Science Park CREALYS
Rue Jean Sonet 4A
5032 - GEMBLOUX - BELGIUM
TEL : + 32(0)81.719.917
FAX : +32(0)81.719.919
e-mail : info@corisbio.com
http://www.corisbio.com

STATEMENT

We, **CORIS BIOCONCEPT** having a registered office at SCIENCE PARK CREALYS, Rue Jean Sonet 4A, 5032 Gembloux, BELGIUM assign SRL Sanmedico, having a registered office at A. Corobceanu street 7A, apt. 9, Chişinău MD-2012, Moldova, as authorized representative in correspondence with the conditions of directive 98/79/EC.

For the purpose of business development and tender participation, we declare that the company mentioned above is authorized to register, notify, renew or modify the registration of medical devices on the territory of the Republic of Moldova.

Gembloux, March 25th, 2021

Rimma DOLOTKAZINA
Sales Director

Coris BioConcept
CORIS BioConcept
Belgium

Digitally signed by Dolgopol Iulian
Date: 2024.05.07 15:01:38 EEST
Reason: MoldSign Signature
Location: Moldova

Certificate BE23/00000111

The management system of

Coris Bioconcept

CREALYS Science Park - Rue Guillaume Fouquet, 11, 5032 Gembloux, Belgium

has been assessed and certified as meeting the requirements of

ISO 13485:2016
EN ISO 13485:2016

For the following activities
Design, development, manufacture and distribution of in vitro diagnostic tests for the detection of pathogens in the diagnosis of respiratory, gastric, enteric and parasitic diseases, the detection of resistance to antibiotics and the detection in urine of therapeutics, used for the treatment of these infectious diseases.
Distribution of instrument for electrochemical detection to be used with Coris' kit.

This certificate is valid from 05 May 2023 until 20 August 2024 and remains valid subject to satisfactory surveillance audits.

Issue 1. Certified since 05 May 2023

Organization certified since 07 April 2021 and first certified by SGS under UKAS since 05 May 2023.

Authorised by
Jonathan Hall
Global Head - Certification Services

SGS United Kingdom Ltd
Rossmore Business Park, Ellesmere Port, Cheshire, CH65 3EN, UK
t +44 (0)151 350-6666 - www.sgs.com

UKAS MANAGEMENT SYSTEMS 0005

CORIS BioConcept	EC Declaration of Conformity according to Annex III of the IVDD

This is to certify that following IVD products:

Product name	Product code
Rota-Strip	C-1001
Rota Uni-Strip	C-1501
Combi-Strip	C-1004
Combi K-SeT	K-1204
Combi K-SeT	K-1504
RSV Respi-Strip	C-1006
RSV K-SeT	K-1206
RSV K-SeT	K-1506
Adeno Respi-Strip	C-1009
Adeno Respi K-SeT	K-1209
Adeno Respi K-SeT	K-1509
Influ A+B K-SeT	K-1212
Influ A+B K-SeT	K-1512
Giardia Strip	C-1013
Giardia K-SeT	K-1513
Legionella K-SeT	K-1215
Legionella K-SeT	K-1515
GastroVir K-SeT	K-1516
Crypto/Giardia Duo-Strip	C-1018
Pylori-Strip	C-1019
Pylori K-SeT	K-1519
Clostridium K-SeT	K-1220
Clostridium K-SeT	K-1520
COVID-19 Ag Respi-Strip	C-1023
COVID-19 Ag Respi-Strip	C-1123
COVID-19 Ag Respi-Strip	C-1223
COVID-19 Ag Respi-Strip	C-1323
COVID-19 Sero NP/RBD	K-1224

COVID-19 Ag K-SeT	K-1525
HAT Sero K-SeT	K-12S2
HAT Sero K-SeT	K-15S2
OXA-48 K-SeT	K-15R1
RESIST-3 O.O.K. K-SeT	K-15R4
RESIST-3 O.O.K. K-SeT	K-15R4/XBRI
RESIST-3 O.O.K. K-SeT	K-11R4/XBRI
RESIST-3 O.K.N. K-SeT	K-15R5
OXA-23 K-SeT	K-15R7
O.K.N.V.I. RESIST-5	K-15R11
O.K.N.V.I. RESIST-5	K-15R11/XBRIT
O.K.N.V.I. RESIST-5	K-11R11/XBRIT
RESIST ACINETO	K-15R13
RESIST CTX-M	K-15R14
IMP K-SeT	K-15R10
BL-RED 25	RED-0001
SARS-CoV-2 RT-LAMP	L-0001
Flu A & FLU B RT-LAMP	L-0002
Negative control	CTR-1000
Rotavirus Positive Control	P-1001
Adenovirus Positive Control	P-1002
RSV Positive Control	P-1006
Influenza A Positive Control	P-1010
Giardia Positive Control	P-1013
Legionella Positive Control	P-1015
Pylori Positive Control	P-1019
C difficile Positive Control	P-1020
RESIST penta O.K.N.V.I. control	P-10R11
OXA-163 Positive Control	P-10R4-1
OXA-23 Positive Control	P-10R7
COVID-19 Ag Positive Control	P-1023
Proguanil / Malarone – Strip	C-10T1
Mefloquine / Lariam - Strip	C-10T2

are manufactured and sold by

Coris BioConcept
CREALYS Science Park
Rue Guillaume Fouquet, 11
5032 Gembloux, BELGIUM

These products:

1. Belong to the Class "Others/General" as they are not for self-testing and do not belong to List A or List B of Annex II of IVDD (98/79 EC).
2. Comply with all Essential Requirements (Annex I) of the IVDD (98/79 EC)
3. This compliance has been properly documented using a checklist created from Annexes I and III of the IVDD, linked to all supporting Technical Documentation. This documentation included both product specific and process (Quality System) specific documents.
4. Have a Quality System in place based on ISO 13485.
5. This Declaration is issued by Coris BioConcept and has an unlimited time validity.
6. This Declaration of Conformity is signed below, certifying these requirements have been met and documented.

For Coris BioConcept, made in Gembloux the 09th of May 2023

Thierry LECLIPTEUX, PhD
CEO
Coris BioConcept

OXA-23 *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
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Produced in BELGIUM

www.corisbio.com
IFU-58R7/EN/02

***In vitro* rapid diagnostic test for the detection of OXA-23 carbapenemase in bacterial culture**

FOR IN VITRO DIAGNOSTIC USE **EN**
FOR PROFESSIONAL USE ONLY
References: K-15R7, 20 cassettes, buffer, 20 tubes and droppers

I. INTRODUCTION

Acinetobacter baumannii is an important opportunistic and multidrug-resistant Gram-negative bacterium responsible for nosocomial infections in health facilities. If left untreated, this infection can lead to septicemia and death. The carbapenem-hydrolysing oxacillinases (OXAs) are the most commonly reported carbapenem-resistance determinants in *Acinetobacter* spp., particularly in *A. baumannii*. Among the OXAs, OXA-23 is the most prevalent carbapenem-resistance determinant in *A. baumannii* isolates.
OXA-23 has been detected in other bacterial species as chromosomal (*P. mirabilis,* Bonnet et al 2002 and Osterblad et al 2016; *A. radioresistans*) or plasmidic gene (*E. coli*, La et al, 2014), which can constitute reservoirs for horizontal transmission of this resistance factor (Poirel et al 2016). The detection of this resistance factor OXA-23, not only in resistant species but also in carrier species, is therefore of paramount importance in the control of antibiotic resistance in the hospital.
Nowadays, definitive confirmation of OXA-23 relies on molecular amplification analysis and DNA sequencing. These tests are expensive and can only be performed in dedicated environment and by skilled staff, hence limiting their more generalized usage.
The 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.
The OXA-23 K-SeT test aimed at a rapid identification of the OXA-23 carbapenemase (and variants of the OXA-23 group) ensures effective treatment of patients and prevention of spread of OXA-23 *Acinetobacter* spp. carrier, especially in hospitals.

II. PRINCIPLE OF THE TEST

This test is ready to use and is based on a membrane technology with colloidal gold nanoparticles. A nitrocellulose membrane is sensitized with a monoclonal antibody directed against one epitope of the OXA-23 carbapenemase. Another monoclonal antibody directed against a second epitope of the OXA-23 carbapenemase is conjugated to colloidal gold particles. This conjugate is dried on a membrane.
This test is aimed at the detection of OXA-23 like carbapenemases in a single bacterial colony growing on agar plate. The sample must be diluted in the dilution buffer supplied with the test. When the provided buffer containing the resuspended bacteria comes into contact with the strip, the solubilized conjugate migrates with the sample by passive diffusion and both the conjugate and sample material come into contact with the anti-OXA-23 antibody that it is adsorbed onto the nitrocellulose strip. If the sample contains the OXA-23 carbapenemase, the conjugate–OXA-23 complex will remain bound to the anti-OXA-23 antibody adsorbed onto the nitrocellulose and a red line will develop. Solution continues to migrate to reach a second reagent (control reagent) that binds the migration control conjugate, thereby producing a red control line that confirms that the test is valid. Result is visible within 15 minutes.

III. REAGENTS AND MATERIALS

1. OXA-23 *K*-SeT (20)
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)
5.

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.
- Reagents' quality 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.

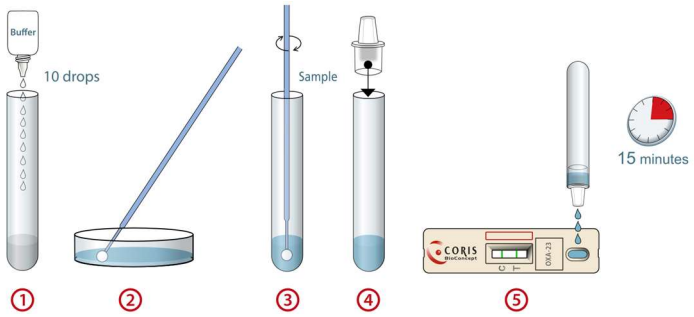
VII. SPECIMEN HANDLING AND COLLECTION

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/OXA-23/FAQ.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:
We recommend the use of fresh bacterial colonies for optimal test performance.

1. Prepare one semi-rigid tube provided in the kit 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 max and read the result.



Positive results may be reported as soon as 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.

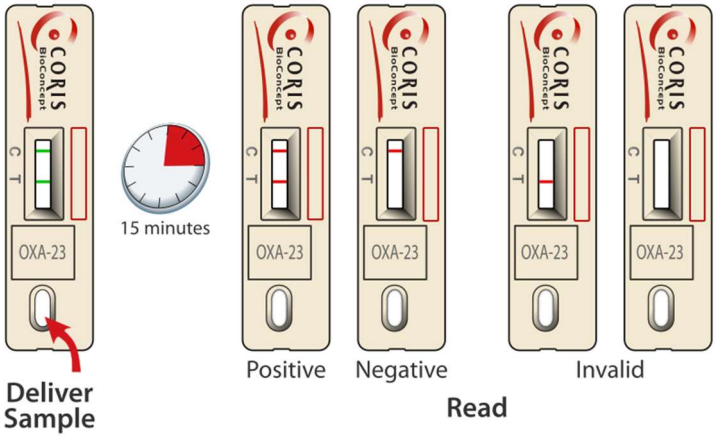
IX. INTERPRETING RESULTS

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 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 was determined with a purified recombinant OXA-23 protein and has been evaluated at 0,156 ng/mL.

B. Validation on collection of reference strains

The OXA-23 *K*-SeT was evaluated on a collection of 108 clinical isolates of carbapenem-resistant *Acinetobacter* spp. fully characterized resistance mechanisms to beta-lactams by phenotypic and molecular tests (Germany).

108 strains	**35 strains** tested positive with the OXA-23 *K*-SeT	**35 strains** carrying OXA-23 carbapenemase	*Acinetobacter baumannii, Acinetobacter pittii, Acinetobacter nosocomialis, Acinetobacter radioresistens*
	73 strains tested negative with the OXA-23 *K*-SeT	**68 strains** carrying a non-OXA-23 carbapenemase	OXA-40, OXA-51, OXA-58, OXA-143, OXA-235
		5 strains carrying class B carbapenemases	Including VIM-2, NDM-1, NDM-2

A second evaluation was retrospectively performed on 448 clinical strains of *Acinetobacter spp*. and 14 oxacillinase-producing Gram-negative bacteria collected in Belgium and in Italy between 2008 and 2018 with an agreement of 100 % versus real-time PCR and molecular sequencing. see Riccobono, 2019

	Italy	Belgium	Total	Test OXA-23 K-SeT
$bla_{OXA\text{-}23\text{-}like}$	170	137	307	307 +
$bla_{OXA\text{-}24\text{-}like}$	5	25	30	negative
$bla_{OXA\text{-}58\text{-}like}$	1	30	31	negative
IS*Aba1* $bla_{OXA\text{-}51\text{-}like}$	11	0	11	negative
$bla_{OXA\text{-}23\text{-}like}$ + $bla_{OXA\text{-}58\text{-}like}$	5	2	7	7 +
$bla_{OXA\text{-}23\text{-}like}$ + IS*Aba1* $bla_{OXA\text{-}51\text{-}like}$	4	0	4	4 +
$bla_{OXA\text{-}23\text{-}like}$ + bla_{NDM}	0	3	3	3 +
$bla_{OXA\text{-}58\text{-}like}$ + bla_{VIM}	0	1	1	negative
bla_{NDM}	0	13	13	negative
$bla_{OXA\text{-}143\text{-}like}$	0	1	1	negative
bla_{IMP}	0	3	3	negative
bla_{VIM}	0	1	1	negative
bla_{GES}	0	1	1	negative
$bla_{OXA\text{-}48\text{-}like}$	0	2	2	negative
$bla_{OXA\text{-}198\text{-}like}$	0	1	1	negative
non-carbapenemase producer	0	46	46	negative
Total	196	266	462	321 +

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

XIII. BIBLIOGRAPHIC REFERENCES

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Last update: 27 NOVEMBER 2019

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

OXA-23 *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
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***In vitro* rapid diagnostic test for the detection of OXA-23 carbapenemase in bacterial culture**

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I. INTRODUCTION

Acinetobacter baumannii is an important opportunistic and multidrug-resistant Gram-negative bacterium responsible for nosocomial infections in health facilities. If left untreated, this infection can lead to septicemia and death. The carbapenem-hydrolysing oxacillinases (OXAs) are the most commonly reported carbapenem-resistance determinants in *Acinetobacter* spp., particularly in *A. baumannii*. Among the OXAs, OXA-23 is the most prevalent carbapenem-resistance determinant in *A. baumannii* isolates.
OXA-23 has been detected in other bacterial species as chromosomal (*P. mirabilis,* Bonnet et al 2002 and Osterblad et al 2016; *A. radioresistans*) or plasmidic gene (*E. coli*, La et al, 2014), which can constitute reservoirs for horizontal transmission of this resistance factor (Poirel et al 2016). The detection of this resistance factor OXA-23, not only in resistant species but also in carrier species, is therefore of paramount importance in the control of antibiotic resistance in the hospital.
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This test is aimed at the detection of OXA-23 like carbapenemases in a single bacterial colony growing on agar plate. The sample must be diluted in the dilution buffer supplied with the test. When the provided buffer containing the resuspended bacteria comes into contact with the strip, the solubilized conjugate migrates with the sample by passive diffusion and both the conjugate and sample material come into contact with the anti-OXA-23 antibody that it is adsorbed onto the nitrocellulose strip. If the sample contains the OXA-23 carbapenemase, the conjugate–OXA-23 complex will remain bound to the anti-OXA-23 antibody adsorbed onto the nitrocellulose and a red line will develop. Solution continues to migrate to reach a second reagent (control reagent) that binds the migration control conjugate, thereby producing a red control line that confirms that the test is valid. Result is visible within 15 minutes.

III. REAGENTS AND MATERIALS

1. OXA-23 *K*-SeT (20)
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)
5.

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.
- Reagents' quality 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.

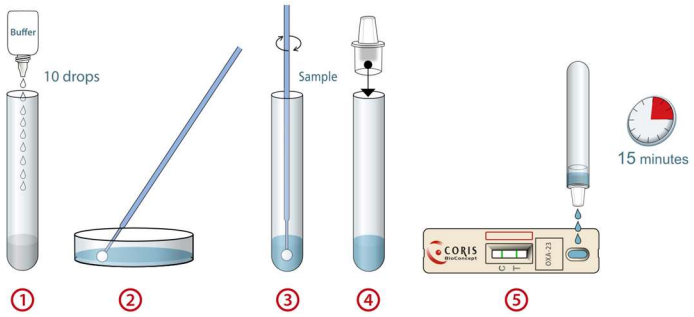
VII. SPECIMEN HANDLING AND COLLECTION

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/OXA-23/FAQ.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:
We recommend the use of fresh bacterial colonies for optimal test performance.

1. Prepare one semi-rigid tube provided in the kit 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 max and read the result.



Positive results may be reported as soon as 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.

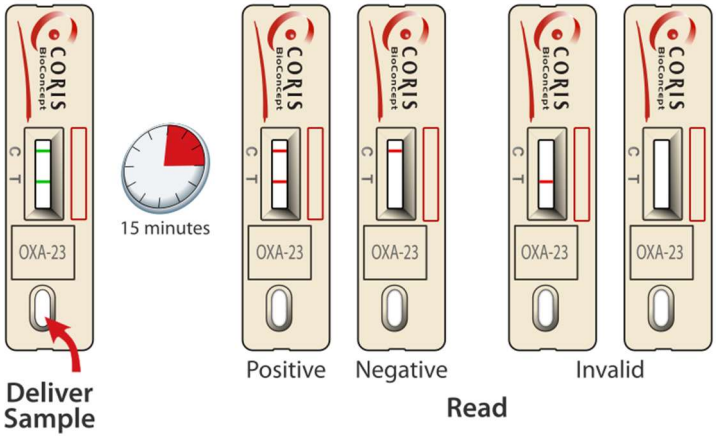
IX. INTERPRETING RESULTS

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 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 was determined with a purified recombinant OXA-23 protein and has been evaluated at 0,156 ng/mL.

B. Validation on collection of reference strains

The OXA-23 *K*-SeT was evaluated on a collection of 108 clinical isolates of carbapenem-resistant *Acinetobacter* spp. fully characterized resistance mechanisms to beta-lactams by phenotypic and molecular tests (Germany).

108 strains	**35 strains** tested positive with the OXA-23 *K*-SeT	**35 strains** carrying OXA-23 carbapenemase	*Acinetobacter baumannii, Acinetobacter pittii, Acinetobacter nosocomialis, Acinetobacter radioresistens*
	73 strains tested negative with the OXA-23 *K*-SeT	**68 strains** carrying a non-OXA-23 carbapenemase	OXA-40, OXA-51, OXA-58, OXA-143, OXA-235
		5 strains carrying class B carbapenemases	Including VIM-2, NDM-1, NDM-2

A second evaluation was retrospectively performed on 448 clinical strains of *Acinetobacter spp*. and 14 oxacillinase-producing Gram-negative bacteria collected in Belgium and in Italy between 2008 and 2018 with an agreement of 100 % versus real-time PCR and molecular sequencing. see Riccobono, 2019

	Italy	Belgium	Total	Test OXA-23 K-SeT
$bla_{OXA\text{-}23\text{-}like}$	170	137	307	307 +
$bla_{OXA\text{-}24\text{-}like}$	5	25	30	negative
$bla_{OXA\text{-}58\text{-}like}$	1	30	31	negative
IS*Aba1* $bla_{OXA\text{-}51\text{-}like}$	11	0	11	negative
$bla_{OXA\text{-}23\text{-}like}$ + $bla_{OXA\text{-}58\text{-}like}$	5	2	7	7 +
$bla_{OXA\text{-}23\text{-}like}$ + IS*Aba1* $bla_{OXA\text{-}51\text{-}like}$	4	0	4	4 +
$bla_{OXA\text{-}23\text{-}like}$ + bla_{NDM}	0	3	3	3 +
$bla_{OXA\text{-}58\text{-}like}$ + bla_{VIM}	0	1	1	negative
bla_{NDM}	0	13	13	negative
$bla_{OXA\text{-}143\text{-}like}$	0	1	1	negative
bla_{IMP}	0	3	3	negative
bla_{VIM}	0	1	1	negative
bla_{GES}	0	1	1	negative
$bla_{OXA\text{-}48\text{-}like}$	0	2	2	negative
$bla_{OXA\text{-}198\text{-}like}$	0	1	1	negative
non-carbapenemase producer	0	46	46	negative
Total	196	266	462	321 +

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

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Last update: 27 NOVEMBER 2019

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

OXA-23 *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
IFU-58R7/EN/02

***In vitro* rapid diagnostic test for the detection of OXA-23 carbapenemase in bacterial culture**

FOR IN VITRO DIAGNOSTIC USE **EN**
FOR PROFESSIONAL USE ONLY
References: K-15R7, 20 cassettes, buffer, 20 tubes and droppers

I. INTRODUCTION

Acinetobacter baumannii is an important opportunistic and multidrug-resistant Gram-negative bacterium responsible for nosocomial infections in health facilities. If left untreated, this infection can lead to septicemia and death. The carbapenem-hydrolysing oxacillinases (OXAs) are the most commonly reported carbapenem-resistance determinants in *Acinetobacter* spp., particularly in *A. baumannii*. Among the OXAs, OXA-23 is the most prevalent carbapenem-resistance determinant in *A. baumannii* isolates.
OXA-23 has been detected in other bacterial species as chromosomal (*P. mirabilis,* Bonnet et al 2002 and Osterblad et al 2016; *A. radioresistans*) or plasmidic gene (*E. coli*, La et al, 2014), which can constitute reservoirs for horizontal transmission of this resistance factor (Poirel et al 2016). The detection of this resistance factor OXA-23, not only in resistant species but also in carrier species, is therefore of paramount importance in the control of antibiotic resistance in the hospital.
Nowadays, definitive confirmation of OXA-23 relies on molecular amplification analysis and DNA sequencing. These tests are expensive and can only be performed in dedicated environment and by skilled staff, hence limiting their more generalized usage.
The 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.
The OXA-23 K-SeT test aimed at a rapid identification of the OXA-23 carbapenemase (and variants of the OXA-23 group) ensures effective treatment of patients and prevention of spread of OXA-23 *Acinetobacter* spp. carrier, especially in hospitals.

II. PRINCIPLE OF THE TEST

This test is ready to use and is based on a membrane technology with colloidal gold nanoparticles. A nitrocellulose membrane is sensitized with a monoclonal antibody directed against one epitope of the OXA-23 carbapenemase. Another monoclonal antibody directed against a second epitope of the OXA-23 carbapenemase is conjugated to colloidal gold particles. This conjugate is dried on a membrane.
This test is aimed at the detection of OXA-23 like carbapenemases in a single bacterial colony growing on agar plate. The sample must be diluted in the dilution buffer supplied with the test. When the provided buffer containing the resuspended bacteria comes into contact with the strip, the solubilized conjugate migrates with the sample by passive diffusion and both the conjugate and sample material come into contact with the anti-OXA-23 antibody that it is adsorbed onto the nitrocellulose strip. If the sample contains the OXA-23 carbapenemase, the conjugate–OXA-23 complex will remain bound to the anti-OXA-23 antibody adsorbed onto the nitrocellulose and a red line will develop. Solution continues to migrate to reach a second reagent (control reagent) that binds the migration control conjugate, thereby producing a red control line that confirms that the test is valid. Result is visible within 15 minutes.

III. REAGENTS AND MATERIALS

1. OXA-23 *K*-SeT (20)
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)
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- 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.
- Reagents' quality 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.

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- 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.
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Specimens to be tested should be obtained and handled by standard microbiological methods.
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We recommend the use of fresh bacterial colonies for optimal test performance.

1. Prepare one semi-rigid tube provided in the kit and add **10** drops of LY-A buffer in the tube.
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3. Stir thoroughly before removing the loop
4. Insert tightly the dropper on the semi-rigid tube.
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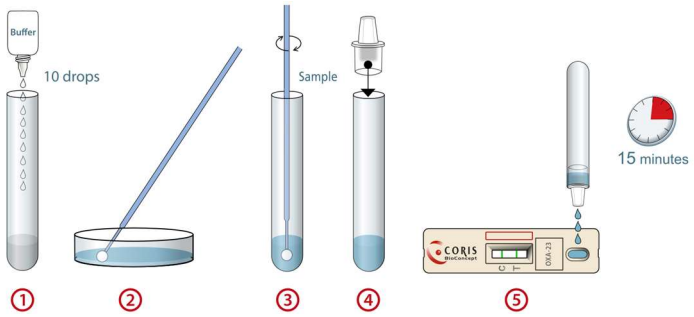

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Do not take the appearance of new lines into account after the reaction time is passed.
The result must be read on still wet strip.

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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.

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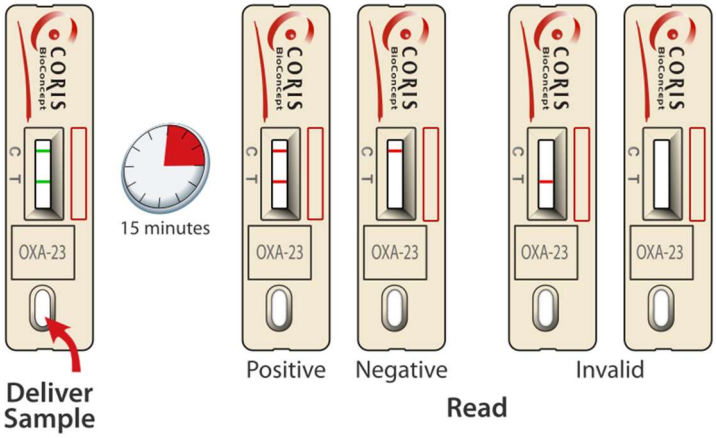

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B. **DW. Wareham, LM. Phee, MHF. Abdul Momin.** Direct detection of carbapenem resistance determinants in clinical specimens using immunochromatographic lateral flow devices. J Antimicrob Chemother. 2018 Mar 22. doi: 10.1093

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Last update: 27 NOVEMBER 2019

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

O.K.N.V.I. RESIST-5

Manufacturer:

Coris BioConcept
CREALYS Science Park
Rue Guillaume Fouquet, 11
5032 GEMBLOUX
BELGIUM
Tel.: +32(0)81.719.917
Fax: +32(0)81.719.919
info@corisbio.com
Produced in BELGIUM

www.corisbio.com
IFU-58R11/EN/06

***In vitro* rapid diagnostic test for the detection of OXA-48, KPC, NDM, VIM and IMP carbapenemases in bacterial culture**

FOR IN VITRO DIAGNOSTIC USE **EN**
FOR PROFESSIONAL USE ONLY
References: K-15R11, 2x20 cassettes, buffer, 20 tubes and transfer pipets

I. INTRODUCTION

Carbapenemase-producing Organisms (CPO), and more specifically, Carbapenem-resistant Enterobacteriaceae (CRE) 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 CREs, CPOs also include nonfermenting 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 worldwide.
Development of new rapid diagnostic tests to track antimicrobial resistance patterns is considered as one of the priority core actions by international experts and health authorities. NDM and KPC represent two of the most increasing and prevalent carbapenemases in many countries. On the other hand, class D OXA-48 type carbapenemases are the most challenging resistance mechanisms to be detected by clinical laboratories. VIM is not only present in Enterobacteriaceae but is also highly prevalent in non-fermenting bacteria. IMP should be regarded as a potential problem since they degrade not only C3G but also carbapenem antimicrobial drug like Imipenem. IMP prevalence is the lowest, apart from Japan where it is more prevalent.
Inhibitor-based phenotypic confirmatory tests exist for the confirmation of class A (KPC) and class B (VIM, IMP, NDM) carbapenemases, Nowadays, definitive confirmation of CPO resistance mechanism 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.
O.K.N.V.I. RESIST-5 test is part of Coris BioConcept RESIST range of antimicrobial resistance diagnostic tests.

II. PRINCIPLE OF THE TESTS

These tests are ready to use and are based on a membrane technology with colloidal gold nanoparticles. Our kit is aimed to detect and identify the carbapenemases from a bacterial colony isolate of Enterobacteriaceae or NFGNB growing on agar plate. Each pouch contains: 2 lateral-flow cassettes for the identification of (i) OXA-48, KPC, NDM and (ii) VIM and IMP.
Identification of OXA-48, KPC and NDM. A nitrocellulose membrane is sensitised with:
(1) a monoclonal antibody directed against OXA-48 carbapenemase and variants (except OXA-163-like enzymes) (“O” line)
(2) a monoclonal antibody directed against KPC carbapenemase (“K” line)
(3) a monoclonal antibody directed against NDM carbapenemase (“N” line)
(4) a control capture reagent (upper “C” line).
Four different colloidal gold nanoparticles conjugates are dried on a membrane: a conjugate directed against a second epitope of the OXA-48 carbapenemase, a conjugate directed against a second epitope of the KPC carbapenemase, a third conjugate specific to NDM carbapenemase and a control conjugate to validate the test conditions.
Identification of VIM and IMP. A nitrocellulose membrane is sensitised with:
(1) a monoclonal antibody directed against VIM carbapenemase (“V” line),
(2) a monoclonal antibody directed against IMP carbapenemase (“I” line)
(3) a control capture reagent (upper “C” line).
Three different colloidal gold nanoparticles conjugates are dried on a membrane: a conjugate directed against VIM carbapenemase, a conjugate directed against IMP carbapenemase and a control conjugate.
When the provided buffer containing the resuspended bacteria comes into contact with the membrane, the solubilised conjugates migrate with the sample by passive diffusion, while conjugates and sample material come into contact with the immobilised respective antibodies that are adsorbed onto the nitrocellulose strip. If the sample contains an OXA-48, KPC, NDM, VIM or IMP carbapenemase, the respective complexes made of the conjugates and either OXA-48, or KPC, or NDM or VIM or IMP will remain bound to their respective specific lines (OXA-48 : “O” line; KPC : “K” line; NDM : “N” line, VIM : “V” line, IMP : “I” line). The migration continues by passive diffusion and both conjugates and sample material come into contact with the (upper) line control reagent that binds a control conjugate (“C” line), thereby producing a red line.
The result is visible within 15 minutes in the form of red lines on the strip.

III. REAGENTS AND MATERIALS

1. O.K.N.V.I. RESIST-5 (2x20 cassettes)
20 sealed pouches containing two lateral-flow cassettes and one desiccant.
Each cassette contains one sensitised strip.
2. LY-D buffer vial (7 mL)
Tris-EDTA solution containing NaN_3 (<0.1%) and a detergent.
3. Instruction for use (1)
4. Disposable collection tubes (20)
5. Disposable transfer pipettes (20)

Materials to be ordered separately:
- RESIST-BC (S-1001): reagents kit for use with blood culture
- ReSCape (S-1002): reagents kits for use with rectal swab

IV. SPECIAL PRECAUTIONS

- All operations linked to the use of the test must be performed in accordance with good laboratory practices.
- 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

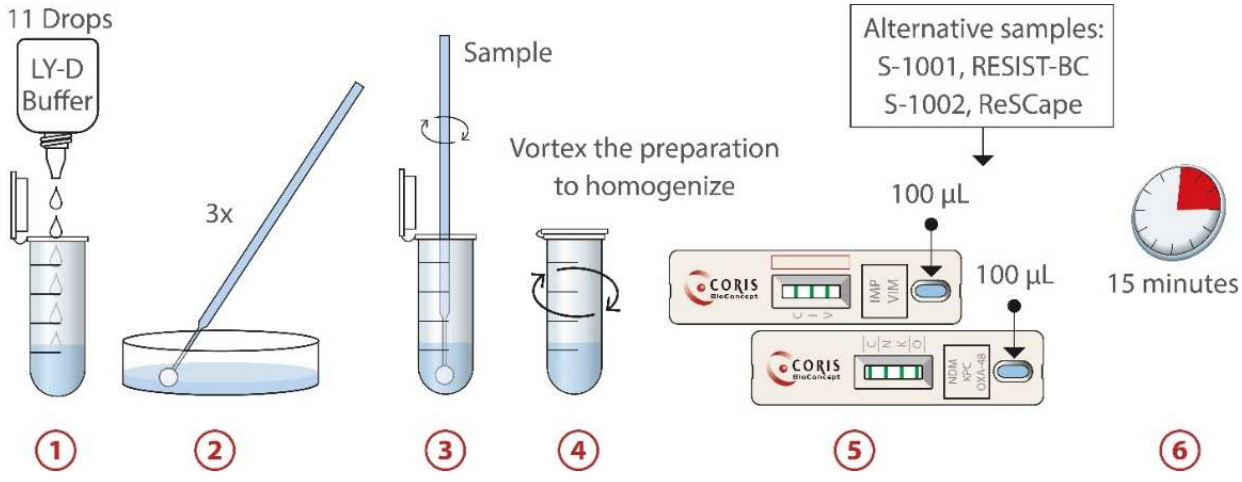
Specimens to be tested should be obtained and handled by standard microbiological methods.
Make sure that the specimens are not treated with solutions containing formaldehyde or its derivatives.
Culture media tested and validated with Coris BioConcept RESIST kits are listed on the website: https://www.corisbio.com/products/oknvi-resist-5/faq

VIII. PROCEDURE

PREPARATIONS OF THE TEST:
Allow kit components, in unopened packaging, and specimens (in the event that the plate containing colony to be tested was kept at 4°C) to equilibrate at 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 been established for rectal swabs and blood cultures.
With rectal swabs and blood cultures, the preparation procedure has to be followed as described in the respective kits (S-1002, ReSCape and S-1001, RESIST-BC)
With bacterial colonies, we recommend the use of fresh agar cultures for optimal test performance and as followed:

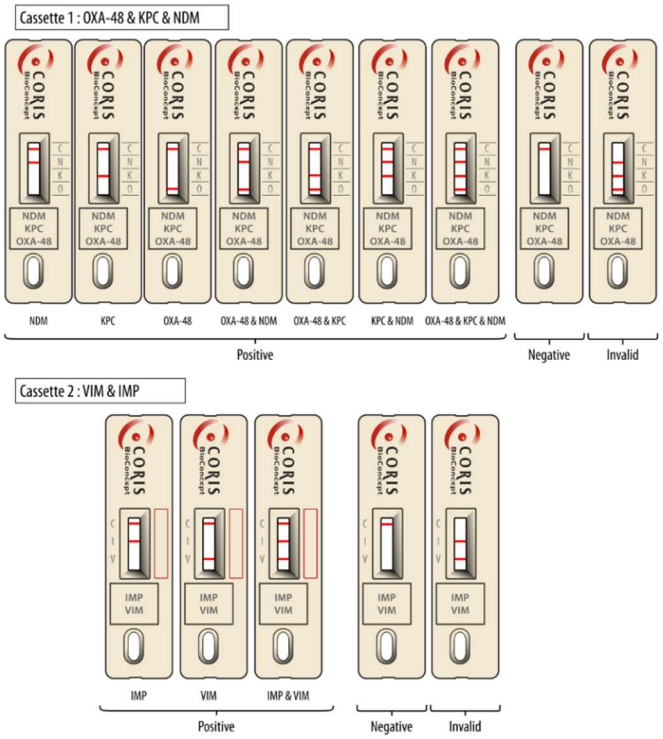
1. Prepare one collection tube and add **11 drops** of LY-D buffer in the tube
2. Harvest bacteria by taking **3 colonies** with a disposable bacteriological loop and dip the loop in the bottom of the tube containing the buffer. The same bacteriological loop can be used to collect the 3 colonies.
3. Stir thoroughly before removing the loop.
4. Close de tube and vortex the preparation to homogenize.
5. Use the transfer pipette provided in the kit and add 100 µL of diluted sample into the sample well of each of the two cassettes labelled (i) NDM, KPC and OXA-48 and (ii) IMP and VIM (**diluted sample must reach the black line indicated on the transfer pipette to accurately aspirate 100 µL**).
6. Allow to react for 15 minutes and read the result.



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

IX. INTERPRETING RESULTS

The results are to be interpreted as follows for each of the two cassettes:
Negative test result: a reddish-purple line appears across the central reading window at the Control line (C) position. No other line is present.
Positive test result: in addition to a reddish-purple line at the Control line (C), a visible reddish-purple line appears at one of the Test lines position ("N" or "K" or "O") on cassette labelled (i) NDM, KPC, OXA-48 or at one of the Test lines position ("I" or "V") on cassette labelled (ii) IMP and VIM. Intensity of the test line may vary according to the quantity of antigens as well as of the variant type present in the sample. Any reddish-purple test line (OXA-48, KPC, NDM, VIM and IMP), even weak, should be considered as a positive result.
If a positive test line appears beside of the "O" mark, the sample contains OXA-48 or OXA-48-like variants. If it appears beside the "K" mark, the sample contains KPC variants; beside the "N" mark, the sample contains NDM; the "V" mark, the sample contains VIM; and beside of the "I" mark, IMP is present in the sample. Combinations of positive test lines can occur.
In this case the sample contains several carbapenemases.
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 positions. It should not be regarded as a positive result.



X. PERFORMANCE

A. Detection Limit

The detection limit determined with purified recombinant proteins of OXA-48, KPC, NDM, VIM and IMP have been evaluated at 0.25 ng/mL, 0.5 ng/mL, 0.0625 ng/mL, 0.23 ng/mL and 0.781 ng/mL, respectively.

B. Retrospective study

The test cassettes were validated by comparison with reference molecular method (validated in house multiplex PCR including sequencing) in a retrospective study performed on 180 non duplicated, consecutive suspected CPE clinical isolates collected between 2012 and 2021 from Belgian hospitals.

Molecular method / OXA-48 test	Positive	Negative	Total
Positive	41	0	41
Negative	0	139	139
Total	41	139	180

95 % Confidence Interval [1]

Sensitivity:	100 %	(89.3 to 100 %)
Specificity:	100 %	(96.6 to 100 %)
Positive Predictive value:	100 %	(89.3 to 100 %)
Negative predictive value:	100 %	(96.7 to 100 %)
Agreement:	100 %	(180/180)

Molecular method / KPC test	Positive	Negative	Total
Positive	24	0	24
Negative	0	156	156
Total	24	156	180

95 % Confidence Interval [1]

Sensitivity:	100 %	(82.8 to 100 %)
Specificity:	100 %	(97.0 to 100 %)
Positive Predictive value:	100 %	(82.8 to 100 %)
Negative predictive value:	100 %	(97.0 to 100 %)
Agreement:	100 %	(180/180)

Molecular method / NDM test	Positive	Negative	Total
Positive	40	0	40
Negative	0	140	140
Total	40	140	180

95 % Confidence Interval [1]

Sensitivity:	100 %	(89.1 to 100 %)
Specificity:	100 %	(96.7 to 100 %)
Positive Predictive value:	100 %	(89.1 to 100 %)
Negative predictive value:	100 %	(96.7 to 100 %)
Agreement:	100 %	(180/180)

Molecular method / VIM test	Positive	Negative	Total
Positive	43	0	43
Negative	3	134	137
Total	46	134	180

95 % Confidence Interval [1]

Sensitivity:	93.5 %	(81.1 to 98.3 %)
Specificity:	100 %	(96.5 to 100 %)
Positive Predictive value:	100 %	(89.8 to 100 %)
Negative predictive value:	97.8 %	(93.2 to 99.4 %)
Agreement:	98.3 %	(177/180)

Molecular method / IMP test	Positive	Negative	Total
Positive	19	0	19
Negative	0	161	161
Total	19	161	180

95 % Confidence Interval [1]

Sensitivity:	100 %	(79.1 to 100 %)
Specificity:	100 %	(97.1 to 100 %)
Positive Predictive value:	100 %	(79.1 to 100 %)
Negative predictive value:	100 %	(97.1 to 100 %)
Agreement:	100 %	(180/180)

The O.K.N.V.I. RESIST-5 kit was also validated with rectal swabs and blood cultures.

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

1. Record the lot number of the kit concerned.
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.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

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Last update : 20 FEBRUARY 2023

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

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