

Diagnostic update

Guide to interpreting minimum inhibitory concentrations (MIC)

We use an automated platform in all our core microbiology laboratories, to support rapid and accurate quantitative antibiotic susceptibility test (AST) reporting, including minimum inhibitory concentrations (MIC). The MIC can provide the ability to precisely determine the concentration of antibiotic required to inhibit growth of a pathogen.

Your IDEXX microbiology results will show the identity of the organism and the appropriate antibiotic sensitivity pattern against each organism. Most antibiograms will include MICs to determine the most effective antibiotic that will result in effective treatment. This guide provides a detailed explanation of the following concepts important in interpreting the MIC:

- + The MIC number is the lowest concentration (in µg/mL) of an antibiotic that inhibits the growth of a given strain of bacteria.
- + The MIC number for one antibiotic CANNOT be compared to the MIC number for another antibiotic. (See the "How are MICs used?" section.)
- + The choice of antibiotic should be based on the MIC number, the site of infection, and an antibiotic's breakpoint.

However, we cannot account for all patient particularities (e.g., age, renal and hepatic function, risk of dysbiosis, pharmacokinetics, etc) and reported antimicrobials should be viewed as a guidance only.

We recognise that antimicrobial prescription considers many patient and clinical factors.

How is the MIC reported?

Next to each antibiotic is the susceptibility interpretation: S (sensitive), I (intermediate), or R (resistant), followed by the MIC in µg/mL, followed by the range of MIC's tested and a visual representation of where the MIC lies in relation to the breakpoint.

If the organism is reported as **sensitive**, it implies that the infection due to the strain may be appropriately treated with the dosage of antimicrobial agent recommended for that type of infection.

Intermediate indicates that the MIC is approaching attainable blood and tissue levels and response rates may be lower than for sensitive strains. There is a high likelihood of therapeutic success if exposure to the antibiotic is increased by adjusting the dosing regimen or by its concentration at the site of infection.

A result of **resistant** indicates that the strain is not inhibited by the usually attainable concentrations of the agent with normal dosage schedules

The breakpoint is the highest effective concentration of the antimicrobial at the site of infection, following systemic administration at established doses. MIC values above or equal to the breakpoint are considered indicative of resistance.

These interpretive standards have been established by the Clinical and Laboratory Standards Institute (CLSI) or by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

Tier classification

Measured MIC

Capitalised letter indicates where MIC lies in relation to breakpoint

Isolate 1

*Growth of: *Proteus mirabilis*

Antibiotic	Result	MIC	Sensitivity Range
*Ampicillin (1)	SENSITIVE	<=2	2 Sssir 32
*Amoxicillin-Clavulanic acid (1)	SENSITIVE	<=2	2 Sssir 32
*Cephalexin (1)	SENSITIVE	16	4 ssSsr 64
*Cefovecin (2)	SENSITIVE	<=0.5	0.5 Sssir 8
*Enrofloxacin (2)	SENSITIVE	0.5	0.12 ssSiir 4
*Marbofloxacin (2)	SENSITIVE	<=0.5	0.5 Ssir 4
*Pradofloxacin (2)	SENSITIVE	0.25	0.12 sSiir 4
*Doxycycline (1)	Resistant	>=16	0.5 ssssiR 16
*Nitrofurantoin (2)	Resistant	128	16 ssiRrr 512
*Potentiated sulphonamides (1)	SENSITIVE	<=20	20 Ssrrr 320
*Amoxicillin (1)	SENSITIVE		

No MIC, as result has been deduced from a class-representative antibiotic

Upper and lower testing limits of antibiotic concentrations

Figure 1. A typical antibiotic report.

In the example above: A strain of *Proteus mirabilis* has a MIC of <=2 µg/mL for ampicillin and a MIC of 16 µg/mL for cephalexin. Looking at the dilutions for ampicillin, at <=2 µg/mL, this MIC is four dilutions away from the breakpoint:

Ampicillin					
Breakpoint for R					
MIC	2	4	8	16	32
Interpretive category	S	S	S	I	R
MIC <= 2µg/ml (4 dilutions below breakpoint)					

Figure 2. An example ampicillin result

For cephalexin, the MIC of 16µg/mL is two dilutions away from the breakpoint:

Cephalexin					
Breakpoint for R					
MIC	4	8	16	32	64
Interpretive category	S	S	S	I	R
MIC 16µg/ml (2 dilutions below breakpoint)					

Figure 3. An example cephalexin result

How are MICs used?

The breakpoint and range of dilutions differ by drug and bacterial species. Therefore, comparing MICs of different antibiotics is not based solely on the numerical value but on how far the MIC is from the breakpoint, the site of the infection, and other considerations, such as the age, species, and health of the animal. Possible side-effects of the drug, price, frequency, and route of administration are also crucial factors.

Tier SYSTEM

Prudent antimicrobial use may lead to a decreased in antimicrobial resistance. Categorisation of antimicrobials can be used as a way of supporting antimicrobial stewardship when selecting antibiotic treatment and may influence the choice of prescription.

Antibiotics (antimicrobials) now show a classification as first-line, second-line, or third-line. These will be indicated by a (1), (2), or (3) after the antibiotic name. These classifications are based on the BSAVA PROTECT guidance and have been refined by our veterinary microbiologists Dr Larry Roberts and Dr Marta Costa.

The classifications are:

1. First-line antimicrobial – this should be considered a first-line antimicrobial where antimicrobial treatment is required
2. Second-line antimicrobials – this is a second-line antimicrobial and should be reserved for when first-line antimicrobials are ineffective or inappropriate for the clinical case.
3. Third-line antimicrobial - this is a third-line antimicrobial and should ideally be reserved for human use

There will be instances where a third-line antimicrobial will appear on the report, and it may be entirely appropriate to prescribe this for your patient (based on culture & sensitivity results and the prescribing cascade)

IDEXX test option and when to test

Intrinsic resistances: intrinsic resistance is defined as inherent or innate antimicrobial resistance; this means the organism is intrinsically resistant and clinical failure is expected even if it appears susceptible in vitro.

Some notable examples are:

- + Clindamycin is not effective against aerobic Gram-negative bacteria e.g., *E. coli*, *P. aeruginosa*, *P. mirabilis*.
- + Polymyxin B is not effective against Gram-positive bacteria e.g., *Staph. pseudintermedius*, *Strep. canis*
- + Cephalosporins for enterococci

When are MICs not reported?

MICs are not reported when:

- + The growth requirements of some organisms require the sensitivity testing to be performed by another method e.g., disk diffusion.
- + Interpretive criteria are not available from CLSI/EUCAST. In these cases, recommended antibiotics will usually be reported based on clinical efficacy studies.
- + Certain antibiotics are not available on our commercial system.
- + If the result has been deduced based on the result of another antibiotic e.g., ampicillin predicts the effectiveness of amoxicillin
- + The drug is known to be clinically ineffective against the organism, regardless of the in vitro results.

When selecting an antibiotic, keep in mind that other factors in addition to the MIC are important. The location of the infection is important because lipid-soluble drugs reach higher levels in the tissue than they do in serum. Some drugs have variable tissue penetration. Drugs excreted by the kidney reach much higher bladder levels than serum levels. Species considerations are also important because certain antibiotics are toxic in some species.

If you need to discuss any microbiology results, please contact our Professional Services team on:

+44 (0)203 788 7508 (if you are in the UK) or
+353 (0) 1562 1211 (if you are in Eire)

Choose option 1 then option 5 from the menu selection. You can then choose from several options to speak to the appropriate specialist.