



Requirements for Screening for Carbapenemase-Producing Enterobacterales (CPE)

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Scope

This document is intended to guide healthcare workers who provide care to people in the acute hospital setting in implementing a programme for screening of people for CPE. There are some other settings that deliver a level of service that is comparable to an acute hospital, such as certain intensive rehabilitation facilities. In this document where the term acute hospital is used it is intended to apply to all settings that deliver a service that is comparable to an acute hospital service. This guidance is particularly relevant to infection prevention and control practitioners and microbiology laboratory service providers.

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This guideline will be reviewed in 12 months (First quarter of 2020) or sooner if significant new evidence emerges.

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Abbreviations and Glossary of Terms

AMAU = Acute Medical Assessment Unit

ED = Emergency Department

IPC= Infection Prevention and Control

CPE = Carbapenemase-Producing Enterobacterales*

***Note.** Until recently the order *Enterobacterales* was considered to include a single family the *Enterobacteriaceae* (so that all *Enterobacterales* were also *Enterobacteriaceae*). Recent studies have led to the conclusion that the members of the order *Enterobacterales* should be divided into multiple families. This means that the term *Enterobacteriaceae* now encompasses only some of the species of bacteria it formerly encompassed. The term *Enterobacterales* is now the term that corresponds most closely to the former meaning of *Enterobacteriaceae*.

Introduction

The following is an updated guideline. It replaces a previous guideline issued in 2018. Hospital groups and hospitals must resource all relevant areas on the ward, the laboratory and the infection prevention and control (IPC) service to achieve this level of screening for CPE. In some circumstances, additional screening beyond that recommended here is required. For additional information related to healthcare associated infection and antimicrobial resistance, or to confirm that you are using the most current version of this guidance, please go to www.hse.ie/infectioncontrol.

What is CPE?

CPE is the latest major wave of antimicrobial resistant organisms that is spreading throughout the world including Ireland. At the moment, spread of CPE in Ireland is mainly a problem in the acute hospital setting.

The gut of every normal, healthy human contains bacteria including a group of bacteria called *Enterobacterales*. This group of bacteria includes *E. coli* and *Klebsiella pneumoniae*. When *Enterobacterales* get into the bladder, kidney or bloodstream, they can cause infection (cystitis, pyelonephritis, sepsis).

Carbapenemase-Producing *Enterobacterales* (CPE) are a particular variant of these common gut bacteria that have become resistant to a critical group of antibiotics, the carbapenems. These bacteria are often also resistant to many other antibiotics. Although they are resistant to antibiotics, in most other respects they are like other *Enterobacterales* bacteria in that they are harmless when they are in the gut.

When people colonised with AMRO including CPE develop clinical evidence of infection, the infection that they have is often caused by bacteria other than the AMRO. For example, upper respiratory tract infection, bronchitis, pneumonia, sinusitis, skin infection and cellulitis are very unlikely to be caused by CPE even in a person colonised with CPE. In a person colonised with CPE, just as in everyone else, these kinds of infection are most likely due to a virus (upper respiratory tract and bronchitis) or the usual bacterial suspects for pneumonia (*pneumococcus*) and cellulitis (*Staphylococcus aureus* or *Group A Streptococcus*). With respect to most people colonised with AMRO the guidance available regarding treatment of infection on www.antibioticprescribing.ie or relevant hospital guidelines remains appropriate most of the time.

CPE in the gut do not cause diarrhoea, vomiting or abdominal pain. In some people who carry CPE in the gut, the CPE may cause cystitis, pyelonephritis or sepsis when it spreads from the gut to other body sites. In this case many of the antimicrobial agents commonly used in the community do not work, however, there are some antibiotics that are effective.

If a person colonised with CPE develops clinical evidence of serious infection they may need prompt treatment directed towards CPE. In that case, in so far as it is appropriate given the persons overall care plan, transfer to an acute hospital is generally appropriate.

See Guidance on treatment of suspected CPE infection available at www.hse.ie/infectioncontrol and <https://www.hse.ie/eng/about/who/cspd/ncps/sepsis/>

CPE Colonisation

A person who carries CPE in the gut, but who has no clinical symptoms related to the CPE is said to be colonised. People may also have asymptomatic CPE colonisation of urine or leg ulcers. Colonisation with CPE (no clinical evidence of infection) should not be treated with antibiotics. Antibiotics do not clear the colonisation from the gut and in fact are likely to make the colonisation more intense and last for longer.

What is Screening for CPE?

Screening for CPE generally means testing a rectal swab or sample of faeces for CPE by selective culture or by molecular methods. In some cases, additional samples may also be tested for CPE. As outlined below screening for CPE encompasses both **population screening** and **screening in the context of contact tracing**.

Are there Ethical Issues Related to CPE Screening?

Yes. As with all investigations, testing of people for colonisation with CPE is performed on the basis that people are entitled to decline testing and to the greatest extent practical should be provided with relevant information about the testing offered.

Detection of asymptomatic colonisation with CPE is of benefit to the person identified as colonised because that knowledge may be critical to the choice of appropriate empirical antimicrobial treatment in the event that they develop serious infection. Guidance on the treatment of people with suspected or confirmed CPE infection is available at www.hse.ie/infectioncontrol

Evidence that a person at high risk of CPE colonisation is not colonised is of benefit to the person because that knowledge may guide a treating clinician towards the use of narrower spectrum and safer antimicrobial therapy if they develop serious infection.

Detection of asymptomatic colonisation with CPE is of benefit to the wider community because it supports measures to control the spread of CPE in the acute hospital setting.

The following are critical issues in relation to the ethical conduct of a programme of screening for CPE

1. Respect for the person's entitlement to refuse testing without prejudice to their access to care.
2. Respect for the entitlement of people identified as colonised with CPE to have the same regard for their privacy and the same level of access to health and social care services as are other people.
3. Respect for the person's right to information about their health. In the event that a person tests positive for CPE they should be informed promptly in accordance with the document "Discussing healthcare associated infection (HCAI) and specific antimicrobial resistant organisms (AMROs) with patients who may have acquired a HCAI, become colonised with an AMRO or been exposed to a specific HCAI/AMR risk. www.hse.ie/infectioncontrol

Timing of Collection of Samples for Screening for CPE

Screening for CPE should generally be performed as soon as possible after admission to an acute hospital. Samples should be submitted within 24 hours of admission. People in whom the requirement to offer screening is not recognized at the time of admission should be offered screening as soon as possible after the requirement is recognised.

If a hospital is using a system of pre-admission screening (see below) a sample collected within the 7 days before the date of hospital admission can be accepted as equivalent to an admission screen.

Healthcare facilities should not require CPE screening in advance of patient transfer between facilities. A requirement for pre-transfer screening is likely to delay patient transfer. In the case of acute hospitals pre-transfer screening cannot replace the

responsibility of the receiving hospital for CPE admission screening of patients transferred to the care of that hospital.

Screening for CPE Outside of the Acute Hospital Setting

Although screening for CPE is not required outside of the acute hospital setting it may be appropriate to facilitate CPE screening for some people in the non-acute hospital setting. It is appropriate to facilitate people identified as CPE Contacts who have left hospital but who wish to be tested for CPE.

It may be pragmatic to offer screening to CPE Contacts who are likely to require re-admission to an acute hospital in the short term.

It may be pragmatic in certain circumstances to offer pre-admission CPE screening to certain non-CPE Contacts in advance of planned admission to an acute hospital. These arrangements may support appropriate patient placement at the time of admission. **Any processes for pre-admission CPE screening implemented must operate to facilitate access to hospital care and must not delay access to care.**

Population Screening in Acute Hospitals

Population screening for CPE (that is CPE screening in people who are not CPE Contacts) generally involves a **single** sample at the beginning of each hospital admission. People with very frequent admission to a general hospital need not be screened on admission more frequently than once per week.

In some circumstances population screening for CPE should involve additional testing for CPE at intervals during the hospital stay. For example, all people admitted to an Intensive Care Unit should be screened weekly for the duration of their stay in ICU (see below).

Who Must be Included in Population Screening?

Two approaches to population screening are outlined below. Whichever option is applied the hospital should conduct periodic audits to assess performance of their CPE screening programme.

Option 1. Targeted Population Risk Based Screening.

The following people **must** be offered screening for CPE in acute hospitals.

- a. All people who were transferred from any other hospital in Ireland or elsewhere.
- b. All people who have been inpatients in any hospital in Ireland or elsewhere any time in the previous twelve months. Any hospital includes previous admissions to the hospital to which they are now being admitted.
- c. All people who normally reside in a long term care facility for older people 1
- d. All admissions to and all transfers to Intensive Care Units and High Dependency Units on admission and weekly thereafter.
- e. All admissions to and all transfers to haematology, oncology and transplant wards on admission and weekly thereafter.
- f. People undergoing renal dialysis for the first time in a dialysis unit, periodically during dialysis treatment (preferably every three months but not less than every six months), and on return from dialysis elsewhere.
- g. All people who were formerly colonised with CPE but who have subsequently met the criteria for removal of that designation.
- h. Other people where CPE screening is requested by the IPC team.

Footnotes. 1. A key challenge for implementation is the ability to identify the people who should be offered screening readily. Information regarding inpatient stay in any other hospital in the previous 12 months and residence in a long -term care facility for older people should wherever possible be recorded routinely by the admissions office and should, whenever possible, be easy to obtain from the patient administration system

2. There is no evidence that the collection of rectal swabs represents a significant risk to people who are neutropenic. Undetected carriage of CPE may be a particular risk for these vulnerable people. Several recent publications report routine screening by rectal swab collection in hematology cohorts including bone marrow transplant recipients.^{2, 3, 4.} These people should be included in screening programs

Option 2. Broader Population Screening Based on Hospital Risk Assessment

Many hospitals have found that the effective identification of people in certain categories for targeted screening is very challenging in practice. Some hospitals have found it more practical to implement broader-based screening. Their experience is that this approach captures most or those people who would require CPE screening with the Targeted Approach (Option 1 above).

Such approaches might include offering of screening to all admissions, or to all emergency admissions. The approach taken must ensure that at a high proportion of those risk groups identified in Option 1 are encompassed in the population offered screening.

Option 2 is generally not appropriate for children's hospitals or maternity hospitals or for discrete children's & maternity units in general hospitals.

Where broad based screening of admissions (for example all admissions, or all emergency admissions) is implemented based on local assessment it is essential that the following elements of targeted CPE screening are also in place.

- a. All admissions to and all transfers to critical care areas Intensive Care Units and High Dependency Units on admission and weekly thereafter.
- b. All admissions to and all transfers to haematology, oncology and transplant wards on admission and weekly thereafter.
- c. People undergoing renal dialysis for the first time in a dialysis unit, periodically during dialysis treatment (preferably every three months but not less than every six months), and on return from dialysis elsewhere.
- d. All people who were formerly colonised with CPE but who have subsequently met the criteria for removal of that designation.
- e. Other people where CPE screening is requested by the IPC team.

CPE Population Screening in Maternity Hospitals/Units.

Targeted population screening for CPE (Option 1 above) is generally appropriate for Maternity Hospitals with the following qualifications.

Pregnant women who have frequent admissions to the same maternity hospital/unit and who have no other indication for CPE screening need not be screened more frequently than once every three months.

Screening for CPE should generally be performed at intervals of less than three months if there has been an intervening admission to a general hospital or other specific risk factors apply, for example, recent hospitalisation outside of Ireland.

Infants transferred between neonatal intensive care units should be screened for CPE on admission to the NICU.

More limited screening for CPE may be justified where a documented local risk assessment by the IPC team indicates that the risk of CPE colonisation is very low and there is no evidence of CPE transmission in the hospital. Any such risk assessment should be reviewed at least annually.

CPE Screening in Children's Hospitals/Units.

Targeted screening for CPE (Option 1 above) is generally appropriate for Children's Hospitals with the following qualifications.

Children who have frequent admissions to the same hospital/unit and who have no other indication for CPE screening need not be screened more frequently than once every three months.

Screening for CPE should generally be performed at intervals of less than three months if specific risk factors apply for example recent hospitalisation outside of Ireland.

More limited screening for CPE may be justified where a documented local risk assessment by the IPC team indicates that the risk of CPE colonisation is very low and there is no

evidence of CPE transmission in the hospital. Any such risk assessment should be reviewed at least annually.

In general no CPE screening is required in relation to an infant born to a woman who is known to be CPE positive if the infant is largely in the care of its parents while in hospital and is promptly discharged to home. The infant need not be designated a CPE Contact.

If an infant born to a CPE positive woman is admitted to a Neonatal Intensive Care Unit CPE screening should be offered on admission and weekly thereafter for the duration of the infants stay in NICU.

Note

The National Emergency Medicine Programme states, “*All patients will undergo Infection Prevention and Control Assessment at Triage*”. This assessment should include assessment of risks for CPE colonisation or contact.

CPE Screening in the Context of Contact Tracing

CPE Contacts are people assessed by IPC professionals or public health doctors as having had a specific exposure(s) that places them at higher risk of having CPE colonisation or infection.

Definition of a CPE Contact

A CPE Contact is a person who has been assessed by an IPC Practitioner or Public Health Doctor as likely to be at a substantially higher risk than the general patient population of colonisation with CPE. Infection Prevention and Control Teams are required to use professional judgement in the designation of exposed people as CPE Contacts.

A person is considered as exposed to CPE if they have shared a multi-bed area or bay and/or **are known to have** shared toilet facilities with a person identified as colonised or infected with CPE. A person may also be exposed if they are accommodated in a room or are known to or are very likely to have used a toilet, shower or other facilities where CPE has been detected on touch surfaces.

In general designation as a CPE Contact will mean that the person has been assessed as having exposure that lasted for 12 hours or more. People who are identified as exposed for periods shorter than 12 hours are generally not considered CPE Contacts.

Identification of CPE Contacts

Each acute hospital should develop a process to ensure, in so far as possible, the identification of CPE Contacts and the flagging of records of all people who are identified as CPE Contacts. This flag may be electronic or manual, but should be capable of being removed if the criteria for removal of the designation as CPE contacts are met. The purpose of flagging of records is to ensure that the people in question are rapidly and readily identifiable if they are admitted to hospital. CPE Contacts admitted to an acute hospital should be offered CPE screening and contact precautions should be applied pending results.

Identifying CPE Exposure and CPE Contacts

For the purposes of this guidance, a person is considered as exposed to CPE if they have shared a multi-bed area or bay and/or **are known to have** shared toilet facilities with a person identified as colonised or infected with CPE. A person may also be exposed if they are accommodated in a room or are known to or are very likely to have used a toilet, shower or other facilities where CPE has been detected on touch surfaces.

Assessment of exposure should take account of time spent in the Emergency Department (ED) and Acute Medical Assessment Units (AMAU). It is acknowledged that identification of exposure in ED can be particularly challenging. In general, only those people who were subsequently admitted to hospital from the ED and who can be positively identified by the IPC team as having received an intensity of care comparable to an in-patient in an open area during the same time that the person colonised or infected with CPE was in the area should be considered as exposed.

When assessing exposure of others in relation to a person colonised or infected with CPE it is sufficient to limit the period under consideration as from the beginning of the period of the acute hospital admission during which CPE was first detected.

If the person has had samples reported as **CPE not detected/CPE Negative** during an admission, but then tests CPE positive later in that admission, it is sufficient to limit the period under consideration as from the date of the most recent sample reported as CPE not detected/CPE Negative.

For example, consider a person admitted on July 1st who tests CPE Not Detected on July 1st and on July 7th, but tests CPE positive on July 14th. Only the period after July 7th need be considered.

In relation to CPE environmental exposure there is generally no practical way to identify at what point the touch surface in question became colonised with CPE. A pragmatic approach

is to limit the identification of contacts to those in patients who are known to have been in that space or are very likely to have been in the space in the two days prior to first detection of CPE on a touch surface. It may be necessary to consider a longer period if there is epidemiological evidence that a particular environment has been clearly associated with CPE transmission.

For example, consider a shower tray sampled on July 1st that tests positive for CPE. Patients who are known to have or are very likely to have used that shower on or after June 29th are regarded as CPE contacts. In the event that a number of those contacts test positive for CPE it may be appropriate to extend back beyond June 29th.

Performing Screening for CPE in the Context of Contact Tracing

Screening of CPE Contacts in the acute hospital setting should commence promptly. Samples should be taken at intervals of at least one week apart. The last sample should be taken at least four weeks after the latest date of exposure.

When an interval of time has elapsed between the latest date of exposure and commencement of screening, the intervals between sampling may be reduced. However the final sample should be taken at least four weeks after the latest date of exposure.

Rationale for the Approach to Screening of CPE Contacts

Screening of Contacts for CPE requires multiple samples. This is because of the limited sensitivity of a single sample. A significant proportion of people that test positive for CPE are not detected on the first sample [Mookerjee *et al.*, 2018]. There is limited data to indicate what the optimum number of samples is. Many guidelines recommend 3 samples. In Ireland 4 samples was selected on the basis of experience of continued detection of new CPE positive patients up to 4 samples.

In relation to screening of CPE Contacts it is appropriate that the first sample is taken promptly. This is because in some circumstances one of the people identified as a CPE Contact may in fact be the source of colonisation of the index case.

In relation to CPE screening an interval of time is required between the date of exposure and taking of the final sample. There is limited data to indicate what the optimum interval should be. In Ireland the interval has been set at 4 weeks based on some experience suggesting that at least four weeks may elapse between exposure and a positive test result.

When does a Contact Cease to be a Contact?

A person may be considered as no longer a CPE Contact if they have at least four samples reported as CPE not detected and if more than four weeks have elapsed since the latest date of the identified exposure.

After the designation of CPE Contact has been removed from a person's record the person should still be included in population screening for CPE on the same basis as other people.

Infection Prevention and Control Precautions with CPE Contacts

In the acute hospital setting **Standard Precautions** and **Contact Precautions** should apply to any contact of a person colonised with CPE. Standard and Contact Precautions should be applied until the person meets the criteria for removal of the designation as CPE Contact.

Is Retesting Required if the Person is Confirmed Positive for CPE?

Retesting of people confirmed positive for CPE is generally **not necessary** however it may be appropriate in some cases.

Some people are particularly distressed by the experience of being designated as CPE colonised and may request a process for removal of that designation.

A person who has been designated as CPE colonised may have that designation removed if more than 12 months have elapsed since the most recent positive CPE detection and there have been four or more CPE screening samples reported as CPE not detected during that 12-month period. At least one of those samples must have been taken more than four weeks after their most recent positive test for CPE.

Note, it is important to provide clear information to the person indicating that while the designation of CPE colonised is removed from their patient record it is not possible to give them an assurance that CPE has definitively cleared. There is reason to believe that in some people CPE may become undetectable for a period of time and yet re-emerge subsequently for example following exposure to antimicrobial agents. Therefore all people formerly designated as positive for CPE but who have had that designation of CPE positive removed should be included in the population screening process.

Sample Collection and Laboratory Screening Methods.

Collection of rectal swabs, rather than waiting for stool samples, lends itself to prompt sample collection and is generally preferred. If rectal swab sampling is not acceptable to a person, stool samples are high quality samples. Generally samples of faeces are appropriate for children.

Note, in some circumstances, samples from additional sites for testing for CPE may also be appropriate based on clinical assessment.

The following are general observations on laboratory methods for CPE screening. More detailed guidance on laboratory methods is in development.

Laboratory screening for CPE should at a minimum mean plating of rectal swabs/faeces on one of the accepted CPE chromogenic agars. Access to rapid methods for direct testing of selected samples and/or for rapid confirmation of suspect CPE from agar plates should be available. Rapid confirmation of suspect colonies may be by immunological (lateral flow) or molecular methods. Results should be reported as CPE detected and acted upon for infection prevention and control purposes based on detection of CPE by lateral flow or molecular methods.

Where screening is based on an initial molecular method those samples that test positive should be cultured to attempt to isolate the organism. It is accepted that in some instances it may not be possible to confirm a molecular result by culture.

If the molecular test used is a CE (European Conformity) marked product or a well validated in-house method, this result is generally sufficient to designate the person as CPE colonised for IPC purposes although this does not meet the criteria for notification of the person as CPE Colonised. All acute hospitals should ensure that CPE screening samples are set up and read 7 days per week and that newly detected CPE are reported to the relevant clinical on the day of detection.

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