥ 17	< 15	See rules (6) and (7).
Isepamicin (H)	30 µg	≤ 8	> 16	≥ 17	< 15	See rules (6) and (7).
Gentamicin	15 µg (10 IU)	≤ 4	> 8	≥ 16	< 14	See rules (6), (8) and (11)
Netilmicin	30 µg	≤ 4	> 8	≥ 19	< 17	See rules (6), (10) and (11)

(H) – Antimicrobial agent for hospital use

Rules for interpretive reading (continued)

Abbreviations . gentamicin (G), tobramycin (T), netilmicin (Nt), amikacin (A), isepamicin (Is)

(6) Apply the zone diameter interpretive standards for each aminoglycoside if a decrease of all aminoglycoside zone sizes is observed. It evokes a reduced permeability.

(7) Interpret $A^{I}Is^{I}$, a G^{S} and $T^{I/R}Nt^{I/R}$ and $A^{S/I}Is^{S/I}$ result, evoking an AAC(6') production, (see also rule 5).

(8) Interpret G^{I}, a G^{S} result when a decrease of the gentamicin alone zone size (16 to 19 mm), evoking an AAC (3)-I production, is observed.

(9) Interpret T^{I}, a T^{S} result when a decrease of the tobramycin zone size (16 to 19 mm) is observed with a $G^{I/R}$ result. This evokes an ANT (2'') production.

(10) Interpret Nt^{I}, a Nt^{S} result when a decrease of the netilmicin zone size (19 to 22 mm) is observed with a $G^{I/R}$ $T^{I/R}$ result. This evokes an AAC(3)-II or AAC(3)-IV production

(11) Among *Providencia spp* , after the verification of the identification, interpret G^{I} T^{I} Nt^{I}, a G^{S} T^{S} Nt^{S} result (intrinsic resistance by AAC (2')-I production)

CAUTION: Phenotypes G^{R} T^{S} Nt^{R} A^{S}, G^{S} T^{R} Nt^{R} A^{S}, G^{S} T^{S} Nt^{R} A^{R} et G^{S} T^{R} Nt^{S} A^{R} are improbable. Check testing and/or repeat identification procedures and verify the interpretive criteria

Table VII (continued) – Minimum inhibitory concentration and zone diameter interpretive standards for *Enterobacteriaceae*.

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Chloramphenicol	30 µg	≤ 8	> 16	≥ 23	< 19	Interpretation valid for thiamphenicol.
Tetracycline	30 IU	≤ 4	> 8	≥ 19	< 17	Interpretation valid for oxytetracycline and doxycycline.
Minocycline	30 IU	≤ 4	> 8	≥ 19	< 17	
Colistin	50 µg	≤ 2	> 2	≥ 15	< 15	Interpretation valid for polymyxin B. Intrinsic resistance of *Proteus* spp., *Providencia* spp., *Morganella* spp. and *Serratia* spp.
Sulfonamides	200 µg	≤ 64	> 256	≥ 17	< 12	Interpretation valid for isolates from urinary tract only.
Trimethoprim	5 µg	≤ 4	> 8	≥ 16	< 12	Interpretation valid for isolates from urinary tract only.
Trimethoprim/sulfamethoxazole	1.25/23.75 µg	≤ 2/38	> 8/152	≥ 16	< 10	Interpretation valid for the other trimethoprim-sulfonamide combinations.
Nitrofurantoin	300 µg	≤ 32	> 128	≥ 17	< 14	Interpretation valid for isolates from urinary tract only.
Oxolinic acid	10 µg	≤ 2	> 4	≥ 20	< 17	It is justified to give a global report for the group of classical quinolones (sometimes called first generation) as a whole by studying only one representative of this group. Interpretation valid for isolates from urinary tract only.
Flumequin	30 µg	≤ 4	> 8	≥ 25	< 21	
Nalidixic acid	30 µg	≤ 8	> 16	≥ 20	< 15	
Pipemidic acid	20 µg	≤ 8	> 16	≥ 19	< 14	
Piromidic acid	25 µg	≤ 16	> 32	≥ 20	< 16	
Norfloxacin	5 µg	≤ 1	> 2	≥ 22	< 19	There is a cross-resistance to the urinary fluoroquinolones but its level of expression can vary for each drug. Interpretation valid for isolates from urinary tract only.
Lomefloxacin	5 µg	≤ 1	> 2	≥ 22	< 19	
Enoxacin	5 µg	≤ 1	> 2	≥ 22	< 19	
Pefloxacin	5 µg	≤ 1	> 4	≥ 22	< 16	There is a cross-resistance to the systemic fluoroquinolones but its level of expression can vary for each drug. The enterobacteriaceae strains susceptible to pefloxacin (PFX) are susceptible to the other fluoroquinolones. For the strains I (or R) to PFX, intrinsic activity differences imply a test and an independent report for the other drugs.
Ofloxacin	5 µg	≤ 1	> 4	≥ 22	< 16	
Ciprofloxacin	5 µg	≤ 1	> 2	≥ 22	< 19	
Levofloxacin (H)	5 µg	≤ 1	> 4	≥ 20	< 15	
Moxifloxacin	*5 µg*	*≤ 1*	*> 2*	*≥ 21*	*< 18*	
Fosfomycin (H)	50 µg	≤ 32	> 32	≥ 14	< 14	Interpretation valid for an intravenous route.

(H) – Antimicrobial agent for hospital use

Table VIII – Minimum inhibitory concentration and zone diameter interpretive standards for *Pseudomonas aeruginosa.*

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Ticarcillin (H)	75 µg	≤ 16	> 64	≥ 22	< 18	See rules (1) to (4). Azlocillin is unavailable in France.
Ticarcillin/clavulanic ac. (H)	75/10 µg	≤ 16/2	> 64/2	≥ 22	< 18	
Azlocillin	75 µg	≤ 16	> 64	≥ 19	< 13	
Piperacillin (H)	75 µg	≤ 16	> 64	≥ 20	< 12	
Piperacillin/tazobactam (H)	75/10 µg	≤ 16/4	> 64/4	≥ 21	< 14	
Imipenem (H)	10 µg	≤ 4	> 8	≥ 22	< 17	A single resistance to imipenem enables to detect a selective impermeability due to porin alteration. Other β-lactams are not concerned by this resistance mechanism. Meroponem is unavailable in France.
Meropenem (H)	10 µg	≤ 4	> 8	≥ 20	< 15	
Aztreonam (H)	30 µg	≤ 4	> 32	≥ 23	< 17	See rules (3) to (5).
Cefoperazone (H)	30 µg	≤ 4	> 32	≥ 21	< 14	See rules (1) to (5).
Ceftazidime (H)	30 µg	≤ 4	> 32	≥ 21	< 15	
Cefsulodin (H)	30 µg	≤ 8	> 32	≥ 22	< 14	
Cefepime (H)	30 µg	≤ 4	> 32	≥ 21	< 15	
Cefpirome (H)	30 µg	≤ 4	> 32	≥ 21	< 15	

(H) – Antimicrobial agent for hospital use

Rules for interpretive reading

Abbreviations TIC, ticarcillin; TCC, ticarcillin + clavulanic acid; PIP, piperacillin; PTZ, piperacillin + tazobactam, AZL, azlocillin; IPM, imipenem; ATM, aztreonam; CFZ, cefoperazone; CFS, cefsulodine, CPO, cefpirome, FEP, cefepime ; CAZ, ceftazidime

(1) Interpret I, a S result to TCC, PIP, PTZ, AZL, CFZ, CFS if a TIC high level resistance (MIC > 256 mg/l, no inhibition zone) is observed.

(2) A TIC ^{S} TCC $^{I/R}$ result is related to an inducible cephalosporinase; Do not change the TIC interpretation.

(3) Interpret I, a S result to TIC, TCC, PTZ, CFZ, CFS, CPO, ATM if a PIP $^{I/R}$ CAZ $^{I/R}$ and TIC ^{S} phenotype is observed.

(4) A TIC $^{I/R}$ TCC $^{I/R}$ and/or ATM $^{I/R}$ result with a conserved susceptibility to other β-lactams (see upwards) evokes an altered drug efflux As there was no sufficient clinical data available, do not change interpretations.

(5) A synergy between TCC and ATM and/or CAZ and/or FEP and/or CPO allows the detection of some extended broad spectrum β-lactamases (ESBL).

Table VIII (continued) – Minimum inhibitory concentration and zone diameter interpretive standards for *Pseudomonas aeruginosa.*

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Tobramycin	10 µg	≤ 4	> 8	≥ 16	< 14	
Amikacin (H)	30 µg	≤ 8	> 16	≥ 17	< 15	
Isepamicin (H)	30 µg	≤ 8	> 16	≥ 17	< 15	See rules (6) and (7).
Gentamicin	15 µg (10 IU)	≤ 4	> 8	≥ 16	< 14	
Netilmicin	30 µg	≤ 4	> 8	≥ 19	< 17	
Chloramphenicol	30 µg	≤ 8	> 16	≥ 23	< 19	Interpretation valid for thiamphenicol.
Tetracycline	30 IU	≤ 4	> 8	≥ 19	< 17	Interpretation valid for tetracyclines, excepted for minocycline.
Minocycline	30 IU	≤ 4	> 8	≥ 19	< 17	
Colistin	50 µg	≤ 2	> 2	≥ 15	< 15	Interpretation valid for polymyxin B.
Pefloxacin	5 µg	≤ 1	> 4	≥ 22	< 16	There is a cross-resistance to the systemic fluoroquinolones but its level of expression can vary for each drug. For *P. aeruginosa*, test ciprofloxacin (CIP) and pefloxacin (PFX) or ofloxacin (OFX). The PFX $^{I/R}$ or OFX $^{I/R}$ strains for which the MIC of CIP is ≤ 1 mg/l (diameter ≥22 mm) are still considered susceptible to CIP.
Ofloxacin	5 µg	≤ 1	> 4	≥ 22	< 16	
Ciprofloxacin	5 µg	≤ 1	> 2	≥ 22	< 19	
Rifampicin	30 µg	≤ 4	> 16	> 19	< 14	
Fosfomycin (H)	50 µg	≤ 32	> 32	≥ 14	< 14	
Sulfonamides	200 µg	≤ 64	> 256	≥ 17	< 12	Interpretation valid for isolates from urinary tract only.

(H) – Antimicrobial agent for hospital use

Rules for interpretive reading (continued)

Abbreviations: G, gentamicin; T, tobramycin; Nt, netilmicin, A, amikacin, Is, isepamicin

(6) - Apply the zone diameter interpretive standards for each aminoglycoside if a decrease of all aminoglycoside zone sizes (< 20 mm), evoking a non enzymatic resistance, is observed

(7) - Interpret A^{I} Is^{I}, an A^{S} Is^{S} and G^{S} and $T^{I/R}$ $Nt^{I/R}$ result which evokes an AAC (6')-1 production.

Table IX – Minimum inhibitory concentration and zone diameter interpretive standards for *Acinetobacter spp., Stenotrophomonas maltophilia* and *Burkholderia cepacia.*

Antimicrobial Agent	Disk content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Ticarcillin (H)	75 µg	≤ 16	> 64	≥ 22	< 18	For use against *Acinetobacter* spp.
Ticarcillin/clavulanic ac. (H)	75/10 µg	≤ 16/2	> 64/2	≥ 22	< 18	For use against *Acinetobacter* spp. and *S. maltophilia.*
Piperacillin (H)	75 µg	≤ 16	> 64	≥ 18	< 12	For use against *Acinetobacter* spp. and *B. cepacia.*
Piperacillin/tazobactam (H)	75/10 µg	≤ 16/4	> 64/4	≥ 19	< 14	For use against *Acinetobacter* spp
Sulbactam (H)		≤ 8	-			The antimicrobial activity evaluation requires MIC determination for *Acinetobacter* spp. and *B. cepacia.*
Imipenem (H)	10 µg	≤ 4	> 8	≥ 22	< 17	
Meropenem (H)	10 µg	≤ 4	> 8	≥ 20	< 15	
Ceftazidime (H)	30 µg	≤ 4	> 32	≥ 21	< 15	Possible synergism with sulbactam + ceftazidime against *Acinetobacter* spp.
Cefepime (H)	30 µg	≤ 4	> 32	≥ 21	< 15	Possible synergism with sulbactam + cefepime against *Acinetobacter* spp.
Cefpirome (H)	30 µg	≤ 4	> 32	≥ 21	< 15	Possible synergism with sulbactam + cefpirome against *Acinetobacter* spp
Tobramycin	10 µg	≤ 4	> 8	≥ 16	< 14	
Amikacin (H)	30 µg	≤ 8	> 16	≥ 17	< 15	
Isepamicin (H)	30 µg	≤ 8	> 16	≥ 17	< 15	For use against *Acinetobacter* spp.
Gentamicin	15 µg (10 IU)	≤ 4	> 8	≥ 16	< 14	
Netilmicin	30 µg	≤ 4	> 8	≥ 19	< 17	
Chloramphenicol	30 µg	≤ 8	> 16	≥ 23	< 19	Interpretation valid for thiamphenicol.
Tetracycline	30 IU	≤ 4	> 8	≥ 19	< 17	For use against *S. maltophilia* and *B. cepacia.*
Colistin	50 µg	≤ 2	> 2	≥ 15	< 15	Interpretation valid for polymyxin B. Intrinsic resistance of *B. cepacia.*
Pefloxacin	5 µg	≤ 1	> 4	≥ 22	< 16	
Ofloxacin	5 µg	≤ 1	> 4	≥ 22	< 16	There is a cross-resistance to the systemic fluoroquinolones but its level of
Ciprofloxacin	5 µg	≤ 1	> 2	≥ 22	< 19	expression can vary for each drug.
Moxifloxacin	*5 µg*	*≤ 1*	*> 2*	*≥ 21*	*< 18*	
Rifampin	30 µg	≤ 4	> 16	≥ 19	< 14	For use against *Acinetobacter* spp. and *S. maltophilia.*
Trimethoprim/sulfamethoxazole	1.25/23.75 µg	≤ 2/38	> 8/152	≥ 16	< 10	Interpretation valid for isolates from urinary tract only.

(H) – Antimicrobial agent for hospital use

Table X – Minimum inhibitory concentration and zone diameter interpretive standards for *Staphylococcus* spp..

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Penicillin G	6 µg (10 IU)	≤ 0.25	> 16	≥ 29	< 8	Interpretation valid for benzyl-penicillin and phenoxymethyl-penicillin. Penicillinase producing strains are resistant to benzyl-penicillin (diameter < 29 mm; MIC > 0.25 mg/l) and other hydrolyzable penicillins (amino-, carboxy- and ureido-penicillins). Only penicillin G must be tested When the diameter is ≥ 29 mm, check the absence of penicillinase production by means of a nitrocefin-based test.
Oxacillin	5 µg	≤ 2	> 2	≥ 20	< 20	The staphylococci resistance to isoxazolyl-penicillins (oxacillin, cloxacillin) which are not hydrolysed by the penicillinases must be searched for with the help of an oxacillin disk 5 µg after 24 h incubation at 30 °C on a medium not supplemented in sodium chloride, or at 37°C on hypersalted medium (2 to 4 % NaCl) with an inoculum of ~ 10^7 CFU/ml. After 24 hours, the staphylococci growth can be weak in the above mentioned conditions. In this case, incubation will be prolonged up to 48 hours. The oxacillin-resistant strains should not be reported as susceptible to all penicillins (whether they are associated or not with a β-lactamase inhibitor), to cephalosporins and to carbapenems. The penicillin R - oxacillin S strains are susceptible to the combination penicillins + β lactamase inhibitors, to cephalosporins and to carbapenems. These molecules can be used within the limit of the A.M.M. indications. It is not relevant to test them routinely.
Streptomycin	10 IU	≤ 8	> 16	≥ 15	< 13	
Kanamycin	30 IU	≤ 8	> 16	≥ 17	< 15	Interpretation valid for neomycin, framycetin, paromomycin, amikacin and isepamicin.
Gentamicin	15 µg (10 IU)	≤ 4	> 8	≥ 16	< 14	Interpretation valid for netilmicin and there is a cross-resistance to all aminoglycosides
Tobramycin	10 µg	≤ 4	> 8	≥ 16	< 14	
Erythromycin	15 IU	≤ 1	> 4	≥ 22	< 17	Interpretation valid for azithromycin, clarithromycin, dirithromycin and roxithromycin.
Telithromycin	*15 µg*	*≤ 0.5*	*> 2*	*≥ 21*	*< 17*	
Spiramycin	100 µg	≤ 1	> 4	≥ 24	< 19	Interpretation valid for josamycin and midecamycin.
Lincomycin	15 µg	≤ 2	> 8	≥ 21	< 17	Interpretation valid for clindamycin.
Pristinamycin	15 µg	≤ 1	> 2	≥ 22	< 19	
Quinupristin/dalfopristin	15 µg	≤ 0.5	> 2	≥ 25	< 19	When the zone size diameter is 19 ≤ Ø < 25 mm, determine the MIC.

(H) – Antimicrobial agent for hospital use

Table X (continued) – Minimum inhibitory concentration and zone diameter interpretive standards for *Staphylococcus spp.*.

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Pefloxacin	5 µg	≤ 1	> 4	≥ 22	< 16	The activity of pefloxacin, ofloxacin, levofloxacin and ciprofloxacin is similar against staphylococci. There is a cross-resistance to the fluoroquinolones and each drug is the representative for all of them.
Ofloxacin	5 µg	≤ 1	> 4	≥ 22	< 16	
Levofloxacin (H)	5 µg	≤ 1	> 4	≥ 20	< 15	
Ciprofloxacin	5 µg	≤ 1	> 2	≥ 22	< 19	
Moxifloxacin	*5 µg*	*≤ 1*	*> 2*	*≥ 21*	*< 18*	
Chloramphenicol	30 µg	≤ 8	> 16	≥ 23	< 19	Interpretation valid for thiamphenicol.
Tetracycline	30 IU	≤ 4	> 8	≥ 19	< 17	Interpretation valid for oxytetracycline and doxycycline.
Minocycline	30 IU	≤ 4	> 8	≥ 19	< 17	
Rifampin	30 µg	≤ 0,5	> 16	≥ 29	< 14	Interpretation valid for an intravenous route.
Fosfomycin (H)	50 µg	≤ 32	> 32	≥ 14	< 14	
Fusidic acid	10 µg	≤ 2	> 16	≥ 22	< 15	
Teicoplanin (H)	30 µg	≤ 4	> 16	≥ 17	-	See the below mentioned note for the detection of *S. aureus* strains of decreased susceptibility to glycopeptides.
Vancomycin (H)	30 µg	≤ 4	> 16	≥ 17	-	
Sulfonamides	200 µg	≤ 64	> 256	≥ 17	< 12	Interpretation valid for isolates from urinary tract only.
Trimethoprim	5 µg	≤ 4	> 8	≥ 16	< 12	Interpretation valid for isolates from urinary tract only.
Trimethoprim/sulfamethoxazole	1.25+23.75 µg	≤ 2/38	> 8/152	≥ 16	< 10	Interpretation valid for the other trimethoprim-sulfonamide combinations.

(H) – Antimicrobial agent for hospital use

Determination of the *in vitro* activity of glycopeptides against *Staphylococcus aureus* : clinical categorization of the strains of putative decreased susceptibility.

Introduction

The *S aureus* strains with a decreased susceptibility to glycopeptides (GISA, GRSA, Hetero-VISA*) have been described for years. In France, this decreased susceptibility concerns nearly only the strains simultaneously resistant to methicillin and gentamicin

Suspicion criteria of reduced susceptibility to glycopeptides.

Routinely, by the disk diffusion test when,

- the inhibition zone diameter is <17mm around the disk of one of the two glycopeptides,
- the inhibition zone diameter around the teicoplanin disk is inferior of at least 3 mm to the one of vancomycin,
- some colonies are present in the inhibition zone of one of the two glycopeptides,
- there is an interaction phenomenon (synergism or antagonism) between one of the glycopeptides and an oxacillin disk at 5 µg

Routinely, by the automated methods when the strains are categorized I or R to at least one of the glycopeptides.

(*) this requires a populational analysis which is not routinely performed (see Chesneau, O., A. Morvan and N. El Solh – JAC, 2000, **45**, 887-890).

By a specific test the decreased susceptibility is suspected by the presence of at least one colony on Mueller-Hinton agar medium (MH) containing 5 mg/L of teicoplanin, seeded by spreading 10 µl of a suspension of 6 10^8 CFU/ml (McFarland 2) after incubation at 35-37°C and reading at 24 and 48 hours It is necessary to include a positive control (*Staphylococcus epidermis* CIP) and a negative control (*Staphylococcus aureus* ATCC 25923) in each series of tests.

Remark : the brain-heart infusion agar (BHI agar) containing 6 mg/L of teicoplanin and seeded by spreading 10 µl of a suspension of 10^8 CFU/ml (Mc Farland 0 5) does not enable to obtain results reproducible from one batch to the other.

Categorization

For the strains of putative decreased susceptibility to glycopeptides, only the determination of the MIC of vancomycin and of teicoplanin, in the conditions described in the yearly report (dilution in Mueller Hinton agar medium) allows their clinical categorization (S,I,R) according to the above mentioned MIC breakpoints

The MIC can also be determined by any technique having shown for these antimicrobial agents, its equivalence with the reference technique

Table XI – Minimum inhibitory concentration and zone diameter interpretive standards for *Enterococcus* spp..

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Ampicillin	10 µg	≤ 4	> 16	≥ 19	< 14	Enterococcus susceptibility to penicillins is assessed by means of an ampicillin disk (10 µg). For *E. faecalis*, interpretation is valid for penicillin G, amoxicillin, mezlocillin, piperacillin and imipenem. For *E. faecium*, the resistance level is higher towards ureidopenicillins and imipenem than towards aminopenicillins. The treatment of severe infections due to enterococcus ampicillin S/I requires higher dosages of penicillin in combination with gentamicin (or streptomycin) to obtain a bactericidal activity.
Streptomycin Kanamycin Gentamicin	500 µg 1000 µg 500 µg	≤ 250 ≤ 250 ≤ 250	> 500 > 500 > 500	≥ 14 ≥ 14 ≥ 17	< 12 < 10 < 11	Only high potency disks of streptomycin (S), kanamycin (K) and gentamicin (G) must be used for streptococci and enterococci which are intrinsically resistant at low level (LLR) to aminoglycosides. They enable to detect a high level acquired resistance (HLR) which abolishes the bactericidal synergistic effect of the concerned aminoglycoside in combination with penicillins. The other aminoglycosides remain usable in combination. Results interpretation : S^{LLR}, K^{LLR} and G^{LLR} (∅ ≥ D ; MIC ≤ c): possible synergy with penicillins in case of susceptibility to the latter antimicrobial agents. S^{HLR}: streptomycin cannot be used. K^{HLR}: kanamycin, amikacin and isepamicin cannot be used. G^{HLR}: kanamycin, tobramycin, dibekacin, gentamicin, sisomicin, amikacin, isepamicin and netilmicin cannot be used. For intermediate zone size diameter, the resistance level must be confirmed by agar dilution or broth dilution containing 500 µg/mL of S, K or G. (HLR : CMI > 500 µg/mL). The S^{HLR} + K^{HLR}, K^{HLR} + G^{HLR} and S^{HLR} + K^{HLR} + G^{HLR} combinations are possible.
Chloramphenicol	30 µg	≤ 8	> 16	≥ 23	< 19	Interpretation valid for thiamphenicol.
Tetracycline	30 IU	≤ 4	> 8	≥ 19	< 17	Interpretation valid for oxytetracycline and doxycycline.

(H) – Antimicrobial agent for hospital use

Table XI (continued) – Minimum inhibitory concentration and zone diameter interpretive standards for *Enterococcus spp.*.

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Erythromycin	15 IU	≤ 1	> 4	≥ 22	< 17	Interpretation valid for azithromycin, clarithromycin, dirithromycin and roxithromycin.
Lincomycin	15 µg	≤ 2	> 8	≥ 21	< 17	Intrinsic resistance of *E. faecalis*
Clindamycin	2 IU	≤ 2	> 2	≥ 15	< 15	Intrinsic resistance of *E. faecalis*.
Pristinamycin	15 µg	≤ 1	> 2	≥ 22	< 19	Spectrum limited to *E. faecium*.
Quinupristin/dalfopristin	15 µg	≤ 0,5	> 2	≥ 25	< 19	Spectrum limited to *E. faecium*.
Levofloxacin	5 µg	≤ 1	> 4	≥ 20	< 15	
Trovafloxacin	10 µg	≤ 1	> 2	≥ 20	< 17	
Teicoplanin (H)	30 µg	≤ 4	> 16	≥ 17	-	If the zone size diameter is < 17 mm, determine MIC.
Vancomycin (H)	30 µg	≤ 4	> 16	≥ 17	-	If the zone size diameter is < 17 mm, determine MIC.
Trimethoprim/sulfamethoxazole	1.25/23.75 µg	≤ 2/38	> 8/152	≥ 16	< 10	
Nitrofurantoin	300 µg	≤ 32	> 128	≥ 17	< 14	Interpretation valid for isolates from urinary tract only.

(H) – Antimicrobial agent for hospital use

Table XII – Minimum inhibitory concentration and zone diameter interpretive standards for *Streptococcus pneumoniae.*

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Penicillin G	-	≤ 0.06	> 1	-	-	An acquired resistance to penicillin G of pneumococci is crossed with all the other β-lactams. The susceptibility to penicillin G is assessed with an oxacillin disk 5 µg (OXA-5) according to the following criteria: OXA-5 diameter ≥ 26 mm = strain susceptible to penicillin G and subsequently to the other β-lactams. OXA – 5 diameter < 26 mm = strain I or R to penicillin G. This test allows neither to differentiate the I strains (low level of resistance LLR) from the R strains (high level of resistance HLR) to penicillin G, nor to evaluate the crossed resistance level to the other β-lactams, depending on each β-lactam. The disk diffusion test cannot be used to validly determine the *in vitro* activity of the β-lactams on the strains OXA-5 < 26 mm. In case of severe infection, clinical failure or with any strain of decreased susceptibility (OXA-5<26 mm), determine the MIC of benzyl penicillin and of the β-lactams whose pharmacodynamic properties are compatible with a therapeutic efficiency: amoxicillin, imipenem, cefuroxime, cefotaxime, ceftriaxone, cefepime, cefpirome. The critical concentrations given above are valid for a parenteral use and, temporarily, for the oral forms of amoxicillin and cefuroxime.
Oxacillin	5 µg	≤ 0.06	-	≥ 26	-	
Ampicillin	-	≤ 0.5	> 2	-	-	
Amoxicillin	-	≤ 0.5	> 2	-	-	
Cefuroxime	-	≤ 0.5	> 2	-	-	
Cefotaxime (H)	-	≤ 0.5	> 2	-	-	
Ceftriaxone	-	≤ 0.5	> 2	-	-	
Cefepime (H)	-	≤ 0.5	> 2	-	-	
Cefpirome (H)	-	≤ 0.5	> 2	-	-	
Imipenem (H)	-	≤ 0.5	> 2	-	-	

(H) – Antimicrobial agent for hospital use

Table XII (continued) - Minimum inhibitory concentration and zone diameter interpretive standards for *Streptococcus pneumoniae.*

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Streptomycin Kanamycin Gentamicin	500 µg 1000 µg 500 µg	≤ 250 ≤ 250 ≤ 250	> 500 > 00 > 500	≥ 14 ≥ 14 ≥ 17	< 12 < 10 < 11	Only high potency disks of streptomycin (S), kanamycin (K) and gentamicin (G) must be used for pneumococci, species intrinsically resistant at low level (LLR) to aminoglycosides. They enable to detect a high level acquired resistance (HLR) which abolishes the bactericidal synergistic effect of the concerned aminoglycoside in combination with penicillins. The other aminoglycosides remain usable in combination. Results interpretation : S^{LLR}, K^{LLR} and G^{LLR} (Ø ≥ D ; MIC ≤ c): possible synergy with penicillins in case of susceptibility to the latter antimicrobial agents. S^{HLR}: streptomycin cannot be used. K^{HLR}: kanamycin, amikacin et isepamicin cannot be used. For intermediate zone size diameter, the resistance level must be confirmed by agar dilution or broth dilution containing 500 µg/mL of S, K or G (HLR : CMI > 500 µg/mL). The S^{HLR} + K^{HLR} combination is possible.
Chloramphenicol	30 µg	≤ 8	> 16	≥ 23	< 19	Interpretation valid for thiamphenicol.
Tetracycline	30 IU	≤ 4	> 8	≥ 19	< 17	Interpretation valid for oxytetracycline and doxycycline.
Erythromycin	15 IU	≤ 1	> 4	≥ 22	< 17	Interpretation valid for azithromycin, clarithromycin, dirithromycin and roxithromycin.
Lincomycin	15 µg	≤ 2	> 8	≥ 21	< 17	Interpretation valid for clindamycin.
Pristinamycin	15 µg	≤ 1	> 2	≥ 22	-	The disk diffusion test cannot be used to determine the *in vitro* activity of pristinamycin if Ø < 22 mm.
Trimethoprim/sulfamethoxazole	1.25/23.75 µg	≤ 2/38	> 8/152	≥ 16	< 10	Interpretation valid for the other trimethoprim-sulfonamide combinations
Fosfomycin (H)	50 µg	≤ 32	> 32	≥ 14	< 14	Interpretation valid for intraveinous route.
Sparfloxacin Levofloxacin Trovafloxacin	5 µg 5 µg 10 µg	≤ 1 ≤ 2 ≤ 1	> 2 > 4 > 2	≥ 20 ≥ 17 ≥ 20	< 16 < 15 < 17	
Teicoplanin (H) Vancomycin (H)	30 µg 30 µg	≤ 4 ≤ 4	> 16 > 16	≥ 17 ≥ 17	- -	If the zone size diameter is < 17 mm, determine MIC. If the zone size diameter is < 17 mm, determine MIC.

(H) – Antimicrobial agent for hospital use

Table XIII – Minimum inhibitory concentration and zone diameter interpretive standards for *Streptococcus* spp. *(S. pneumoniae* excepted).

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Penicillin G	6 µg (10 IU)	≤ 0.25	> 16	≥ 29	< 8	Interpretation valid for phenoxymethyl-penicillin.
Ampicillin	10 µg	≤ 4	> 16	≥ 19	< 14	Interpretation valid for bacampicillin, metampicillin, pivampicillin.
Amoxicillin	25 µg	≤ 4	> 16	≥ 21	< 14	
Streptomycin	500 µg	≤ 250	> 500	≥ 14	< 12	Only high potency disks of streptomycin (S), kanamycin (K) and gentamicin (G) must be used for streptococci, species intrinsically resistant at low level (LLR) to aminoglycosides. They enable to detect a high level acquired resistance (HLR) which abolishes the bactericidal synergistic effect of the concerned aminoglycoside in combination with penicillins. The other aminoglycosides remain usable in combination. Results interpretation : S^{LLR}, K^{LLR} and G^{LLR} (∅ ≥ D ; MIC ≤ c): possible synergy with penicillins in case of susceptibility to the latter antimicrobial agents. S^{HLR}: streptomycin cannot be used. K^{HLR}: kanamycin, amikacin et isepamicin cannot be used. For intermediate zone size diameter, the resistance level must be confirmed by agar dilution or broth dilution containing 500 µg/mL of S, K or G (HLR : CMI > 500 µg/mL). The S^{HLR} + K^{HLR} combination is possible.
Kanamycin	1000 µg	≤ 250	> 500	≥ 14	< 10	
Gentamicin	500 µg	≤ 250	> 500	≥ 17	< 11	

(H) – Antimicrobial agent for hospital use

Table XIII (continued) – Minimum inhibitory concentration and zone diameter interpretive standards for *Streptococcus* spp. *(S. pneumoniae* excepted).

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Chloramphenicol	30 µg	≤ 8	> 16	> 23	< 19	Interpretation valid for thiamphenicol.
Tetracycline	30 IU	≤ 4	> 8	≥ 19	< 17	Interpretation valid for oxytetracycline and doxycycline.
Erythromycin	15 IU	≤ 1	> 4	≥ 22	< 17	Interpretation valid for azithromycin, clarithromycin, dirithromycin and roxithromycin.
Telithromycin	*15 µg*	*≤ 0.5*	*> 2*	*≥ 21*	*< 17*	
Lincomycin	15 µg	≤ 2	> 8	≥ 21	< 17	
Clindamycin	2 IU	≤ 2	> 2	≥ 15	< 15	
Pristinamycin	15 µg	≤ 1	> 2	≥ 22	< 19	
Levofloxacin	5 µg	≤ 2	> 4	≥ 17	< 15	
Trovafloxacin	10 µg	≤ 1	> 2	≥ 20	< 17	
Teicoplanin (H)	30 µg	≤ 4	> 16	≥ 17	-	If the zone size diameter is < 17 mm, determine MIC.
Vancomycin (H)	30 µg	≤ 4	> 16	≥ 17	-	If the zone size diameter is < 17 mm, determine MIC.
Rifampin	30 µg	≤ 4	> 16	≥ 19	< 14	
Trimethoprim/sulfamethoxazole	1.25/23 75 µg	≤ 2/38	8/152	≥ 16	< 10	Interpretation valid for the other trimethoprim-sulfonamide combinations.

(H) – Antimicrobial agent for hospital use

Table XIV – Minimum inhibitory concentration and zone diameter interpretive standards for *Haemophilus influenzae.*

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Ampicillin Cephalotin (H) Amoxicillin/clavulanic ac.	2 µg 30 µg 20/10 µg	- - ≤ 4/2	> 1 > 8 -	- - ≥ 21	< 20 < 17 -	The β-lactamase production is detected by means of a nitrocefin-based test right from the isolate and renders the strain resistant to amino-, carboxy- and ureido- penicillins. The activity of these β-lactams is restored when they are combined with a β-lactamase inhibitor. The detection of a decreased susceptibility to β-lactams (β-lactamase non producing ampicillin resistant strain) can be made with an ampicillin disk 2 µg (diameter < 20 mm) or, failing that, with a cefalotin disk 30 µg (diameter < 17 mm). Since some of these strains have a weak growth on HTM medium, a chocolate PolyViteX® agar culture plate is then used. This low-level resistance to the aminopenicillins is more pronounced for the first generation cephalosporins and imipenem. The third generation cephalosporins activity is only slightly altered. The clinical consequences of this resistance are unknown.
Cefotaxime (H) Ceftriaxone						Usable without interpretive standards as there is no clinical failure due to resistance mechanisms.
Tetracycline	30 IU	≤ 2	> 4	≥ 23	18	Interpretation valid for the other tetracyclines.

(H) – Antimicrobial agent for hospital use

Table XIV (continued) - Minimum inhibitory concentration and zone diameter interpretive standards for *Haemophilus influenzae.*

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Trimethoprim/sulfamethoxazole	1.25/23.75 µg	≤0.5/9.5	> 1/19	≥ 24	-	Cannot be tested with chocolate agar plate. Use HTM agar.
Chloramphenicol	30 µg	≤ 2	> 4	≥ 28	< 24	
Rifampin	30 µg	≤ 2	> 4	≥ 24	< 20	
Kanamycin	30 IU	≤ 8	> 16	≥ 18	< 15	
Gentamicin	15 µg	≤ 2	> 4	≥ 16	< 14	
Macrolides	-	-	-	-	-	The study of these molecules is not justified because *H. influenzae* generally appears as intermediate to the macrolides with a cycle at 14 and 15 atoms and to pristinamycin, and resistant to the macrolides with a cycle at 16 atoms and to the lincosamides.
Lincosamides	-	-	-	-	-	
Pristinamycin	-	-	-	-	-	
Ofloxacin	5 µg	≤ 1	-	≥ 22	-	
Levofloxacin	5 µg	≤ 1	-	≥ 22	-	
Ciprofloxacin	5 µg	≤ 1	-	≥ 22	-	

Table XV – Minimum inhibitory concentration and zone diameter interpretive standards for *Neisseria meningitidis.*

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Penicillin G	-	≤ 0.06	> 1	-	-	A decreased susceptibility to β-lactams can be routinely detected with an oxacillin disk (1 μg or 5 μg) according to the following criteria: oxa 1 μg ≥ 11 mm or oxa 5 μg ≥ 18 mm, β-lactam susceptible strain oxa 1 μg < 11 mm or oxa 5 μg < 18 mm, strain with a decreased susceptibility to penicillin G and/or amoxicillin to be confirmed by agar dilution test. The high level resistance to β-lactams by β-lactamase production is very seldom. It can be detected by means of a nitrocefin-based test.
Amoxicillin	-	≤ 0.25	> 2	-	-	
Oxacillin	5 μg	-	-	≥ 18	-	
Oxacillin	1 μg	-	-	≥ 11	-	
Cefotaxime (H)	-	≤ 0.25	-	-	-	
Ceftriaxone	-	≤ 0.25	-	-	-	
Chloramphenicol	30 μg	≤ 2	> 4	≥ 30	-	
Rifampin	30 μg	≤ 0.25	-	≥ 30	-	For meningococcal prophylaxis

(H) – Antimicrobial agent for hospital use

Table XVI – Minimum inhibitory concentration and zone diameter interpretive standards for *Neisseria gonorrhoeae.*

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L) S	MIC Breakpoints (mg/L) R	Zone Diameter Breakpoints (mm) S	Zone Diameter Breakpoints (mm) R	Comments
Penicillin G	-	≤ 0.06	> 1	-	-	The β-lactamase production is detected by means of a nitrocefin-based test right from the isolate and renders the strain resistant to amino-, carboxy- and ureido-penicillins. The activity of these β-lactams is restored when they are combined with a β-lactamase inhibitor. The detection of a decreased susceptibility to β-lactams can be routinely made by penicillin G MIC determination and agar dilution test using chocolate PolyViteX® agar medium; if the E-test® method is used, seed by swabbing.
Amoxicillin	-	≤ 0.25	> 2	-	-	
Ceftriaxone		≤ 0.25	-			
Spectinomycin	100 µg	≤ 64	> 64	≥ 20	< 20	
Chloramphenicol		≤ 4	> 16			
Tetracycline	30 IU	≤ 1	> 4	-	< 19	Interpretation valid for doxycycline and minocycline. A zone size diameter < 19 mm evokes a resistance due to *tetM* gene.
Erythromycin		≤ 1	> 4	-	-	
Nalidixic acid	30 µg			-	< 25	The detection of a decreased susceptibility to fluoroquinolones can be made by using a nalidixic acid disk (30 µg). If the zone size diameter is less than 25 mm, check MIC of ofloxacin or ciprofloxacin.
Ciprofloxacin	-	≤ 0.06	> 0.06	-	-	
Ofloxacin	-	≤ 0.12	> 0.12	-	-	

Table XVII – Minimum inhibitory concentration and zone diameter interpretive standards for *Campylobacter* spp.

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Ampicillin	10 µg	≤ 4	> 16	≥ 19	< 14	See rule (1).
Amoxicillin/clavulanic ac.	20/10 µg	≤ 4/2	> 16/2	≥ 21	< 14	See rule (1).
Cephalotin (H)	30 µg	≤ 8	> 32	≥ 18	< 12	See rule (1).
Cefotaxime (H)	30 µg	≤ 4	> 32	≥ 21	< 15	See rule (1).
Imipenem (H)	10 µg	≤ 4	> 8	≥ 22	< 17	See rule (1).
Streptomycin	10 IU	≤ 8	> 16	≥ 15	< 13	See rule (1) and (2).
Gentamicin	15 µg (10 IU)	≤ 4	> 8	≥ 16	< 14	See rule (1) and (2).
Kanamycin	30 IU	≤ 8	> 16	≥ 17	< 15	See rule (1) and (2).
Tobramycin	10 µg	≤ 4	> 8	≥ 16	< 14	See rule (1) and (2).
Erythromycin	15 IU	≤ 1	> 4	≥ 22	< 17	See rule (1). Interpretation valid for clarithromycin.
Nalidixic acid	30 µg	≤ 8	> 16	≥ 20	< 15	See rule (1).
Ciprofloxacin	5 µg	≤ 1	> 2	≥ 22	< 19	See rule (1).
Tetracycline	30 IU	≤ 4	> 8	≥ 19	< 17	
Chloramphenicol	30 µg	≤ 8	> 16	≥ 23	< 19	

(H) – Antimicrobial agent for hospital use

Rules for interpretive reading

Note : according to antimicrobial agents, the correlation between MICs and zone diameters is sometimes difficult to establish. If the results obtained by the disk diffusion test seem doubtful, determine MICs by agar dilution method or by any technique having shown its equivalence with the reference technique for these antimicrobial agents.

(1) For *Campylobacter* spp , no inhibition zone diameter around β-lactam, aminoglycoside, macrolide or quinolone disks evokes a high level resistance.
(2) Taking into account the incubation conditions (anaerobic or micro-aerophilic), the zones of inhibition around aminoglycoside disks are always reduced

Table XVIII – Minimum inhibitory concentration and zone diameter interpretive standards for *Helicobacter pylori.*

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Erythromycin	15 IU	≤ 1	> 4	≥ 22	< 17	Interpretation valid for clarithromycin.

Supplemental note

Testing with erythromycin is more appropriate to determine the susceptibility to clarithromycin using the disk diffusion test Susceptibility to amoxicillin is best determined using a MIC method Some isolates have a decreased susceptibility *in vitro* to amoxicillin (CMI>0 1 mg/L), that does not preclude its use for therapy.

Table XIX – Minimum inhibitory concentration and zone diameter interpretive standards for anaerobes.

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Amoxicillin		≤ 0.5	> 1	-	-	Interpretation valid for gram-negative anaerobes only. See rules (1) and (2).
Amoxicillin	25 µg	≤ 4	> 16	≥ 21	< 14	Interpretation valid for gram-positive anaerobes only. See rules (5). Interpretation valid for penicillin G and ampicillin.
Amoxicillin/clavulanic ac.	20/10 µg	≤ 4/2	> 16/2	≥ 21	< 14	
Ticarcillin (H)	75 µg	≤ 16	64	≥ 22	< 18	Against *Bacteroides fragilis*, interpretation valid for piperacillin.
Ticarcillin/clavulanic ac. (H)	75/10 µg	≤ 16/2	> 64/2	≥ 22	< 18	
Piperacillin (H)	75 µg	≤ 8	> 64	≥ 20	< 12	Against *Bacteroides fragilis*, interpretation valid for ticarcillin.
Piperacillin/tazobactam (H)	75/10 µg	≤ 8/4	> 64/4	≥ 21	< 14	
Imipenem (H)	10 µg	≤ 4	> 8	≥ 22	< 17	See rule (4)
Cefoxitin (H)		-	> 32	-	-	
Cefotetan (H)		-	> 32	-	-	
Cefotaxime (H)	30 µg	≤ 4	> 32	≥ 21	< 15	See rule (5)

(H) – Antimicrobial agent for hospital use

Rules for interpretive reading

Note : according to antimicrobial agents, the correlation between MICs and zone diameters is sometimes difficult to establish and is different according to species especially for fastidious organisms If the results obtained by the disk diffusion test seem doubtful, determine MICs by agar dilution method or by any technique having shown its equivalence with the reference technique for these antimicrobial agents.

(1) Among *Fusobacterium*, ß-lactamase production, detected by means of a nitrocefin-based test right from the isolate, renders the strain resistant to amino-, carboxy- and ureido-penicillins The activity of these β-lactams is restored when they are combined with a β-lactamase inhibitor.

(2) Among *Prevotella* , ß-lactamase production, detected by means of a nitrocefin-based test right from the isolate, renders the strain resistant to aminopenicillins, first-generation cephalosporin, cefamandole, cefuroxime oral third-generation cephalosporins.·The activity of these β-lactams is restored when they are combined with a β-lactamase inhibitor

(3) Among *Clostridium butyricum*, *C clostridioforme* and *C ramosum*, ß-lactamase production detected by means of a nitrocefin-based test right from the isolate Only the ß-lactamase of *C butyricum* is inhibited, with therapeutic concentrations, by β-lactamase inhibitors.

(4) Imipenem resistance is found in France among *Bacteroides fragilis* (carbapenemase) or *B distasonis*. There is a cross resistance for all ß-lactams even if they are combined with a β-lactamase inhibitor

(5) For *Bacteroides* group *fragilis*, interpret I any S result for third-generation cephalosporins.

Table XVIII (continued) – Minimum inhibitory concentration and zone diameter interpretive standards for anaerobes.

Antimicrobial Agent	Disk Content	MIC Breakpoints (mg/L)		Zone Diameter Breakpoints (mm)		Comments
		S	R	S	R	
Chloramphenicol	30 µg	≤ 8	> 16	≥ 23	< 19	
Clindamycin	2 IU	≤ 2	> 2	≥ 15	< 15	Requires a full 48 hours incubation because they are false susceptible results after 24 hours.
Spiramycin	100 µg	≤ 1	> 4	≥ 24	< 19	Valid for anaerobes from dental infections.
Pristinamycin	15 µg	≤ 1	> 2	≥ 22	< 19	Do not test against *Bacteroides* group *fragilis*.
Vancomycin	30 µg	≤ 4	> 16	≥ 17	-	Interpretation valid for gram positive anaerobes.
Teicoplanin	30 µg	≤ 4	> 16	≥ 17	-	Interpretation valid for gram positive anaerobes.
Ofloxacin	5 µg	≤ 1	> 4	≥ 22	< 16	Only relevant against *Peptostreptococcus* and propionibacteria from bone or brain infections.
Rifampin	30 µg	≤ 4	> 16	≥ 19	< 14	
Metronidazole	Tabs 16 µg	≤ 4	> 16	-	< 21	Interpretation valid for ornidazole . See rule (6).
Vancomycin	5 µg	-	-	-	< 10	Aid to identification of gram-negative rods. See rule (7).
Kanamycin	1000 µg	-	-	-	< 10	Aid to identification of gram-negative rods. See rule (7).
Colistin	10 µg	-	-	-	< 10	Aid to identification of gram-negative rods. See rule (7).

Rules for interpretive reading (continued)

(6) Metronidazole Neosensitabs® (Rosco) allow the susceptibility testing of this antimicrobial agent by the disk diffusion test. For susceptible strains, zone size diameters are > 35 mm. Among *Clostridium* and gram-negative anaerobes, 5 nitro-imidazole resistance is very seldom. It must be confirmed by MIC determination. Some strains appear false resistant if the anaerobic conditions are not perfect. Metronidazole high level resistance is exceptional In France, 2 to 3% of *Bacteroides* group *fragilis* strains have a decreased susceptibility to 5 nitro-imidazole (MIC between 8 and 16 mg/L)

(7) These three disks, with special contents, are an aid to identification of gram-negative rods: *Bacteroides* group *fragilis* are resistant to kanamycin, colistin and vancomycin, *Prevotella* are resistant to kanamycin and vancomycin, colistin susceptibility varying according to species; *Porphyromonas* are susceptible to vancomycin and resistant to kanamycin and colistin; *Fusobacterium* are susceptible to kanamycine and colistin, resistant to vancomycin