Test Definition: ZMMLS

Susceptibility, Aerobic, MIC

Overview

Useful For

Determining the in vitro susceptibility of aerobic bacteria involved in human infections

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
MIC	Susceptibility, MIC	No	Yes

Testing Algorithm

When this test is ordered, the reflex tests may be performed at an additional charge.
All aerobically growing bacteria submitted will automatically have susceptibility testing performed and billed as appropriate. Antimicrobial agents appropriate to the organism and specimen source will be tested according to Mayo Clinic's practice and the laboratory's standard operating procedures.
If appropriate, testing for *mecA* will be performed by polymerase chain reaction (PCR) under MARP1 / *mecA*, Molecular Detection, PCR (Bill Only). Indications for *mecA* testing include inadequate growth by phenotypic antimicrobial susceptibility testing, lack of current organism breakpoints for oxacillin or cefoxitin, and assessment of discrepancies between cefoxitin and oxacillin phenotypic testing results.
In the event that an isolate of *Helicobacter pylori* does not grow from a client sample or does not grow for susceptibility testing, reflex testing for HPCR1 / *Helicobacter pylori* with Clarithromycin Resistance Prediction, Molecular Detection, PCR (Bill Only) may be added.
The following tables provide a listing of the antimicrobials routinely tested as well as antimicrobials that may be tested upon request. These tables are organized by isolate groups and are not all inclusive. Call 800-533-1710 and ask to speak to the Bacteriology Antimicrobial Susceptibility Testing Laboratory if the organism or antimicrobial of interest are not listed in these tables.
-Aerobic Gram-Negative Bacilli Antimicrobials
-Additional Gram-Negative Bacteria Antimicrobials
-Staphylococcus, Enterococcus, Bacillus, and Related Genera Antimicrobials
-Additional Gram-Positive Bacteria Antimicrobials
For test utilization options, see *Helicobacter pylori* Diagnostic Algorithm in Special Instructions.

Special Instructions

- Helicobacter pylori Diagnostic Algorithm
- Infectious Specimen Shipping Guidelines
- Aerobic Gram-Negative Bacilli Antimicrobials
- Additional Gram-Negative Bacteria Antimicrobials
- Staphylococcus, Enterococcus, Bacillus, and Related Genera Antimicrobials
- Additional Gram-Positive Bacteria Antimicrobials

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
RMALD	Ident by MALDI-TOF mass spec	No	No
BLA	Beta Lactamase	No	No
SUS	Susceptibility	No	No

HPCR1	H pylori + Clarithro Resistance PCR	No	No
MARP1	mecA PCR (Bill Only)	No	No

Method Name

Minimal Inhibitory Concentration (MIC) (Agar Dilution or Broth Microdilution or Gradient Diffusion) or Disk Diffusion(if appropriate)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

Mayo Clinic Laboratories will not perform susceptibility testing on select agents (eg, *Bacillus anthracis*, *Brucella* species, *Burkholderia mallei*, *Burkholderia pseudomallei*, *Francisella tularensis*, and *Yersinia pestis*). Consult with your state health department or the CDC regarding antimicrobial susceptibility testing of such isolates.

Shipping Instructions

1. See Infectious Specimen Shipping Guidelines in Special Instructions.
2. Place specimen in a large infectious container and label as an etiologic agent/infectious substance.

Necessary Information

Organism identification and specimen source are required.

Specimen Required

Supplies: Infectious Container, Large (T146)
Container/Tube: Agar slant or other appropriate media
Specimen Volume: Organism in pure culture
Collection Instructions:
1. Perform isolation of infecting bacteria.
2. Organism must be in pure culture, actively growing. **Do not submit mixed cultures.**

Forms

If not ordering electronically, complete, print, and send a Microbiology Test Request (T244) with the specimen.

Reject Due To

Agar plate	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Frozen		

	Refrigerated		

Clinical & Interpretive

Clinical Information

Antimicrobial susceptibility testing (AST) determines the minimal inhibitory concentration (MIC) of antimicrobial agents. The MIC is a measurement of the activity of an antimicrobial agent against an organism. It is defined as the lowest concentration of an antimicrobial agent that inhibits growth of the microorganism. Clinical breakpoints are derived from a number of data including:

-The pharmacokinetics/pharmacodynamics of an antimicrobial agent

-The MIC distribution of a large number of isolates

-Clinical outcome data for a patient population treated with the antimicrobial of interest

AST should be performed on pure culture isolates of pathogenic bacteria (or those potentially pathogenic in special situations) grown from specimens that have been appropriately collected so as not to confuse clinically significant isolates with normal or contaminating microbiota. Susceptibility testing is indicated for any organism that contributes to an infectious process warranting antimicrobial chemotherapy if its susceptibility cannot be reliably predicted from the organism's identity.

The MIC obtained during AST is helpful in indicating the concentration of antimicrobial agent required at the site of infection necessary to inhibit the infecting organism. For each organism-antimicrobial agent combination, the Clinical and Laboratory Standards Institute and/or the European Committee on Antimicrobial Susceptibility Testing provides interpretive criteria for determining whether the MIC should be interpreted as susceptible, susceptible dose dependent, intermediate, nonsusceptible, resistant, or epidemiological cutoff value if applicable.

Reference Values

Susceptibility results are reported as minimal inhibitory concentration (MIC) in mcg/mL Breakpoints (also known as "clinical breakpoints") are used to categorize an organism as susceptible, susceptible-dose dependent, intermediate, resistant, or nonsusceptible according to breakpoint setting organizations, either the Clinical and Laboratory Standards Institute (CLSI) or the European Committee on Antimicrobial Susceptibility Testing (EUCAST), as applicable.

In some instances, an interpretive category cannot be provided based on available data and the following comment will be included: "There are no established interpretive guidelines for agents reported without interpretations."

Clinical and Laboratory Standards Institute (CLSI) Interpretive Category Definitions:

Susceptible:

A category defined by a breakpoint that implies that isolates with an MIC at or below or a zone diameter at or above the susceptible breakpoint are inhibited by the usually achievable concentrations of antimicrobial agent when the dosage recommended to treat the site of infection is used, resulting in likely clinical efficacy.

Susceptible-Dose Dependent:

A category defined by a breakpoint that implies that susceptibility of an isolate depends on the dosing regimen that is used in the patient. To achieve levels that are likely to be clinically effective against isolates for which the susceptibility testing results (either MICs or zone diameters) are in the susceptible-dose dependent (SDD) category, it is necessary to use a dosing regimen (ie, higher doses, more frequent doses, or both) that results in higher drug exposure than that achieved with the dose that was used to establish the susceptible breakpoint. Consideration should be given to the maximum literature-supported dosage regimens, because higher exposure gives the highest probability of adequate coverage of a SDD isolate. The drug label should be consulted for recommended doses and adjustment for organ function.

Intermediate:

A category defined by a breakpoint that includes isolates with MICs or zone diameters within the intermediate range that approach usually attainable blood and tissue levels and/or for which response rates may be lower than for susceptible isolates.

Note: The intermediate category implies clinical efficacy in body sites where the drugs are physiologically concentrated or when a higher than normal dosage of a drug can be used. This category also includes a buffer zone, which should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations, especially for drugs with narrow pharmacotoxicity margins.

Resistant:

A category defined by a breakpoint that implies that isolates with an MIC at or above or a zone diameter at or below the resistant breakpoint are not inhibited by the usually achievable concentrations of the agent with normal dosage schedules and/or that demonstrate MICs or zone diameters that fall in the range in which specific microbial resistance mechanisms are likely, and clinical efficacy of the agent against the isolate has not been reliably shown in treatment studies.

Nonsusceptible:

A category used for isolates for which only a susceptible breakpoint is designated because of the absence or rare occurrence of resistant strains. Isolates for which the antimicrobial agent MICs are above or the zone diameters are below the value indicated for the susceptible breakpoint should be reported as nonsusceptible.

Note: An isolate that is interpreted as nonsusceptible does not necessarily mean that the isolate has a resistance mechanism. It is possible that isolates with MICs above the susceptible breakpoint that lack resistance mechanisms may be encountered within the wild-type distribution after the time the susceptible-only breakpoint was set.

Epidemiological Cutoff Value:

The MIC that separates microbial populations into those with and without phenotypically detectable resistance (non-wild-type or wild-type, respectively). The epidemiological cutoff value (ECV) defines the highest MIC for the wild type population of isolates. ECVs are based on in vitro data only, using MIC distributions. ECVs are not clinical breakpoints, and the clinical relevance of ECVs for a particular patient has not yet been identified or approved by CLSI or any regulatory agency.

When an ECV is reported, an interpretive category is not assigned, and the following comment will be included: "This MIC is consistent with the Epidemiological Cutoff Value (ECV) observed in isolates (WITH / WITHOUT) acquired resistance; however, correlation with treatment outcome is unknown."

-Wild-type (WT) – an interpretive category defined by an ECV that describes the microbial population with no phenotypically detectable mechanisms of resistance or reduced susceptibility for an antimicrobial agent being evaluated.

-Non-wild-type (NWT) – an interpretive category defined by an ECV that describes the microbial population with phenotypically detectable mechanisms of resistance or reduced susceptibility for the antimicrobial agent being evaluated.

Note: MIC values for which ECV's are defined are not to be interpreted or reported as susceptible, intermediate or resistant but rather as WT or NWT. The ECV's should not be used as clinical breakpoints.(Clinical and Laboratory Standards Institute [CLSI]. Performance Standards for Antimicrobial Susceptibility Testing. 31st ed. CLSI supplement M100. CLSI; 2021:4-6, 268-269)

European Committee on Antimicrobial Susceptibility Testing (EUCAST) Interpretive Category Definitions:

S - Susceptible, standard dosing regimen: A microorganism is categorized as "Susceptible, standard dosing regimen", when there is a high likelihood of therapeutic success using a standard dosing regimen of the agent

I - Susceptible, increased exposure*: A microorganism is categorized as "Susceptible, Increased exposure*" when there is a high likelihood of therapeutic success because exposure to the agent is increased by adjusting the dosing regimen or by its concentration at the site of infection.

R - Resistant: A microorganism is categorized as "Resistant" when there is a high likelihood of therapeutic failure even when there is increased exposure*.

*Exposure is a function of how the mode of administration, dose, dosing interval, infusion time, as well as distribution and excretion of the antimicrobial agent will influence the infecting organism at the site of infection.
(The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. v11.0, 2021. Available at www.eucast.org.)

Interpretation

A "susceptible" category result and a low minimum inhibitory concentration value indicate in vitro susceptibility of the organism to the antimicrobial tested.
Refer to Reference Values for interpretation of various antimicrobial susceptibility interpretive categories (ie, susceptible, susceptible-dose dependent, intermediate, nonsusceptible, resistant, or epidemiological cutoff value).

Cautions

In vitro susceptibility does not guarantee clinical response. Therefore, the decision to treat with a particular agent should not be based solely on the antimicrobial susceptibility testing result.

Clinical Reference

1. Jorgensen JH, Ferraro MJ: Antimicrobial susceptibility testing: a review of general principles and contemporary practices. Clin Infect Dis. 2009 Dec 1;49(11):1749-1755
2. Jenkins SG, Schuetz AN: Current concepts in laboratory testing to guide antimicrobial therapy. Mayo Clin Proc. 2012 Mar;87(3):290-308
3. Procop GW, Church DL, Hall GS, et al: Antimicrobial susceptibility testing. In: Koneman's Color Atlas and Textbook of Diagnostic Microbiology. 7th ed. Wolters Kluwer Health; 2017:1074-1171

Performance

Method Description

An agar dilution method is used for routine testing. The agar dilution method employs the use of antimicrobial agents incorporated in agar plates. The antimicrobial is added to agar in various concentrations depending upon levels attainable in serum, urine, or both. A standardized suspension of the organism is applied to the agar plates, which are incubated for a minimum of 16 to 18 hours at 35 degrees C. Complete inhibition of all but one colony or a very fine residual haze represents the end point.(Clinical and Laboratory Standards Institute [CLSI]: Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically. 11th ed. CLSI standard M07.CLSI; 2018.)
Daptomycin and tigecycline are tested by agar gradient diffusion.(Clinical and Laboratory Standards Institute [CLSI]: Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically. 11th ed. CLSI standard M07. CLSI; 2018; package insert: Etest Biomerieux;15203E-EN-2016/07. Available at: www.biomerieux.com/techlib)
Colistin is tested by the CLSI-approved Colistin agar test for Enterobacterales and *Pseudomonas aeruginosa*. (Clinical and Laboratory Standards Institute [CLSI]. Performance Standards for Antimicrobial Susceptibility Testing. 31st ed. CLSI supplement M100. CLSI; 2021: 142-147.).
Cefiderocol is tested by disk diffusion.(Clinical and Laboratory Standards Institute [CLSI]. Performance Standards for Antimicrobial Disk Susceptibility Tests. 13th ed. CLSI standard M02. CLSI; 2018.)

PDF Report

No

Specimen Retention Time

Bacterial isolates: 30 days.

Performing Laboratory Location

Rochester

Fees & Codes

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

87077-Ident by MALDI-TOF mass spec (if appropriate)

87185-Beta lactamase (if appropriate)

87186-Antimicrobial Susceptibility, Aerobic Bacteria, MIC-per organism for routine battery (if appropriate)

87181-Susceptibility per drug and per organism for drugs not in routine battery (if appropriate)

87150-H pylori + Clarithro Resistance PCR (if appropriate)

87150-mecA PCR (if appropriate)