ComASP® Cefiderocol 0.008-128

ENGLISH

System for cefiderocol susceptibility testing with broth microdilution method according to ISO 20776-1.

INTENDED PURPOSE

ComASP® Cefiderocol 0.008-128 is an *in vitro* diagnostic product for antimicrobial susceptibility testing (AST) of clinical isolates based on growth of the test organism in the presence of various concentrations of an antimicrobial agent.

This ComASP® system is used for quantitative determination of the minimum inhibitory concentration (MIC) of cefiderocol against the following non-fastidious organisms:

Gram-negative bacteria
Enterobacterales
Pseudomonas aeruginosa
Acinetobacter baumannii complex
Stenotrophomonas maltophilia

DESCRIPTION

ComASP® Cefiderocol 0.008-128 is a 2-test panel containing the dried-up antibiotic in 15 two-fold dilutions:

Cefiderocol concentration ranges 0.008 to 128 µg/ml.

The ComASP® system is a compact version of the broth microdilution (BMD) reference method allowing to perform the antimicrobial susceptibility testing of Cefiderocol as recommended by international standards (i.e. CLSI, EUCAST, ISO) but in a simpler and less time-consuming way. The procedure identified in this type of devices is for manual testing only.

KIT CONTENT

- 4 Systems (panels) of ComASP® Cefiderocol 0.008-128
  (panels individually packed in foil with silica gel desiccant)
- 8 Tubes of Iron-Depleted Mueller Hinton Broth (ID-MHB) (3.6 ml)
- Sealing Film
- Instructions Sheet and Test Results Form

MATERIALS REQUIRED BUT NOT PROVIDED

Standard microbiological supplies and equipment such as:

- loops - pipettes - physiological solutions - swabs - culture media - incubator
- test tubes - 0.5 McFarland turbidity standard - quality control organisms

CONFIGURATION

Test	Cefiderocol Concentration (µg/ml)							
A	Growth	0.008	0.016	0.032	0.064	0.125	0.25	0.5
	1	2	4	8	16	32	64	128
B	Growth	0.008	0.016	0.032	0.064	0.125	0.25	0.5
	1	2	4	8	16	32	64	128

Growth indicates growth control: No antimicrobial agent in the well.

PRINCIPLE OF THE METHOD

Each panel of ComASP® Cefiderocol 0.008-128 is used for testing two bacterial isolates (test A and test B). All wells of test A and B are rehydrated with a standardized microbial suspension. After an incubation of 16-20 hours the growth in the wells is observed and the MIC, i.e. the lowest concentration of antibiotic that inhibits visible growth, is established in terms of µg/ml.

SPECIMEN COLLECTION AND PREPARATION

ComASP® Cefiderocol 0.008-128 is not for use directly with clinical or other specimens. The product is used to indicate appropriate patient treatment against infections caused by microorganisms that can be isolated from clinical samples of adult, juvenile and pediatric patients. There are no different indications for use according to sample source. The microorganism to be tested must first be isolated on a nonselective culture medium, such as blood agar or tryptic soy agar (TSA). In case of mixed culture, selected colonies should be purified by subculturing. Differential media harboring chromogenic or fluorogenic substrates should not be used for the subculture. It is recommended that cultures be no more than 24 hours old unless additional incubation is required to achieve sufficient growth.

TEST PROCEDURE

1. Take a panel from its envelope and leave it at room temperature for 10 min, DO NOT DISCARD THE ENVELOPE until both tests have been carried out.
2. Prepare a suspension of the test organism using either the direct colony suspension or growth method.
3. Standardize the suspension to the density of a McFarland 0.5 standard.
4. Optimally within 15 min of preparation, dilute the adjusted suspension 1:20 in saline; this will be the **Solution A**.
5. Add 0.4 ml of Solution A to a tube of Iron-Depleted Mueller Hinton Broth (ID-MHB) * provided in the kit to obtain the **Solution B**.
6. Dispense 100 µl of Solution B into each well (test 1 or 2).
7. Cover the panel with the lid provided and incubate at 36 ± 2°C for 16-20 hours in ambient air.

* Iron-Depleted Mueller Hinton Broth (ID-MHB): Beef Extract 3.0 g; Acid Hydrolysate of Casein 17.5 g; Starch 1.5 g; Distilled Water 1000 ml; pH 7.3 ± 0.1 (final concentrations of cations and iron: Ca^{++} 20-25 mg/l, Mg^{++} 10-12.5 mg/l, Zn^{++} 0.5-1.0 mg/l, Fe^{++} ≤0.03 mg/l).

READING THE RESULTS

At the end of the incubation period observe the growth in the wells and establish the MIC, i.e. the lowest concentration of antibiotic that inhibits visible growth (Clear End Point).

The result can be read visually or automatically. Reading by the naked eye can be improved by use of bright indirect lighting against a dark background.

Growth appears as turbidity or as a button at the bottom of the well (compare with the amount of growth in the growth-control well).

The growth-control well should be evaluated first. Make sure it is positive for growth. If not, check the viability of the colonies picked and repeat the test using a new row in the same panel or a new panel and a microbial culture of recent growth.

Note the results on the Test Results Form included in the kit (copy as many form as necessary).

INTERPRETATION OF THE RESULTS

The MIC obtained should be interpreted according to current CLSI or EUCAST interpretative criteria (see below).

Antimicrobial agent	Organism	MIC Criteria (µg/ml)				
		CLSI			EUCAST	
		S≤	I	R≥	S≤	R>
Cefiderocol	Enterobacterales	4	8	16	2	2
	Pseudomonas aeruginosa	4	8	16	2	2
	Acinetobacter baumannii complex	4	8	16	-	-
	Stenotrophomonas maltophilia	4	-	-	-	-

Disclaimer: This breakpoint table might be out-of-date and does not replace the CLSI and EUCAST published guidelines, which always should be consulted before MIC categorization.

NOTE: Each individual panel is used for performing two tests. If only one test has been performed, use the film provided in the kit to seal the inoculated rows so to prevent any leakage of contaminated fluids. Then, return the panel into its own desiccant envelope and into the refrigerator (see STORAGE).

USER QUALITY CONTROL

Quality control of ComASP® Cefiderocol 0.008-128 is performed using the following reference strains:

Control strain	MIC QC range (µg/ml)
Escherichia coli ATCC® 25922; NCTC 12241	0.06 – 0.5
Pseudomonas aeruginosa ATCC® 27853; NCTC 12903	0.06 – 0.5

PERFORMANCE CHARACTERISTICS

Accuracy

Accuracy of ComASP® Cefiderocol 0.008-128 was determined by evaluating the agreement of the AST system result with the result generated for the same isolate with the broth microdilution (BMD) reference method. To assess accuracy, Essential Agreement (EA) was calculated. EA occurs when the MIC of the ComASP® system and the reference method agree exactly or is within ± 1 dilution of each other.

Bias

Bias of the method is the evaluation of test device results to determine whether the results that differ from the reference method are significantly skewed or predominantly in one direction.

A total of 300 clinical isolates were tested by three operators.
The following table summarizes performance data from these studies.

Antimicrobial agent	Organism	N	%EA	%Bias
Cefiderocol	Enterobacterales	173	94.2	
	Pseudomonas aeruginosa	65	95.4	
	Acinetobacter baumannii	57	93.0	
	Stenotrophomonas maltophilia	5	100.0	
	TOTAL	300	94.3	-6.7

N, Number of isolates **EA**, Essential Agreement

Reproducibility
95.9 % of ComASP® Cefiderocol 0.008-128 results (3 *E. coli*, 3 *P. aeruginosa*, 2 *A. baumannii* and 2 *S. maltophilia* tested in triplicate by 3 operators on 3 days) were within a doubling dilution of reference microdilution results.

Repeatability
96.7 % of ComASP® Cefiderocol 0.008-128 results (3 *E. coli*, 3 *P. aeruginosa*, 2 *A. baumannii* and 2 *S. maltophilia* tested in triplicate) were within a doubling dilution of reference microdilution results.

LIMITATIONS

Invalid results can be caused by poor specimen quality, improper sample collection, improper transportation, improper laboratory processing, or a limitation of the testing technology. The operator should understand the principles of the procedures, including its performance limitations, in advance of operation to avoid potential mistakes.

WARNINGS AND PRECAUTIONS

1) **For *in vitro* diagnostic use (IVD) only.**
2) **For laboratory professional use only.**
3) Operators must be trained and have certain experience. Please read the instructions carefully before using the kit. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this document.
4) Do not use if a panel, tube or packaging appears to be damaged.
5) Follow standard precautions. All patient specimens should be considered potentially infectious and handled accordingly.
6) Handle all specimens as if infectious using safe laboratory procedures. Dispose of hazardous or biologically contaminated materials according to the practices of your institution.
7) Avoid cross-contamination of samples by using disposable tips and changing them after each sample.
8) Do not mix reagents of different batches. Please use the kit within the validity period.
9) Do not eat, drink, smoke, apply cosmetics or handle contact lenses in areas where reagents and human specimens are handled
10) Results should be interpreted by a trained professional in conjunction with the patient's history and clinical signs and symptoms, and epidemiological risk factors.
11) Ensure laboratory equipment is calibrated and maintained in accordance with the laboratory's procedure.
12) When test results are transmitted from the laboratory to an informatics centre, attention has to be done to avoid erroneous data transfer.

STORAGE

Store ComASP® Cefiderocol 0.008-128 at 2-8°C in the original packaging. Once an envelope is opened the panel shall be used within 7 days and stored at 2-8°C. Do not use the panels beyond the expiry date indicated on the label. Eliminate without using if there are signs of deterioration.

DISPOSAL OF USED MATERIAL

After use, ComASP® Cefiderocol 0.008-128 and material that has come into contact with the sample must be decontaminated and disposed of in accordance with guidelines used in the laboratory for decontamination and disposal of potentially infected material.

SUGGESTIONS FOR TROUBLESHOOTING

For out-of-range QC, first repeat the test with a pure culture or a freshly subcultured QC strain. If the issue is unresolved, follow this guidance for additional suggestions for troubleshooting out-of-range QC results and unusual clinical isolates results.

Observation	Probable Cause	Comments/Suggested Actions
MIC too low	Inoculum too light	Repeat using McFarland 0.5 turbidity standard or standardizing device. Check expiration date and proper storage if using barium sulfate or latex standards. Check steps in inoculum preparation and incubation procedure. Perform colony count check of growth control well immediately after inoculation and before incubation (*E. coli* ATCC® 25922 closely approximates 5 x 10^5 CFU/ml)
MIC too high	Inoculum too heavy	
MIC too high	Antimicrobial agent is degrading	Use alternative lot. Check STORAGE and package integrity
Skipped wells	Contamination. Inadequate mixing of inoculum or improper inoculation of panel	Repeat QC test

In case of other malfunctions or defects, contact immediately Liofilchem (*) or the local representative.

In case of incident associated with the device, notify immediately Liofilchem (*) or its local representative and the National Competent Authority.

*Please login to https://www.liofilchemstore.it/login.php (user ID and password required) and click on Complaint.

REFERENCES

1. CLSI. Performance Standards for Antimicrobial Susceptibility Testing. 34nd ed. CLSI Supplement M100S. Wayne, PA: Clinical and Laboratory Standards Institute; 2024.
2. CLSI. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically. 12th ed. CLSI standard M07. Wayne, PA: Clinical and Laboratory Standards Institute; 2024.
3. CLSI. Verification of Commercial Microbial Identification and Antimicrobial Susceptibility Testing Systems. 1st ed. CLSI guideline M52. Wayne, PA: Clinical and Laboratory Standards Institute; 2015.
4. The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 14.0, 2024. http://www.eucast.org.
5. The European Committee on Antimicrobial Susceptibility Testing. Routine and extended internal quality control for MIC determination and disk diffusion as recommended by EUCAST. Version 14.0, 2024. http://www.eucast.org.
6. ISO 20776-2:2021. Clinical laboratory testing and in vitro diagnostic test systems — Susceptibility testing of infectious agents and evaluation of performance of antimicrobial susceptibility test devices — Part 2: Evaluation of performance of antimicrobial susceptibility test devices against reference broth micro-dilution
7. EUCAST Guidance Document on Cefiderocol BMD; 2020. https://www.eucast.org/eucastguidancedocuments/
8. ISO 20776-1:2019. Clinical laboratory testing and in vitro diagnostic test systems —Susceptibility testing of infectious agents and evaluation of performance of antimicrobial susceptibility test devices — Part 1: Broth micro-dilution reference method for testing the in vitro activity of antimicrobial agents against rapidly growing aerobic bacteria involved in infectious diseases.

A Summary of Safety and Performance (SSP) will be available on Eudamed (subject to Eudamed availability). This summary is also available on request at liofilchem@liofilchem.com

Product	Packaging	Ref.
ComASP® Cefiderocol 0.008-128	4x2 tests	75009

CE 0123 IVD

Table of Symbols

IVD	*In Vitro* Diagnostic Medical Device
REF	Catalogue number
LOT	Batch code
	Do not reuse
	Fragile, handle with care
CE 0123	Identification number of notified body
	Manufacturer
	Use by
Σ	Contains sufficient for <n> tests
	Consult instructions for use
	Temperature limits

Revision History

Revision	Release Date	Change Summary
1	23 Sep 2024	Updated layout and content in compliance with IVDR 2017/746
0	04 Apr 2022	Initial release

Note: Minor typographical, grammar, and formatting changes are not included in revision history.

This document is also available from the online Support Center: **liofilchem.com/ifu-sds**

For other language translations, please contact your local Liofilchem representative or **liofilchem.com**

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CE IVD

Liofilchem®
Microbiology products since 1983

TEST RESULTS FORM

ComASP® Cefiderocol 0.008-128

Patient data
Name
Surname
Age
Gender
Specimen
Notes

Indicate with the sign **+** the microbial growth.

Indicate with the sign **−** the absence of microbial growth.

Read the MIC and interpret the result according to the current EUCAST or CLSI interpretative criteria.

TEST	**Cefiderocol concentration (µg/ml)**								**MIC VALUE AND INTERPRETATION**
1	Growth	0.008	0.016	0.032	0.064	0.125	0.25	0.5	.....
									.....
	1	2	4	8	16	32	64	128	.....
2	Growth	0.008	0.016	0.032	0.064	0.125	0.25	0.5	.....
									.....
	1	2	4	8	16	32	64	128	.....

Use a distinct test results form for each sample under investigation. A horizontal line should be drawn on the empty spaces related to an unused test, if any.

Date of Test	**Operator**