Microbiology guide to interpreting minimum inhibitory concentration (MIC)

Historically, in vitro susceptibility testing was routinely performed by disk diffusion (Kirby-Bauer) method. The size of the growth-free zone determined whether the bacterium was considered to be susceptible, resistant, or intermediate to a particular antibiotic.

Although a useful guide for selecting an effective antibiotic, Kirby-Bauer testing could not tell the clinician the exact concentration of antibiotic needed to achieve a therapeutic result. The VITEK® 2 (BioMerieux) automated platform, used in all our microbiology laboratories, supports rapid and accurate quantitative antibiotic susceptibility test (AST) reporting, including minimum inhibitory concentration (MIC). The MIC provides 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 in order to determine the most effective antibiotic that will result in effective treatment.

This guide provides a detailed explanation of the following concepts important in implementing 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. (See the "What is an MIC?" section.)
- An 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. Consider safety, ease of use, and cost when determining the optimum antibiotic.
- The attached tables will aid in MIC interpretation and antibiotic selection.

What is an MIC?

The MIC, or minimum inhibitory concentration, is the lowest concentration (in µg/mL) of an antibiotic that inhibits the growth of a given strain of bacteria. At IDEXX, a commercial automated system is used to determine MICs. A quantitative method of susceptibility testing, an MIC helps determine which class of antibiotic is most effective. This information can lead to an appropriate choice of an antibiotic that will increase chances of treatment success and help in the fight to slow antibiotic resistance.

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. Sensitive implies that the organism is inhibited by the serum concentration of the drug that is achieved using the usual dosage; intermediate implies that the organisms are inhibited only by the maximum recommended dosage; and resistant implies that the organisms are resistant to the usually achievable serum drug levels. These interpretive standards have been established by the Clinical and Laboratory Standards Institute (CLSI).

Urine culture susceptibility result

Organism: *E.coli*

Antibiotics	MIC (µg/mL)	Interpretation
Amoxicillin	≤2	Sensitive
Amoxicillin/clavulanic acid	≤2	Sensitive
Cephalexin	8	Sensitive
Cefpodoxime	≤0.25	Sensitive
Ceftiofur	≤1	Sensitive
Cefovecin	≤2	Sensitive
Ceftazidime	≤4	Sensitive
Cefotaxime*		Sensitive
Imipenem	2	Sensitive
Amikacin	≤2	Sensitive
Gentamicin	≤0.5	Sensitive
Tobramycin	≤1	Sensitive
Enrofloxacin	0.5	Sensitive
Marbofloxacin	0.5	Sensitive
Ciprofloxacin	≤1	Sensitive
Doxycycline	≥16	Resistant
Nitrofurantoin	32	Sensitive
Chloramphenicol	8	Sensitive
Trimethoprim/sulfa	≤10	Sensitive

*MIC not available

When are MICs not performed?

MICs are not performed when:

- The growth requirements of some organisms require the sensitivity testing to be performed by another method.
- Interpretive criteria is not available from CLSI. In these cases, recommended antibiotics will usually be reported based on clinical efficacy studies.
- Certain antibiotics are not available on our commercial system.
- The drug is known to be clinically ineffective against the organism, regardless of the in vitro results.

How are MICs used?

The breakpoint and range of dilutions differ by drug and bacterial species (see chart on next page). 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 important factors.

For example: A strain of *Escherichia coli* has an MIC of 2 µg/mL for amoxicillin and for cefovecin. Looking at the dilutions for amoxicillin, at 2 µg/mL, this strain of *E. coli* is four dilutions away from the breakpoint. For cefovecin, the same strain of *E. coli* at an MIC of 2 µg/mL is two dilutions away from the breakpoint. So, based on MICs, this strain of *E. coli* is more susceptible to amoxicillin than cefovecin. Other factors to take into consideration are the site of the infection, the animal's health, frequency and route of administration, and cost of the antibiotic.

An antibiotic breakpoint is the dilution where bacteria begin to show resistance.

In vitro efficacy of amoxicillin (predicts ampicillin)

Sensitive (MIC)			Intermediate	Resistant
2	4	8	16	32
Tested concentrations of amoxicillin (µg/mL)				Breakpoint

In vitro efficacy of cefovecin

Sensitive (MIC)	Intermediate	Resistant
2	4	8
Tested concentrations of cefovecin (µg/mL)		Breakpoint

For example: Amoxicillin is four dilutions away from its breakpoint while cefovecin is only two dilutions away from its breakpoint. Therefore, in this case, the *E. coli* strain is more susceptible to amoxicillin.

Our consultants are available to help you interpret test results.

Class-reference antibiotics

Some antibiotics are used to determine the susceptibility of other antibiotics in the same class. For example, the presence of methicillin-resistant staphylococci (MRS) is tested in the laboratory with oxacillin and not methicillin. The name MRS is used because of convention over years of use in scientific articles and textbooks.

Antibiotic	Further application
Amoxicillin/clavulanic acid	Predicts susceptibility of Clavamox®.
Amoxicillin	Predicts susceptibility of ampicillin.
Cephalexin	Predicts susceptibility of all first-generation cephalosporins, except cefazolin.
Clindamycin	Predicts susceptibility of lincomycin. Should not be used in horses, rabbits, and other herbivores. Not effective against aerobic gram-negative bacteria.
Erythromycin	Predicts susceptibility of azithromycin and clarithromycin. Not effective against aerobic gram-negative bacteria.
Oxacillin	Predicts susceptibility to methicillin.
Trimethoprim/sulfa	Predicts susceptibility of other potentiated sulfonamides.

Antibiotics

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. Drugs excreted by the kidney reach much higher bladder levels than serum levels. Also, some drugs are more effective against gram-negative bacteria than gram-positive bacteria and vice versa. Species considerations are also important because certain antibiotics are toxic in some species.

Current antibiotic MIC ranges for canine and feline patients are listed below:

Antibiotic	Susceptible	Intermediate	Resistant breakpoint
Amikacin	≤4	8	≥16
Amoxicillin (skin and soft tissue)*	≤0.25	0.5	≥1
Amoxicillin (urine)*	≤8	16	≥32
Amoxicillin/clavulanic acid (skin and soft tissue)*	≤0.25	0.5	≥1
Amoxicillin/clavulanic acid (urine)*	≤8	16	≥32
Benzylpenicillin *Enterococcus*	≤8		≥16
Benzylpenicillin *Staphylococcus*	≤0.12		≥0.25
Cefovecin (skin and soft tissue)	≤0.5	1	≥2
Cefovecin (urine)	≤2	4	≥8
Cefpodoxime	≤2	4	≥8
Ceftazidime Enterobacteriaceae	≤4	8	≥16
Ceftazidime *Pseudomonas*	≤8	16	≥32
Cephalexin (skin and soft tissue)	≤2	4	≥8
Cephalexin (urine)	≤16		≥32
Chloramphenicol	≤8	16	≥32
Clindamycin gram-positive	≤0.5	1–2	≥4
Ciprofloxacin gram-negative	≤1	2	≥4
Doxycycline (respiratory, skin, and soft tissue)†	≤0.12	0.25	≥0.5
Doxycycline (urine)†	≤4	8	≥16
Enrofloxacin	≤0.5	1–2	≥4
Erythromycin	≤0.5	1–4	≥8
Florfenicol	≤2	4‡	≥8
Gentamicin gram-negative	≤2	4	≥8
Gentamicin *Staphylococcus*	≤4	8	≥16
Imipenem gram-negative	≤2	4	≥8
Marbofloxacin	≤1	2	≥4
Minocycline (skin and soft tissue)	≤0.5	1	≥2
Nitrofurantoin (only reported on urine cultures)	≤32	64	≥128
Oxacillin *Staphylococcus aureus*	≤2		≥4
Oxacillin *Staphylococcus* (non-*S. aureus*)	≤0.25		≥0.5
Polymyxin B (not reported on urine cultures)	≤2	4	≥8
Pradofloxacin	≤0.25	0.5–1	≥2
Trimethoprim/sulfa	≤40		≥80

*Amoxicillin and amoxicillin/clavulanic acid may appear sensitive when tested in vitro, but they may not achieve effective levels at the site of skin and soft-tissue infections with standard dosing.

†CLSI breakpoints for doxycycline against staphylococci isolated from respiratory, skin, and soft tissue are ≤0.12 (susceptible), 0.25 (intermediate), and ≥0.5 (resistant). Currently, the lowest concentration reportable for doxycycline in the IDEXX automated platform is 0.5. An internal study of 120 *Staphylococcus* isolates submitted to IDEXX Reference Laboratories with an MIC result of <0.5 were confirmed to be uniformly susceptible when measured by Kirby-Bauer method. Therefore, an MIC of ≤0.5 will be reported as susceptible. ǂ

‡The lowest MIC reportable for florfenicol in our automated platform is ≤4. The breakpoints reported in this table are based on CLSI guidelines for systemic treatment. Higher concentrations are expected when used topically. Organisms are expected to be susceptible to topical florfenicol treatment when a concentration of ≤4 is reported.

Customer support services

IDEXX supports your practice with our customer support, technical support, and medical consulting services teams, including our diagnostic support veterinarians and board-certified veterinary specialists. Call **1-800-667-3411** if you have questions.

The information contained herein is intended to provide general guidance only. As with any diagnosis or treatment, you should use clinical discretion with each patient based on a complete evaluation of the patient, including history, physical presentation and complete laboratory data. With respect to any drug therapy or monitoring program, you should refer to product inserts for a complete description of dosages, indications, interactions and cautions.

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