

# **National Pilot Study of Carbapenemase-producing Carbapenem Resistant Enterobacteriaceae (CRE) in Critical Care Units in the Republic of Ireland**

## **Study Protocol**

**Version 1.4**

**June 2011**

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## **Pilot Study Summary**

This is a pilot four week surveillance study designed to assess, for the first time, the current prevalence of carbapenemase-producing carbapenem resistant Enterobacteriaceae, hereafter known as CRE, in critical care units in Ireland.

## **Study Working Group Membership**

Dr Karen Burns – Locum Consultant Microbiologist, Health Protection Surveillance Centre (HPSC) & Health Service Executive Critical Care Programme (HSE CCP) & Beaumont Hospital.

Dr Fidelma Fitzpatrick – Consultant Microbiologist, HPSC & Beaumont Hospital & Health Service Executive-Royal College of Physicians in Ireland (HSE-RCPI) Healthcare associated infection (HCAI) Clinical Lead.

Dr Robert Cunney – Consultant Microbiologist, HPSC & Children’s University Hospital.

Mr Stephen Murchan – Surveillance Scientist, HPSC.

Dr Michael Power – Consultant in Intensive Care Medicine & Anaesthesia, Beaumont Hospital, HSE CCP Clinical Lead & Intensive Care Society of Ireland representative.

Prof Martin Cormican – Consultant Microbiologist Galway University Hospital & Director National Salmonella Reference Laboratory.

Dr Dearbhaile Morris – Lecturer in Bacteriology, Antimicrobial Resistance and Microbial Ecology Group, National University of Ireland, Galway.

Dr Ed Smyth – Consultant Microbiologist, Beaumont Hospital & President, Irish Society of Clinical Microbiologists (ISCM).

Dr Kirsten Schaffer – Consultant Microbiologist, St Vincent’s University Hospital & Chairperson of Strategy for the control of antimicrobial resistance in Ireland (SARI) subcommittee on management of multi-drug resistant organisms.

Dr Cathal Collins – Specialist Registrar Clinical Microbiology, St James’s Hospital.

Dr Anne Sheahan – Consultant in Public Health Medicine. HSE-South.

## Introduction

Carbapenems (meropenem, imipenem, ertapenem, doripenem) are broad spectrum intravenous antimicrobials, which have traditionally been reserved for therapy of suspected or confirmed infection in patients who are critically ill and/or patients known or suspected to be colonised with multi-drug resistant Gram-negative bacilli (MDR-GNB), including extended spectrum  $\beta$  lactamase (ESBL)-producing Enterobacteriaceae. In Ireland and throughout the world, the use of carbapenems has increased in recent years. This is partly due to concerns about emergence of more resistant GNB and the need to provide antimicrobials with good activity against such organisms. In the last decade, there have been new and emerging reports of Enterobacteriaceae which have become resistant to carbapenems (CRE). CRE have been widely reported mainly from Greece, USA, parts of China and Israel and more recently in India and Pakistan. Enterobacteriaceae have developed the capability to produce an enzyme which has the ability to hydrolyse or destroy the carbapenem (also known as a carbapenemase), rendering the antimicrobial ineffective. The predominant genetic mechanisms of carbapenemase production differ from country to country. Prior to 2010, there had been only one reported case of a CRE in Ireland. However, since 2010, the Health Protection Surveillance Centre (HPSC) has received several reports of isolated CRE cases and CRE outbreaks, mainly in critical care settings. Some of these cases have had a history of travel abroad but others have had no travel history. The emergence of CRE in Ireland is a cause for major concern. In addition to genes which confer resistance to carbapenems, these organisms commonly carry genes which confer resistance to almost all classes of antimicrobial agents. In March 2011, the detection of CRE from a patient became notifiable to the relevant department of public health. CRE should be notified regardless of whether or not the detection of CRE from a patient reflects colonisation or infection.

## Methods

### Inclusion Criteria

- All patients admitted to a participating adult or paediatric critical care unit during the four week study period

### Exclusion Criteria

- Infants admitted to neonatal intensive care units (NICU)

Every critical care unit and the corresponding microbiology laboratory will be invited to participate in this one-month pilot study.

A short questionnaire regarding existing surveillance and laboratory practices will be issued with the invitation to participate (See **Appendix A**). Each unit will be requested to complete the questionnaire in conjunction with the microbiology laboratory, to indicate their intention to participate in the study and to nominate a study contact in the critical care unit and a second study contact in the microbiology laboratory. The critical care unit and microbiology laboratory contacts should agree locally who will be responsible for the completion and return of enhanced surveillance forms.

An information leaflet for staff working in critical care units will be devised (See **Appendix B**).

### Summary of role of the participating critical care unit:

- 1) Agree to participate in the pilot four week study.
- 2) Nominate a local critical care unit study contact. This may be a member of the critical care unit staff or a member of the infection prevention and control team and should be decided locally.
- 3) Perform a weekly rectal screening swab for CRE carriage on a pre-determined day, to be agreed locally with the microbiology laboratory.

- 4) Complete a weekly denominator form (See **Appendix C**) on the date that the weekly CRE screening swabs are taken for each of the four weeks of the study and return the completed denominator form to HPSC at the end of the study period.
- 5) Agree locally the nominated person who will be responsible for the completion of the enhanced patient surveillance form (in conjunction with the named local microbiology laboratory study contact) for every patient from whom a confirmed carbapenemase-producing CRE is isolated. Agree locally the nominated person who will return the completed enhanced surveillance form to HPSC at the end of the study period and retain a photocopy of the form for local records. See **Appendix E** for enhanced patient surveillance form.
- 6) Notify the relevant department of public health in the event that CRE is confirmed.

### **Summary of role of the participating microbiology laboratory:**

- 1) Agree to participate in the pilot four week study.
- 2) Nominate a local microbiology laboratory study contact.
- 3) Perform CRE screen in accordance with this pilot study laboratory protocol, on weekly rectal screening swabs taken in the critical care unit on a pre-determined day, to be agreed locally.
- 4) Complete a weekly form regarding the total number of CRE screening swabs received by the microbiology laboratory from the critical care unit(s) for each of the four weeks of the study (See **Appendix D**), the number of queried carbapenemase-producing isolates [isolated from both CRE rectal screening swabs and any clinical specimens taken from patients in critical care unit(s)] referred to the reference laboratory, Galway, during the study period and the number of confirmed carbapenemase-producing isolates identified during the study and return the completed form to HPSC at the end of the study period.
- 7) Agree locally, the nominated person who will be responsible for the completion of the enhanced patient surveillance form (in conjunction with the named local critical care unit study contact) for every patient from whom a confirmed carbapenemase-

producing CRE is isolated. Agree locally the nominated person who will return the completed enhanced surveillance form to HPSC at the end of the study period and retain a photocopy of the form for local records. See **Appendix E** for enhanced patient surveillance form.

- 5) Notify the relevant department of public health in the event that CRE is confirmed.

## **CRE Screening Protocol for Participating Critical Care Units**

Each participating critical care unit will be requested to perform a rectal swab on every patient admitted to the critical care unit on a pre-determined day weekly for each of the four weeks of the study.

The CRE screening protocol for the participating unit will depend upon existing practices within that unit:

**Option 1: Unit does not currently undertake any rectal screening swabs for surveillance of vancomycin resistant enterococci (VRE) or carbapenem resistant Enterobacteriaceae (CRE)**

The participating unit will be requested to liaise with the local microbiology laboratory in advance of the start date to decide locally on a suitable day for performing rectal screening swabs for each of the four weeks of this pilot study. Once a suitable day has been agreed locally, every patient present on the unit on the appointed day will have a rectal screening swab taken, for four consecutive weeks (e.g., every Tuesday). The rectal swab should be legibly labelled by the critical care unit staff member with the relevant patient details that would normally accompany any patient specimen sent to the microbiology laboratory:

- Patient name
- Date of birth – DD/MM/YY
- Hospital/chart number (unique patient number used locally)
- Admitting consultant

- Patient location - ICU
- Date swab taken
- Site from which swab taken – rectal swab
- Requested test - **CRE screen**

The specimen should then be transported to the local microbiology laboratory with an accompanying request form/computerised order for a CRE screen to be performed on the swab. The microbiology laboratory should then process the swab in accordance with the specimen processing guideline provided with this protocol.

### **Option 2: Unit currently undertakes weekly rectal screening swabs for surveillance of VRE**

If an individual critical care unit already has a weekly rectal screening policy in place for VRE, the VRE rectal screening swab can be simultaneously tested by the laboratory for CRE and there should be no need to take a second rectal swab for CRE testing. The individual critical care unit should liaise with the local microbiology laboratory in advance of the start date to ensure systems are in place in the microbiology laboratory to ensure that rectal swabs received from the unit are simultaneously processed for VRE and CRE. The rectal swab should be legibly labelled by the critical care unit staff member with the relevant patient details that would normally accompany any patient specimen sent to the microbiology laboratory:

- Patient name
- Date of birth – DD/MM/YY
- Hospital/chart number (unique patient number used locally)
- Admitting consultant
- Patient location - ICU
- Date swab taken



- Site from which swab taken – rectal swab
- Requested test - **VRE AND CRE screen**

The specimen should then be transported to the local microbiology laboratory with an accompanying request form/computerised order for a VRE AND CRE screen to be performed on the swab. The microbiology laboratory should then process the swab in accordance with the specimen processing guideline provided with this protocol.

### **Option 3: Unit currently undertakes weekly rectal screening swabs for surveillance of CRE**

If an individual critical care unit already has a weekly rectal screening policy in place for CRE, there will be no need to make any changes to the existing policy. Staff in the critical care unit should continue to follow the local weekly CRE screening policy on the predetermined day per week. The microbiology laboratory should then process the swab in accordance with the specimen processing guideline provided with this protocol.

#### **Admission rectal screening swabs**

Every critical care unit participating in this study will be requested to perform a weekly rectal screening swab for CRE carriage on a pre-determined day, to be agreed locally with the microbiology laboratory. If an individual unit already has an existing policy of performing rectal screening swabs on the day of patient admission to the unit (e.g., CRE screen or both VRE and CRE screen) in addition to weekly rectal screening swabs, the microbiology laboratory should also process the admission rectal screening swabs for CRE in accordance with the specimen processing guideline provided with this protocol.

For the purposes of calculating the denominator for the study, the denominator form (See **Appendix C**) will be completed based only on the weekly screening swabs taken in the unit for that week.

The nominated study contact for each participating critical care unit will be requested to complete the weekly CRE screening swab denominator form on the date that the weekly CRE screening swabs are taken for each of the four weeks of the study. The denominator

form should be retained in the unit until the final weekly screening swab data is entered on the form. The completed denominator form should be photocopied and retained for local records and the original completed form returned to:

Mr Stephen Murchan, National CRE Project Data Manager, Health Protection Surveillance Centre, 25-27 Middle Gardiner St, Dublin 1.

## **Protocol for Participating Microbiology Laboratories**

Each participating microbiology laboratory will be requested to perform a CRE screen on a rectal swab taken from every patient present in the critical care unit on a pre-determined day weekly for each of the four weeks of the study.

The protocol for the participating laboratory will depend upon existing CRE screening practices within the corresponding critical care unit:

**Option 1: Unit does not currently undertake any rectal screening swabs for surveillance of vancomycin resistant enterococci (VRE) or carbapenem resistant Enterobacteriaceae (CRE)**

The local microbiology laboratory and participating critical care unit(s) should liaise with each other in advance of the study start date to decide locally on a suitable day for performing rectal screening swabs for each of the four weeks of this pilot study. Once a suitable day has been agreed locally, every patient present in the unit on the appointed day will have a rectal screening swab taken, for four consecutive weeks (e.g., every Tuesday). The rectal swab should be legibly labelled by the critical care unit staff member with the relevant patient details that would normally accompany any patient specimen sent to the microbiology laboratory:

- Date swab taken
- Site from which swab taken – rectal swab
- Requested test - **CRE screen**

The microbiology laboratory should then process the swab in accordance with the specimen processing guideline provided with this protocol.

### **Option 2: Unit currently undertakes weekly rectal screening swabs for surveillance of VRE**

If an individual critical care unit already has a weekly rectal screening policy in place for VRE, the VRE rectal screening swab can be simultaneously tested by the laboratory for CRE and there should be no need to take a second rectal swab for CRE testing. The individual critical care unit should liaise with the local microbiology laboratory in advance of the start date to ensure systems are in place in the microbiology laboratory to ensure that rectal swabs received from the unit are simultaneously processed for VRE and CRE. The rectal swab should be legibly labelled by the critical care unit staff member with the relevant patient details that would normally accompany any patient specimen sent to the microbiology laboratory:

- Date swab taken
- Site from which swab taken – rectal swab
- Requested test - **VRE AND CRE screen**

The microbiology laboratory should then process the swab in accordance with the specimen processing guideline provided with this protocol.

### **Option 3: Unit currently undertakes weekly rectal screening swabs for surveillance of CRE**

If an individual critical care unit already has a weekly rectal screening policy in place for CRE, there will be no need to make any changes to the existing policy. Staff in the critical care unit should continue to follow the local weekly CRE screening policy on the pre-determined day per week and the microbiology laboratory should process the swab in accordance with the specimen processing guideline provided with this protocol.

## Admission rectal screening swabs

Every critical care unit participating in this study will be requested to perform a weekly rectal screening swab for CRE carriage on a pre-determined day, to be agreed locally with the microbiology laboratory. If an individual critical care unit already has an existing policy of performing rectal screening swabs on the day of patient admission to the unit (e.g., CRE screen or both VRE and CRE screen), in addition to weekly rectal screening swabs thereafter, the microbiology laboratory should also process the admission rectal screening swabs for CRE in accordance with the specimen processing guideline provided with this protocol.

## CRE Screening Swab Specimen Processing Guideline

The recommended laboratory protocol for detection of carbapenemase-producing CRE in this pilot study is adapted from that recommended by the US Centers for Disease Control and Prevention, which can be accessed in full [here](#) and is summarised below.

**Summary of laboratory protocol: In addition to each patient sample to be processed with the weekly screen, it is advised that a positive control (NCTC 13438) and a negative control (ATCC 25922) are set up with each of the four weekly CRE screening batches.**

### DAY 1

**Step 1:** Aseptically place a 10µg disc containing ertapenem AND a 5µg disc containing vancomycin into 5ml of trypticase soy broth (TSB) labelled as per local laboratory protocol.

**Step 2:** Immediately inoculate the TSB (containing antimicrobial discs) with a rectal screening swab.

**Step 3:** Incubate aerobically overnight at 35 ±2°C.

### DAY 2

**Step 1:** Vortex the TSB bottle.

**Step 2:** Subculture 100µl of the incubated TSB culture onto MacConkey agar plate.

**Step 3:** Streak out the inoculated plates.

**Step 4:** Aseptically, place a 10µg meropenem disc on the streaked out MacConkey agar plate.

**Step 5:** Incubate aerobically overnight at 35±2°C.

### **DAY 3**

**Step 1:** Examine MacConkey plate for growth up to the meropenem disc or a reduced zone of inhibition around the meropenem disc. A zone of inhibition of less than 27mm around the meropenem disc should be taken as the cut-off for performing further work on the isolate.

**Step 2:** Note, if there is more than one colony morphology present, this may represent different species of Enterobacteriaceae. It may be necessary to subculture different colony types to MacConkey plates for purity. If there are no suspect colonies and no reduced zone of inhibition, report swab result as “CRE not isolated” or according to current local laboratory protocol.

**Step 3:** Select suspect colony for full identification and susceptibility testing using local methodology for organism identification and antimicrobial susceptibility testing.

**Step 4:** In addition to local methodology for identification and antimicrobial susceptibility testing, set up “E-tests” to both ertapenem and meropenem against suspected colony .

**Step 5:** Inform clinical microbiologist and infection prevention and control team of the possible isolation of Enterobacteriaceae with reduced susceptibility to carbapenems, pending further results.

### **DAY 4**

**Step 1:** Read organism identification and susceptibility results in accordance with local laboratory protocol.

**Step 2:** Read “E-test” MIC results in accordance with local laboratory protocol.

**Step 3:** If organism identification belongs to Enterobacteriaceae family and carbapenem susceptibility results suggest intermediate susceptibility or resistance, according to local

interpretive criteria inform clinical microbiologist and infection prevention and control team of latest results.

**Step 4:** Set up two slopes of the suspect isolate – Retain one slope locally.

**Step 5:** Send the second slope to the reference laboratory, Galway along with a photocopy of completed page 3 of enhanced surveillance form – Laboratory information (See **Appendix E** for enhanced patient surveillance form and **Appendix G** for instructions on specimen transport).

The CDC protocol for CRE detection refers to the Modified Hodge Test (MHT). This test has low specificity for carbapenemase detection and can be difficult to interpret. The recommendation for this study is that any suspected Enterobacteriaceae isolate with intermediate susceptibility or resistance to carbapenems should be referred to the reference laboratory, Galway, regardless of the MHT results.

The nominated study contact for each participating microbiology laboratory will be requested to complete a weekly microbiology laboratory form (See **Appendix D**). This form contains details regarding the total number of CRE screening swabs received by the microbiology laboratory from the critical care unit(s) for each of the four weeks of the study, the number of queried carbapenemase-producing isolates [isolated from both CRE rectal screening swabs and any clinical specimens taken from patients in critical care unit(s)] referred to the reference laboratory, Galway during the study period and the number of confirmed carbapenemase-producing isolates identified during the study and return the completed form to HPSC at the end of the study period. The microbiology laboratory form should be retained in the laboratory until the final weekly screening swab data is entered on the form. The completed laboratory form should be photocopied and retained for local records and the original completed form returned to:

Mr Stephen Murchan, National CRE Project Data Manager, Health Protection Surveillance Centre, 25-27 Middle Gardiner St, Dublin 1.

## **Criteria for Referral of Suspected Carbapenemase-producers to Reference Laboratory, Galway**

Any suspected carbapenemase-producing Enterobacteriaceae isolate should be referred to the reference laboratory, Galway, for confirmation of carbapenemase production and the underlying resistance mechanism.

- Suspect isolates identified from rectal screening swabs should be referred
- Suspect isolates identified from clinical specimens (e.g., sputum, blood cultures, urine, wound swabs etc.) should be referred

In the event that there is any local concern regarding an Enterobacteriaceae isolate, the microbiology laboratory is advised to refer that isolate to the reference laboratory, Galway. This may particularly be the case for microbiology laboratories who are undertaking CRE screening for the first time.

The CDC protocol for CRE detection refers to the Modified Hodge Test (MHT). This test has low specificity for carbapenemase detection and can be difficult to interpret. The recommendation for this study is that any suspected Enterobacteriaceae isolate with intermediate susceptibility or resistance to carbapenems should be referred to the reference laboratory, Galway, regardless of the MHT results.

# Instructions for Completion of Enhanced Patient Surveillance Form (version 1.5)

## Form completed by:

Please provide the name, work telephone number (direct office extension) and work e-mail address of the person who has completed this enhanced surveillance form

## Section 1: Demographic Information

1. **Hospital Code:** This is a unique code assigned to every hospital by the Health Protection Surveillance Centre (HPSC) also known as the EARS-Net code. The code facilitates identification of the hospital by HPSC upon receipt of the completed enhanced surveillance form.
2. **Patient ID:** This is a unique number (e.g., medical record number or chart number) which permits the referring hospital to identify the patient in the event that further clarification is required. The patient ID has no meaning outside of the referring hospital
3. **Age:** Infants admitted to neonatal intensive care units (NICU) are excluded from this study. Neonates (0-1 month) admitted to paediatric intensive care units (PICU) are included in this study. For neonates, provide the age in days (e.g., 24D). For children aged 1-12 months – provide the age in months (e.g., 11M). For all aged >12 months, provide the age in years (e.g., 88Y)
4. **Sex:** Tick box for patient's gender. M = Male, F = Female, Unk = Gender unknown. Please make every effort to provide complete data
5. **Date of hospital admission:** Please provide the date the patient was admitted to your hospital. If the patient was transferred to your hospital from elsewhere, please provide the date of admission to your hospital as the date of hospital admission
6. **Date of ICU admission:** Please provide the date the patient was admitted to your critical care unit. If the patient was admitted directly to critical care, the date of hospital admission and date of ICU admission will be the same date.
7. **Admitted to this healthcare facility (HCF) from:** Tick the most appropriate box
  - a. Home – The patient's own home



- b. Other hospital – The patient was transferred to this HCF from another hospital
- c. Long-term care facility – The patient was admitted to this HCF from a long-term care facility (e.g. residential facility)
- d. Nursing home – The patient was admitted to this HCF from a nursing home
- e. Other – The patient was admitted to this HCF from somewhere not fitting the definitions of a-d above

## Section 2: Clinical Information

1. **At the time of CRE detection, was the patient already known to be colonised or infected with another HCAI pathogen?** Please tick appropriate box: Yes or No
2. If the response is Yes, the patient was already colonised or infected with another HCAI pathogen, **Please indicate the organism(s)** with which the patient was colonised or infected by ticking the appropriate box(es);
  - a. Meticillin resistant *Staphylococcus aureus* (MRSA)
  - b. Vancomycin resistant enterococcus (VRE)
  - c. Extended spectrum Beta-lactamase (ESBL)-producing Enterobacteriaceae
  - d. Other organism (e.g. *Clostridium difficile*, multi-drug resistant *Acinetobacter sp*)
3. **Was this patient transferred to this healthcare facility (HCF) from a hospital abroad?** Please tick the appropriate box: Yes or No
4. If the response is Yes, the patient was transferred to this HCF from a hospital abroad, please **provide the name of the country from which the patient was repatriated**
5. **Does the patient have a history of travel abroad in the 12 months prior to hospitalisation?** Please tick the appropriate box: Yes or No or Unknown. Please make every effort to provide complete data
6. If the response is Yes, the patient does have a history of travel abroad in the 12 months prior to hospitalisation, **please provide the name(s) of the country(ies) visited.** Up to two countries can be included here. In the event that the patient has visited more than two countries, provide the names of the two countries most recently visited. There is more space to write at the bottom of Page 2 – Section 4: Other Relevant Clinical Information if further travel information has been collected

7. If the response to travel abroad in the past 12 months is Yes, **please state the reason(s) for travel abroad:**
- a. Holiday
  - b. Work
  - c. Medical intervention/procedure/care
  - d. Visiting friends and relatives
  - e. Other reason (Please specify other reason in box provided)
  - f. Unknown reason (Please make every effort to provide complete data)
8. **Risk factors for CRE:** Please tick box(es) that apply to this patient;
- a. Hospitalisation in the past 12 months
  - b. ICU admission in the last 12 months
  - c. Surgery in the last 6 months
  - d. Immunocompromised (includes patients with malignancy, solid organ or haematopoietic stem cell transplantation, immunosuppressive therapy, including chronic steroid use, HIV infection or asplenia)
  - e. Diabetes mellitus
  - f. End-stage renal disease or renal replacement therapy (haemodialysis or peritoneal dialysis)
  - g. Chronic lung disease
  - h. Chronic liver disease
  - i. Recurrent urological problems
  - j. None of the above risk factors apply to this patient
  - k. Unknown risk factors (Please make every effort to provide complete data)
9. **Isolation of CRE from this patient represents:** Please tick the appropriate box.
- a. Infection
  - b. Colonisation

In the event that the initial suspected CRE isolate referred to the reference laboratory, Galway for confirmation of carbapenemase production, is from a rectal screening swab, then it is likely that the isolate represents colonisation. In the event that the initial suspected CRE isolate referred to the reference laboratory, Galway for confirmation of carbapenemase production, is from a clinical specimen (e.g., wound swab or CVC tip), the admitting clinician, critical

care clinician and microbiologist will be required to decide whether or not the detection of CRE from the clinical sample reflected colonisation or infection. In the event that antimicrobial therapy is administered to target the CRE, then it is likely that the isolate represents infection. If the initial specimen was felt to represent colonisation but the patient subsequently developed infection due to the CRE, then it is advised to tick the box that states that isolation of CRE from this patient represents Infection.

**10. If Yes to infection, the likely source is:** Please tick the appropriate box that represents the most likely source of the patient's CRE infection. There is more space to write at the bottom of Page 2 – Section 4: Other Relevant Clinical Information if further information regarding source of infection is available.

- a. Bacteraemia (positive blood cultures for CRE) without an obvious focus/source
- b. Central nervous system (e.g., meningitis, intracranial abscess)
- c. Respiratory tract (e.g., healthcare-associated pneumonia, ventilator-associated pneumonia, lung abscess, empyema)
- d. Urinary tract (e.g., UTI, Catheter-associated UTI, pyelonephritis, prostatic abscess)
- e. Intra-abdominal (e.g., peritonitis, ascending cholangitis, cholecystitis, liver abscess, intraabdominal abscess)
- f. Genital tract (e.g., choramnionitis, abscess)
- g. Skin/soft tissue (e.g., cellulitis, gangrene)
- h. Surgical wound (e.g., superficial incisional, deep incisional, organ space wound infection)
- i. Infection of device or prosthetic material (e.g., central venous catheter-related infection, prosthetic joint infection, prosthetic cardiac valve infection, intracardiac device infection)
- j. Other source not listed above – please state other source in box provided

**11. Outcome:** Please tick the appropriate box that applies to the patient's outcome on the date that the enhanced surveillance form is completed.

- a. The patient has survived and remains an inpatient in ICU – Please tick if this is the appropriate box

- b. The patient has survived and has been discharged from ICU – If this is the appropriate box, please provide the date of discharge from ICU
- c. The patient died in ICU – If this is the appropriate box, please provide the date of death

### **Section 3: Antimicrobial Information**

#### **1. Antimicrobials administered during this admission PRIOR to CRE being detected**

**from this patient:** Please tick the appropriate box(es) to demonstrate the antimicrobial classes that the patient would have been exposed to during this hospital admission, prior to being identified as being colonised or infected with CRE. If the patient was transferred to ICU from the ward, please also include any antimicrobial classes administered prior to ICU admission.

- a. Beta-lactam + Beta lactamase inhibitor combination (e.g., co-amoxiclav, piperacillin-tazobactam)
- b. Cephalosporin (e.g., cefuroxime, cefotaxime, ceftriaxone, ceftazidime)
- c. Meropenem
- d. Ertapenem
- e. Aztreonam
- f. Fluoroquinolone (e.g., ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin)
- g. Gentamicin
- h. Tobramycin
- i. Amikacin
- j. Tigecycline
- k. Colistin
- l. Chloramphenicol
- m. Co-trimoxazole or trimethoprim-sulfamethoxazole

#### **2. If the isolation of CRE from this patient, represents infection; Please tick the appropriate box for the agent(s) used to treat the infection and the number of days each agent was administered for:**

- a. Meropenem & number of days of therapy
- b. Ertapenem & number of days of therapy
- c. Aztreonam & number of days of therapy

- d. Fluoroquinolone (e.g., ciprofloxacin, ofloxacin) & number of days of therapy
  - e. Gentamicin & number of days of therapy
  - f. Tobramycin & number of days of therapy
  - g. Amikacin & number of days of therapy
  - h. Tigecycline & number of days of therapy
  - i. Colistin & number of days of therapy
  - j. Chloramphenicol & number of days of therapy
  - k. Co-trimoxazole or trimethoprim-sulfamethoxazole & number of days of therapy
3. In the event that a patient in critical care develops symptoms or signs suggestive of infection, antimicrobial therapy is usually initiated empirically pending the results of microbiological culture and susceptibility. **Did the initial choice of empiric antimicrobial therapy provide cover for the CRE isolated from this patient?** Please tick the appropriate box: Yes or No
4. If the response is No, the initial choice of empiric antimicrobial therapy did not provide activity against the CRE isolated from this patient, **please provide the number of days that elapsed before the provisional antimicrobial susceptibility results were available to guide appropriate antimicrobial therapy.** This may be calculated by subtracting the date of initiation of empiric antimicrobial therapy from the date that provisional (local microbiology laboratory) antimicrobial susceptibility results for the CRE became available to guide a change in antimicrobial therapy to an agent that would be expected to provide appropriate activity against CRE

#### **Section 4: Other Relevant Clinical Information**

This section provides a blank space for writing in any additional relevant clinical information regarding the isolation of CRE from this patient. In the event that the patient has a history of foreign travel to more than two countries in the past 12 months, details of the 3<sup>rd</sup> most recent and subsequently visited countries can be provided in this section. If there is more detailed clinical information regarding the clinical source of the patient's CRE infection, such information can be provided in this section. If there is no additional relevant clinical information, then Section 4 may be left blank by the individual completing the form.

### **Page 3 of 3: National Pilot Study of Carbapenemase-Producing CRE in ICU**

Page 3 should be completed as far as possible, by the named individual responsible for completing the enhanced surveillance form or the named individual from the microbiology laboratory. This person is asked to provide their name, work e-mail address and work telephone number (direct office extension) at the top of Page 3. This information is very important as it is essential that the reference laboratory, Galway can efficiently and rapidly communicate any positive results with a named person in the referring laboratory. It is important that the named person understands the significance of any positive result being communicated and understands what subsequent internal communication and infection prevention and control actions are required in the event that the reference laboratory, Galway provides a provisional verbal result confirming isolation of a carbapenemase-producing CRE.

In addition to providing enhanced surveillance information, Page 3 of the enhanced surveillance form contains the details required by the reference laboratory, Galway for processing the suspected carbapenemase-producing CRE isolate. Therefore, during this study, Page 3 of the form, once complete, can be photocopied and the photocopy of Page 3 sent to the reference laboratory, Galway along with the suspected carbapenemase-producing CRE isolate (See instructions for specimen transport to the reference laboratory, Galway: **Appendix G**). The original enhanced surveillance form (Pages 1, 2 and 3) should be retained in the referring hospital, by the individual responsible for final completion of the form pending further results from the reference laboratory, Galway. In the event that the reference laboratory, Galway confirm the presence of a carbapenemase-producing CRE in the referred specimen, the named individual in the referring hospital laboratory will be contacted via telephone with the verbal positive result. If the named individual is not contactable, the reference laboratory, Galway will telephone the verbal positive result to the Consultant Microbiologist on-call for the referring hospital, via the hospital switchboard. The e-mail address of the named individual will be used in the event that the reference laboratory, Galway has a non-urgent query regarding the referred suspect isolate or the accompanying copy of Page 3 of the enhanced surveillance form. The reference laboratory, Galway will produce a written report and the report will be posted to the named individual on Page 3 of the enhanced surveillance form.

Upon receipt of the written confirmation of carbapenemase-producing CRE, the referring laboratory can now complete the original enhanced surveillance form, ticking the box that states the CRE is confirmed and ticking the box that represents the resistance gene detected by the reference laboratory, Galway. At this point, the named individual responsible for completing the enhanced surveillance form should review the entire form and ensure that as far as possible the data provided is as complete and as accurate as possible, including patient outcome. The completed original enhanced surveillance form Pages 1, 2 and 3, should be returned to HPSC with all other requested documentation at the end of the study period, via registered post (See instructions for return of enhanced surveillance forms and study forms). The relevant department of public health should also be informed in the event that a patient is confirmed to be colonised or infected with a carbapenemase-producing CRE.

### **Section 5: Laboratory Information**

It is important to note that for some hospitals there may be a slight difference between the assigned laboratory code and hospital code. The reason for this is that a regional microbiology laboratory may process microbiology specimens for several hospitals in the region. Therefore, there will be one regional microbiology laboratory code, identifying the laboratory that processed the specimens but the hospital code will be slightly different, identifying the hospital to which the patient was admitted and from where the microbiology specimen was sent to the regional laboratory.

1. **Laboratory Code:** This is a unique code assigned to every microbiology laboratory by the Health Protection Surveillance Centre (HPSC) also known as the EARS-Net code. The code facilitates identification of the referring laboratory by HPSC upon receipt of the completed enhanced surveillance form
2. **Hospital Code:** This is a unique code assigned to every hospital by the Health Protection Surveillance Centre (HPSC) also known as the EARS-Net code. The code facilitates identification of the hospital by HPSC upon receipt of the completed enhanced surveillance form
3. **Patient ID:** This is a unique number (e.g., medical record number or chart number) which permits the referring hospital to identify the patient in the event that further

clarification is required. The patient ID has no meaning outside of the referring hospital

4. **Patient Date of Birth:** Along with the Patient ID, the patient date of birth permits the referring hospital to identify the patient in the event that further clarification is required
5. **Sex:** Tick box for patient's gender. M = Male, F = Female, Unk = Gender unknown. Please make every effort to provide complete data
6. **Specimen Number:** This is the unique specimen number assigned by the referring laboratory which enables easy identification of that specimen and linkage of that specimen to other specimens received from that patient. The specimen number has no meaning outside of the referring laboratory but permits the referring laboratory to append to that specimen report any subsequent confirmatory test results received from the reference laboratory, Galway
7. **Specimen Date:** This is the date that the specimen was collected from the patient
8. **Specimen Type:** Please tick the appropriate box for the specimen type from which the suspected carbapenemase-producing CRE was identified.
  - a. Non-sterile site - Rectal screening swab
  - b. Sterile site - Blood culture
  - c. Sterile site - Cerebrospinal fluid (CSF)
  - d. Other Sterile site (e.g., urine, joint fluid, ascitic fluid, bronchoalveolar lavage taken from a patient without pre-existing lung disease) – Please state sterile site specimen taken from in box provided
  - e. Other non-sterile site (e.g. surgical wound swab, leg ulcer swab, catheter specimen urine) – Please state sterile site specimen taken from in box provided
9. **Referring laboratory's identification of the organism** suspected to be a carbapenemase-producing CRE. Please tick the appropriate box or write the name of the organism identified at the referring laboratory. Please note that *Pseudomonas sp* and *Acinetobacter sp* are NOT regarded as belonging to the Enterobacteriaceae.
  - a. *Escherichia coli*
  - b. *Klebsiella pneumoniae*



- c. Other Enterobacteriaceae (e.g., *Enterobacter sp*, *Citrobacter sp*, *Proteus sp* etc)

**10. Antimicrobial susceptibility testing (AST) method in use in the referring laboratory:**

Please tick the appropriate box:

- a. European Committee on Antimicrobial Susceptibility Testing (EUCAST)
- b. Clinical and Laboratory Standards Institute (CLSI)
- c. British Society for Antimicrobial Chemotherapy (BSAC)

**11. Antimicrobial susceptibility testing results recorded by the referring laboratory**

(AST results are interpreted based on the local AST method in use by the laboratory).

For each antimicrobial provided, please tick the appropriate box for the AST results recorded by your laboratory for that agent. If your laboratory does not perform AST for a particular antimicrobial, leave blank the results for that antimicrobial

- a. Meropenem: R = Resistant, I = Intermediate susceptibility, S = Full susceptibility. If I or R, the minimum inhibitory concentration (MIC) for the isolate against meropenem should be recorded
- b. Imipenem: R, I or S. If I or R, the minimum inhibitory concentration (MIC) for the isolate against imipenem should be recorded
- c. Ertapenem: R, I or S. If I or R, the minimum inhibitory concentration (MIC) for the isolate against ertapenem should be recorded
- d. Third generation cephalosporin (e.g., cefotaxime, ceftriaxone or ceftazidime):  
R, I, S
- e. Aztreonam: R, I or S
- f. Gentamicin: R, I or S
- g. Tobramycin: R, I or S
- h. Amikacin: R, I or S
- i. Fluoroquinolone (e.g., ciprofloxacin or ofloxacin): R, I or S
- j. Tigecycline: R, I or S
- k. Colistin: R, I or S
- l. Chloramphenicol: R, I or S
- m. Co-trimoxazole or trimethoprim-sulfamethoxazole: R, I or S

**12. Is this case part of a suspected CRE outbreak?** (Applies whether isolate represents colonisation or infection). Please tick the appropriate box Yes or No

**13. Was this suspected carbapenemase-producing CRE referred to the reference laboratory, Galway for confirmation of carbapenemase production?** Please tick the appropriate box Yes or No. It is recommended that when an Enterobacteriaceae isolate has reduced susceptibility to carbapenem antimicrobials (exceptions are: *Enterobacter cloacae* and ertapenem, *Proteus mirabilis* or *Morganella morganii* and imipenem), the isolate should always be referred to a reference laboratory for confirmation of resistance to carbapenems and confirmation of the mechanism of resistance

**14. The case classification of this carbapenemase-producing CRE is:** Please tick the appropriate box that applies on the date the enhanced surveillance form is being returned to HPSC. In the event that during the study period, a referring laboratory, in conjunction with the local infection prevention and control team suspects that there may be an outbreak of suspected CRE (observed cases exceeds expected cases and/or  $\geq 2$  epidemiologically-linked cases), pending reference laboratory confirmation, then that suspected outbreak of infection should be notified to the relevant department of public health as soon as possible and the completion of enhanced surveillance forms expedited. The case classification "Probable" can be selected for isolates where reference laboratory confirmation is still pending.

- a. Confirmed = Any person with reference laboratory confirmation of a carbapenemase-producing CRE
- b. Probable = Any person with phenotypic laboratory evidence of a carbapenem-non-susceptible Enterobacteriaceae, pending confirmation by a reference laboratory. This option should only be selected in the event of a suspected CRE outbreak, which should be notified as soon as possible to the relevant department of public health

**15. If confirmed, please state resistance gene:** Once the reference laboratory, Galway has confirmed carbapenemase production by the suspected isolate, a verbal provisional result will be telephoned to the referring laboratory. This will be followed by a written report addressed to the named individual on Page 3 of the enhanced surveillance form. Once the confirmed report has been received, the referring laboratory can complete the original enhanced surveillance form, ticking the appropriate box for resistance gene detected by the reference laboratory, Galway:

- a. VIM
- b. KPC
- c. NDM
- d. IMP
- e. OXA
- f. Other: Please provide details in box provided

### **Section 6: Other Relevant Laboratory Information**

This section provides a blank space for recording any other relevant laboratory information regarding the isolation of a suspected carbapenemase-producing CRE from this patient. For example, if the suspected isolate was identified in multiple clinical and screening samples but only one sample was sent to the reference laboratory, this could be recorded here.

## **Checklist at Study Completion**


### **A) Participating ICUs**

1. Completed weekly ICU denominator form to be photocopied; retain one copy locally and return the original completed form to HPSC.
2. Liaise with microbiology laboratory nominated contact regarding any confirmed positive CRE isolates from patients in critical care unit during the study period. Ensure that for each CRE-positive patient, an enhanced surveillance form is completed in full. Photocopy the form(s); retain one copy locally and return the original completed form(s) to HPSC: Mr Stephen Murchan, National CRE Project Data Manager, Health Protection Surveillance Centre, 25-27 Middle Gardiner St, Dublin 1.
3. Ensure that the relevant department of public health has received a clinical notification of each CRE positive patient detected during the study period.

## **B) Participating Microbiology Laboratories**

1. Completed weekly microbiology laboratory form to be photocopied; retain one copy locally and return the original completed form to HPSC via registered post.
2. Liaise with critical care unit nominated contact regarding any confirmed positive CRE isolates from patients in critical care unit during the study period. Ensure that for each CRE-positive patient, an enhanced surveillance form is completed in full. Photocopy the form(s); retain one copy locally and return the original completed form(s) to HPSC via registered post: Mr Stephen Murchan, National CRE Project Data Manager, Health Protection Surveillance Centre, 25-27 Middle Gardiner St, Dublin 1.
3. Ensure that the relevant department of public health has received a laboratory notification of each CRE positive patient detected during the study period.

**Appendix A – Pre-study Questionnaire: To be completed by all invited participants regardless of whether or not the hospital agrees to participate in the study**

 <p><b>NATIONAL PILOT STUDY OF CARBAPENEMASE-PRODUCING CRE IN CRITICAL CARE UNITS – PRE-STUDY QUESTIONNAIRE</b></p>	
Name of your hospital	
Number of critical care units in your hospital	
Number of critical care beds open in your hospital	
Is rectal screening for VRE routinely performed in your critical care unit(s)? If yes, tick appropriate box:	Yes <input type="checkbox"/> No <input type="checkbox"/> On admission to unit <input type="checkbox"/> Weekly screen <input type="checkbox"/>
Is rectal screening for Carbapenem-resistant Enterobacteriaceae (CRE) routinely performed in your critical care unit(s)? If yes, tick appropriate box:	Yes <input type="checkbox"/> No <input type="checkbox"/> On admission to unit <input type="checkbox"/> Weekly screen <input type="checkbox"/>
To date, has the microbiology laboratory undertaken CRE screening on any patient sample from any clinical location in the hospital?	Yes <input type="checkbox"/> No <input type="checkbox"/>

<p>Does the microbiology laboratory routinely perform full identification and susceptibility testing on all Enterobacteriaceae isolated from patients admitted to the critical care unit?</p>	<p>Yes <input type="checkbox"/> No /only on request <input type="checkbox"/></p>
<p>Does the microbiology laboratory routinely test susceptibility to a carbapenem (meropenem, imipenem or ertapenem) for all Enterobacteriaceae undergoing antimicrobial susceptibility testing</p>	<p>Yes <input type="checkbox"/> No <input type="checkbox"/></p>
<p>Following local consultation between critical care unit(s) and microbiology laboratory, does your hospital agree to participate in the national 4 week pilot CRE screening in ICU project?</p> <p>If no, please provide reason why the hospital is not in a position to participate</p>	<p>Yes <input type="checkbox"/> No <input type="checkbox"/></p>
<p>If yes, please provide contact details (name, work e-mail address and work telephone number [direct extension]) of two nominated local contacts for the study</p>	<p><b>1.Critical care unit contact</b></p> <p>Name:</p> <p>E-mail:</p> <p>Tel:</p> <p><b>2: Microbiology laboratory contact</b></p> <p>Name:</p> <p>E-mail:</p> <p>Tel:</p>

\*Completed questionnaire can be e-mailed to [karen.burns1@hse.ie](mailto:karen.burns1@hse.ie) or returned via post to: Dr. Karen Burns. Health Protection Surveillance Centre, 25-27 Middle Gardiner St, Dublin 1.

## Appendix B – Staff information

### What is CRE?

CRE stands for Carbapenem resistant Enterobacteriaceae. This term is used to describe a group of well-known bacteria, such as *E. coli* and *Klebsiella pneumoniae*, which have managed to develop resistance to powerful antibiotics belonging to the carbapenem group. These antibiotics, such as meropenem and ertapenem, have traditionally been used to treat infection in patients who are seriously ill or who are suspected to have infection due to resistant bacteria. Historically, these antibiotics have been very effective treatments. In recent years there have been increasing numbers of reports from many countries, such as Greece, Israel, Eastern USA, India and Pakistan of Enterobacteriaceae that have developed resistance to meropenem and CRE bacteria are now very common in those countries. Not only do these bacteria carry enzymes that break down the meropenem, rendering it useless. They also carry enzymes that break down many other classes of antibiotics. CRE bacteria are frequently resistant to almost all available antibiotic therapies and there have been reports that patients who develop invasive infection due to CRE bacteria are more likely to die from the infection due to a lack of effective therapy.

*E. coli*, *Klebsiella pneumoniae* and related organisms, belong to the family Enterobacteriaceae, which describes bacteria that commonly live in the enteric tract or bowel. These bacteria are often called colonising flora or bystanders, and do no harm to the patient. Critically ill patients are often immunocompromised or vulnerable to infection because of breaches in the normal skin barrier or insertion of invasive devices (surgical wounds, central venous catheters, endotracheal tubes etc.). Such patients are at risk of invasive

infection due to colonising bacteria. If the colonising bacteria are CRE, then the usual choices of antimicrobial therapy are ineffective and it may take several days for the laboratory to be in a position to tell what antibiotics are effective. Like any bacteria, CRE could potentially be transferred between patients in the event that there is sub-optimal compliance with standard precautions, including hand hygiene and personal protective equipment use. Because this bug is so resistant and there are hardly any treatments, it is vitally important to ensure that it cannot spread between patients.

### **How can CRE be detected?**


Because CRE is usually carried in the patient's bowel, a rectal swab can be taken and tested in the microbiology laboratory to detect asymptomatic carriage of CRE. Sometimes, the CRE may be detected in a clinical sample from the patient, such as a catheter specimen of urine or a wound swab or in serious cases, from blood cultures. Currently, our national guidelines recommend that if a person has a history of hospital admission abroad in the past year or admission to a hospital in the mid-west of Ireland in the past year, then that patient should have a rectal swab taken to rule out CRE carriage. It is very important to know if a patient is a CRE carrier as this alerts healthcare workers to the need to apply additional transmission based precautions to prevent the bacteria from spreading (patient isolation, dedicated equipment and nursing care etc.) In the event that the CRE colonised patient develops signs of sepsis, it is also helpful to know what antibiotics could be used to treat the infection.




## **What is the reason for this CRE study?**

Before 2010, CRE had only been reported in Ireland on one occasion. Since then, CRE has been detected on several occasions and there have been some outbreaks of infection, mainly in patients admitted to critical care units. Some of the patients had a history of admission to a hospital abroad. This is a four week study in which it is anticipated that all patients in critical care units in Ireland will be screened to check if they are carrying the CRE bacteria in the bowel. This study will help us decide if we need to recommend that all patients in critical care units are routinely screened for CRE carriage and it will also ensure that all microbiology laboratories have experience in picking up these resistant bacteria.

## Appendix C: Weekly Denominator Form to be completed by the Critical Care Unit

 <p><b>NATIONAL PILOT STUDY OF CARBAPENEMASE-PRODUCING CRE IN CRITICAL CARE UNITS: WEEKLY DENOMINATOR FORM FOR CRITICAL CARE</b></p>				
<b>FORM COMPLETED BY:</b>				
<b>WORK E-MAIL ADDRESS:</b>				
<b>HOSPITAL NAME:</b>		<b>UNIT NAME:</b>		
<b>WEEK OF STUDY</b>	<b>DATE WEEKLY CRE SCREENING SWABS TAKEN</b>	<b>DAY OF WEEK WHEN THE WEEKLY CRE SCREENING SWABS TAKEN</b>	<b>NUMBER OF PATIENTS ADMITTED TO THE UNIT AT THE TIME CRE SCREENING SWABS TAKEN</b>	<b>NUMBER OF CRE SCREENING SWABS TAKEN</b>
<b>WEEK 1</b>				
<b>WEEK 2</b>				
<b>WEEK 3</b>				
<b>WEEK 4</b>				
<b>TOTAL</b>				

# Appendix D: Weekly Microbiology Laboratory Specimen Form

 <p><b>NATIONAL PILOT STUDY OF CARBAPENEMASE-PRODUCING CRE IN CRITICAL CARE UNITS: WEEKLY MICROBIOLOGY LABORATORY SPECIMEN FORM</b></p>				
<p><b>FORM COMPLETED BY:</b></p> <p><b>WORK E-MAIL ADDRESS:</b></p>				
<p><b>HOSPITAL LABORATORY NAME:</b></p>		<p><b>NAMES OF CRITICAL CARE UNITS SERVED BY THIS MICROBIOLOGY LABORATORY:</b></p>		
WEEK OF STUDY	TOTAL CRE SCREENING SWABS RECEIVED IN LABORATORY  (WEEKLY SCREENS +/- ADMISSION SCREENS)*	NUMBER OF QUERY CARBAPENEMASE CRE ISOLATES FROM SCREENING SWABS	NUMBER OF QUERY CARBAPENEMASE CRE ISOLATES FROM CLINICAL SAMPLES	NUMBER OF CONFIRMED CARBAPENEMASE PRODUCERS CONFIRMED BY REFERENCE LABORATORY
WEEK 1				
WEEK 2				
WEEK 3				
WEEK 4				
TOTAL				

**\*As per study protocol, all participants are requested to perform weekly rectal swabs for CRE. In the event that a unit already has a policy in place where admission screening is performed, then that policy should remain.**

# Appendix E – Enhanced Patient Surveillance form – Version 1.5



## National Pilot Study of Carbapenemase-Producing Carbapenem-Resistant Enterobacteriaceae (CRE) in ICU Enhanced Surveillance Form, v1.5 (June 2011)

Please complete as fully and legibly as possible



CONTACT DETAILS IN CASE FURTHER DISCUSSIONS OF THIS CASE ARE REQUIRED:

Name:   
 Telephone Number:  Email:

### Section 1: Demographic information:

Hospital code:  Patient ID (MRN or Chart No.):  Sex: M  F  Unk   
 Age:  If <1 year, please state if age in days (D) or months (M): D  M   
 Date of hospital admission:  /  /  Date of ICU admission:  /  /   
 Admitted to this healthcare facility (HCF) from:  
 Home  Other Hospital  Long-term care facility  Nursing Home  Other

### Section 2: Clinical Information:

At the time of CRE detection was the patient already colonised or infected with another HCAI pathogen?  
 Yes  No

If YES, please indicate organism(s):  
 MRSA  
 VRE  
 ESBL-producing Enterobacteriaceae  
 Other / multi-drug resistant organism → Please state:

Was this patient transferred to this HCF from a hospital abroad?  Yes  No

If YES to hospitalisation abroad, please state country:

Did the patient travel abroad in the 12 months prior to hospitalisation?  Yes  No  Unk

If YES to travel abroad, please state country/ies:

If YES to travel abroad, please state reason(s) for travel:  
 Holiday  Visiting friends and relatives  
 Work  Other → Please state:   
 Medical  Unk

Risk Factors for CRE:  
 Hospitalisation in last 12 months  Chronic lung disease  
 ICU admission in last 12 months  Chronic liver disease  
 Surgery in last 6 months  Recurrent urological problems  
 Immunocompromised  None of the above  
 Diabetes mellitus  Unk  
 End-stage renal disease or renal replacement therapy

Isolation of CRE from this patient represents:  Infection or  Colonisation



55791

Patient ID (MRN or Chart No.):

Please repeat Patient ID above to allow adequate form matching

If YES to infection, the likely source is:

- |  |   |
|--|---|
| <input type="checkbox"/> Bacteraemia without obvious focus | <input type="checkbox"/> Genital tract                              |
| <input type="checkbox"/> Central nervous system            | <input type="checkbox"/> Skin / soft tissue                         |
| <input type="checkbox"/> Respiratory tract                 | <input type="checkbox"/> Surgical wound                             |
| <input type="checkbox"/> Urinary tract                     | <input type="checkbox"/> Infection of prosthetic material           |
| <input type="checkbox"/> Intra-abdominal                   | <input type="checkbox"/> Other → Please state: <input type="text"/> |

Outcome:

- |   |   |
|---|---|
| <input type="checkbox"/> Survived and remains an inpatient in ICU |   |
| <input type="checkbox"/> Survived and discharged from ICU →       | Date of discharge: <input type="text"/> / <input type="text"/> / <input type="text"/> 20 <input type="text"/> |
| <input type="checkbox"/> Died →                                   | Date of death: <input type="text"/> / <input type="text"/> / <input type="text"/> 20 <input type="text"/>     |

### SECTION 3: ANTIMICROBIAL INFORMATION

Antimicrobials administered during this admission PRIOR to CRE isolation:

- |   |  |
|---|--|
| <input type="checkbox"/> Beta-Lactam + beta-lactamase inhibitor | <input type="checkbox"/> Tobramycin      |
| <input type="checkbox"/> Cephalosporin                          | <input type="checkbox"/> Amikacin        |
| <input type="checkbox"/> Meropenem                              | <input type="checkbox"/> Tigecycline     |
| <input type="checkbox"/> Ertapenem                              | <input type="checkbox"/> Colistin        |
| <input type="checkbox"/> Aztreonam                              | <input type="checkbox"/> Chloramphenicol |
| <input type="checkbox"/> Fluoroquinolone                        | <input type="checkbox"/> Co-trimoxazole  |
| <input type="checkbox"/> Gentamicin                             |  |

If this represents CRE infection, please state the agents used to treat this infection:

- |  | Number of days given:     |
|--|---------------------------|
| <input type="checkbox"/> Meropenem       | <input type="text"/> days |
| <input type="checkbox"/> Ertapenem       | <input type="text"/> days |
| <input type="checkbox"/> Aztreonam       | <input type="text"/> days |
| <input type="checkbox"/> Fluoroquinolone | <input type="text"/> days |
| <input type="checkbox"/> Gentamicin      | <input type="text"/> days |
| <input type="checkbox"/> Tobramycin      | <input type="text"/> days |
| <input type="checkbox"/> Amikacin        | <input type="text"/> days |
| <input type="checkbox"/> Tigecycline     | <input type="text"/> days |
| <input type="checkbox"/> Colistin        | <input type="text"/> days |
| <input type="checkbox"/> Chloramphenicol | <input type="text"/> days |
| <input type="checkbox"/> Co-trimoxazole  | <input type="text"/> days |

Did initial choice of empiric antimicrobial therapy cover the CRE isolated?  Yes  No

If NO, how many days elapsed between date of culture and date of initiation of appropriate antimicrobial therapy?

days

### SECTION 4: OTHER RELEVANT CLINICAL INFORMATION:

**NATIONAL PILOT STUDY OF CARBAPENEMASE-PRODUCING CRE IN ICU  
Enhanced Surveillance Form, v1.5 (June 2011)**

**LABORATORY CONTACT DETAILS IN CASE FURTHER DISCUSSIONS OF THIS ISOLATE ARE REQUIRED:**

Name:		
Telephone Number:		Email:

**SECTION 5: LABORATORY INFORMATION:**

Laboratory code:	Hospital code:	Patient ID (MRN or Chart No.):
<input type="text"/>	<input type="text"/>	<input type="text"/>
Date of birth:	<input type="text"/> / <input type="text"/> / <input type="text"/>	Sex: M <input type="checkbox"/> F <input type="checkbox"/> Unk <input type="checkbox"/>
Specimen number:	Specimen date:	
<input type="text"/>	<input type="text"/> / <input type="text"/> / 20 <input type="text"/>	
Specimen Type:		
<input type="checkbox"/> Rectal screen	<input type="checkbox"/> Other sterile site	➔ Please state: <input type="text"/>
<input type="checkbox"/> Blood	<input type="checkbox"/> Other non-sterile site	➔ Please state: <input type="text"/>
<input type="checkbox"/> CSF		
Organism:	Other - please state:	
<input type="checkbox"/> <i>E. coli</i>	<input type="checkbox"/> <i>K. pneumoniae</i>	<input type="text"/>
Antimicrobial susceptibility testing (AST) method used:	<input type="checkbox"/> EUCAST	<input type="checkbox"/> CLSI
	<input type="checkbox"/> BSAC	
AST results:		
Meropenem <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	Meropenem MIC, if I/R:	<input type="text"/> mg/L
Imipenem <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	Imipenem MIC, if I/R:	<input type="text"/> mg/L
Ertapenem <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	Ertapenem MIC, if I/R:	<input type="text"/> mg/L
3rd-Generation Cephalosporin <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	Fluoroquinolone <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	
Aztreonam <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	Tigecycline <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	
Gentamicin <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	Colistin <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	
Tobramycin <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	Chloramphenicol <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	
Amikacin <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	Co-trimoxazole <input type="checkbox"/> R <input type="checkbox"/> I <input type="checkbox"/> S	
Is this case part of a suspected outbreak? <input type="checkbox"/> Yes <input type="checkbox"/> No		
Was this isolate referred to the Reference Laboratory (NUI Galway) for confirmation of the CRE? <input type="checkbox"/> Yes <input type="checkbox"/> No		
The case classification of this carbapenemase-producing CRE is: <input type="checkbox"/> Confirmed <input type="checkbox"/> Probable		
<input type="checkbox"/> VIM <input type="checkbox"/> IMP		
If CONFIRMED, please state resistance gene: <input type="checkbox"/> KPC <input type="checkbox"/> OXA		
<input type="checkbox"/> NDM <input type="checkbox"/> Other	➔ Please state:	<input type="text"/>

**SECTION 6: OTHER RELEVANT LABORATORY INFORMATION:**

--

Please return the ORIGINAL form to HPSC, 25-27 Middle Gardiner Street, Dublin 1 and a COPY to your local Dept of Public Health

## Appendix F – Case Definition for CRE

Isolation of a carbapenemase-producing carbapenem resistant Enterobacteriaceae (CRE) from a patient specimen.

**Clinical Criteria:** Invasive infection due to CRE may have differing clinical manifestations, depending on the site of infection. Patients colonised with CRE may not manifest any signs or symptoms of infection.

**Laboratory Criteria** for case definition:

- Isolation of a carbapenemase-producing carbapenem-resistant Enterobacteriaceae (CRE) from a patient specimen
- Any Enterobacteriaceae isolate with reduced or non-susceptibility to carbapenem agents should be referred for molecular confirmation of the resistance mechanism\*. Pending referral for confirmation of resistance, suspected CRE isolates should be sloped and stored in the isolating laboratory.

**Case Classification:**

- A. Possible Case: Not applicable
- B. Probable Case: Any person with phenotypic laboratory evidence of a carbapenem-resistant Enterobacteriaceae, pending molecular confirmation by a reference laboratory
- C. Confirmed Case: Any person with reference laboratory confirmation of a carbapenemase producing CRE

A confirmed case should be notified to the relevant public health department once carbapenemase production has been confirmed by a reference laboratory. In the event that the case is part of a suspected outbreak of infection, the medical officer of health should be notified of a probable case pending reference laboratory confirmation and all usual outbreak control measures should be implemented in the interim.

\*There are certain genera of Enterobacteriaceae which have intrinsic mechanisms of resistance to imipenem other than carbapenemase production (*Proteus*, *Morganella*) and isolated ertapenem resistance in *Enterobacter* has

been described as a result of derepression of AmpC. Such isolates are not notifiable.

Carbapenem resistance which arises as a result of extended spectrum  $\beta$  lactamase or Amp C expression combined with impermeability mechanism or porin loss is not notifiable.

Testing for susceptibility to more than one carbapenem may provide more specific selection for acquired carbapenem resistance in Enterobacteriaceae.

**Definition of Enterobacteriaceae:** Gram-negative; rod shaped; non-spore forming organisms which may be found in the intestinal flora. They grow well on MacConkey agar; grow both aerobically and anaerobically; are active biochemically; ferment sugars and are oxidase negative. The following genera are included in the family Enterobacteriaceae:

- *Escherichia*
- *Klebsiella*
- *Citrobacter*
- *Enterobacter*
- *Serratia*
- *Proteus*
- *Morganella*
- *Providencia*
- *Salmonella*
- *Shigella*

**Definition of Carbapenems:** Meropenem, Imipenem, Ertapenem, Doripenem



## Appendix G – Instructions for Specimen Transport to Reference Laboratory, Galway

Direct link to National Salmonella Reference Laboratory user guide [here](#)

### Transportation of samples

Slopes must be packaged and transported according to IATA regulations.

- Grow isolate overnight on a small nutrient agar slope and remove any fluid accumulating at the bottom of the slope using a sterile Pasteur pipette.
  - Place slope(s) into an inner crushproof hard plastic container and place this into a cardboard box or envelope.
  - Label with an emergency contact number for the sender and an Infectious substance label.
  - Label box with UN3373 and add sticker with “BIOLOGICAL SUBSTANCE, CATEGORY B”.
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- This can be then sent to the *Salmonella* Reference laboratory via a courier company, e.g. Hays DX (01-8421088), Capital Freight (01-8852064), Claymon (1800-252967) or Nightline couriers (091-795100).
  - A number of slopes may be sent in each crush-proof container but each slope must be individually wrapped in an adsorbent material to prevent breakage during transit.