April 2023

# Characterizing other genera for detection of targeted carbapenemases special study

## Background information

The AR Lab Network focuses detection of targeted carbapenemase genes *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{OXA-48-like}$, *bla*$_{IMP}$, *bla*$_{VIM}$ in carbapenem resistant Enterobacterales, *Pseudomonas aeruginosa* and in carbapenem resistant *Acinetobacter baumannii,* *bla*$_{OXA-23-like}$, *bla*$_{OXA-24/40-like}$ and *bla*$_{OXA-58-like}$ are also targeted for detection. However, public health laboratories in the Network have reported an increased interest from their submitting laboratories to test for the presence of carbapenemase genes in non-*aeruginosa Pseudomonas* (NAP) and non-*baumannii Acinetobacter* (NBA) isolates. Most AR Lab Network laboratories cannot not speciate all NBA/NAP isolates due to limitations in their MALDI database. Additionally, laboratories are not validated to perform AST on these organisms and there are no CLSI approved carbapenemase production testing methods available. There have also been reports in the literature that these organisms can harbor carbapenemase genes and therefore represent an emerging threat to public health that requires additional surveillance and monitoring.

Based on these findings, OLSA proposes a special project to assess whether NAP and NBA species harbor carbapenemase genes in the AR Lab Network.

## Objectives

The primary objective of this project is to determine the frequency of NAP/NBA organisms and the frequency of targeted carbapenemase genes within these species, across time in a sentinel network of laboratories. Genes targeted for detection will include *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{OXA-48-like}$, *bla*$_{IMP}$, *bla*$_{VIM}$ and for NBA isolates only, *bla*$_{OXA-23-like}$, *bla*$_{OXA-24/40-like}$ and *bla*$_{OXA-58-like}$.

Secondary objectives include:

- Using NAP isolates to validate carbapenemase production methods such as mCIM to better detect carbapenemase production in these isolates.
- Contributing a subset of NAP isolates for CLSI studies to update CLSI breakpoints.
- Provide a list of isolates public health laboratories in the AR Lab Network can use to validate AST for NAP and NBA and mCIM for NAP.
- Understanding the susceptibility profiles of these isolates with and without the targeted carbapenemase genes.

## Timeframe for study

Active surveillance will begin on or around May 1, 2023 with a tentative end date of December 31, 2023. Isolate collections will be evaluated routinely to determine an appropriate end date. We hope to conclude isolate collection by December 2023, but the study period may be extended as needed and if partners agree.

Any confirmed or suspected NBA/NAP isolates collected before the start of the study will be requested for additional characterization at CDC.

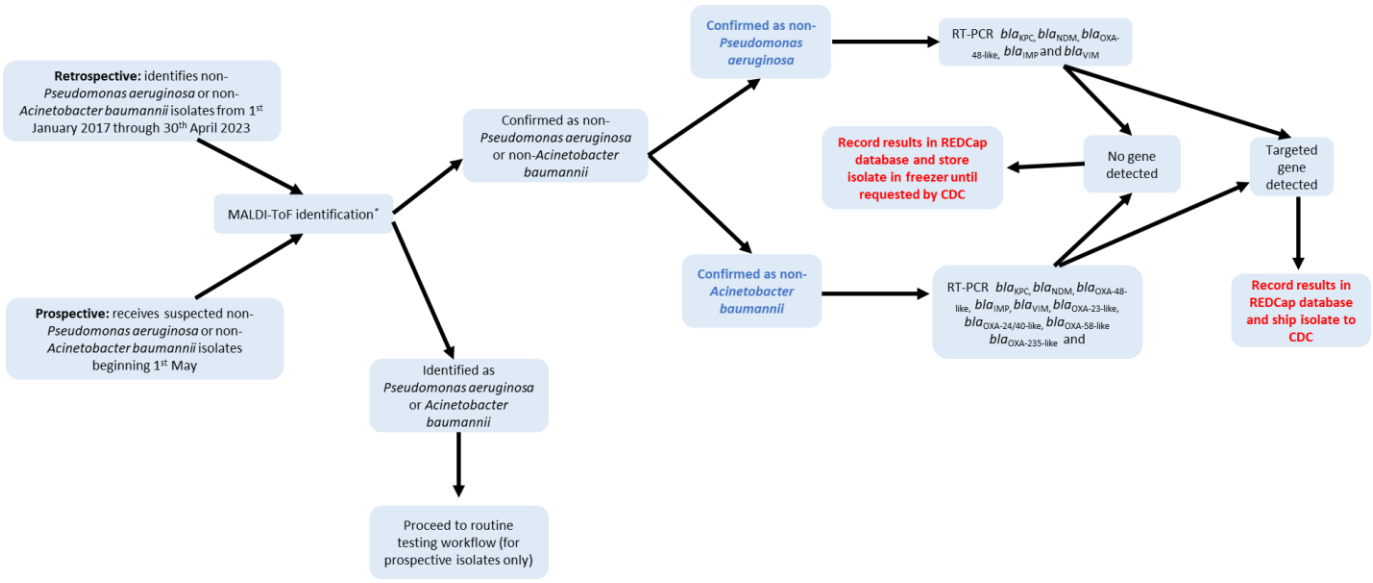
## Participating laboratories

Participating laboratories will recruit a minimum of 2 laboratories to submit confirmed or suspected NBA/NAP isolates. Suspected NAP/NBA isolates are defined as isolates that have been ruled out as being *Pseudomonas aeruginosa* or *Acinetobacter baumannii* using MALDI-ToF MS, but species level

identification was not possible (e.g., *Pseudomonas/Acinetobacter* spp.). Confirmed NAP/NBA isolates are defined as isolates that have been identified by MALDI-ToF MS to the species level (e.g., *Pseudomonas putida or Acinetobacter radioresistens*).
Participating laboratories include:

1. Regional laboratories (e.g., UT) that will send confirmed or suspected NBA/NAP isolates received from submitters but will not perform any additional testing. These isolates will be sent to CDC for testing.
2. Regional laboratories (e.g., NY, MD, TN, WI, MN and WA) that will perform organism identification and RT-PCR on isolates received from submitters in their jurisdiction and on behalf of participating jurisdictions in their region that cannot perform testing on confirmed or suspected NBA/NAP isolates.
    a. Non-regional laboratories that will send NBA/NAP isolates received from submitters but will not perform any additional testing. Upon agreement by the regional laboratory, these isolates will be sent to their regional laboratory for the testing indicated above.
3. Non-regional laboratories that will perform organism identification and RT-PCR on isolates received from submitters in their jurisdiction on confirmed or suspected NBA/NAP isolates.

**Figure 1. Testing workflow in AR Lab Network laboratories***




**Testing approach**

Participating public health laboratories will receive confirmed and suspected NBA/NAP isolates from participating clinical laboratories. PHLs will confirm organism identification using MALDI-ToF. Isolates confirmed as NBA/NAP will be tested for targeted carbapenemase genes as outlined in figure 1. Any laboratory that does not have ability to test NBA isolates for *bla*$_{\text{OXA-23-like}}$, *bla*$_{\text{OXA-24/40-like}}$ and *bla*$_{\text{OXA-58-like}}$ may send these isolates to their regional laboratory for testing upon agreement with that regional laboratory. All data will be recorded in a dedicated REDCap project and a subset of isolates will be sent to CDC as indicated in figure 1.

*Any laboratory already performing any testing on NBA/NAP i.e., AST, PCR or WGS, should continue to follow their routine testing workflows.

Testing at CDC will include:

- Confirmation of organism identification using MALDI-ToF.
- Carbapenemase production testing (mCIM for NAP isolates only)
- Real time PCR for carbapenemase genes; *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{OXA-48-like}$, *bla*$_{IMP}$, *bla*$_{VIM}$ and for NAB isolates only, *bla*$_{OXA-23-like}$, *bla*$_{OXA-24/40-like}$, *bla*$_{OXA-58-like}$, and *bla*$_{OXA-235-like}$.
- Reference broth microdilution (GN1, GN2, GN3 panels) for carbapenemase gene positive NBA/NAP and a subset of NBA/NAP isolates (exact number will depend on total volume of isolates received).
- A subset of confirmed NAP/NBA may undergo whole genome sequencing.

**Data reporting**
Participating laboratories will be given access to a new REDCap project entitled 'Characterizing other genera for detection of targeted carbapenemases'. Data variables will include:

- Date entry entered to REDCap
- Submitter information (public health laboratory)
- Reason for submission from clinical lab (misidentification from clinical lab, recruited for study)
- Specimen source
- Date of specimen collection
- Genera
- Species (can include 'unknown')
- Method used for carbapenemase gene detection
- Carbapenemase genes detected
- Additional testing performed (AST, mCIM, WGS)
- Isolate requested by CDC
- Date isolate requested and received by CDC
- CDC CSID

**Alert reporting**
CDC will check REDCap database for any isolates found to harbor a carbapenemase gene. These will be transferred to the 'Alerts' database by CDC so that containment reponses can be implemented.

**Isolate shipping to CDC**
Isolates will be shipped to CDC using the Global File Accession Template provided for this study. Results will not be reported until the study is completed.

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