OPERATIONAL SUPPORT

# Reporting protocol for epidemiological, microbiological and genomic investigation of outbreaks and emerging resistance mechanisms for carbapenem-resistant Enterobacterales – version 3.0

European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net)

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Suggested citation: European Centre for Disease Prevention and Control. Reporting protocol for epidemiological, microbiological and genomic investigation of outbreaks and emerging resistance mechanisms for carbapenem-resistant Enterobacterales – version 3.0. Stockholm: ECDC; 2026.

Stockholm, June 2026

ISBN 978-92-9498-889-8
doi: 10.2900/2627820
Catalogue number TQ-01-26-034-EN-N

# Contents

# Abbreviations

| | |
|---|---|
| AD | allelic difference |
| AMR | antimicrobial resistance |
| AMRISO | EpiPulse dataset for antimicrobial resistant isolates |
| AST | antimicrobial susceptibility testing |
| CCRE | carbapenem- and/or colistin-resistant Enterobacterales |
| cgMLST | core genome multilocus sequence typing |
| cgSNP | core genome single nucleotide polymorphism |
| CRE | carbapenem-resistant Enterobacterales |
| EEA | European Economic Area |
| EMMa | ECDC Map Maker tool |
| ENA | European Nucleotide Archive |
| EpiPulse | European Surveillance Portal |
| EU | European Union |
| EUCAST | European Committee on Antimicrobial Susceptibility Testing |
| EURGen-Net | European Antimicrobial Resistance Genes Surveillance Network |
| EURGen-RefLabCap | European Antimicrobial Resistance Genes Reference Laboratory Capacity Building Project |
| EURL-PH-AMR | European Reference Laboratory for Public Health on Antimicrobial Resistance in Bacteria |
| EWRS | Early Warning and Response System |
| MDR | multidrug resistance |
| MIC | minimum inhibitory concentration |
| MLST | multilocus sequence typing |
| NCBI | National Center for Biotechnology Information |
| NDM | New Delhi metallo-beta-lactamase |
| NRL | National reference laboratory |
| NUTS | Nomenclature of territorial units for statistics |
| OCP | Operational Contact Point |
| OXA | oxacillinase |
| PDR | pandrug-resistant |
| RRA | rapid risk assessment |
| ST | sequence type |
| WGS | whole-genome sequencing |

# Executive summary

Antimicrobial resistance (AMR) threatens the ability to treat common infections, results in prolonged illness, disability, and death, and increases the cost of healthcare. Outbreaks of infections with antimicrobial-resistant microorganisms and the emergence of resistance mechanisms, including new high-risk multidrug-resistant (MDR) clones, should be detected and controlled as early as possible to avoid or reduce further spread.

The European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net) is a network for genomic-based surveillance of healthcare-associated MDR bacteria, coordinated by ECDC. National reference laboratories (NRLs) or equivalent expert laboratories of European Union (EU), European Economic Area (EEA) and candidate countries currently participate in EURGen-Net. The primary objectives of EURGen-Net are to monitor the occurrence and geographic distribution of high-risk clones and resistance genes of public health importance and to support cross-border investigations of MDR pathogens outbreaks and related emerging resistance mechanisms. EURGen-Net has been conducting CRE outbreak investigations since 2018 and improved related procedures over time. The purpose of this protocol is to standardise the data collection and enable the conduct of cross-border epidemiological, microbiological and genomic investigations of outbreaks and emerging resistance mechanisms, facilitating rapid detection and investigation via harmonised, structured, and standardised data collection from EU/EEA and candidate countries.

# Background

Outbreaks of antimicrobial-resistant pathogens and the emergence of resistance mechanisms, including new high-risk multidrug-resistant (MDR) clones need to be detected and controlled as early as possible. The emergence and spread of antimicrobial resistance (AMR) threaten the ability to treat common infections. The consequences of antimicrobial resistance can be prolonged illness, disability, and death, as well as increases in healthcare costs due to prolonged hospital stays and the requirement for more intensive healthcare procedures [1]. Without effective antimicrobials for the prevention and treatment of infections, medical procedures such as organ transplantation, chemotherapy, and major surgery have a high risk of a negative outcome for patients [1].

The European Centre for Disease Prevention and Control (ECDC) is mandated to gather and analyse data on emerging public health threats and developments to protect public health in the European Union (EU)/European Economic Area (EEA) [2]. Regulation 2022/2371 of the European Parliament and the Council of 23 November 2022 on cross-border threats to health specifically mentions the role of ECDC in response coordination and collection of 'pathogen data, including at molecular level, if required for epidemiological surveillance and for detecting or investigating serious cross-border threats to health' [2]. Since 2025, the role of the European Reference Laboratory for Public Health for Antimicrobial-Resistant Bacteria (EURL-PH-AMR) is to support ECDC outbreak investigations for antimicrobial-resistant bacteria.

The European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net) is a network for genomic-based surveillance of healthcare-associated MDR bacteria, coordinated by ECDC [3]. National reference laboratories (NRLs) or equivalent expert laboratories of 39 European countries currently participate in EURGen-Net. The primary objectives of EURGen-Net are to monitor the occurrence and geographical distribution of high-risk clones and resistance genes of public health importance in the EU/EEA, and to support cross-border investigations of outbreaks of MDR pathogens and emerging resistance mechanisms. The purpose of this protocol is to enable rapid cross-border genomic and epidemiological investigations of carbapenem-resistant Enterobacterales (CRE) outbreaks and related emerging resistance mechanisms, via harmonised, structured, and standardised data collection from EU/EEA and candidate countries.

Since 2017, EURGen-Net has mostly focused on surveillance of CRE [4]. Besides the structured survey of carbapenem and/or colistin-resistant Enterobacterales (CCRE) with a focus on carbapenem-resistant *Escherichia coli* and *Klebsiella pneumoniae* [5], this also included investigations of high-risk clones and emerging resistance mechanisms [6,7] and related ECDC rapid risk assessments addressing the cross-border emergence of CRE [8-11] and supporting national CRE investigations [12]. A more detailed overview of the history of EURGen-Net and its investigations has been described in the article 'From structured surveys to outbreak investigations: advancing genomic surveillance of carbapenem-resistant Enterobacterales within the European Antimicrobial Resistance Genes Surveillance Network' [13].

# Objectives of the EURGen-Net investigations

The primary EU-level public health objective of the EURGen-Net investigations is to investigate any acute increase in the occurrence and geographical distribution of healthcare-associated MDR bacterial and fungal pathogens. This includes population dynamics and/or transmissible resistance/genetic elements of critical public health importance in Europe, to target preventive and control measures.

The secondary objectives are:

- Early confirmation of multi-country/cross-border dimension of outbreaks;
- Identification of genetic vector/modes/sources of transmission;
- Support national investigations;
- Support the development of national technical capabilities and proficiency in genomic-based surveillance;
- Development and implementation of strategies to reduce the incidence and impact of MDR bacterial and fungal outbreaks in different populations and settings;
- Support enhancing communication, collaboration and coordination among stakeholders involved in the management of AMR outbreaks;
- Identify epidemiological risk factors for infection and/or colonisation with MDR pathogens at bacterial clonal and sub-genomic level.

# Triggers for EURGen-Net investigations

## 1. EpiPulse Events, EWRS notifications and country requests for support

EpiPulse is the European Surveillance Portal for infectious diseases, launched by ECDC, that integrates indicator- and event-based surveillance. The portal offers nominated users the possibility to report, collect and explore data on infectious diseases. The platform facilitates interdisciplinary collaboration to discuss findings and connects users from different sectors under a One Health approach. Reporting in EpiPulse is voluntary for EU/EEA Member States but highly encouraged to communicate and exchange information that will facilitate prompt detection of signals and allow their monitoring and timely assessment.

Investigations following an event posting from an EU/EEA country on the ECDC EpiPulse platform [14] or any other third parties with access to the EpiPulse, following a notification via the EU Early Warning and Response System (EWRS) or based on EU/EEA country requests for support will be given priority.

An event in EpiPulse is defined as:

- case(s)/cluster(s)/outbreak(s)/epidemiological situation(s)/incident(s)/public health risk situation(s);
- detected in/reported by one or several countries;
- that are assessed to pose or may pose a public health risk for the EU/EEA.

**Examples** of EURGen-Net investigations and Rapid Risk Assessments triggered by EpiPulse events are described in the 'Rapid Risk Assessment on carbapenemase-producing (OXA-48) *Klebsiella pneumoniae* ST392 in travellers previously hospitalised in Gran Canaria, Spain' [10], the 'Rapid Risk Assessment on the increase in OXA-244-producing *Escherichia coli* in the European Union/European Economic Area and the UK since 2013, first update' [9], and the 'Rapid Risk Assessment on the emergence of hypervirulent *Klebsiella pneumoniae* ST23 carrying carbapenemase genes in EU/EEA countries' [8]. An example for ECDC support to a country investigation is described in the 'Rapid Risk Assessment on combined clonal and plasmid-mediated outbreak of carbapenemase-producing Enterobacterales, Lithuania, 2019–2020' [12].

## 2. Emergence/increase of resistance and virulence mechanisms and high-risk clones

Reports of emerging resistance/virulence markers and high-risk clones detected at the national level or at the EU/EEA level via standardised surveys (such as the CCRE survey mentioned above) will be further investigated if deemed relevant for EU-level surveillance.

**Examples** are the investigations of the increase of OXA-244-producing *E. coli* and hypervirulent *K. pneumoniae* ST23 mentioned above [8,9]. An example of an investigation triggered by preliminary results of an increasing resistance mechanism detected in the standardised CCRE survey is the cross-border investigation into the emergence of New Delhi metallo-beta-lactamase (NDM)-5-producing *E. coli* [15].

## 3. Outbreaks of highly drug-resistant bacteria detected by ECDC epidemic intelligence

Signals on outbreaks and the emergence of highly-drug resistant bacteria or increasing resistance/virulence mechanisms detected by the ECDC epidemic intelligence team will be followed up with respective countries and a cross-border investigation will be initiated when deemed relevant.

An **example** of such an investigation is described in the 'Rapid Risk Assessment on the outbreak of carbapenemase-producing (NDM-1 and OXA-48) and colistin-resistant *Klebsiella pneumoniae* ST307, north-east Germany, 2019' [11].

## 4. Spread of extensively drug-resistant strains or strains with phenotypic resistance to critical antimicrobials

Evidence of the spread of pandrug-resistant (PDR) strains or critical resistance gene combinations would also be a reason for an EU-level outbreak investigation.

**Examples** could be detecting the spread of strains phenotypically resistant to critical antimicrobials such as ceftazidime-avibactam resistance, or extensively drug-resistant (XDR) or PDR strains which are resistant to all antimicrobials tested in ECDC standardised surveys. While the 'Rapid Risk Assessment on the outbreak of NDM-1- and oxacillinase (OXA)-48-co-producing and colistin-resistant *K. pneumoniae* sequence type (ST) 307 in Germany' [11] mentioned in the above paragraph addressed a phenotypically highly-drug resistant pathogen, criteria based on phenotypic resistance in the absence of an outbreak have so far not been used to trigger EURGen-Net investigations. Nevertheless, with increasingly fewer treatment options available, this may be an important reason for further investigation.

## 5. New mode/source of transmission of healthcare-associated pathogens

Previously unknown modes and sources of healthcare-associated pathogens may also require an EU-level investigation, even in the absence of or with limited AMR of involved pathogens.

This has so far not been the focus of EURGen-Net investigations that have mainly concentrated on highly resistant pathogens. However, an investigation that could serve as an example of an EU-level investigation is the investigation described in the ECDC 'Rapid Risk Assessment on invasive cardiovascular infection by *Mycobacterium chimaera* associated with the 3T heater-cooler system used during open-heart surgery' [16].

The criteria outlined under points 1-5 above are intended to guide decision-making for the initiation of EURGen-Net epidemiological and genomic investigations. However, they should not preclude investigations based on other criteria if considered relevant.

# Definitions and inclusion criteria

## Pathogens

This protocol is intended to provide a framework and standardisation for outbreak investigations of CRE. However, in principle, this protocol can be used for other ECDC investigations of gram-negative and gram-positive bacterial pathogens related to healthcare-associated infections and emerging healthcare-associated fungal pathogens if there is evidence for potential new modes/sources of transmission, emerging resistance or virulence mechanism, or extensive spread, to be evaluated on a case-by-case basis.

## Case definition

A case definition should be defined for each event, based on molecular criteria, affected geographical area(s) and period. For investigations of outbreaks of pathogens and emerging resistance mechanisms, the case definition can be based on, but not limited to,

- Specific period or geographical distribution (this may include particular settings, e.g., hospitals);
- Specific patient population (e.g., inpatients and/or outpatients);
- Specific pathogens and/or STs;
- Specific phenotypic antimicrobial susceptibility profile under investigation (e.g., resistance to carbapenems);
- Specific resistance genes (e.g., carbapenemase gene carriage);
- Specific virulence factors;
- Combinations of specific genetic markers.

Using the above criteria, a case definition should capture as many associated cases as possible. Case definitions can be revised and specified as additional information becomes available over the course of the investigation.

**Example case definition:** reported cases of OXA-48-producing *K. pneumoniae* ST392 in travellers returning from and having been hospitalised in Gran Canaria in 2018 [10].

## Biological samples

Non-duplicate isolates of a pathogen from patients meeting the case definition, preferably the first isolate per patient during the study period, should be included. Isolates from clinical specimens collected for diagnostic purposes (e.g. blood, urine, sputum, wound secretion, etc.) should be given priority, but screening samples can also be relevant depending on the specific investigation. Biological samples required for genomic and epidemiological investigations must be tailored to each event and may include screening or environmental samples.

## Sample size

Depending on the investigation and prevalence, all isolates fitting the case definition can be collected (low prevalence setting) or a limited number of consecutive isolates from each sampling site can be chosen (high prevalence setting). Comparator isolates which are not part of the case definition might be included in the sampling frame when relevant (for example for a case-control study).

## Sample metadata

Each isolate is accompanied by microbiological, clinical, and epidemiological metadata according to the AMR isolate (AMRISO) record type as outlined below. However, lack of metadata should not impair rapid sharing of WGS data as a first step to confirm a multi-country outbreak and the extent of transmission. After confirmation of an outbreak, further epidemiological data might be required for a detailed investigation tailored to each event and may include variables that are supplementary to the AMRISO record type. An example of such a detailed questionnaire on patient exposures is provided in the Annex.

## Species identification and phenotypic antimicrobial susceptibility testing

Species identification and characterisation should be performed following respective national laboratory diagnostic protocols. Antimicrobial susceptibility testing (AST) and the identification of resistance mechanisms should be conducted in accordance with the European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints and guidelines for detection of resistance mechanisms valid at the time of investigation. Detection and characterisation of carbapenem and colistin resistance in Enterobacterales is also outlined in the ECDC consensus protocols for the CCRE survey [17,18].

# Data collection and management

Metadata collection includes variables at the isolate level (microbiological data) and the patient level (epidemiological and clinical data) as described in the AMRISO and AMRISO$AST subject. Data will be transferred to ECDC through the EpiPulse Cases platform, which is only accessible by nominated users such as the OCPs for AMRISO as well as ECDC. The specifications of the AMRISO and AMRISO$AST subjects at the time of submission apply and can be found in the EpiPulse Cases metadata set. A list of variables to be collected for outbreak investigations and related definitions can also be found below. The mandatory variables for a successful data submission to the EpiPulse Cases platform are highlighted in red below. In case of discrepancy, the AMRISO as well as AMRISO$AST subject specifications apply. Hospital denominator data will not be collected for outbreak investigations. WGS data should be generated at the national level and FASTQ files should also be submitted (i) directly via the EpiPulse Cases platform or (ii) indirectly by providing run identifiers from the public repositories such as European Nucleotide Archive (ENA) or Sequence Read Archive (SRA) (see Whole genome sequencing section below). It is possible to instead submit assembled genomes as FASTA files, but raw data are preferable.

## Event identifier

To be able to identify isolates related to outbreak investigations within the large CRE datasets already in EpiPulse, and to differentiate them from other ongoing investigations and surveys, it is important to allocate a unique event identifier to any submission. This code is the EpiPulse event code allocated by EpiPulse upon posting any specific event with the format YYYY-ARH-XXXXX. This code should be included in the **ItemCode** variable in the AMRISO subject to link the data to the corresponding event.

Available metadata should be reported as follows:

## General subject data

The generic variables should be filled out as follows:

- Health topic (**HealthTopic**): the code of the health topic that is being reported should be set as AMRISO.
- Status (**Status**): the Status value is used to provide the functionality for a record within EpiPulse Cases database:
  - default value: NEW/UPDATE. If set to DELETE, the record with the specified **NationalRecordId** is deleted (invalidated) from EpiPulse Cases database, if it exists;

    - if set to NEW/UPDATE, the record is inserted into the database;
    - if the same **NationalRecordId** already exists for the same data source and subject code, then the current submitted record updates (replaces) the existing one.
- Data source (**DataSource**): the data source (surveillance system) that the record originates from; the DataSource value must be a special reference value from EpiPulse Cases metadata set and usually consists of two-letter country code followed by *-AMRISO*, e.g. SE-AMRISO for Sweden.
- Subject code (**SubjectCode**): this variable is a reporting model for a disease/health topic and identifies the reporting structure and format of a record (case based or aggregate reporting); for the outbreak investigation, in the appropriate templates, subject code should be set to:
    - AMRISO for the metadata reporting in the AMRISO subject template (Template_AMRISO.csv);
    - AMRISO$AST for the phenotypic AST data reporting in the AMRISO$AST subject template (Template_AMRISO$AST.csv).
- Reporting country (**ReportingCountry**): the country reporting the record (two-letter location code from the EpiPulse Cases metadata set).
- Isolate unique identifier (**NationalRecordId**).
- Date used for statistics (**DateUsedForStatistics**): the most epidemiologically relevant date for the isolate in the outbreak investigations is date of sampling if available; if not, please use the date of receipt in the source laboratory, and if that is not available, the date of receipt in the NRL (yyyy-mm-dd).

# Isolate data

## Microbiological data

- Bacterial species (**Pathogen**): mainly expected under this protocol: KLEPNE – *K. pneumoniae* SC or ESCCOL – *E. coli*; Other relevant enterobacteria codes can be found in the EpiPulse Cases metadata set.
- Date of sampling (**DateOfSampling**): date the sample from which the isolate was derived was taken (yyyy-mm-dd);
- Date of receipt source laboratory (**DateOfReceiptSourceLab**): date of receipt in source laboratory, i.e. the laboratory the sample was first sent to (yyyy-mm-dd);
- Date of receipt reference laboratory (**DateOfReceiptReferenceLab**): if sample collection date is not available, date of receipt in NRL can be included (yyyy-mm-dd);
- Sample origin (**SampleOrigin**): source that the isolate was obtained from (most commonly: human;
- Specimen source of human samples (**SpecimenSource**): clinical or screening sample;
- Type of human clinical specimen (**Specimen**): aspirate, blood, bone marrow, catheter exit site, cerebrospinal fluid, faeces, gastrointestinal tract, lower respiratory tract, reproductive tract, skin, soft tissue, urine, wound, other.

## Antimicrobial susceptibility testing

- Antimicrobial susceptibility testing results and method(s) will be collected and interpreted based on EUCAST clinical breakpoints for the following antimicrobial agents (**AntimicrobialAgent**) using AMRISO$AST subject:
    - Aminoglycosides: amikacin (AMK), tobramycin (TOB), gentamicin (GEN);
    - Beta-lactams/monobactams: aztreonam (ATM);
    - Beta-lactams/cephalosporins: cefotaxime (CTX), ceftazidime (CAZ), cefiderocol (FDC);
    - Beta-lactams/carbapenems: ertapenem (ETP), imipenem (IPM), meropenem (MEM);
    - Beta-lactam - beta-lactamase inhibitor combinations: piperacillin-tazobactam (TZP), ceftazidime-avibactam (CZA), meropenem-vaborbactam (MEV), aztreonam-avibactam (AZA), imipenem-relebactam (IMR), ceftolozane-tazobactam (CZT);
    - Fluoroquinolones: ciprofloxacin (CIP), levofloxacin (LVX);
    - Tetracyclines: tigecycline (TGC, *E. coli* only);
    - Polymyxins: colistin (COL);
    - Other: trimethoprim-sulfamethoxazole (SXT), fosfomycin (FOS, *E. coli* only).
- AST record identifier (**NationalRecordId**): unique identifier for each antimicrobial susceptibility test selected and generated by the country reporting the record
- Parent national record identifier (**ParentNationalRecordId**): the corresponding parent identifier for each record (i.e. pseudonymised identifier corresponding to the specific isolate in AMRISO subject); a record with no corresponding parent identifier will not be added to EpiPulse Cases database
- AST method used for the antimicrobial agent (**ASTMethod**): automated instrument method, broth microdilution, antimicrobial gradient, disc diffusion test
- Minimum inhibitory concentration (MIC) sign (**MICSusceptibilitySign**):

    - < (Less than)
    - <= (Less than or equal)
    - = (Equal)
    - > (Greater than)
    - >= (Greater than or equal)
- MIC value (**MICValueAST**): in mg/l; use '.' as decimal delimiter, e.g. 0.25
- Disk diffusion zone diameter sign (**DDZDSusceptibilitySign**):
    - < (Less than)
    - <= (Less than or equal)
    - = (Equal)
    - > (Greater than)
    - >= (Greater than or equal)
- Disk diffusion zone diameter value (**DDZDValueAST**): in mm

## Whole genome sequencing

It is expected that WGS data are collected from NRLs or produced by an appointed central laboratory for a centralised WGS analysis approach. The following variables will be collected:

- protocol used for sequencing, limited to the sequencing technology used and the read length (**WGSProtocol**):
    - ILLUMINA: Illumina short-read sequencing (<1000 bp);
    - IONTORRENT: Ion Torrent short-read sequencing (<1000 bp);
    - MGI: MGI short-read sequencing (<1000 bp);
    - ONT: Oxford Nanopore long-read sequencing (>1000 bp);
    - PACBIO: Pacific Biosciences long-read sequencing (>1000 bp).
- WGS accession identifier (**WgsAccession**): ENA or SRA run identifier, based on which, the sequence read data can be retrieved from the public domain. Starts with ERR or SRR, i.e. not the sample or experiment which start with ERS/ERX or SRS/SRX.
- If assemblies are provided instead of raw reads (not recommended), the assembly software used should be reported in **WgsAssembler**.

Any isolates that are part of outbreak investigations should be stored with a suitable method to preserve their viability until the end of the investigation. If there are difficulties with appropriate long-term storage, isolates can be sent to the ECDC strain collection for storage.

# Patient data

## Demographic data

- age (**Age**): age of patient in years at the date of sampling;
- gender (**Gender**): female, male or other;
- type of patient (**PatientType**): admission category of the patient, inpatient, outpatient or other;
- type of unit/ward (**HospitalUnitType**): hospital department at sample collection: emergency department, intensive care unit (ICU), infectious diseases ward, inpatient ward, internal medicine, obstetrics/gynecology, haematology/oncology, paediatrics/neonatal, paediatrics/neonatal ICU, primary health care, surgery, urology ward, other;
- healthcare facility NUTS-2 level location (**HealthcareFacilityLocation**): NUTS-2 region of the healthcare facility where the respective isolate is originating from;
- date of hospitalisation (**DateOfHospitalisation**): date of hospitalisation or outpatient visit (yyyy-mm-dd).

## Epidemiological and clinical data

- clinical significance (**ClinicalSignificance**): colonisation or infection or undetermined/unknown clinical significance;
- organ/system or location of infection/colonisation (**SiteOfInfection**): intra-abdominal, bloodstream, lower respiratory tract, skin or soft tissue, urinary tract, other;
- hospital-acquired or community-onset (**HospitalAcquiredSample**):
    - Yes: hospital-acquired colonisation/infection if the sample is collected from an inpatient later than 48 h post-admission;
    - No: community-onset if the sample is collected from an outpatient or from a hospitalised patient earlier than 48 h post-admission.

## Healthcare exposure/referral history

- direct hospital transfer (**HospitalTransfer**): direct transfer of patient from another hospital to the current hospital where patient is admitted:
  - Yes, same country: another hospital in the same country (specify country in **CountryOfHospitalTransfer**);
  - Yes, other country: a hospital in another country (specify country in **CountryOfHospitalTransfer**);
  - No.
- previous hospitalisation within six months before sampling date (**PriorHospitalisation**):
  - Yes, same country: another hospital in the same country (specify country in **CountryOfPriorHospitalisation**);
  - Yes, other country: a hospital in another country (specify country in **CountryOfPriorHospitalisation**);
  - No.
- previous residence in a long-term/elderly care facility, direct transfer or within six months before sampling date (**PriorResidenceInLTCF**):
  - Yes, same country (specify country in **CountryOfPriorResidenceInLTCF**);
  - Yes, other country (specify country in **CountryOfPriorResidenceInLTCF**);
  - No.

## Travel history

- recent (past six months) travel history to another country prior to sample date (**Travel**):
  - Yes (specify country in **TravelLocation**);
  - No.

## Data not collected for the CRE outbreak investigations

The following variables are present in the AMRISO dataset but will NOT be collected for CRE outbreak investigations:

- AMRISO subject:
  - hospital identifier (**HospitalId**);
  - date of onset of disease (**DateOfOnset**);
  - date of discharge (**DateOfDischarge**);
  - date of death (**DateOfDeath**);
  - outcome of hospital stay (**OutcomeHospital**);
  - prescribed antimicrobial agent (**PrescribedAntimicrobial**);
  - sample identifier (**SampleId**);
  - laboratory code (**LaboratoryCode**);
  - WGS assembled genome (**WgsAssembly**);
  - WGS raw sequence reads (**WgsRawReads**).
- AMRISO$AST subject:
  - AST guideline (**ReferenceGuidelinesSIR**).

In addition, all variables of the AMRISODENOM subject are NOT collected for CRE outbreak investigations.

## Whole genome sequencing data

WGS data are either produced by a central typing laboratory or collected from the national reference/expert laboratories for a centralised WGS analysis approach. Sequencing data should ideally be submitted as FASTQ files. To ensure data comparability, EQA exercises will be offered by EURL-PH-AMR activities to Member States. Both short-read and long-read sequencing technologies can be employed depending on the objectives of the investigation. For more information on CRE WGS recommendations, refer to the EURGen-RefLabCap proposed protocol, 'EURGen-RefLabCap harmonized common WGS-based genome analysis methods and standard protocols for national CCRE surveillance and integrated outbreak investigations'.

Based on needs, WGS efforts can be supported by ECDC. Should WGS support be required, information on sample preparation, management, and shipment can be obtained by contacting typing@ecdc.europa.eu. Isolates should be transferred directly from the NRL to relevant contractors. Packaging should comply with international shipment regulations for biohazardous material. ECDC recommends sharing genome sequence data in the public domain, e.g., European Nucleotide Archive (ENA) or GenBank maintained by the National Center for Biotechnology Information (NCBI), to allow easy access for all international stakeholders. If WGS data is generated using the ECDC WGS support contract, they will be uploaded to public repositories by default.

# Data protection

Submitting EU/EEA and candidate countries should pseudonymise all personal data relevant for an outbreak investigation before transferring them to ECDC. ECDC will process all personal data in accordance with Regulation (EU) 2018/1725. Epidemiological data and pathogen sequencing data will be stored on ECDC's digital platforms for surveillance with restricted access for a period of ten years from their collection, and will be anonymised afterwards. Upon request, ECDC may grant access to subsets of epidemiological data to third parties for scientific or other purposes in public interest after having priorly consulted the submitting countries. For further information about the rules on the access to data stored in ECDC's surveillance platforms, please consult the document on "Data protection governance for Epipulse".

# Data analysis

## Epidemiological analysis

Epidemiological information received from countries will be aggregated into a master line list that will be used to perform a descriptive analysis by time, place, and person. An epidemic curve will be prepared displaying the number of cases over time on the appropriate time scale. Cases numbers will be presented by country or higher geographic resolution as applicable, using the nomenclature of territorial units for statistics (NUTS) [19]. Respective maps will be prepared using a geospatial data tool, e.g. the ECDC Map Maker tool (EMMa) [20]. Demographic and epidemiological characteristics of cases will be tabulated in an aggregated format. Text and figures will be prepared using the ECDC style guide and the ECDC guidelines for presentation of surveillance data [21].

## Bioinformatic analysis

WGS data can be submitted to ECDC in the form of assemblies or raw reads. If raw reads are submitted, these will be assembled using the standard ECDC bioinformatics pipeline, currently using SPAdes and post-assembly mapping and error correction. All WGS data will be subjected to quality control following standard criteria:

- for raw reads: read length, coverage, number of reads;
- for assemblies: number of contigs, N50, genome coverage and expected genome size with at least 90% core genome loci covered using a defined core genome multilocus sequence typing (cgMLST) scheme when available.

If submitting assembled genomes, it is recommended that relevant quality parameters are shared with ECDC. For more details on sequence quality control refer to the EURGen-RefLabCap protocols mentioned above.

Subsequently, sequence-derived information, such as ST, cgMLST profile, predicted AMR determinants (resistome) and virulence determinants (virulome) will be retrieved through taxonomic and functional gene identification algorithms and nomenclature annotation through public access typing and bioinformatic analyses platforms ;

- EnteroBase as a source of cgMLST schemes and sometimes for finding relevant background isolate data;
- Bacterial Isolate Genome Sequence Database at the Institut Pasteur for cgMLST schemes;
- Software and databases provided by the Center for Genomic Epidemiology at Technical University of Denmark (e.g., MLST, ResFinder, PointFinder), installed locally at ECDC;
- Centre for Genomic Pathogen Surveillance software (e.g., PathogenWatch);
- Kleborate for specific analyses for *Klebsiella*, installed locally at ECDC and/or used through PathogenWatch;
- NCBI Pathogen Detection for finding relevant background isolate data for inclusion in the analysis, based on e.g. resistance determinants, ST, or clustering with outbreak reference isolates;
- Other relevant open-access tools and databases as needed.

Phylogenetic trees based on core genome allelic differences (ADs) will be generated to visualise genetic clusters and to determine the phylogenetic relationships between isolates. Cluster definitions may be determined per investigation, but as a baseline, for *E. coli* 10 cgMLST ADs (Enterobase scheme) single linkage; for *K. pneumoniae* 10 cgMLST ADs (Riddom scheme) single linkage may be used. In special cases, core genome single nucleotide polymorphisms (cgSNPs) or whole genome single nucleotide polymorphisms (wgSNPs) can also be used for more in-depth analysis. Outbreak investigations and related analysis can be supported by the EURL-PH-AMR.

# Reporting of results

Preliminary results will be reported, as soon as available, to the country's nominated Operational Contact Points (OCPs) for Epidemiology/Microbiology/Bioinformatics – Antimicrobial-Resistant Isolates (AMRISO), and the analysis results will be made available to OCPs in a molecular typing tool through the EpiPulse platform. A draft report will be prepared by ECDC and sent to the above mentioned OCPs for review including consultation on the next steps of the investigation. Depending on the results and input from the OCPs, event information alongside a brief situation assessment will be included in EpiPulse as well as the daily and weekly Communicable Disease Threat Report. If required, a confidential collaboration site (ECON-site) will be established for data sharing between involved countries. Investigation results will be published in an ECDC surveillance report or in a Rapid Risk Assessment based on the decision taken at the ECDC round table. If relevant, a scientific publication might also be prepared together with involved national contact points. Any output will only be published after explicit written approval from countries that have provided data for the investigation.

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# Annex

# Example questionnaire template for patient exposures for CRE outbreak investigations

The questionnaire below gives an example of a patient exposure questionnaire used for a EURGen-Net multi-country outbreak investigation. The questionnaire was initially developed for cases of OXA-244 producing *E. coli*. Part A and B of the current version were used for investigation of cases of NDM-5-producing *Enterobacter hormaechei* in several EU countries in 2025-2026. The pathogen under investigation will need to be added to the template for each specific investigation.

## PART A – for healthcare providers

**Introduction**

This section is to be completed with information about the outbreak relevant for healthcare providers. This questionnaire is intended to collect information on possible sources as part of the outbreak investigation.

**Case definition:** This section is to be completed with the case definition (example: any patient with NDM-5-producing *E. hormaechei* ST1344 detected from a clinical or screening sample in the European Union/European Economic Area in 2025).

Name of respondent to this questionnaire: _____

Email address: _____

**Basic demographic and clinical information of the patient**

1. Country (of residence of the patient) _____
2. Age (of patient) _____ (in years)
3. Sex (of patient): female ☐ / male ☐ / unknown ☐
4. Date of first sample positive for (pathogen to be added)_____ (= sample collection date) _____
5. Type of sample _____and reason for sampling _____
6. Did the patient have symptoms of infection caused by (pathogen to be added)_____?

   Yes ☐ / No ☐ / Unknown ☐, if yes, please specify which symptoms and date of symptom onset

   _____

   _____
7. Did the patient have any significant comorbidities or conditions causing immunosuppression?

Yes ☐ / No ☐ / Unknown ☐, if yes, please specify

_____

_____

8. Did the patient travel in the six months prior to the sample positive for (pathogen to be added)?
   Yes ☐ / No ☐ / Unknown ☐, if yes, please specify to which countries

   _____

**Hospitalisation and healthcare contact history**

9. Was the patient hospitalised at the time of the sample positive for (pathogen to be added)?
   Yes ☐ / no ☐ / Unknown ☐
   If hospitalised, please specify:
   - Date of hospitalisation_____
   - Diagnosis/reason for admission _____
   - Planned hospitalisation ☐, unplanned hospitalisation ☐, Unknown ☐
     - If unplanned, did hospitalisation take place via an emergency unit?

       Yes ☐ / No ☐ / Unknown ☐
     - How did the patient arrive in the hospital?

       Ambulance ☐, Private transport ☐, Unknown ☐

10. Has the patient undergone any medical procedure including invasive procedures (for example surgery, endoscopic procedures, balloon angioplasty, stenting, ventilation, dialysis etc.) or non-invasive procedures (for example diagnostic imaging) within six months before detection of (pathogen to be added)?

    Yes ☐ / No ☐ / Unknown ☐, if yes, please specify below:
    - Procedure 1 _____month/year_____
      place (hospital, department, city) of the procedure_____
    - Procedure 2 _____month/year_____
      place (hospital, department, city) of the procedure_____
    - Procedure 3 _____month/year_____
      place (hospital, department, city) of the procedure_____
    - Procedure 4 _____month/year_____
      place (hospital, department, city) of the procedure_____
    - Procedure 5 _____month/year_____
      place (hospital, department, city) of the procedure_____
    - Procedure 6 _____month/year_____
      place (hospital, department, city) of the procedure_____

- Procedure 7 _____month/year_____
  place (hospital, department, city) of the procedure_____
- Procedure 8 _____month/year_____
  place (hospital, department, city) of the procedure_____
- Procedure 9 _____month/year_____
  place (hospital, department, city) of the procedure_____
- Procedure 10 _____month/year_____
  place (hospital, department, city) of the procedure_____

11. Has the patient had any previous hospital admissions within six months prior to detection of (pathogen to be added)? Yes ☐ / No ☐ / Unknown ☐ If yes, please specify below
    - Admission 1 from_____to_____and place (hospital, department, city) of admission_____
    - Admission 2 from_____to_____and place (hospital, department, city) of admission_____
    - Admission 3 from_____to_____and place (hospital, department, city) of admission_____
    - Admission 4 from_____to_____and place (hospital, department, city) of admission_____
12. Did the patient have contact with patients or shared a room with patients known to be infected or colonised (carrier) with a similar or another multidrug-resistant pathogen within six months prior to detection of (pathogen to be added)?
    Yes ☐ / No ☐ / Unknown ☐ If yes, please specify which pathogen_____
13. Has the patient had any invasive medical devices within six months prior to detection of (pathogen to be added)?
    Peripheral intravenous line ☐, Central venous catheter ☐, Urinary catheter ☐, Surgical drain ☐Other, please specify _____ no invasive medical devices ☐ Unknown ☐
14. Has the patient lived in a nursing home or residential care facility within the six months prior to detection of (pathogen to be added)? Yes ☐ / No ☐ / Unknown ☐
15. Did the patient receive home healthcare services within six months prior to detection of (pathogen to be added)? Yes ☐ / No ☐ / Unknown ☐
16. Did the patient have any wounds or skin infection within six months prior to detection of (pathogen to be added)*?* Yes ☐ / No ☐ / Unknown ☐ if yes, which kind of wound/infection
    _____
17. Did the patient receive any total parenteral nutrition, enteral nutrition or supplementary medical nutrition within six months prior to detection of (pathogen to be added)?

Yes ☐ / No ☐ / Unknown ☐, if yes which type of nutrition/brand_____

_____

**18. Medication** received within six months prior to detection of (pathogen to be added).

If a separate medication list is available, it can be attached to this questionnaire instead of completing the list below. If details such as dose, treatment duration or route of administration are not available, please complete the list of substances and leave the respective other fields empty.

Substance 1_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 2_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 3_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 4_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 5_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 6_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 7_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 8_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 9_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 10_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 11_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 12_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 13_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 14_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 15_____, dose_____ duration of treatment from_____to_____

route of administration oral ☐, intravenous ☐ other ☐, please specify_____

Substance 16_____, dose_____ duration of treatment from_____to_____
route of administration oral ☐, intravenous ☐ other ☐, please specify_____
Substance 17_____, dose_____ duration of treatment from_____to_____
route of administration oral ☐, intravenous ☐ other ☐, please specify_____
Substance 18_____, dose_____ duration of treatment from_____to_____
route of administration oral ☐, intravenous ☐ other ☐, please specify_____
Substance 19_____, dose_____ duration of treatment from_____to_____
route of administration oral ☐, intravenous ☐ other ☐, please specify_____
Substance 20_____, dose_____ duration of treatment from_____to_____
route of administration oral ☐, intravenous ☐ other ☐, please specify_____

**19. Medical/care products and disposable material** used for the patient within six months prior to detection of (pathogen to be added) (for example dressings, sutures (absorbable/non-absorbable), wound debridement products, cleansers, creams, wash lotions, washing wipes, products related to diagnostic imaging such as ultrasound gels). Please also include any nutritional treatment (including protein powder or whey protein) and laxatives here if not already listed under questions 17. or 18. above.

Product 1_____, purpose/place of use_____
Product 2_____, purpose/place of use_____
Product 3_____, purpose/place of use_____
Product 4_____, purpose/place of use_____
Product 5_____, purpose/place of use_____
Product 6_____, purpose/place of use_____
Product 7_____, purpose/place of use_____
Product 8_____, purpose/place of use_____
Product 9_____, purpose/place of use_____
Product 10_____, purpose/place of use_____
Product 11_____, purpose/place of use_____
Product 12_____, purpose/place of use_____
Product 13_____, purpose/place of use_____
Product 14_____, purpose/place of use_____
Product 15_____, purpose/place of use_____
Product 16_____, purpose/place of use_____
Product 17_____, purpose/place of use_____
Product 18_____, purpose/place of use_____
Product 19_____, purpose/place of use_____
Product 20_____, purpose/place of use_____
Product 21_____, purpose/place of use_____

Product 22_____, purpose/place of use_____

Product 23_____, purpose/place of use_____

Product 24_____, purpose/place of use_____

Product 25_____, purpose/place of use_____

Please enter any other product or medication that could not be included above here:

_____

_____

_____

Please let us know if you have any further observations that could be helpful in finding the source:

_____

_____

_____

## PART B – for patients (interview or filled by the patient)

An antibiotic-resistant bacterium was detected from a sample that you have provided on _____. The purpose of the questions below is to gather more information on how or where you could have acquired this antibiotic-resistant bacterium and to identify a potential source. All questions below refer to the period before the detection of this antibiotic-resistant bacterium (date of sample as mentioned above).

**Questions on prior medical treatment**

1. In the six months prior to detection of the antibiotic-resistant bacterium, have you been admitted to a hospital? Yes ☐ / No ☐ / Do not know ☐ If yes, please specify further below:

    - Admission 1: Due to which illness/treatment? _____
      In which hospital and department? _____
      When (admission and discharge dates)? _____
    - Admission 2: Due to which illness/treatment? _____
      In which hospital and department? _____
      When (admission and discharge dates)? _____
    - Admission 3: Due to which illness/treatment? _____
      In which hospital and department? _____
      When (admission and discharge dates)? _____
    - Admission 4: Due to which illness/treatment? _____
      In which hospital and department? _____
      When (admission and discharge dates)? _____
    - Admission 5: Due to which illness/treatment? _____
      In which hospital and department? _____
      When (admission and discharge dates)?_____

2. In the six months before detection of the antibiotic-resistant bacterium, have you visited a doctor or healthcare centre without hospitalisation?
   Yes ☐ / No ☐ / Do not know ☐ If yes, please specify below

    - Visit 1: Due to which illness/treatment? _____
      Which doctor/healthcare centre _____
      When (on which dates)? _____
    - Visit 2: Due to which illness/treatment? _____
      Which doctor/healthcare centre? _____
      When (on which dates)? _____
    - Visit 3: Due to which illness/treatment? _____

Which doctor/healthcare centre? _____

When (on which date(s))? _____

- Visit 4: Due to which illness/treatment? _____

  Which doctor/healthcare centre? _____

  When (on which date(s))? _____
- Visit 5: Due to which illness/treatment? _____

  Which doctor/healthcare centre? _____

  When (on which date(s))? _____
- Visit 6: Due to which illness/treatment? _____

  Which doctor/healthcare centre? _____

  When (on which date(s))? _____
- Visit 7: Due to which illness/treatment? _____

  Which doctor/healthcare centre? _____

  When (on which date(s))? _____
- Visit 8: Due to which illness/treatment? _____

  Which doctor/healthcare centre? _____

  When (on which date(s))? _____

3. Please list any medication you have taken within six months before detection of the antibiotic-resistant bacterium, including any medication received with or without prescription, and any supplements, laxatives or herbal remedies here:
   - Medication 1_____, dose_____ duration of treatment from_____to_____
   - Medication 2_____, dose_____ duration of treatment from_____to_____
   - Medication 3_____, dose_____ duration of treatment from_____to_____
   - Medication 4_____, dose_____ duration of treatment from_____to_____
   - Medication 5_____, dose_____ duration of treatment from_____to_____
   - Medication 6_____, dose_____ duration of treatment from_____to_____
   - Medication 7_____, dose_____ duration of treatment from_____to_____
   - Medication 9_____, dose_____ duration of treatment from_____to_____
   - Medication 10_____, dose_____ duration of treatment from_____to_____
   - Medication 11_____, dose_____ duration of treatment from_____to_____
   - Medication 12_____, dose_____ duration of treatment from_____to_____
   - Medication 13_____, dose_____ duration of treatment from_____to_____
   - Medication 14_____, dose_____ duration of treatment from_____to_____
   - Medication 15_____, dose_____ duration of treatment from_____to_____

**Questions on family members and other contacts**

4. How many people live in your household? _____
   How many of those are:
   Adult _____, children aged 2-16 years _____, or children less than 2 years old _____
5. In the six months before detection of the antibiotic-resistant bacterium, has anyone in your household been hospitalised Yes ☐ / No ☐ / Do not know ☐. If yes, please specify:

   - Who (relation)? _____When (admission and discharge dates) _____
   - Who (relation)? _____When (admission and discharge dates) _____
   - Who (relation)? _____When (admission and discharge dates) _____
   - Who (relation)? _____When (admission and discharge dates) _____
   - Who (relation)? _____When (admission and discharge dates) _____

6. In the six months before or any time after detection of the antibiotic-resistant bacterium, had any of your household members a similar or another antibiotic-resistant bacterium?

   Yes ☐ / No ☐ / Do not know ☐. If yes, please specify:
   Who (relation)? _____ When was it detected? _____

**Questions on travel**

7. In the six months before detection of the antibiotic-resistant bacterium, did you travel to another country (even if only for a day)? Yes ☐ / No ☐ / Do not know ☐. If yes, please specify

   - Country 1 _____ when (dates) _____
   - Country 2 _____ when (dates) _____
   - Country 3 _____ when (dates) _____
   - Country 4 _____ when (dates) _____
   - Country 5 _____ when (dates) _____
   - Country 6 _____ when (dates) _____
   - Country 7 _____ when (dates) _____
   - Country 8 _____ when (dates) _____
   - Country 9 _____ when (dates) _____
   - Country 10_____ when (dates) _____
   - If yes to question 7, have you visited a doctor, healthcare centre or hospital in any of the countries that you travelled to? Yes ☐ / No ☐ / Do not know ☐. If yes, please specify:

Healthcare centre/clinic name and location: _____

8. In the six months before detection of the antibiotic-resistant bacterium, did anyone else in your household travel to other countries? Yes ☐ / No ☐ / Do not know ☐. If yes, please specify:

   - Country 1 _____ when (dates) _____
   - Country 2 _____ when (dates) _____
   - Country 3 _____ when (dates) _____
   - Country 4 _____ when (dates) _____
   - Country 5 _____ when (dates) _____
   - Country 6 _____ when (dates) _____
   - Country 7 _____ when (dates) _____
   - Country 8 _____ when (dates) _____
   - Country 9 _____ when (dates) _____
   - Country 10_____ when (dates) _____

   - If yes, did your household member visit a doctor, healthcare centre or hospital in any of the countries that they travelled to? Yes ☐ / No ☐ / Do not know ☐. If yes, please specify

     Healthcare centre/clinic name and location:_____

**Questions on employment setting and potential exposures**

9. Do you work in any of the following settings? Healthcare facility ☐, Community facility ☐, Veterinary facility ☐, Food service setting ☐, Other ☐, please specify your occupation _____ Not applicable (not employed) ☐

   If you work in a healthcare facility, have you cared, in the past six months, for patients with a similar or another antibiotic-resistant bacterium?

   Yes ☐ / No ☐ / Do not know ☐. If yes, please specify _____

**Questions on animal contact**

10. Do you have pets, or did you have contact with pets or farm animals or their food or their droppings, e.g. visit to the farm, petting zoo, professional activity (in the one month before detection of the antibiotic-resistant bacterium)?

    Yes ☐ / No ☐ Do not know ☐. If yes, which of the following*?*

| Contact with pets, animals or their food | Yes | Probably yes | Probably not | No |
|---|---|---|---|---|
| Bird | ☐ | ☐ | ☐ | ☐ |
| Cat | ☐ | ☐ | ☐ | ☐ |
| Dog | ☐ | ☐ | ☐ | ☐ |
| Dog treats like pig ears, rawhide chews | ☐ | ☐ | ☐ | ☐ |
| Chicken/baby chicks | ☐ | ☐ | ☐ | ☐ |
| Cow/bull/steer/calves | ☐ | ☐ | ☐ | ☐ |
| Goat, sheep, or lamb | ☐ | ☐ | ☐ | ☐ |
| Horse | ☐ | ☐ | ☐ | ☐ |
| Pig | ☐ | ☐ | ☐ | ☐ |
| Turkey | ☐ | ☐ | ☐ | ☐ |
| Reptile (including snakes, iguanas or other lizards, and turtles) | ☐ | ☐ | ☐ | ☐ |
| Amphibian (such as frogs) | ☐ | ☐ | ☐ | ☐ |
| Tropical fish | ☐ | ☐ | ☐ | ☐ |

**Questions on nutritional habits**

11. Is your diet predominantly or frequently based on:
    - Vegetarian or vegan food?

      Yes ☐ / No ☐ / Unknown ☐
    - A religious rule (e.g. kosher, halal)?

      Yes ☐ / No ☐ / Unknown ☐
    - Uncooked, cured meat or raw sausage, e.g. sausages, cold meat, salami, etc.?

      Yes ☐ / No ☐ / Unknown ☐
    - A medical diet due to food allergies/intolerances, weight loss, etc.?

      Yes ☐ / No ☐ / Unknown ☐
12. In the month before detection of the antibiotic-resistant bacterium, did you receive and consume food that someone brought to you from other countries?

    Yes ☐ / No ☐/ Unknown ☐. If yes, what and when and which country of origin?

    _____

13. In the month before detection, did you take any of the following: dietary or food supplements ☐, laxatives (for example macrogel laxatives) ☐, fibre supplements (for example psyllium husk) ☐ probiotics ☐. If yes, please specify which ones

_____

14. In the month before detection, have you used any of the following: protein drinks ☐, whey proteins ☐, dried milk powder ☐, dried egg powder ☐, dried fruit ☐? If yes, please specify which ones_____

15. Is there any additional information that you would like to share that could help us with the investigation about the source of infection?

_____

_____

_____

_____

_____

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**European Centre for Disease Prevention and Control (ECDC)**

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of the European Union