

Canadian Nosocomial Infection Surveillance Program (CNISP)

Surveillance Protocol for Vancomycin Resistant *Enterococci* Bloodstream Infections in CNISP Hospitals

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### **BACKGROUND**

Vancomycin resistant *Enterococci* (VRE) cause significant morbidity and mortality in hospitalized patients with immunocompromised conditions and intensive care needs, with few effective antimicrobial interventions available<sup>1</sup>. In Canada, the incidence of VRE bloodstream infections has been increasing steadily over the past several years. Divergence in infection prevention and control practices – including cessation of screening and isolation of hospitalized patients in some hospitals – has been postulated as the main driver of these changes<sup>2</sup>. In addition, a novel strain of vancomycin resistant *Enterococcus faecium*, which was previously "non-typeable" by multi-locus sequence typing (MLST) due to the loss of the *pstS* gene was first described in Australia and was identified in CNISP hospitals in 2013. In Canada, this novel strain was assigned the sequence type ST1478. An increase in ST1478 (from <5% of isolates in 2013 to 38.7% in 2018) coincides with an increase in VRE BSI rates. This strain is also associated with non-susceptibility to daptomycin and high level gentamicin resistance.

### **OBJECTIVES**

- 1. To determine the incidence of VRE BSIs among CNISP hospitals.
- 2. To provide a Canadian benchmark for VRE BSIs rates.
- 3. To describe the epidemiology of VRE BSIs.
- 4. To characterize the susceptibility profile and molecular subtype of VRE BSI isolates.

### **METHODS**

### **Site Eligibility**

All CNISP hospitals are eligible to participate.

### Case Eligibility

### **Inclusion Criteria**

Criterion 1: Isolation of Enterococcus faecalis or faecium from blood

#### AND

Criterion 2: Vancomycin MIC ≥ 8 ug/ml

#### AND

Criterion 3: Patient must be admitted to the hospital

#### AND

**Criterion 4:** Is a "newly identified VRE BSI" at a CNISP hospital at the time of hospital admission or identified during hospitalization.

A newly identified VRE BSI is defined as a positive VRE blood isolate > 14 days after completion
of therapy for a previous infection and felt to be unrelated to previous infection in accordance
with best clinical judgement by Infection Control physicians and practitioners

### **Exclusion Criteria**

Emergency, clinic, or other outpatient cases who are **not admitted** to the hospital.

### **Numerators**

### **Case Identification**

For each **VRE BSI** that meets the above criteria, a <u>APPENDIX 3 - VRE</u> BSI Patient Questionnaire should be completed by reviewing the patients' chart and reported to the Public Health Agency of Canada (PHAC).



**IMPORTANT:** For patients with more than one VRE BSI during the same calendar year, **NEW** infections are to be identified by entering as a new case and 'linking' to the patient's original VRE BSI by entering the original unique patient identifier at the end of the patient questionnaire. This will enable the identification of duplicate patients.

### **Exposure Classification**

Once the patient has been identified with a VRE BSI, they will be classified as healthcare-associated acquired in your acute-care facility, healthcare-associated any other healthcare exposure or community-associated based on the following criteria and in accordance with the best clinical judgement of the healthcare and/or infection prevention and control practitioner (ICP).

### Healthcare-associated acquired in your acute-care facility (HA-YAF)

• Patient is on or beyond calendar day 3<sup>1</sup> of their hospitalization

#### OR

• Has been hospitalized in your facility in the last 7 days or up to 90 days<sup>2</sup> depending on the source of the infection

#### OR

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

### Healthcare-associated any other healthcare exposure (HA-OTHER)

Any patient who has a bacteremia not acquired at your facility that is thought to be associated with any other healthcare exposure (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 bacteremia (using best clinical judgement<sup>3</sup>) and does not meet the criteria for healthcare-associated BSI

<sup>&</sup>lt;sup>1</sup> Calendar day 1 is the day of hospital admission

<sup>&</sup>lt;sup>2</sup>For example, a VRE bacteremia from a surgical wound that occurs 3 weeks after a surgical procedure completed in your facility should be considered HA – your acute-care facility (up to 90 days after procedure if implant). A VRE bacteremia secondary to UTI occurring >7 days after discharge from your facility should not be considered HA – your acute-care facility.

<sup>&</sup>lt;sup>3</sup> Consideration should be given to the frequency and nature of exposure to a medical device and/or procedure. For example, pediatric patients with clinic visits for otitis media, asthma, well-baby etc., may or may not be considered as HA while pediatric patients with clinic visits that involved invasive procedures or day surgery may be more likely to be considered HA. Adult patients attending dialysis, receiving chemotherapy, outpatient visits involving invasive procedures or day surgery may be more likely to be considered HA compared to adult patients with occasional outpatient or community health clinic visits.

### **Denominator Data**

Denominator data will be collected on the quarterly denominator form and submitted in CNPHI.

The data collected will include:

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

### **Data Management and Reporting**

### **Case Reporting**

All denominator and patient questionnaire data (<u>SEE APPENDIX 3 - VRE</u> BSI Patient Questionnaire) should be submitted online through the Canadian Network for Public Health Intelligence (CNPHI) at <u>www.cnphircrsp.ca</u>.

### **Laboratory Reporting**

**Blood Isolates:** One blood isolate is required for every eligible VRE BSI and submitted to the NML. For patients with more than one VRE BSI in a calendar year, please indicate the patient's previous unique patient ID on the Laboratory Shipping Form (Appendix 2).

**Mandatory Shipping Form:** Each shipment of eligible VRE blood isolates must be accompanied by a Laboratory Shipping Form. Please complete the template found in the Laboratory Shipping Form and ensure it is included in the shipment. Please note that the Laboratory Shipping Form must also be emailed to the NML at <a href="mailto:phac.nml.ARNI-RAIN.lnm.aspc@canada.ca">phac.nml.ARNI-RAIN.lnm.aspc@canada.ca</a>.

### Instructions for submitting laboratory specimens:

- Vancomycin-resistant *E. faecium* and *E. faecalis* isolated from a blood infection will be identified by the submitting lab's preferred methods (e.g. grows on a VRE screen plate and identified by phenotypic methods).
- The isolate in pure culture and properly labelled with a CHEC number (in indelible ink/marker) should be stored by an appropriate method (i.e. swab at 4°C, cryobeads or glycerol stock at-20°C). Isolates can be stockpiled for bulk shipment to the NML.
- Unique patient ID must use the following syntax: Site number (alphanumeric) e.g. 01A, year (2 digits) e.g. 20, strain number (3 digits) e.g. CHEC #, would be 01AYY001.



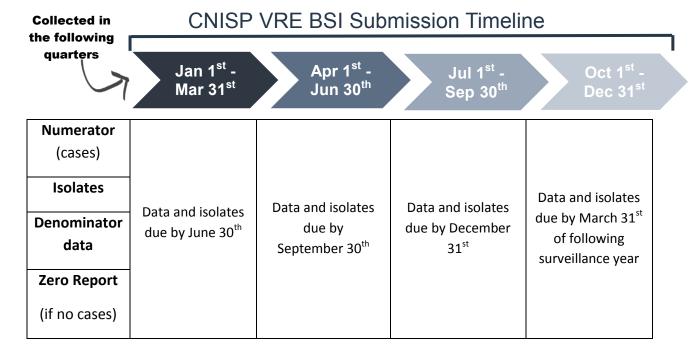
Note: The unique patient ID for the isolate must match the unique patient ID on the corresponding submitted VRE questionnaire.

### **Surveillance Algorithm**

The ERROR! REFERENCE SOURCE NOT FOUND. has been provided to assist in surveillance activities.

### **Submission Timeline**

Please submit VRE BSI data and isolates according to the following timeline:



### Zero report

For any quarter with no cases at your site, a zero report must be made in the CNPHI VRE module so that quarters with zero counts can be differentiated from missing data. If no cases are submitted and you are missing zero reports for a surveillance year, your hospital data will not be included in the rates.



### **Analysis**

Regional and national BSI rates (per 1,000 admissions and per 10,000 inpatient-days), descriptive epidemiology, sequence type and resistance data will be calculated each year by PHAC and NML staff. Data will be reported through PHAC surveillance reports, presentations, publications, and published on the Agency and/or AMMI website.

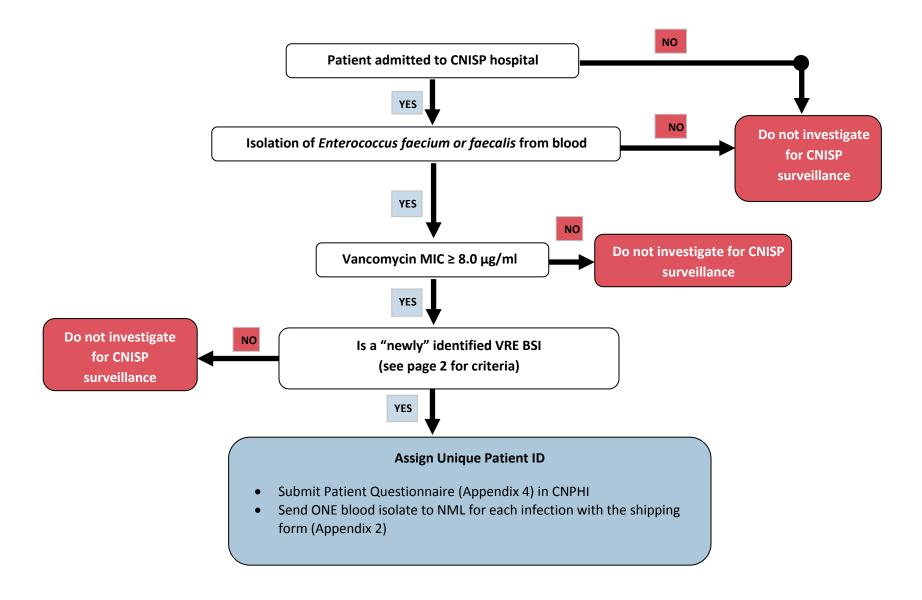
### **ETHICS**

While this surveillance project is observational and does not involve any alteration in patient care, ethics approval may be sought at some hospital sites. Surveillance for healthcare-associated infections is a routine component of quality assurance and patient care in Canadian healthcare institutions and therefore informed consent is not required. A unique identifier linked to patient name will only identify patients at the local CHEC site and is not transmitted to the Agency. All data submitted to the Agency are kept strictly confidential.

### **PRIVACY**

There is current demand for public disclosure of hospital-associated infections. Any data released by CNISP will be in summary format and will not identify individual hospitals. Hospital administrators should be made aware that national reporting of aggregate data will occur.

### Appendix 1 - Algorithm for VRE BSI surveillance



### Appendix 2 - Laboratory Shipping Form

Include the following form with the shipment AND email to the NML address provided.

# Send isolates to: Dr. George Golding National Microbiology Laboratory

1015 Arlington St., Winnipeg, Manitoba R3E 3R2

Tel: 204 784 8096 Fax: 204 789 5020

Use FedEx billing number: 6327-8173-3

In addition, email the shipping form to

phac.nml.ARNI-RAIN.lnm.aspc@canada.ca

Please click on the icon below to access the excel shipping form:



### Appendix 3 - VRE BSI Patient Questionnaire

Please note: this form is only to be completed for bloodstream infections.

1.	Does this patient meet the criteria for a VRE bloodstream infection (refer to inclusion and exclusion criteria)?  — Yes — if yes, please complete the remainder of the questionnaire  — No — if no, do NOT complete this questionnaire.		
2.	CHEC Site:		
3.	Unique Patient ID: (CHEC site #)	YY(year) (case number)	
4.	Age:	hs 🗆 Days	
5.	Postal Code (first 3 digits):		
6.	Sex:   Male   Female		
7.	Date of admission://		
8.	Date of patient's positive culture:/_ DD I	/ MMM YYYY	
9.	Source of blood infection:		
	<ul> <li>□ IV catheter associated</li> <li>□ Primary bacteremia (source unknown/cannot determine)</li> <li>□ Skin or soft tissue/burn wound</li> <li>□ Surgical site infection</li> <li>□ Endocarditis</li> </ul>	<ul> <li>□ Urinary tract infectio</li> <li>□ GI (e.g. intraabdomin ascending cholangitis e</li> <li>□ Mucosal barrier injur</li> <li>□ Other, specify:</li> </ul>	nal abscess, peritoneal fluid, tc.) Y
10.	Where was this VRE BSI acquired? Check one response only:		

	<ul> <li>□ Healthcare-associated – acquired in your acute-care facility (HA-YAF)<sup>4</sup></li> <li>□ Healthcare-associated – acquired from any other healthcare exposure<sup>5</sup></li> <li>□ Community-associated (CA)<sup>6</sup></li> <li>□ Unknown</li> </ul>
11.	Was the patient receiving any of the following treatments at the time of positive blood culture?  (Check ALL that apply)  No Chemotherapy Radiation therapy Hemodialysis Peritoneal hemodialysis
	□ Unknown
12.	Did the patient have a central venous catheter <sup>7</sup> at the time of positive blood culture?  □ Yes □ No □ Unknown
13.	Was the patient a bone marrow or stem cell transplant recipient?
	☐ Yes, please specify date of procedure://  DD MMM YYYY  ☐ No ☐ Unknown
14.	Was the patient a solid organ transplant recipient?
	□ <b>Yes</b> , please specify date of procedure://  DD MMM YYYY □ No □ Unknown

<sup>&</sup>lt;sup>4</sup> Patient is on or beyond calendar day 3<sup>4</sup> of their hospitalization OR has had a healthcare exposure (inpatient or outpatient) at your facility that would have resulted in this infection or colonization (using best clinical judgement) <sup>5</sup> Any patient who has an infection or colonization <u>not</u> acquired at your facility that is thought to be associated with another healthcare exposure (e.g. another acute-care facility, long-term care, rehabilitation facility, clinic or exposure to a medical device).

<sup>&</sup>lt;sup>6</sup> 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.

<sup>&</sup>lt;sup>7</sup> Central Venous Catheter (CVC) include non-tunnelled (standard) CVC, coated or not, peripherally inserted CVC (PICC), tunnelled devices (e.g. Broviac, Hickman), tunnelled haemodialysis line, intra-cardiac catheters such as intra-arterial & and ventricular lines, dual function lines such as temperature/venous catheters (e.g. Cool line catheters, Quattro catheters, introducers etc.), pulmonary catheters, umbilical artery and vein catheters and implanted catheters (including ports).

15.	Please indicate which treatment(s) the patient received for the VRE BSI ONLY (please do not report treatment received for other infections)		
	□ Linezolid		
	□ Daptomycin		
	□ Tigecycline		
	□ Other, specify:		
	□ Unknown		
	□ None		
16.	Please indicate which antimicrobials the patient received 30 days prior to their positive blood culture Check <b>ALL</b> that apply:		
	□ Vancomycin	_ 10	
	☐ Fluoroquinolones	□ Linezolid	
	☐ Cephalosporins	□ Daptomycin	
	□ Carbapenems	Other, specify:	
	□ Penicillins	□ None □ Unknown	
	□ Macrolides	U UIIKIIOWII	
17.	Was the patient admitted to an ICU within 30 days of positive blood culture?		
	$\hfill\Box$ Patient was already in an ICU at the time the posit	ive blood culture was obtained	
	$\hfill\Box$ Yes, please indicate the date of ICU admission:	//	
	DI	D MMM YYYY	
	□ No		
	□ Unknown		
18.	What was the outcome at 30 days from the date of p	ositive blood culture?	
	☐ Patient discharged or transferred alive, please spe	cify date://	
	☐ Patient still alive and in hospital		
	☐ Patient died, please specify date of death:	//	
	DD	MMM YYYY	
	□ Unknown		
19.	Is this a NEW infection in a patient previously identifi	ed with a VRE BSI in this surveillance year?	
	□ No		
	☐ Yes, enter the <i>original/previous unique Patient ID</i> :		
	(C	HEC site #) (year) (case number)	

### Appendix 4 - Data Dictionary

Definitions and notes for completing <u>APPENDIX 3 - VRE BSI PATIENT QUESTIONNAIRE</u> **Appendix 3 - VRE BSI Patient Questionnaire** 

### 1. Does this patient meet the criteria for a VRE BSI infection?

Please refer to the inclusion and exclusion criteria under the CASE ELIGIBILITY

If the patient meets the criteria for a VRE BSI, please complete the remainder of this questionnaire. If the case does NOT meet the criteria for VRE BSI, please do NOT complete this questionnaire.

### 2. 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.

### 3. Unique patient ID

This 10 character code should consist of the 3 character CHEC site # (e.g., 09A), the surveillance year the infection occurred in (e.g., 20), and a consecutive number starting at 001 and continuing on with each additional case. An example of the first case in an institution would be 09A20001. An example of the thirty-fifth case would be 09A20035, and so on.

### Note: Always label the laboratory isolate with this same unique patient ID.

As a patient may have more than one VRE BSI during the same calendar year, **NEW** infections are to be identified by entering as a new case and 'linking' to the patient's original VRE BSI by entering the original unique patient ID at the end of the questionnaire.

### 4. Age

Please enter the patient's age (in years, months or days) at the time of positive culture.

### 5. Postal code (first 3 digits)

Please indicate the patient's residential postal code (first 3 digits).

#### 6. Sex

Check male or female as appropriate.

#### 7. Date of admission

Please indicate the date when the patient was admitted to the hospital.

### 8. Date of this patient's positive culture

For the current admission, please indicate when the positive blood isolate for VRE was obtained.

### 9. Source of blood infection.

Please select the source of infection from which the positive blood culture was obtained.

The National Healthcare Safety Network (NSHN) definition of mucosal barrier injury:

Patient with at least one blood culture growing an eligible intestinal organism or at least two blood cultures with viridans group streptococci but no other organisms isolated who meets any National Healthcare Safety Network criteria for Mucosal Barrier Injury BSI: specifically, allogeneic hematopoietic stem cell transplant recipient who meets National Healthcare Safety Network criteria; or a neutropenic patient meeting National Healthcare Safety Network criteria.

Please refer to the National Healthcare Safety Network document <a href="https://www.cdc.gov/nhsn/PDFs/pscManual/4PSC\_CLABScurrent.pdf">https://www.cdc.gov/nhsn/PDFs/pscManual/4PSC\_CLABScurrent.pdf</a> for complete definitions (CDC, January 2020).

### 10. Source of acquisition

Please indicate whether the BSI was acquired in a healthcare setting or in the community according to the following definitions. If the source of acquisition cannot be determined, please report as unknown.

### Healthcare-associated acquired in your acute-care facility (HA-YAF)

• Patient is on or beyond calendar day 3<sup>8</sup> of their hospitalization

### OR

• Has been hospitalized in your facility in the last 7 days or up to 90 days<sup>9</sup> depending on the source of the infection

#### OR

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

<sup>&</sup>lt;sup>8</sup> Calendar day 1 is the day of hospital admission

<sup>&</sup>lt;sup>9</sup>For example, a VRE bacteremia from a surgical wound that occurs 3 weeks after a surgical procedure completed in your facility should be considered HA – your acute-care facility ( up to 90 days after procedure if implant). A VRE bacteremia secondary to UTI occurring >7 days after discharge from your facility should not be considered HA – your acute-care facility.

### Healthcare-associated any other healthcare exposure (HA-OTHER)

Any patient who has a bacteremia not acquired at your facility that is thought to be associated with any other healthcare exposure (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 bacteremia (using best clinical judgement<sup>10</sup>) and does not meet the criteria for healthcare-associated BSI

### 11. Receiving treatment at the time of positive culture

Please indicate if the patient was receiving any of the following treatments: chemotherapy, radiation therapy, hemodialysis, peritoneal dialysis at the time of positive blood culture.

### 12. Patient with central venous catheter (CVC) at the time of positive blood culture

Please indicate if the patient had a CVC at the time of positive blood culture. Central Venous Catheter (CVC) refers to non-tunnelled (standard) CVC, coated or not, peripherally inserted CVC (PICC), tunnelled devices (e.g. Broviac, Hickman), tunnelled haemodialysis line, intra-cardiac catheters such as intra-arterial and ventricular lines, dual function lines such as temperature/venous catheters e.g. Cool line catheters, Quattro catheters, introducers etc., pulmonary catheters, umbilical artery and vein catheters and implanted catheters (including ports).

### 13. Bone marrow or stem cell transplant recipient

Please indicate if the patient was a bone marrow or stem cell transplant recipient. If yes, please specify the transplant date.

### 14. Solid organ transplant recipient

Please indicate if the patient was a solid organ transplant recipient. If yes, please specify the transplant date.

### 15. Treatment for VRE BSI

Please indicate all of the treatments that the patient received for their VRE BSI. Please do not include treatment for other infections.

<sup>&</sup>lt;sup>10</sup> Consideration should be given to the frequency and nature of exposure to a medical device and/or procedure. For example, pediatric patients with clinic visits for otitis media, asthma, well-baby etc., may or may not be considered as HA while pediatric patients with clinic visits that involved invasive procedures or day surgery may be more likely to be considered HA. Adult patients attending dialysis, receiving chemotherapy, outpatient visits involving invasive procedures or day surgery may be more likely to be considered HA compared to adult patients with occasional outpatient or community health clinic visits.

### 16. Antimicrobials exposure within past 30 days

Please indicate which antimicrobials the patient received 30 days prior to their positive blood culture.

### 17. ICU admission within 30 days

Please indicate if the patient was admitted or transferred to the ICU within 30 days following the date of positive blood culture.

### 18. Outcome at 30 days

Please indicate what the patient's outcome was at 30 days following the date of positive blood culture.

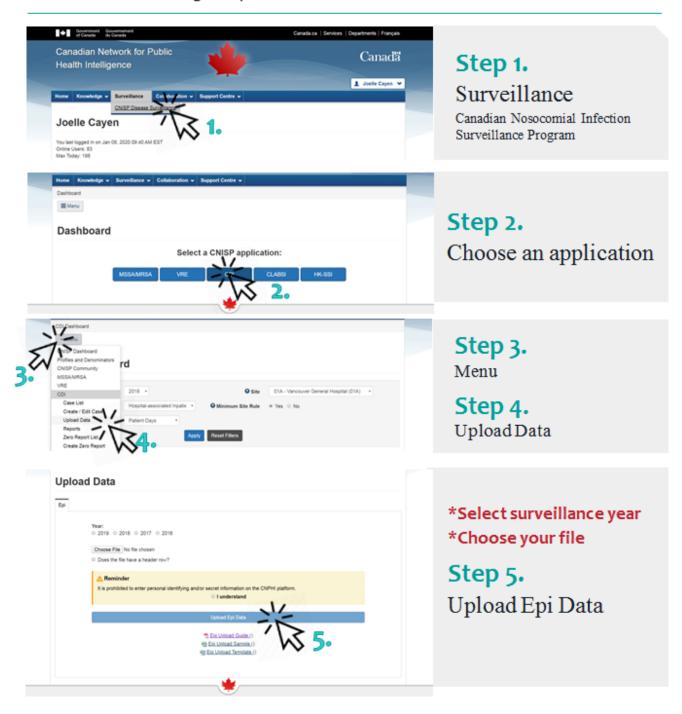
### 19. Is this a NEW infection in a patient previously identified with a VRE BSI in this surveillance year?

Please indicate whether this is a new infection in a patient previously identified with a VRE BSI in this surveillance year. If yes, please indicate the unique PID of the original/previous case

### Appendix 5 - Data Uploader on CNPHI

## **CNPHI – UPLOAD DATA FILES**

How to submit data using the uploader on CNPHI



### References

- 1. Johnstone J, Chen C, Rosella L et al. Patient and hospital level predictors of vancomycin-resistant *Enterococcus* (VRE) bacteremia in Ontario, Canada. *Am J Infect Control* 2018; **46**(11):1266-1271.
- 2. Johnstone J, Policarpio ME, Lam F et al. Rates of blood cultures positive for vancomycin-resistant Enterococcus in Ontario: a quasi-experimental study. *CMAJ Open* 2017; **5**(2): E273-E280.
- 3. Carter GP, Buultjens AH, Ballard SA et al. Emergence of endemic MLST non-typeable vancomycin-resistant *Enterococcus faecium*. *J Antimicrob Chemother* 2016; **71**: 3367–71.
- 4. Van Hal SJ, Beukers AG, Timms VJ et al. Relentless spread and adaptation of non-typeable vanA vancomycin resistant *Enterococcus faecium*: a genome-wide investigation. *J Antimicrob Chemother* 2018; **73**: 1487–1491

### **Revision History**

Date	Revisions Made	
May 1, 2014	Added question 9 to the questionnaire addressing the 30-day outcome of	
-	patients with VRE bacteremia	
October 30, 2014	Began making changes to homogenize CNISP protocol formatting	
November 3, 2014	Case definition' renamed to 'inclusion criteria'	
	2. 'Numerator Data' moved under 'Inclusion Criteria'	
November 5, 2014	<ol> <li>'Introduction' added (copied from VRE Report 'Background').</li> </ol>	
	2. 'Data Analysis' and 'Ethics' copied from the CDI protocol.	
November 12, 2014	Edited 'Unique identifier code' in the Data Dictionaries	
November 27, 2014	Updated protocol to reflect 2015 surveillance year	
December 29, 2014	Added Q9-18 to collect additional data for blood stream infections only	
October 30, 2015	1. Additional question added for blood isolates: "Did the patient have a	
	central venous catheter at the time of positive blood culture?"	
	2. Question 14 was changed from 3 months to 30 days prior to the	
	positive blood culture 'Data Analysis' and 'Ethics' copied from the CDI	
	protocol.	
December 29, 2016	Addition of antimicrobials for Q15. Addition of definitions for Surgical Wound and Urine in Data Dictionary.	
November 10, 2017	The following updates were made to the 2018 protocol:	
	Surveillance of bloodstream infections only.	
	2. Added additional sources of blood infection (Q9).	
	<ol> <li>Updated healthcare and community-associated definitions.</li> <li>Update to inclusion/exclusion criteria – defined new VRE BSI in the</li> </ol>	
	same calendar year.	
	5. Added Q18 to the patient questionnaire - for patients with multiple	
	VRE BSI in the same calendar year, indicate the original case PID.	
October 15, 2018	Removed all references to a specific surveillance year as protocol may	
	not be updated annually.  Added the following response options to source of blood infection:	
	<ol><li>Added the following response options to source of blood infection: mucosal barrier injury and GI</li></ol>	
	3. Added first 3 digits of postal code and removed DOB	
February 7, 2019	Updated format (numbering)	

September 30, 2019	In the data dictionary included in the January 2019 NHSN definition of mucosal barrier injury	
January 8, 2020	Updated the background section	
	<ol><li>In the data dictionary, included the 2020 NHSN definition of mucosal barrier injury</li></ol>	