IMP *K*-SeT

Manufacturer:

Coris BioConcept
Science Park CREALYS
Rue Jean Sonet 4A
B – 5032 GEMBLOUX
BELGIUM
Tel.: +32(0)81.719.917
Fax: +32(0)81.719.919
info@corisbio.com

Produced in BELGIUM

www.corisbio.com
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***In vitro* rapid diagnostic test for the detection of IMP carbapenemase in bacterial culture**

FOR IN VITRO DIAGNOSTIC USE ***EN***
FOR PROFESSIONAL USE ONLY
References: K-15R10, 20 cassettes, buffer, 20 tubes and droppers

I. INTRODUCTION

Carbapenemase-producing Organisms (CPO), and more specifically, Carbapenem-producing Enterobacteriaceae (CPE) represent a major public health concern worldwide due to their broad spectrum of resistance to antibiotics including, besides carbapenems, most classes of antimicrobial agents, and thus leaving very few options for the management of infected patients. Besides CPEs, CPOs also include non fermenting gram-negative *bacilli* (NFGNB), such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii* that exhibit resistance not only to beta lactam and other groups of antibiotics, but also to carbapenems. The rapid spread of CPOs and genes encoding these resistances has led to nosocomial outbreaks and endemic situations in several countries in Europe as well as elsewhere worldwide.

Metallo-ß-lactamase (MBL), extended-spectrum ß lactamase (ESBL) and AmpC ß-lactamase are part of the ß-lactamase family. IMP-type MBL are detected from Gram negative bacteria mostly in asian countries, even if prevalence is now increasing in Europe and some areas of North and South America as well.

Class B IMP-type is a plasmid-mediated carbapenemase that should be regarded as a major potential problem since they degrade not only C3G but also carbapenem antimicrobial drug like Imipenem. Inhibitor-based phenotypic confirmatory tests exist for the confirmation of class A (KPC) and class B (VIM, IMP, NDM) carbapenemases, Nowadays, definitive confirmation of IMP relies on molecular assays. These tests are expensive and can only be performed in dedicated environment and by skilled personnel, hence limiting their more generalized usage.
Development of new rapid diagnostic tests to track antimicrobial resistance patterns is considered as one of the priority core action by international experts and health authorities.

IMP *K*-SeT test is part of Coris BioConcept RESIST range of antimicrobial resistance diagnostic tests.

II. PRINCIPLE OF THE TEST

This test is ready to use and is based on a membrane technology with colloidal gold nanoparticles. Our kit is aimed to the detection of IMP carbapenemase from a single bacterial colony isolate of Enterobacteriaceae or NFGNB. A nitrocellulose membrane is sensitized with a monoclonal antibody directed against one epitope of the IMP carbapenemase. Another monoclonal antibody directed against a second epitope of the IMP carbapenemase is conjugated to colloidal gold particles. This conjugate is dried on a membrane.
This test is aimed to the detection of IMP like carbapenemases on colonies of Enterobacteriaceae isolates or Non Fermenting Gram Negative Bacteria growing on agar plate.
When the provided buffer containing the resuspended bacteria comes into contact with the strip, the solubilised conjugate migrates with the sample by passive diffusion and both the conjugate and sample material come into contact with the anti-IMP antibody that it is adsorbed onto the nitrocellulose strip. If the sample contains the IMP carbapenemase, the conjugate–IMP complex will remain bound to the anti-IMP antibody adsorbed onto the nitrocellulose. The result is visible within 15 minutes in the form of a red line that develops-on the strip. The solution continues to migrate to reach a control reagent that binds a control conjugate, thereby producing a second red line.

III. REAGENTS AND MATERIALS

1. IMP *K*-SeT (20 cassettes)
20 sealed pouches containing one device and one desiccant. Each device contains one sensitized strip.
2. LY-A buffer vial (15 mL)
Saline solution buffered to pH 7.5 containing TRIS, NaN_3 (<0,1%) and a detergent.
3. Instruction for use (1)
4. Semi-rigid disposable collection tubes with droppers (20)

IV. SPECIAL PRECAUTIONS

- All operations linked to the use of the test must be performed in accordance with Good Laboratory Practices (GLP).
- All reagents are for *in vitro* diagnostic use only.
- Pouch must be opened with care:
- Avoid touching nitrocellulose with your fingers.
- Wear gloves when handling samples.
- Never use reagents from another kit.
- Green lines indicate immunoreagents adsorption sites. Green colour disappears during the test.
- The quality of the reagents cannot be guaranteed beyond their shelf-life dates or if reagents are not stored under required conditions as indicated in the insert.

V. WASTE DISPOSAL

- Dispose of gloves, swabs, test tubes and used devices in accordance with GLP.
- Each user is responsible for the management of any waste produced, and must ensure that it is disposed of in accordance with the applicable legislation.

VI. STORAGE

- An unopened pouch may be kept at between 4 and 30°C and used until the shelf-life date indicated on the packaging. Once the pouch is opened, run the test immediately.
- Avoid freezing devices and buffer.

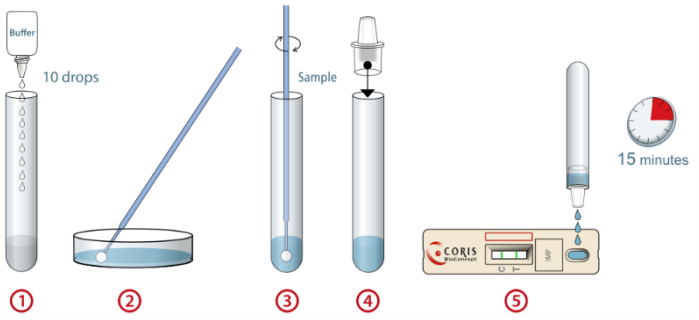
VII. SPECIMEN HANDLING AND COLLECTION

Specimens to be tested should be obtained and handled by standard microbiological methods.
Make sure that the specimens are not treated with solutions containing formaldehyde or its derivatives.
Culture media tested and validated with Coris BioConcept RESIT kits are listed on the website: https://www.corisbio.com/Products/Human-Field/IMP.php

VIII. PROCEDURE

PREPARATIONS OF THE TEST:
Allow kit components, in unopened packaging, and specimens (in case the plate containing colony to be tested was kept at 4°C) to reach room temperature (15-30°C) before performing a test.
Open the pouch and remove the device. Once opened, run the test immediately. Indicate the patient's name or specimen number on the device (one device per sample).
SPECIMEN PREPARATION PROCEDURE:
Performance claims with regard to sample types other than bacterial colonies have not been established. We recommend the use of fresh bacterial colonies for optimal test performance.

1. Prepare one semi-rigid tube and add **10** drops of LY-A buffer in the tube.
2. Harvest bacteria by taking one colony with a disposable bacteriological loop and dip the loop in the bottom of the semi-rigid tube containing the buffer.
3. Stir thoroughly before removing the loop
4. Insert tightly the dropper on the semi-rigid tube.
5. Vortex the preparation to homogenize. The entire bacterial colony must be suspended into the buffer.
6. Invert the test tube and add slowly **3** drops of diluted sample into the sample well of the cassette. Alternatively, add 100µl with a micropipette into the sample well of the cassette.
7. Allow to react for 15 min maximum and read the result.



Positive results may be reported sooner the moment the test and control lines become visible.
Do not take the appearance of new lines into account after the reaction time is passed.
The result must be read on still wet strip.

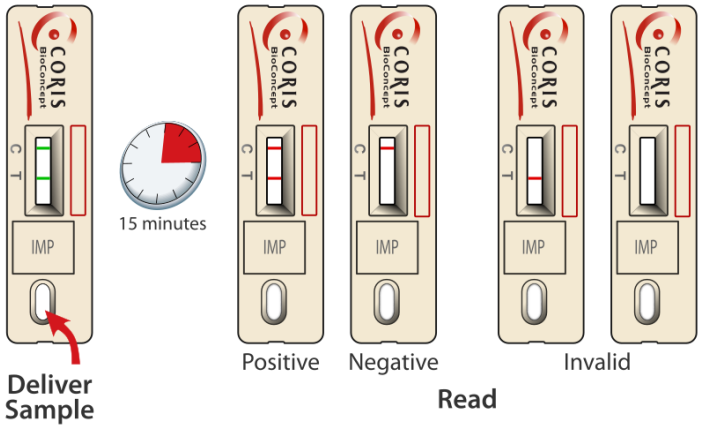
IX. INTERPRETING RESULTS

The results are to be interpreted as follows:

Negative test result: a reddish-purple line appears across the central reading window at the Control line (C) position. No other band is present.

Positive test result: in addition to a reddish-purple band at the Control line (C), a visible reddish-purple band appears at the Test line position (T). Intensity of the test line may vary according to the quantity of antigens as well as of the IMP variant type present in the sample. Any reddish-purple line (T), even weak, should be considered as a positive result.

Invalid test result: The absence of a Control line indicates a failure in the test procedure. Repeat invalid tests with a new test device.
Note: during the drying process, a very faint shadow may appear at the Test line position. It should not be regarded as a positive result.



X. PERFORMANCE

A. Detection Limit

The detection limit determined with purified recombinant proteins of IMP has been evaluated at 1,5625 ng/mL.

B. Validation on collection of reference strains

The IMP *K*-SeT was evaluated on a collection of 94 fully-characterized clinical strains in the National Reference Laboratory for Multidrug-Resistant Gram Negative Bacilli (Belgium) and by the Laboratory of Microbiology of University Hospital in Brussels (Belgium).

Status / IMP *K*-SeT	Positive	Negative	Total
Positive	32	0	32
Negative	1	61	62
Total	33	61	94

		95 % Confidence Interval [1]
Sensitivity:	97,0 %	(82,5 to 99,8 %)
Specificity:	100 %	(92,6 to 100 %)
Positive Predictive value:	100 %	(86,7 to 100 %)
Negative predictive value:	98,4 %	(90,2 to 99,9 %)
Agreement:	98,9 %	(93/94)

C. Repeatability and reproducibility

To check intra-batch accuracy (repeatability), the same positive samples and a buffer solution were processed 15 times on kits of the same production batch in the same experimental conditions. All observed results were confirmed as expected.
To check inter-batch accuracy (reproducibility), some samples (positive and buffer) were processed on kits from three different production batches. All results were confirmed as expected.

XI. LIMITS OF THE KIT

The test is qualitative and cannot predict the quantity of antigens present in the sample. Clinical presentation and other test results must be taken into consideration to establish diagnosis.
A positive test does not rule out the possibility that other antibiotic resistance mechanisms may be present.

XII. TECHNICAL PROBLEMS/COMPLAINTS

If you encounter a technical problem or if performances do not correspond with those indicated in this package insert:

1. Record the kit batch number
2. If possible, keep the sample in the appropriate storage condition during the complaint management
3. Contact Coris BioConcept (client.care@corisbio.com) or your local distributor.

[1] Newcombe, Robert G. "Two-Sided Confidence Intervals for the Single Proportion: Comparison of Seven Methods," *Statistics in Medicine*, **17**, 857-872 (1998).

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F. **Notake S., Matsuda M., Tamai K., Yanagisawa H, Hiramatsu K. and Kikuchi K. .** Detection of IMP Metallo-ß-Lactamase in Carbapenem-Nonsusceptible Enterobacteriaceae and Non-Glucose-Fermenting Gram-Negative Rods by Immunochromatography Assay. Journal. of Clinical Microbiology 2013 51(6) 1762-1768

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REF	Catalogue number		Manufacturer
IVD	*In vitro* diagnostic medical device		Temperature limits
Σ	Contains sufficient for <n> tests	LOT	Lot number
	Consult instructions for use		Do not reuse
	Keep dry		Use by
DIL SPE	Diluent specimen	CONT NaN_3	Contains Sodium azide