

## Canadian Nosocomial Infection Surveillance Program (CNISP)

### Surveillance Protocol for Carbapenemase-Producing Organisms (CPO) in CNISP Healthcare Facilities

*January 29, 2019*

*Final*

#### **Working Group:**

Elizabeth Bryce, Chelsey Ellis, Joanne Embree, Susy Hota, Kevin Katz (co-chair), Pamela Kibsey, Allison McGeer, Jessica Minion, Sonja Musto, Jocelyn Srigley, Kathy Suh, Geoff Taylor, Nisha Thampi, Nathalie Turgeon, Titus Wong, Jerome Leis, Christian Lavallée (co-chair), Michael Mulvey (NML), David Boyd (NML), Laura Mataseje (NML), Kanchana Amaratunga (PHAC) and Robyn Mitchell (PHAC)

#### **Contact:**

Ottawa: [phac.cnisp-pcsin.aspc@canada.ca](mailto:phac.cnisp-pcsin.aspc@canada.ca)

NML: [phac.nml.ARNl-RAlN.lnm.aspc@canada.ca](mailto:phac.nml.ARNl-RAlN.lnm.aspc@canada.ca)

## OBJECTIVES

1. To identify and describe the epidemiology and clinical outcomes of inpatients infected or colonized with a carbapenemase-producing organism (CPO), specifically carbapenemase-producing *Enterobacteriales* (CPE) and carbapenemase-producing *Acinetobacter* (CPA) in participating CNISP hospitals.
2. To describe the molecular epidemiologic information of the carbapenemase-producing isolates collected, including the resistance genes present and the infecting microorganisms identified.
3. To determine the incidence of patients infected and colonized with a CPO, specifically CPE and CPA in participating CNISP hospitals.
4. To provide national benchmark rates that hospitals may use for external comparison.

## RATIONALE

Carbapenems are a class of beta-lactam antibiotics with broad-spectrum activity recommended as first-line therapy for severe infections caused by certain gram negative organisms and as directed therapy for organisms that are resistant to narrower spectrum antibiotics. Carbapenem resistance can be due to changes in the permeability of the organism to the antibiotic and/or the up-regulation of efflux systems that “pump” the antibiotic out of the cell, usually concomitant with the presence of an acquired extended-spectrum beta-lactamase (ESBL) or AmpC enzyme or the hyperproduction of intrinsic chromosomally – located beta-lactamase(s). More recently, resistance is increasingly due to the acquisition of enzymes that break down the carbapenems: carbapenemases. These latter subsets of carbapenem-resistant organisms are called carbapenemase-producing organisms (CPOs) and are of particular concern because of their ability to transfer resistance easily across different genera and species of bacteria. They are quickly becoming a public health problem not only because of the ability to cause healthcare acquired infections which have limited treatment options, but because of the potential for colonizing both inpatient and outpatient populations due to their ease of transmissibility, thus, creating a reservoir of bacterial resistance.

The intent of this surveillance is to describe the epidemiology and clinical outcomes of patients identified as harbouring a carbapenemase. There is a specific focus on this subset of organisms that are carbapenemase producers because this type of resistance is not endemic in Canadian populations at this point in time, but is known to be associated with transmission and outbreaks in health care facilities. We need to understand the epidemiology and scope of the problem while it is still an emerging event, and identify the potential impact of CPOs on infection prevention and control programs and patient treatment strategies.

## METHODOLOGY

### **a) Eligible facilities**

All CNISP hospitals are eligible to participate.

### **b) Eligible cases**

- (i) Patient admitted to a CNISP participating hospital
- (ii) Laboratory confirmation of carbapenem resistance or carbapenemase production (see **Appendix A** for laboratory criteria) in *Enterobacteriales* and *Acinetobacter spp.*

Note: Following molecular testing, only isolates determined to be harbouring a carbapenemase will be included in surveillance.

### **c) Case identification and isolate submission**

All patient specimens with eligible *Enterobacteriales* and/or *Acinetobacter spp.* (as per **Appendix A**) will be identified by the hospital microbiology laboratory and sent to the NML with a minimum data set (**Appendix B**) for detection or confirmation of carbapenemase production. Laboratories who perform their own molecular testing should submit to the NML only isolates which are confirmed to produce carbapenemases, or which they suspect contain a carbapenemase not detected by their testing. If there are multiple isolates from one patient and laboratories are only sending one isolate, please submit the isolate from the most invasive specimen, and otherwise please submit all isolates.

**Note:** Appendix B must be included with the shipment **AND** emailed to the NML at **phac.nml.ARNIRAIN.Inm.aspc@canada.ca**. It is important that when isolates are submitted to the NML that they are identified as CNISP isolates otherwise they will not be included in CNISP surveillance.

The NML will send the carbapenemase testing results via email to the CNISP hospital.

### **d) Case reporting**

The carbapenemase testing results may be used to confirm the hospital's own molecular testing or if the hospital does not do molecular testing this report will indicate for which isolate(s) to submit a patient questionnaire. A patient questionnaire (**Appendix C**) should be completed for all carbapenemase-producing *Enterobacteriales* and/or *Acinetobacter spp.* For data quality purposes, please ensure that data submitted on Appendix B matches data submitted on the patient questionnaire (Appendix C) (e.g. age, sex, pathogen, site of isolation etc.). The patient questionnaire (Appendix C) should be completed based on the isolate submitted to the NML (Appendix B).

Please submit all patient questionnaires by email to CNISP at **phac.cnisp-pcsin.aspc@canada.ca**.

Please assign a unique patient identifier as follows: CHEC site number, surveillance year then consecutive number (e.g., 99ZY001). Note: When multiple isolates are submitted for the same patient in the same surveillance year, please indicate by adding a suffix A or B etc. to the case number (e.g. 99ZY001A and 99ZY001B).

**e) Denominator data**

Denominator data will be collected on the quarterly denominator form.

The data collected will include:

- 1) total number of patient admissions per year
- 2) total number of inpatient-days per year

**f) Data management and reporting**

The NML will maintain a database of all eligible isolates. This database will include all data submitted on Appendix B and laboratory testing results. The Ottawa CNISP team will maintain an epi database of all patient questionnaire data. Once the laboratory analysis is complete, the lab and epi data will be merged.

Patients with multiple CPO positive isolates will only be included in the rates once based on the isolate from the most invasive site. If the patient was initially colonized with a CPO and subsequently develops a CPO infection with the same gene, within the surveillance year, the colonization will be excluded from the rates and only the infection will be included.

**g) Environmental sampling**

**If possible**, please consider screening drains at discharge for CPO positive patients. Please swab all drains in the patient room and bathroom before a cleaning protocol is implemented. Please complete and send Appendix B to the NML along with the CPO positive environmental swab(s). On Appendix B, under site of isolation please select environmental (ENV) and indicate site (drain, sink, etc.). Please use the same unique PID assigned to the patient whose room was swabbed and add a suffix E1 or E2 etc. to the case number (e.g. 99ZYY001E1 and 99ZYY001E2).

**Attached Appendices:**

*Appendix A. Laboratory considerations for determining carbapenem resistance and carbapenemase production in Gram-negative bacilli to determine eligibility for inclusion in surveillance*

*Appendix B. Carbapenemase-Producing Gram-Negative Bacilli Specimen Surveillance Form*

*Appendix C. CPO Patient Questionnaire*

*Appendix D. Algorithm for CNISP CPO Surveillance*

*Appendix E. Carbapenem-Resistant Gram-Negative (CRGN) Organisms*

*Appendix F. Data dictionary – definition and notes for patient questionnaire*

**APPENDIX A – Laboratory considerations for determining carbapenem resistance and carbapenemase production in Gram-negative bacilli to determine eligibility for inclusion in surveillance**

All *Enterobacteriales* and *Acinetobacter spp.* that meet at least one of the following criteria should be submitted to the NML:

- 1) Tested fully resistant to a carbapenem based on the current CLSI.2018.M100-ED28<sup>1</sup> zone diameters and/or MIC values as listed below:

At least ONE of the following:	<i>Enterobacteriales:</i>	
	MIC ( $\mu\text{g/ml}$ )	Disk diffusion (mm)
Imipenem	$\geq 4$	$\leq 19$
Meropenem	$\geq 4$	$\leq 19$
Doripenem	$\geq 4$	$\leq 19$
Ertapenem	$\geq 2$	$\leq 18$

At least ONE of the following:	<i>Acinetobacter:</i>	
	MIC ( $\mu\text{g/ml}$ )	Disk diffusion (mm)
Imipenem	$\geq 8$	$\leq 18$
Meropenem	$\geq 8$	$\leq 14$
Doripenem	$\geq 8$	$\leq 14$

- 2) Tested positive for a carbapenemase in laboratories that conduct molecular testing (PCR) or immunochromatographic lateral flow assay for specific enzymes (e.g. K-SeT). Laboratories should be aware that commercial tests may include only the most common carbapenemases i.e. KPC, OXA-48, NDM, and may not include more rare ones i.e. VIM, IMP, GES, NMC-A/IMI, SME, and others. If the molecular test is negative but a laboratory suspects the presence of a carbapenemase, the isolate should be further tested by the submitting laboratory, their Provincial Laboratory, or the NML. Isolates then confirmed to harbour a carbapenemase are eligible for inclusion in surveillance.
- 3) Tested positive for carbapenemase production by a phenotypic test such as the mCIM, CARBA-NP or a commercial equivalent, or Beta-Carba test. These tests can help determine if a suspected CPO that was negative by molecular testing does in fact harbour a carbapenemase. Note however, that these tests can produce false negatives for poorly expressed enzymes (likely have low MICs), enzymes that only slowly hydrolyze carbapenems (e.g. OXA-48-group, GES-type), or non-specificity of the test for certain enzymes (e.g. SME, NMC-A/IMI, GES-type by Beta-Carba test).

<sup>1</sup> CLSI. Performance standards for antimicrobial susceptibility testing; 24<sup>th</sup> informational supplement. CLSI document M11-S27. CLSI, Wayne, PA.

Due to the importance of the timely identification of these organisms for treatment and infection control purposes, we strongly encourage you to send isolates that meet the study definition to the NML as soon as possible – **at least once every three months**. Timely submission is especially important if you have additional evidence (phenotypic or molecular) that the isolate is harbouring a carbapenemase or if you suspect it is part of an outbreak. In addition, we strongly recommend you alert your provincial public health authorities.

To ensure that the NML receives all isolates (and avoids receiving duplicate isolates), we would appreciate if you would inform the NML if the isolate(s) you shipped to the NML were also sent to your provincial laboratory. The provincial laboratory may have forwarded the same isolates to the NML for routine testing (non-CNISP) and they would have been assigned an NML number (e.g. N18-01234). Therefore, **if you have an NML number please include on Appendix B with a CNISP PID.**

Isolates and Appendix B should be submitted to Dr. George Golding at the address below.

Dr. George Golding  
National Microbiology Laboratory  
1015 Arlington St.  
Winnipeg, Manitoba  
R3E 3R2  
Tel: 204-789-8096  
Fax: 204-789-5020  
Use FedEx billing number: 6636-8403-5

Email: [phac.nml.ARNI-RAIN.lnm.aspc@canada.ca](mailto:phac.nml.ARNI-RAIN.lnm.aspc@canada.ca)

## **APPENDIX B – Carbapenemase-Producing Gram-Negative Bacilli Specimen Surveillance Form**

Instructions: All fields of this questionnaire should be filled out and sent to the NML (care of Dr. Golding) along with the patient specimens.  
The specimens should be clearly labelled with their unique patient identifier.

**Important: Please email [phac.nml.ARN1-RAIN.Inm.aspc@canada.ca](mailto:phac.nml.ARN1-RAIN.Inm.aspc@canada.ca) the day of shipping to allow tracking of the shipment**

PLEASE CLICK ON THE ICON BELOW TO ACCESS THE EXCEL SHIPPING FORM



Appendix B\_CPO  
Standardized Shipping

**APPENDIX C – CPO Patient Questionnaire**

**Surveillance for inpatients with Carbapenemase-Producing Enterobacterales (CPE) or Carbapenemase-Producing Acinetobacter (CPA) Infection or Colonization**

1	Which laboratory conducted carbapenemase confirmatory testing for this case?	<input type="checkbox"/> NML <input type="checkbox"/> Provincial laboratory <input type="checkbox"/> Hospital laboratory
2	Does this patient meet the criteria for an infection or colonization?	<input type="checkbox"/> Infection <sup>2</sup> <input type="checkbox"/> Colonization
3	CHEC site # _____	
4	Unique patient identifier	_____ <i>(CHEC site #) (year) (case number)</i>
5	Patient ward	<input type="checkbox"/> ICU <input type="checkbox"/> NICU <input type="checkbox"/> Medical ward <input type="checkbox"/> Surgical ward <input type="checkbox"/> Other, specify _____ <input type="checkbox"/> Unknown
6	Date of birth _____/_____/_____ <i>dd mmm yyyy</i>	<b>OR</b> Age _____ <input type="checkbox"/> Years <input type="checkbox"/> Months <input type="checkbox"/> Days
7	Sex	<input type="checkbox"/> Male <input type="checkbox"/> Female <input type="checkbox"/> Unknown
8	Date of admission	_____/_____/_____ <i>dd mmm yyyy</i>
9	Type of CPO isolate	<input type="checkbox"/> Screening isolate <input type="checkbox"/> Clinical isolate
10	Date of positive culture <i>(Specimen collection date from which the positive organism was isolated)</i>	...../...../..... <i>dd mmm yyyy</i>

<sup>2</sup> Infection is determined using the 2017 CDC/NHSN surveillance definitions for specific infections, and in accordance with the best judgment of the healthcare practitioner. These criteria can be accessed at [URL:www.cdc.gov/nhsn/PDFs/pscManual/17pscNosInfDef\\_current.pdf](http://www.cdc.gov/nhsn/PDFs/pscManual/17pscNosInfDef_current.pdf)





19a	Were any sinks or shower drains tested for CPO related to this patient?	<input type="checkbox"/> No (end of patient questionnaire) <input type="checkbox"/> Yes, please go to Q18b.
19b	If yes, please complete if possible:	
	Patient sink in bathroom	<input type="checkbox"/> positive <input type="checkbox"/> negative <input type="checkbox"/> culture not done _____ (CHEC site #) _____ (year) _____ E _____ (case number)
	Staff hand hygiene sink	<input type="checkbox"/> positive <input type="checkbox"/> negative <input type="checkbox"/> culture not done _____ (CHEC site #) _____ (year) _____ E _____ (case number)
	Patient shower/tub drain	<input type="checkbox"/> positive <input type="checkbox"/> negative <input type="checkbox"/> culture not done _____ (CHEC site #) _____ (year) _____ E _____ (case number)
	Communal shower drain	<input type="checkbox"/> positive <input type="checkbox"/> negative <input type="checkbox"/> culture not done _____ (CHEC site #) _____ (year) _____ E _____ (case number)
	Other, specify: _____	<input type="checkbox"/> positive <input type="checkbox"/> negative <input type="checkbox"/> culture not done _____ (CHEC site #) _____ (year) _____ E _____ (case number)

## APPENDIX D: ALGORITHM for CNISP CPO SURVEILLANCE

Patient admitted to any ward/department of your hospital and identified with carbapenem-resistant *Enterobacterales* AND / OR *Acinetobacter* spp.

No

Exclude from surveillance

Yes

**Hospital laboratory identifies eligible isolate(s) for surveillance using 1 or more of the following 3 methods:**

- 1-See table to the right
- 2-**POSITIVE** molecular testing (PCR) or immunochromatographic lateral flow assay for carbapenemase presence
- 3-**POSITIVE** phenotypic test such as the mCIM, CARBA-NP, Beta-Carba or a commercial equivalent

At least ONE of:	<i>Enterobacterales</i> :		<i>Acinetobacter</i> :	
	MIC (µg/mL)	Disk diffusion (mm)	MIC (µg/mL)	Disk diffusion (mm)
Imipenem	≥4	≤19	≥8	≤18
Meropenem, Doripenem	≥4	≤19	≥8	≤14
Ertapenem	≥2	≤18	n/a	n/a

No

Exclude from surveillance

Yes

Complete the Specimen Surveillance Form (**Appendix B**) and send it with the isolate(s) to the NML (care of Dr. Golding). Please also email Appendix B to the NML at [phac.nml.ARNI-RAIN.Inm.aspc@canada.ca](mailto:phac.nml.ARNI-RAIN.Inm.aspc@canada.ca)

PCR detection (by NML) of isolated *Enterobacterales* spp. and/or *Acinetobacter* spp. for the presence of a carbapenemase  
**If a carbapenemase is detected**

No

Yes

Yes

The NML sends a report of all PCR results to the CHEC site

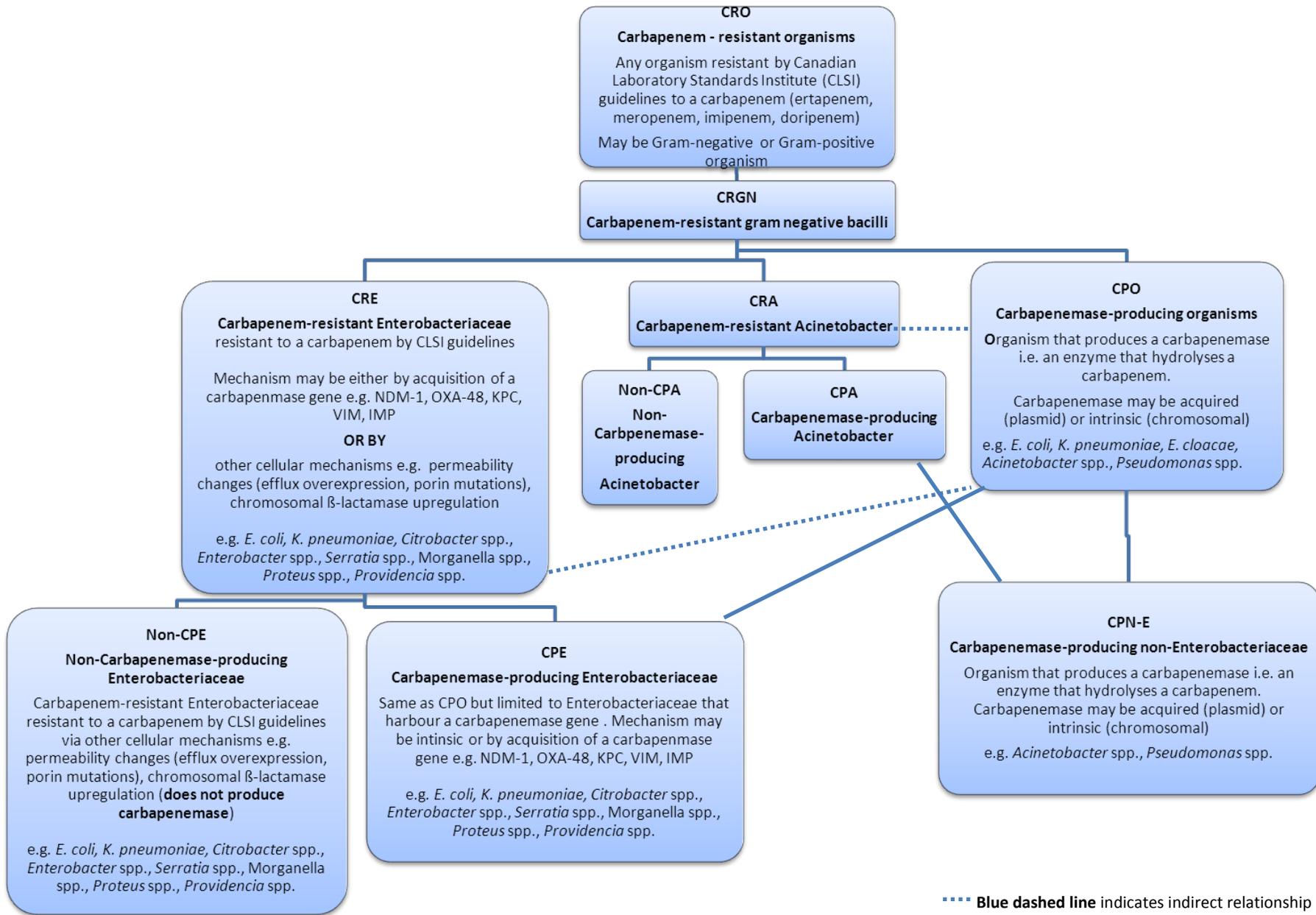
**Dr. George Golding**

National Microbiology Laboratory  
1015 Arlington St.  
Winnipeg, Manitoba R3E 3R2

Tel: 204-789-8096; Fax: 204-789-5020  
FedEx billing number: 2299-8435-7  
Email [george.golding@canada.ca](mailto:george.golding@canada.ca)

CHEC site completes a patient questionnaire (**Appendix C**) for all CPE and CPA infections and colonizations and submits to:  
[phac.cnisp-pcsin.aspc@canada.ca](mailto:phac.cnisp-pcsin.aspc@canada.ca).

## APPENDIX E: Carbapenem-Resistant Gram-Negative (CRGN) Organisms



## APPENDIX F - Data Dictionary - Definitions and notes for Patient Questionnaire (Appendix C)

### 1. Which laboratory conducted confirmatory carbapenemase testing for this case?

Please indicate which laboratory confirmed that this case is CPO positive. Please check all that apply.

### 2. Does this patient meet the criteria for an infection or colonization?

Please indicate if this case is colonized or infected. Infection is determined using the CDC/NHSN surveillance definitions for specific infections **AND** in accordance with the best judgment of the infection control and/or healthcare practitioner. These criteria can be accessed at URL:

[http://www.cdc.gov/nhsn/PDFs/pscManual/17pscNosInfDef\\_current.pdf](http://www.cdc.gov/nhsn/PDFs/pscManual/17pscNosInfDef_current.pdf)

### 3. CHEC Site #

This will be the **3-character** alphanumeric number assigned to your institution. It will always begin with the two digit number assigned to your CHEC member e.g., 07, 15, and a letter assigned by the CHEC member for that specific institution e.g., A, B, C, etc. The CHEC site # for each institution should always be the same for all the CHEC/CNISP surveillance projects and will always have all three alphanumeric digits reported as the CHEC site #, e.g., 07A, 15A.

### 4. Unique patient identifier

Please assign a unique patient identifier as follows: CHEC site number, surveillance year then consecutive number (e.g., 99ZY001). Note: When multiple isolates are submitted for the same patient in the same surveillance year, please indicate by adding a suffix A or B etc. to the case number (e.g. 99ZY001A and 99ZY001B).

Note: The unique patient identifier assigned to the isolate on Appendix B should correspond to the unique patient identifier on the patient questionnaire (Appendix C).

### 5. Patient ward

Please indicate the ward the patient was on when the positive specimen was collected (e.g., medical, surgical, ICU).

### 6. Date of birth

Please enter Day (##), Month (May) and Year (1973) in this order. If the date of birth is not available please enter the patient's age (in years, months or days) at the time of positive culture.

### 7. Sex

Check male, female or unknown as appropriate.

### 8. Date of admission

Please indicate the date when the patient was admitted to the hospital using the following format Day (##), Month (May) and Year (1973).

### 9. Type of CPO isolate

Please indicate whether the isolate was obtained as a result of screening, a clinical isolate (wound, surgical site, respiratory etc.) or a blood culture.

### 10. Date of positive culture

For the current admission, please indicate when the isolate that tested CPO positive was collected.

### 11. Organism isolated

Please select the organism isolated as reported by the laboratory.

## 12. Site of isolation

Please indicate the site of isolation for the isolate that was submitted to the NML.

### 13a. Where was CPO acquired?

Please indicate whether the infection was acquired in a healthcare setting (HA) or in the community (CA) according to the following definitions and in accordance with the best clinical judgement of the healthcare and/or infection prevention and control practitioner (IPC). If the site of acquisition cannot be determined, please report as 'unable to determine'.

#### Healthcare-associated (HA) your facility:

Patient is on or beyond calendar day 3<sup>7</sup> of their hospitalization

OR

Has had a healthcare exposure at your facility that would have resulted in this infection or colonization (using best clinical judgement)

#### Healthcare-associated (HA) other Canadian healthcare exposure:

Any patient who has an infection or colonization not acquired at your facility that is thought to be associated with another healthcare exposure in Canada (e.g. another acute-care facility, long-term care, rehabilitation facility, clinic or exposure to a medical device).

#### Healthcare-associated (HA) other healthcare facility outside of Canada

Any patient who has an infection or colonization not acquired at your facility that is thought to be associated with another healthcare exposure outside of Canada (e.g. another acute-care facility, long-term care, rehabilitation facility, clinic or exposure to a medical device).

#### Community-associated (CA):

No exposure to healthcare that would have resulted in this infection or colonization (using best clinical judgement) and does not meet the criteria for a healthcare-associated infection or colonization.

### 13b. If healthcare-associated (your facility), is there evidence of any of the following modes of transmission?

Please indicate whether there is any evidence to suggest that this patient became infected/colonized with this CPO through any of the modes listed. If contact with another patient, please specify the unique patient ID of this patient.

### 14a. Is there any evidence of international travel in the 12 months prior to CPO diagnosis?

Please indicate if the patient has travelled internationally in the 12 months prior to the date of positive culture.

### 14b. If travelled internationally, is there evidence the patient received medical care where they travelled to?

If answered 'yes' to question 14a, please indicate (if possible) whether the patient received medical care while travelling internationally.

---

<sup>7</sup>Calendar day 1 is the day of hospital admission

**15. Is there any evidence of international travel by a member of the household or caregiver in the 12 months prior to the patient's CPO diagnosis??**

Please indicate (if possible) whether there is any evidence of international travel by a member of the household and/or a caregiver in the 12 months prior to the patient's CPO diagnosis.

**16. Does the patient have any underlying medical conditions?**

Please indicate whether the patient has any underlying medical conditions – if yes, check all that apply.

**Note:** Q16 & Q17 are only to be completed for infected cases

**17. Was ICU admission required due to complications associated with CPO infection?**

Please indicate whether the patient required admission to ICU as a result of complications associated with acquiring a CPO infection.

**18. Patient outcome 30 days after positive CPO culture?**

Thirty days after the date of positive culture please select one of the outcome options available.

**19. Were any sinks or shower drains tested for CPE related to this patient?**

Please indicate yes or no if sinks and/or shower drains were tested for CPE related to this patient. If yes, please indicate the type of sink or drain, whether the swab was CPO positive, negative or not collected and if possible indicate the PID associated with the environmental swab. Please use the same unique PID assigned to the patient whose room was swabbed and add a suffix E1 or E2 etc. to the case number (e.g. 99ZYY001E1 and 99ZYY001E2).

## Revision History

June 3, 2014 - added response 'unable to determine' to Q8 "Where CPO acquired?" – now Final v2

June 9, 2014 - corrected numbering of questions – now Final v3

July 15, 2014 - added ER visits to denominator data collection – was already added to separate 'quarterly denominator form' – now Final v4

October 30, 2014 - Began making changes to homogenize CNISP protocol formatting

December 15, 2014 - Updated the unique patient ID for multiple organisms and/or re-admission to reflect previous nomenclature (i.e. adding suffix A or B).

December 30, 2014 - Updated Q8 to include 'other Canadian healthcare facility' and 'other healthcare facility outside of Canada'. Changed wording of Q13 to clarify evidence of transmission.

2015 - Question Q13 "Is there any evidence that this was a nosocomial-acquired case?" was removed in the 2015 protocol.

October 28, 2015 - Question 15c related to what medical procedure patients were subjected to if they received medical care abroad has been removed.

November 2017 - Added Q13b regarding possible sources/modes of transmission

- Added Q19 - for patients with more than one CPE or CPA infection or colonization in a calendar year, please report the PID of the previous case

- Project name updated to CPO surveillance. Note: reflected in PID format

- Update to PID format: For multiple pathogens, infections, colonizations etc. within same the admission use the same PID with suffix A, B, C etc. **NEW** – use a new PID for a new admission.

July 2018

- Discontinued CPO surveillance of ER and outpatients
- Updated Appendix A to reflect sites that conduct their own molecular testing
- Removed surveillance year as protocol will no longer be updated annually
- Added inclusion and exclusion surveillance criteria
- Removed Q1 from pt questionnaire (Appendix C) and added a question regarding who/where carbapenemase confirmation is conducted.
- Updated definitions for healthcare and community associated

Nov 2018

- Added section on environmental sampling and updated Appendix B accordingly
- Added Q18 – Added question - were any sinks or drains tested for CPO related to this patient
- Added Q14c – Added question regarding evidence of international travel by a member of the household or caregiver