

**General guidelines for laboratory
detection of carbapenemase in
Pseudomonas spp. and
Acinetobacter spp. in Belgium**

NRC Antibiotic-resistant Gram-negative bacilli

Multidrug resistance (MDR) criteria in *P. aeruginosa* and *Acinetobacter* spp.

- **DO NOT USE NATURAL RESISTANCES as criteria for MDR in *Pseudomonas*/*Acinetobacter*:**
 - **Natural R to β -lactams : aminopenicillins, amoxicillin+clavulanate, cephalosporins gen1/gen2, ceftriaxone/cefotaxime, temocillin, ertapenem**

***P. aeruginosa* MDR (NSIH-AMR-BE):**

Resistance (R according to EUCAST criteria) to ≥ 3 of the following classes of antibiotics:

- Cephalosporins gen3/gen4 (ceftazidime or cefepime)
- Carbapenems (meropenem or imipenem)
- Fluoroquinolones (ciprofloxacin or levofloxacin)
- Aminoglycosides (tobramycin or amikacin)

***Acinetobacter* MDR:**

Resistance (R according to EUCAST criteria) to ≥ 2 of the following classes of antibiotics:

- Carbapenems (meropenem or imipenem)
- Fluoroquinolones (ciprofloxacin or levofloxacin),
- Aminoglycosides (tobramycin or amikacin)

Types of carbapenemase in *Pseudomonas* spp. and *Acinetobacter* spp. vs *Enterobacteriales*

Ambler molecular class	Carbapenemase family	<i>Enterobacteriales</i> (CPE)	<i>Pseudomonas</i> spp.	<i>Acinetobacter</i> spp.
A (sérine)	KPC	+++	-	-
	GES	(+)	+	(+)
	IMI, NMC, SME, SFC...	+	-	-
B (Métallo βL)	VIM	+++	+++	+
	NDM	+++	+	++
	IMP	+	+	+
	AIM, DIM, GIM, SIM, SPM...	-	(+)	(+)
D (Sérine)	OXA-48-like	+++	-	-
	OXA-427	+	-	-
	OXA-198	(+)	+	-
	OXA-23-like	(+)	-	+++
	OXA-24-like	(+)	-	++
	OXA-58-like	(+)	-	++

P. aeruginosa

(Class B MBL): VIM > IMP / NDM

A. baumannii

(Class D): OXA-23 > OXA-24 / OXA-58

(Class B): NDM > IMP / VIM

➤ No OXA-48 nor KPC (extremely rare) in Europe in *Pseudomonas* and *Acinetobacter* spp.

Screening tests for carbapenemase in *P. aeruginosa* and *Acinetobacter* spp.

- **Criteria for suspicion of carbapenemase:**

- *P. aeruginosa*:

- 1) R to a carbapenem (meropenem OR imipenem)

- AND**

- 2) R to ceftolozane/tazobactam OR MDR profile (see slide 2)

- *P. aeruginosa imipenem-R and meropenem-I/R without criterion 2) is suggestive of resistance due to porin deficiency OprD)*

- *Acinetobacter* spp.:

- R to a carbapenem (meropenem OR imipenem)

- **Carbapenem hydrolysis tests* (one of the following):**

- Modified Carbapenem Inactivation Method: for *P. aeruginosa*

- RAPIDEC (BioMérieux): for *P. aeruginosa* and *Acinetobacter* spp.

- Rapid CARB Screen, Rapid CARB Blue (ROSCO): for *P. aeruginosa*

- Beta-Carba test (BioRad): for *P. aeruginosa*

- MBT Star Carba (Bruker): *P. aeruginosa* et *Acinetobacter* spp. (prolonged incubation)

***NB: usually poorer performance for *Acinetobacter* spp and NON-class-B carbapenemase (GES, OXA-carbapenemases...)**

Confirmatory carbapenemase assays for *P. aeruginosa* and *Acinetobacter* spp.

- **Synergy tests with inhibitor (EDTA/DPA) for suspected class B MBL in *P. aeruginosa*:**
 - Paper discs or tablets (ROSCO): IMI +/- EDTA or MERO +/- DPA
 - Gradient diffusion strip: IMI +/- EDTA or MERO +/- DPA
 - Requires confirmation/identification of the type of MBL (VIM, IMP, NDM,...) by other tests

NB1: Synergy assays with boronic acid-derived inhibitors for the detection of class A carbapenemase (KPC type) non-validated in *P. aeruginosa* or *Acinetobacter* spp (false-positive results related to overproduction of AmpC cephalosporinase)

NB2: No phenotypic test with inhibitors for the detection of OXA class D carbapenemase (OXA-23, -24, -58) in *Acinetobacter* spp. (with potential false-positive results +)

- **Immunochromatography assays:** identification of carbapenemase family
 - Class B: VIM, NDM, IMP
 - Class D: OXA-23, OXA-40, OXA-58
- **Molecular assays** (PCR assays, DNA microarray, isothermal amplification, sequencing...): identification of carbapenemase family and/or enzyme variant
 - Avoid isolated detection (without surrounding genetic characterization) of intrinsic chromosomal genes (OXA-50-like, OXA-51-like)

Criteria for rejection or delay of analyses for confirmation of carbapenemase in *Pseudomonas*/*Acinetobacter* by the NRC

- Application form missing or without minimal mandatory **information** (including copy of antibiogram results)
- **Damaged** sample (crushed agar plate, broken glass tube,....)
- **Contaminated** culture
- Isolate sent/identified by the NRC as belonging to a **genus/species other** than *Pseudomonas* spp. or *Acinetobacter* spp
- Isolate with a susceptibility profile not meeting the **criteria** for suspected carbapenemase (see slide 4)
- **Duplicated** isolates (strains of the same species from the same patient): only the most resistant isolate according to the antibiogram provided will be analyzed