

REGIONAL OFFICE FOR Europe

Central Asian and Eastern European Surveillance of Antimicrobial Resistance

CAESAR Manual Version 2, 2015

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Central Asian and Eastern European Surveillance of **Antimicrobial Resistance**

> CAESAR Manual Version 2, 2015

Abstract

This document describes the objectives, methodology and organization of the Central Asian Eastern European Surveillance of Antimicrobial Resistance network. The document provides the steps that have to be taken by a country for participation, the steps for routine data collection, and the protocols and AMR case definitions to be used. As CAESAR is fully complementary to and compatible with the European Antimicrobial Resistance Surveillance Network at the European Center for Disease Prevention and Control, this manual is an adaptation from the EARS-Net reporting protocol (version 4, 2014)2 and the EARSS manual 2005.

Keywords

ANTIMICROBIAL RESISTANCE NATIONAL SURVEILLANCE NETWORKS ANTIMICROBIAL SUSCEPTIBILITY TESTING DATA COLLECTION DATA ANALYSIS

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Abbreviations

AMR	Antimicrobial resistance
AST	Antimicrobial susceptibility test
CAESAR	Central Asian and Eastern European Surveillance of Antimicrobial Resistance
CLSI	Clinical and Laboratory Standards Institute
CSF	Cerebrospinal fluid
EARS-Net	European Antimicrobial Resistance Surveillance Network
EARSS	European Antimicrobial Resistance Surveillance System
ECDC	European Centre for Disease Prevention and Control
ESBL	Extended-spectrum beta lactamase
ESCMID	European Society of Clinical Microbiology and Infectious Diseases
ESGARS	ESCMID Study Group for Antimicrobial Resistance Surveillance
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FTP	File transfer protocol
ICM	Intersectoral coordination mechanism
ICU	Intensive care unit
MIC	Minimal inhibitory concentration
MRSA	Methicillin-resistant Staphylococcus aureus
MSSA	Methicillin-susceptible Staphylococcus aureus
PNSP	Penicillin nonsusceptible Streptococcus pneumoniae
RIVM	National Institute for Public Health and the Environment (in the Netherlands)
RIVM-Cib	Centre for Infectious Disease Control of RIVM
S/I/R	Susceptible/Intermediate/Resistant
VRE	Vancomycin-resistant enterococci
WHO	World Health Organization
WHONET	WHO microbiology laboratory database software



Introduction

1.1. What is CAESAR?

CAESAR stands for Central Asian and Eastern European Surveillance of Antimicrobial Resistance. The CAESAR network is a joint initiative of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), the National Institute for Public Health and the Environment (RIVM) in the Netherlands and the World Health Organization (WHO) Regional Office for Europe, to survey, contain and prevent emergence and spread of antibiotic resistance in a selected number of countries in the WHO European Region.

Antimicrobial resistance (AMR) and especially resistance to antibiotics is an increasing global public health problem. The WHO European Region is no exception, and resistance of some pathogens now reaches over 50% in some countries and new resistance mechanisms are emerging and spreading rapidly. Surveillance of antibiotic resistance is undertaken by all 28 countries of the European Union, as well as in Norway, Iceland and Liechtenstein under the EARS-Net (European Antimicrobial Resistance Surveillance Network) system of the European Commission coordinated by the European Centre for Disease Prevention and Control (ECDC). This system is a well-developed and accepted surveillance network to report and survey trends in antibiotic resistance. However, the emergence and spread of antibiotic resistance does not acknowledge borders. Therefore, to safeguard public health in Europe it is of paramount importance to develop a harmonized and coordinated surveillance network in all 53 countries of the WHO European Region.

The aim of the CAESAR network is to gradually set up a network of national surveillance systems of antibiotic resistance in all countries of the WHO European Region that are not part of, or affiliated with, EARS-Net. In order to enable compilation and comparison of data in the whole European Region, the methodology of EARS-Net will be used in close collaboration with ECDC. In the future, this approach will enable joined reports of antibiotic resistance for all 53 countries based on the same standards and methodologies.

The CAESAR network is a fundamental step in the implementation of the European strategic action plan on antibiotic resistance that was adopted by the WHO Regional Committee for Europe in Baku, Azerbaijan in September 2011¹. CAESAR meets the first two of the seven strategic objectives of the European strategic action plan on antibiotic resistance: 1) promoting national coordination and 2) strengthening surveillance of antibiotic resistance. In addition, CAESAR is a good starting point in achieving the other objectives: 3) promoting rational use of antibiotics, including surveillance of antibiotic consumption; 4) improving infection control and stewardship of antibiotic use in health care settings; 5) promoting surveillance, prevention and control of antibiotic resistance in the food chain; 6) promoting research and innovation on new antibiotics; and 7) improving awareness of antibiotic use and the risk of increasing resistance.

1.2. Objectives for AMR surveillance

The CAESAR strategy for AMR surveillance is in line with the one adopted by the former European Antimicrobial Resistance Surveillance System (EARSS) and EARS-Net. Therefore, the approach is to maintain a comprehensive surveillance system that links national networks and provides comparable and validated data on the prevalence and trends in AMR of a core group of invasive bacteria.

The specific objectives are as follows:

- collect comparable and validated AMR data;
- analyse trends over time;

¹ http://www.euro.who.int/__data/assets/pdf_file/0008/147734/wd14E_AntibioticResistance_111380.pdf

- provide timely AMR data that constitute a basis for policy decisions;
- encourage the implementation, maintenance and improvement of national AMR surveillance programmes;
- support national systems in their efforts to improve diagnostic accuracy and quality at every level of the surveillance chain;
- link AMR data to factors influencing the emergence and spread of AMR, such as antibiotic use data;
- link the European scientific and professional community to exchange experience and expertise; and
- initiate, foster and complement scientific research in Europe in the field of AMR.

1.3. CAESAR manual and related EUCAST guidelines

This document describes the objectives, methodology and organization of CAESAR, the steps that have to be taken by a country for participation, the steps for routine data collection and the protocols and AMR case definitions to be used. As CAESAR is fully complementary to and compatible with EARS-Net, this manual is an adaptation from the EARS-Net reporting protocol (version 4, 2014)² and the EARSS manual 2005. In addition to the CAESAR manual, the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance is available on the EUCAST website³. The guideline includes definitions of the mechanisms of resistance, an outline description of the recommended methods of detection, and references that detail descriptions of the methods of detection for:

- 1. carbapenemase-producing Enterobacteriaceae
- 2. extended-spectrum β -lactamase-producing Enterobacteriaceae
- 3. acquired AmpC β-lactamase-producing Enterobacteriaceae
- 4. methicillin-resistant Staphylococcus aureus (MRSA)
- 5. glycopeptide nonsusceptible S. aureus
- 6. vancomycin-resistant enterococci (VRE)
- 7. penicillin nonsusceptible *Streptococcus pneumoniae* (PNSP).

3 http://www.eucast.org/resistance_mechanisms/

² http://ecdc.europa.eu/en/activities/surveillance/EARS-Net/Documents/2015-EARS-Net-reporting-protocol.pdf

CHAPTER 1





Organization of the CAESAR network

2.1. The CAESAR project group at the international level

The CAESAR project group consists of three representatives from WHO Regional Office for Europe, and two from the ESCMID Study Group for Antimicrobial Resistance Surveillance (ESGARS-ESCMID) and WHO Collaborating Centre for AMR Epidemiology and Surveillance at the Centre for Infectious Disease Control (Clb) of RIVM (RIVM-Clb); see Chapter 3.2 for contact details:

- Dr Danilo Lo Fo Wong (WHO Regional Office for Europe)
- Dr Nienke van de Sande Bruinsma (WHO Regional Office for Europe)
- Dr Saskia Nahrgang (WHO Regional Office for Europe)
- Dr Christian Giske (ESGARS-ESCMID)
- Dr Robert Skov (ESGARS-ESCMID)
- Jos Monen, MSc (RIVM-CIb)
- Dr Tjalling Leenstra (RIVM-CIb)

Figure 1. CAESAR organization structure



WP1 – Country situation analysis; WP2 – Laboratory capacity building; WP3 – Set up surveillance network on the national level; WP4 – Collect AMR surveillance data of the participating countries in the CAESAR database platform; WP5 – Project output

2.2. The national networks

Each participating country needs to appoint an AMR focal point and a national data manager. The main task of the AMR focal point is to connect the CAESAR-specific activities of the participating laboratories and ensure that the laboratories generate their antimicrobial susceptibility test (AST) data according to CAESAR protocols, as published in this manual. The main task of the national data manager is to collect, approve and forward resistance data every quarter or year and to assist the AMR focal point. Often the data requested by the CAESAR network is already collected via the national surveillance system that is already in place in a country. Alternatively, a national surveillance network will need to be developed using CAESAR methodology as described in this manual. The role of the AMR focal point is to coordinate the national surveillance system on AMR. In this role, they encourage the participation of laboratories and hospitals such that a good representation of the population is achieved. Preferably, coverage should exceed 20% of the national population, and health care systems should be represented with respect to the mix of academic/tertiary care hospitals and general hospitals. Furthermore, geographic distribution should be even and include urban and rural catchment areas.

2.3. Collecting and processing data

CAESAR data collection includes routinely collected susceptibility test results of invasive isolates and background information about patients. Laboratories are asked to report the first isolate from blood per species or cerebrospinal fluid per patient per year. According to the specifications of the CAESAR exchange format⁴ (see Chapter 5) the system requires the following: laboratory code, isolate sample number, isolate source, date of sample collection, sex, month and year of birth, hospital code, hospital department, origin of patient, level of care (ambulant, hospitalized, etc.), bacterial species and AST results as specified in the protocols. Furthermore, optional data are collected including susceptibility data for other antibiotics and the serotype of the reported *S. pneumoniae* strains.

In order for CAESAR to provide a representative description of the antimicrobial susceptibility in the country, all patients presenting with signs of a bloodstream infection (systemic inflammatory response syndrome) or meningitis should be sampled, if possible, prior to initiation of antimicrobial therapy. Including only special patient categories (e.g. only patients in intensive care units [ICU] or tertiary care institutions), patients with chronic or recurring infections, or with relapses or treatment failure will overestimate the resistance proportion because these patients were subjected to selective pressure of antimicrobials.

2.4. Laboratories

Participating laboratories can opt for one of two methods of data submission: electronically (WHONET, Excel, LIS) or on conventional isolate record forms (paper and Microsoft-Excel-based electronic data entry forms). CAESAR recommends laboratories to use WHONET, a free Windows-based database software that is downloadable from the WHO website⁵. This software was developed for the management and analysis of microbiology laboratory data with a special focus on collection and analysis of AST results, and includes an automated export function dedicated to the EARS-Net/CAESAR data format.

Isolate record forms are now available as Microsoft-Excel-based data entry forms (see Annex 2), enabling the electronic capture of CAESAR data at local laboratory level without the need for a dedicated laboratory information system. Data are stored in .xls spreadsheet format and are readily exported in the required CAESAR data format. Additionally, the data entry form automatically checks for completeness, and it ensures sensible data. The data form can be configured to any language. The required translation can

⁴ In concordance with the EARS-Net exchange format

⁵ http://www.who.int/drugresistance/whonetsoftware/en/

be made by any user, without the need for programming skills. The data entry form and instructions for use can be obtained from the international data manager by email (caesar@rivm.nl).

Laboratories are asked to collect and forward all AST data specified by the standard CAESAR protocols described in this manual to the national data manager on a quarterly basis. Before submission, laboratories are asked to check their data for:

- adherence to CAESAR protocol;
- microbiological consistency/plausibility; and
- consistency with AST methods and clinical S/I/R breakpoints according to the respective guideline issued by an appropriate board or committee (EUCAST⁶ or the Clinical and Laboratory Standards Institute [CLSI]⁷).

2.5. AMR focal point and the national data manager

At national level, data are processed by the national data manager in consultation with the AMR focal point in a stepwise procedure.

- Data are recorded from all participating laboratories (completeness).
- Manual data entries are made in cases in which paper isolate records forms are used.
- Data are merged from all participating laboratories into one single file.
- Duplicate reports are removed. Only primary isolates per patient per quarter or year are included in the database. Duplicate records per patient are ignored.
- Data are converted into EARS-Net exchange format.
- Data are approved by the AMR focal point who checks for adherence to CAESAR protocol, microbiological consistency and whether S/I/R interpretations are in agreement with the minimal inhibitory concentrations or disk inhibition zones (mm) reported.
- Data are transferred to the international data manager on a quarterly or yearly basis.

2.6. Feedback from CAESAR

Accurate and timely feedback is essential for surveillance systems. Once made available to CAESAR, data are analysed and returned as a standard feedback report to the AMR focal point. This feedback contains information on pathogens with important (MRSA, PNSP and VRE) and unusual resistance patterns, and contains information on the validity and completeness of the data. Subsequently, the AMR focal point is asked to confirm the correctness of the results. With this approval, the data will be added to the CAESAR database. The data from the CAESAR database are used to prepare annual reports, newsletters and publications that are disseminated to the participants, policy makers and to a broader public. In addition, a WHO website will be developed for display of the data.

⁶ http://www.eucast.org/

⁷ http://www.clsi.org/



Steps in setting up a national network

This chapter describes the steps that are needed in setting up the national coordination and a network of laboratories to enable national AMR surveillance according to CAESAR methodology.

3.1. Ministry of health

The main objective of CAESAR is to supply reliable information on AMR in participating countries. One of the main parties interested in this information is the national ministry of health. Therefore, it is essential to involve the national ministry of health when setting up a national surveillance network on AMR and to gain their support.

3.2. Contact the CAESAR project group

For more information and support in setting up a national network please contact Dr Danilo Lo Fo Wong or Dr Nienke van de Sande-Bruinsma at the WHO Regional Office for Europe, Copenhagen, Denmark.

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3.3. Appoint an AMR focal point and a national data manager

In each participating country an AMR focal point is appointed by the ministry of health. The AMR focal point has several responsibilities, including the coordination of AMR surveillance in the country and appointing a national data manager. The AMR focal point also has other responsibilities, as described in the European strategic action plan on antibiotic resistance. One is to set up and/or sustain an intersectoral coordination mechanism (ICM) for AMR (e.g. taskforce, steering committee, board or council). The ICM should encompass representatives from the relevant stakeholders for AMR (e.g. ministry of health, ministry of agriculture, national reference laboratories, public health institutes, national medicines agency, academia, nongovernmental organizations and the private sector). Another responsibility is to develop or review a national AMR action plan (including objectives, policies, surveillance and control). Through the



ICM, the national AMR focal point ensures regular data collection and information sharing and facilitates effective communication and coordination between its members and their constituents.

3.4. Selection of laboratories and hospitals participating in CAESAR

Results reported to CAESAR must be based on routine clinical samples. To base the data collection on strains sent to specialist laboratories for reference purposes (reference centres) would severely bias the results. If a participating laboratory asks the reference laboratory to conduct an MIC, for example of vancomycin for an MRSA strain, then these MICs should be included in the report from this participating laboratory.

3.4.1. Synchronization of laboratories

Key staff members from laboratories expressing an interest in national surveillance are invited to a meeting with the national management team by the AMR focal point in order to explain the aims of the CAESAR network and what they will be expected to do. PowerPoint presentations are available from the CAESAR project group or a member of the CAESAR project group could be invited to attend the meeting.

3.4.2. Assignment of laboratory and hospital codes

The national management team assigns laboratory and hospital codes to the (potential) CAESAR participants. Laboratory codes consist of the first two letters of the country code (e.g. RU for Russian Federation) plus three digits (e.g. 001), resulting in codes such as RU001, RU002 and RU003. Hospital codes preferably should consist of four characters: the three characters of the laboratory plus one letter (e.g. 001A).

3.4.3. Data management at the participating laboratories

For the participating laboratories, there are several ways to report data to the national data manager.

- If WHONET is used at laboratory level, data export is simple, as exporting EARS-Net files is a standard feature of WHONET, and CAESAR is compatible with EARS-Net (TESSy). To create a CAESAR export file, choose the option to export TESSy(CSV) format. The exported CSV file can be sent to CAESAR. It is important that WHONET is set up properly, with the exact tests as used in the laboratory, and choosing the breakpoints according to the standard used. As with EARS-Net, the preferred standard for laboratories participating in CAESAR is EUCAST (alternatively CLSI). If another standard is used, efforts should be made to calibrate results to EUCAST. If configured this way, interpretation is carried out automatically by WHONET according to these breakpoints. This prevents discrepancies between zone diameter or MIC and the interpretation.
- If the laboratory uses a laboratory information system based on a database, there are several possibilities.
 - Laboratory information system export functionality (query language) can be used.
 - In order to export CAESAR files directly, a skilled programmer is needed to make the export query. Difficulties can arise because a numeric identifier needs to be derived from the patient identifier. In addition, the date format needs to adhere to the CAESAR specification.
 - If it is too difficult to produce CAESAR files directly, the program BACLINK can be used. This program is bundled with WHONET and can be used to import any export format into

WHONET. No special programming skills are needed to configure BACLINK. When data are imported into WHONET, CAESAR export can be performed as described above.

- For laboratories not using a laboratory information system or WHONET, or small laboratories with few isolates, the CAESAR team developed an Excel file with forms that can be used to enter data manually. The forms generate the correct codes, and automatically check for completeness of the data. The data form can be configured for each country or each laboratory, meaning that only the antibiotics that are tested will be visible. Moreover, the forms can be translated into any language. The required configuration and translation can be made by any user, without the need of programming skills. To receive a copy of this Excel tool or WHONET please email to the international data manager (Caesar@rivm.nl)
- For (small) laboratories not having access to computers, paper forms can be used. The national data manager can use the Excel tool to enter the data from the paper forms.

3.4.4. Test phase laboratory data

If the national data manager receives data from the individual laboratories on paper (isolate record forms), manual data entry into the electronic database is required. Regardless, if the data arrive in electronic format or on paper, they always need to be checked for consistency with CAESAR protocols and for microbiological plausibility.

- Do the AST data reported follow the CAESAR protocol? For example, are MRSA strains reported with a vancomycin MIC?
- Do the data make sense? For example, an ampicillin-susceptible *Escherichia coli* strain with a ceftriaxone MIC of 15 probably reflects an error in data entry or laboratory practice.
- Are the S/I/R interpretations consistent with the breakpoints used by the laboratory? To check this, the national data manager needs to know what kind of guidelines the individual laboratories are using (preferably EUCAST, or CLSI).
- The data also need to be checked for adherence with the CAESAR data exchange format.

3.4.5. Finalization of the list of participating laboratories

When both the laboratories and the AMR focal point have agreed on the participation in CAESAR, a letter of agreement may be signed (Annex 1). The AMR focal point should ensure that the selection of laboratories participating in CAESAR provides a representative sample of the national population. If it is suspected that this is not the case, the AMR focal point should attempt to recruit additional laboratories to increase the representativeness of the sample.

3.4.6. Laboratory/hospital questionnaire

After the finalization of the laboratory list, the AMR focal point needs to ensure that laboratories provide certain details on the laboratory and hospital characteristics and population denominators using the questionnaire (Chapter 9). If one laboratory serves, for example, two hospitals, then two laboratory/ hospital questionnaires need to be filled out (the laboratory information will be repeated in the second questionnaire). More detailed information on the questionnaire is given in Chapter 9.

3.4.7. Test phase data

National data managers are encouraged to submit a first complete (merged) data set to CAESAR that can then be checked for consistency and adherence with the EARS-Net data exchange format. At this point, the international data manager of CAESAR and the national data manager will communicate frequently to improve the quality of the data, if necessary.

3.4.8. Start of regular reporting to CAESAR

Full data reporting to CAESAR should preferably start with the full (all participating laboratories) data set of one entire quarter, via email or secure FTP account. Data can be sent on a quarterly basis, but the ultimate deadline for sending in data of the whole previous year is June.

3.4.9. Contact information regarding data reporting

Jos Monen,

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AMR case definitions for data exchange

Given the typology of data for AMR surveillance (which refers to laboratory isolates rather than to cases of disease), the following case definition has been implemented.

- The bacterial species under surveillance⁸ are *S. pneumoniae* (STRPNE), *S. aureus* (STAAUR), *Enterococcus faecalis* (ENCFAE), *E. faecium* (ENCFAI), *E. coli* (ESCCOL), *Klebsiella pneumoniae* (KLEPNE), *Pseudomonas aeruginosa* (PSEAER) and Acinetobacter spp. (ACISPP).
- All isolates from blood (STRPNE, STAAUR, ENCFAE, ENCFAI, ESCCOL, KLEPNE, PSEAER, ACISPP) and/or cerebrospinal fluid (STRPNE, ESCCOL, KLEPNE, PSEAER, ACISPP), for which a susceptibility test has been performed, have to be included.
- Duplicates from the same patients are ignored, only the first by date of sample collection and isolate source per species is taken into account. The bug/source/drug combinations to be reported are listed in table 1. If records referring to additional combinations are uploaded, they will be collected but not be reported in the regular reports.
- The minimal panel recommended by EUCAST and ESGARS-ESCMID for CAESAR reporting has been included as a separate column.
- Additionally, a column has been added regarding antimicrobials for which EUCAST has specific recommendations in terms of detection of resistance mechanisms⁹.
- In accordance with the EARS-Net reporting protocol, a number of additional antimicrobial agents have been added to the list of agents for which it is possible to report AST results (marked with an * in Table 1 below).

Pathogen	Source/ specimen	Antibiotic	EUCAST/ESGARS minimum panel for CAESAR reporting	EUCAST guidelines for detection of resistance mechanisms
Streptococcus pneumoniae (STRPNE)	Blood (BLOOD); cerebrospinal fluid (CSE)	Penicillin (PEN) Oxacillin (OXA) Ceftriaxone (CRO) OR Cefotaxime (CTX)	Penicillin Oxacillin (screen)	Penicillin
		Erythromycin (ERY) OR Clarithromycin (CLR) OR Azithromycin (AZM) Norfloxacin (NOR) OR Levofloxacin (LVX) OR Moxifloxacin (MFX)	Erythromycin Norfloxacin (screen) OR Levofloxacin OR Moxifloxacin	

Table 1. The pathogen, source and antibiotic combinations to be reported to CAESAR, including the minimal panel for reporting and available guidelines for detection of resistance mechanisms according to EUCAST

8 In the initial implementation phase of CAESAR, the number of bacterial species under surveillance can be limited to fewer.

9 http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Consultation/EUCAST_guidelines_detection_of_resistance_mechanisms_121222.pdf

Pathogen	Source/ specimen	Antibiotic	EUCAST/ESGARS minimum panel for CAESAR reporting	EUCAST guidelines for detection of resistance mechanisms
Staphylococcus aureus (STAAUR)	Blood (BLOOD)	Oxacillin (OXA) OR Cefoxitin (FOX) Norfloxacin (NOR) OR Ciprofloxacin (CIP) OR Ofloxacin (OFX) OR Levofloxacin (LVX) Rifampicin (RIF) Linezolid (LNZ) Vancomycin (VAN)* Daptomycin (DAP)*	Cefoxitin (disk screen) Vancomycin	Cefoxitin (disk screen) Vancomycin
Enterococcus faecalis (ENCFAE)	Blood (BLOOD)	Ampicillin (AMP) OR Amoxicillin (AMX) Gentamicin-High (GEH) Vancomycin (VAN) Teicoplanin (TEC) Linezolid (LNZ)	Ampicillin Gentamicin-High Vancomycin	Vancomycin
Enterococcus faecium (ENCFAI)	Blood (BLOOD)	Ampicillin (AMP) OR Amoxicillin (AMX) Gentamicin-High (GEH) Vancomycin (VAN) Teicoplanin (TEC) Linezolid (LNZ)	Ampicillin Gentamicin-High Vancomycin	Vancomycin
Escherichia coli (ESCCOL) and Klebsiella pneumoniae (KLEPNE)	Blood (BLOOD); cerebrospinal fluid (CSF)	Ampicillin (AMP) OR Amoxicillin (AMX) Piperacillin-tazobactam (TZP) OR Amoxicillin-clavulanic acid (AMC)* Gentamicin (GEN) OR Tobramycin (TOB) OR Amikacin (AMK) Netilmicin (NET)* Ceftriaxone (CRO) OR Cefotaxime (CTX) OR Cefotaxime (CAZ) Cefepime (FEP)* Ciprofloxacin (CIP) OR Ofloxacin (OFX) OR Levofloxacin (MFX)* Meropenem (MEM) OR Imipenem (IPM) OR Ertapenem (ETP) * Tigecycline (TGC)* Colistin (COL)* Polymyxin B (POL)*	Piperacillin-tazobactam OR Amoxicillin-clavulanic acid Gentamicin OR Tobramycin OR Amikacin Ceftriaxone OR Cefotaxime OR Ceftazidime Ciprofloxacin OR Ofloxacin OR Levofloxacin Meropenem OR Imipenem OR Ertapenem	Ceftriaxone Cefotaxime Ceftazidime Meropenem Imipenem Ertapenem
Pseudomonas aeruginosa (PSEAER)	Blood (BLOOD); cerebrospinal fluid (CSF)	Piperacillin (PIP) Piperacillin/tazobactam (TZP) Ceftazidime (CAZ) Cefipime (FEP)* Ciprofloxacin (CIP) OR Levofloxacin (LVX) Gentamicin (GEN) OR Tobramycin (TOB) OR Amikacin (AMK) Netilmicin (NET)* Imipenem (IPM) OR Meropenem (MEM)	Piperacillin/tazobactam Ceftazidime Cefipime Ciprofloxacin OR Levofloxacin Gentamicin OR Tobramycin OR Amikacin Imipenem OR Meropenem	

16)

Pathogen	Source/ specimen	Antibiotic	EUCAST/ESGARS minimum panel for CAESAR reporting	EUCAST guidelines for detection of resistance mechanisms
Acinetobacter spp. (ACISPP)	Blood (BLOOD); cerebrospinal fluid (CSF)	Ciprofloxacin (CIP) OR Levofloxacin (LVX) Gentamicin (GEN) OR Tobramycin (TOB) OR Amikacin (AMK)* Netimicin (NET)* Imipenem (IPM) OR Meropenem (MEM) Colistin (COL)* Polymyxin B (POL)*	Ciprofloxacin OR Levofloxacin Gentamicin OR Tobramycin OR Amikacin Imipenem OR Meropenem	

* In accordance with the EARS-Net reporting protocol, a number of additional antimicrobial agents have been added to the list of agents for which it is possible to report AST results.





Dataset for AMR surveillance

The set of variables for isolate-based AMR reporting consists of eight technical variables and 29 epidemiological variables, which are further classified into variables at patient/isolate level and variables at AMR test level. The first level includes data referring to the isolate, which are repeated in all records reporting the AST performed for that isolate (see table 2). The variables are described in more detail, including the validation rules, in Chapter 6.

CHAPTER 5

Variable name	Mandatory	Explanation
Technical variables		
 RecordId RecordType RecordTypeVersion Subject DataSource ReportingCountry DateUsedForStatistics Status 	Yes Yes Yes Yes Yes	Unique identifier (primary key) Fixed: AMRTEST Version number of the variable set (now 2) Fixed: AMR Code for local surveillance system Country code Date of sample collection New/update or delete
Epidemiological variables	at isolate level	
 PatientCounter Specimen PatientCounter Gender Age Isolateld Hospitalld PatientType HospitalUnitType Pathogen DateOfHospitalisation ResultPCRmec ResultPbp2aAggl Serotype ESBL ResultCarbapenemases 	Yes Yes Yes	Laboratory code: two letter country code + three digits lab no. Material: BLOOD or CSF Anonymized patient ID, must be numeric Gender of the patient M/F/O/UNK Age of the patient in years Isolate sample identifier Hospital code, recommended format lab no. + one letter Origin of patient: INPAT/OUTPAT/O/UNK Hospital department (see Annex 3) Pathogen code (see Annex 3) Date of admission, YYYY-MM-DD PCR mec-gene: POS/NEG/UNK Serotype coded according to the Danish system ESBL present: POS/NEG/UNK
Epidemiological variables a	at AMR test level	
 25. Antibiotic 26. SIR 27. ResultZoneSign 28. ResultZoneValue 29. ResultZoneSIR 30. ResultMICSign 31. ResultMICValue 32. ResultMICSIR 33. ResultEtestSign 34. ResultEtestValue 35. ResultEtestSIR 36. DiskLoad 37. ReferenceGuidelinesSIR 	Yes Yes	Antibiotic code (see Annex 4) Interpretation of susceptibility: S/I/R Sign used in the zone diameter (> < =) Zone value (mm) Interpretation of susceptibility from the zone: S/I/R Sign used in the MIC (> < =) MIC (mg/l) Interpretation of susceptibility from the MIC: S/I/R Sign used in the MIC from a gradient strip test (> < =) MIC value from gradient strip test (mg/l) Interpretation of susceptibility from the gradient strip test: S/I/R Disk load (text) The used guideline (CLSI/EUCAST/NAT/O)

Table 2. Set of variables for isolate-based AMR reporting to CAESAR



Preparing national datasets

This chapter for AMR data submission describes the dataset structure and the variable coding. Questions regarding coding, upload of data, etc. should be directed to the international data manager Jos Monen (email: caesar@rivm.nl; phone: +31 (0)30 274 3956).

If the data collection at laboratory level has been performed manually by filling in isolate record forms (Annex 2), the national data manager should create the fields "Age" and "PatientCounter" starting from the available information in the paper forms ("Year of birth" and "Patient ID/Code"). It is possible to generate a number from an ID in a reproducible way by means of a "hash function". The international data manager can provide tools to produce the patient counter. If data are read into WHONET all of this is done automatically.

6.1. Check for duplicate records

Before the national data manager sends the data to RIVM, they have to revise the laboratory data and check for duplicates (records with the same RecordID). If there are duplicates they should be eliminated by merging/selecting records. Recommendations for merging and selecting records are shown below.

- The recommended format of the RecordID is the combination of the following fields: ReportingCountry; LaboratoryCode; PatientCounter; Pathogen; Specimen; Antibiotic; DateUsedForStatistics.
- The first proposed step to deal with this problem is to identify the multiple isolates within the same day (using the field "Isolateld" when available) and select the first one per day (DateUsedForStatistics).
- If there are still duplicates after the first step, the further merging/selection of records should be carried out according to the recommended method, which is summarized in examples 1, 2 and 3.

Pathogen	Antibiotic	SIR	ResultZoneSIR	ResultMICValue	ResultMICSIR
STAAUR	FOX	R	R		
STAAUR	FOX	S		1	S

Example 1 – Duplicates: same bug/drug combination but different microbiological tests

- The two records above refer to the same patient and the same bug/drug combination from the same source (blood) on the same day.
- To avoid this unsuccessful outcome, it is possible to merge the reported data in one row.
- For the final interpretation, the presence or absence of *mecA* or *mecC* will determine the susceptibility reporting (SIR).

Pathogen	Antibiotic	SIR	ResultZoneSIR	ResultMICValue	ResultMICSIR
STAAUR	FOX	S	R	1	Pending PCR

Pathogen	Antibiotic	SIR	ResultZoneSIR	ResultMICValue	ResultMICSIR
STAAUR	FOX	R	R	8	R
STAAUR	FOX	S	S	1	S

Example 2 – Duplicates: same drug/bug combination, same test, different SIR results

Select the first in this order $R \rightarrow I \rightarrow S$ (therefore, the most resistant is selected). This is a rare occurrence and this rule is implemented to have a standard algorithm for filtering the duplicates.

Example 3 – Duplicates: same drug/bug combination, same test, same SIR results

Pathogen	Antibiotic	SIR	ResultZoneSIR	ResultMICValue	ResultMICSIR
STAAUR	FOX	S	S	1	S
STAAUR	FOX	S	S	1	S

If the records have the same SIR result (true duplicates) just select one of them, taking into account the completeness of the other variables.







Data management and analysis

After data uploading, RIVM will provide a validation/feedback report that should be assessed by the AMR focal point and data manager before approval. The report shows summary statistics of the data from the uploaded batch. The analysis outputs are obtained using the same methodology that is used for the annual reports.

7.1. Preparing the dataset for analysis at RIVM

At RIVM, the international data manager will upload the country dataset into the database platform. During the upload, a quality control will be performed and remaining duplicate isolates will be selected out, and the following steps will be performed:

- for each record, and each pathogen/antibiotic line, mandatory fields will be checked;
- if mandatory fields are missing, the line is not included;
- the pathogen/antibiotic records are combined into one record per isolate;
- only the first isolates per pathogen per patient per year is kept, the others are ignored; and
- the validation/feedback report will be produced and sent back to the AMR focal point and data manager for data control and confirmation.

7.2. Analysis

The proportion of resistance is often calculated considering an antibiotic group (instead of a single antibiotic), and other specifications are needed to perform the analysis. The groups often but not always represent an antibiotic class. An example of an antibiotic group is the third-generation cephalosporins for *E. coli* (ESCCOL). This antibiotic group includes three antibiotics: ceftriaxone (CRO), cefotaxime (CTX) and ceftazidime (CAZ). The full set of bug/antibiotic-group combinations under surveillance is displayed in table 3).

Table 3. Pathogens and antibiotic-group combinations under surveillance

Pathogen	Antibiotics in the group	Group name (results to be reported)
ENCFAE/ENCFAI	AMX, AMP	Aminopenicillins (I+R)
ENCFAE/ENCFAI	GEH	High-level gentamicin (R)
ENCFAE/ENCFAI	VAN	Vancomycin (R)
ENCFAE/ENCFAI	TEC	Teicoplanin (R)
ENCFAE/ENCFAI	LNZ	Linezolid (I+R)
ESCCOL	AMX, AMP	Aminopenicillins (R)
ESCCOL/KLEPNE	AMC, TZP	Aminopenicillin + β-lactamase inhib. (R; I+R)
ESCCOL/KLEPNE	CTX, CRO, CAZ	3rd gen. cephalosporins (R; I+R)
ESCCOL/KLEPNE	AMK, GEN, TOB, NET	Aminoglycosides (R)
ESCCOL/KLEPNE	CIP, OFX, LVX, MFX	Fluoroquinolones (R; I+R)
ESCCOL/KLEPNE	IPM, MEM, ERT	Carbapenems (R; I+R)
ESCCOL/KLEPNE	COL, POL	Polymyxins (R)
ESCCOL/KLEPNE	TGC	Glycylcyclines (R)
PSEAER	PIP, TZP	Piperacillin ± tazobactam (R)
PSEAER	CAZ	Ceftazidime (R)
PSEAER/ACISPP	GEN, TOB, AMK, NET	Aminoglycosides (R)
PSEAER/ACISPP	CIP, LVX	Fluoroquinolones (R)
PSEAER/ACISPP	IPM, MEM	Carbapenems (R; I+R)
PSEAER/ACISPP	COL, POL	Polymyxins (R)
STAAUR	FOX	MRSA (R)
STAAUR	CIP, OFX, LVX, NOR	Fluoroquinolones (R)
STAAUR	RIF	Rifampin (R)
STAAUR	LNZ	Linezolid (R)
STAAUR	VAN	Vancomycin (R)
STAAUR	DAP	Daptomycin (R)
STRPNE	PEN, OXA	Penicillins (R; I+R)
STRPNE	ERY, CLR, AZM	Macrolides (R; I+R)
STRPNE	CTX, CRO	3rd gen. cephalosporins (R; I+R)
STRPNE	LVX, NOR, MFX	Fluoroquinolones (R)



General rule to calculate the proportion of resistance

If two or more antibiotics (records) are reported for the same bug/antibiotic group combination, count only one of them; the choice must accord with the final interpretations of the susceptibility test (field=SIR; priority sequence $R \rightarrow I \rightarrow S$). i.e. the most resistant result is used for group-resistance.

Specific rule for *S. pneumoniae* and nonsusceptibility to penicillin

The antibiotics considered for MRSA are penicillin (PEN) and oxacillin (OXA). If both are reported, give priority to penicillin.

Specific rule to define MRSA

The antibiotic considered for this resistance is cefoxitin (FOX). Other tests (equivalents) are also considered as confirmation tests: PCR mecA or PBP2a detection. Hierarchical levels to assess MRSA are as follows: 1) confirmation test (PCR mecA and/or PBP2a); and 2) cefoxitin (MIC or disc diffusion).

The definition of MRSA is based on the following criteria: 1) if at least one between ResultPCRmec and ResultPbp2aAggl is positive then MRSA; 2) if at least one between ResultPCRmec and ResultPbp2aAggl is negative and the other one is not positive then MSSA (methicillin-susceptible *S. aureus*); and 3) if both ResultPCRmec and ResultPbp2aAggl are missing then consider SIR to define susceptibility (if SIR=S then MSSA; if SIR=I or R then MRSA).

Future rules to perform the resistance trend analysis

The temporal trends of AMR by country are calculated and reported in the final annual report. The statistical significance of trends is assessed by the Cochrane Armitage test. Countries reporting less than 20 isolates per year or providing data for less than 3 years within the considered period are not included in the analysis. A sensitivity analysis, considering all laboratories or only those reporting for the full period, is carried out to exclude bias in assessing the significance of the trends.

Web application and outputs

On the WHO CAESAR web page¹⁰, outputs of the validated and approved data including European maps, bar charts and tables will become available in the future. These outputs will be available as soon as data are stored in the RIVM data warehouse (shortly after data approval). A country-specific and laboratory-specific summary report providing detailed results for the country referring to the bug/drug combinations under surveillance will be available to the user.

10 http://www.euro.who.int/en/health-topics/disease-prevention/antimicrobial-resistance/antimicrobial-resistance/central-asian-and-easterneuropean-surveillance-of-antimicrobial-resistance-caesar



Description of the set of variables for AMR surveillance

Technical variables	
VariableName Description Required (what happens if not submitted) Data type	 1 – RecordID Unique anonymized identifier for each record within and across the national surveillance system and subject – MS selected and generated. Recommended format: "[ReportingCountry][LaboratoryCode] [Patient Counter][Pathogen] [Specimen][Antibiotic][DateUsedForStatistics]" Yes (Error) String (Max length: 80)
VariableName	2 - RecordType
Description	Structure and format of the data
Required	Yes
(what happens if not submitted)	(Error)
Data type	Coded Value
Code	AMRTEST (fixed value for EARS-Net/CAESAR)
VariableName Description Required Data type Code	3 – RecordTypeVersion There may be more than one version of a RecordType. This element indicates which version the sender uses when generating the message Yes Numeric 2 (CAESAR uses AMRTEST version 2)
VariableName	4 - Subject
Description	Subject of the data to report
Required	Yes
(what happens if not submitted)	(Error)
Data type	Coded Value
Code	AMR (fixed value for EARS-Net/CAESAR)
VariableName	5 - DataSource
Description	The data source (surveillance system) that the record originates from
Required	Yes
(what happens if not submitted)	(Error)
Data type	Coded Value
Code	<name national="" of="" surveillance="" the=""> to be decided, and then fixed</name>
VariableName	6 - ReportingCountry
Description	The country reporting the record
Required	Yes
(what happens if not submitted)	(Error)
Data type	Coded Value
Code	Two letter country codes, same as Internet suffix
VariableName	7 – DateUsedForStatistics
Description	Date when sample was taken
Required	Yes
(what happens if not submitted)	(Error)
Data type	Date
Code	Exact date only, "YYYY-MM-DD"

Technical variables	
VariableName Description	8 - Status Status of reporting "NEW/UPDATE" or "DELETE"
	Default if left out: NEW/UPDATE. If set to DELETE, the record with the given RecordId will be deleted from the database (or better stated, invalidated). If set to NEW/UPDATE or left empty, the record is entered into the database. If the same recorded was already present, that record will be replaced.
Required	Yes
Data type	Coded Value
Code	NEW/UPDATE OR DELETE

Epidemiological variables at isolate level		
VariableName Description Required (what happens if not submitted) Data type	9 - LaboratoryCode Laboratory code unique for each laboratory within the country Yes Error Coded Value Recommended format: [ReportingCountry]-[code of three characters]	
VariableName Description Required Data type Code	10 - Specimen The source of the isolate (e.g. blood) Yes (lgnore): data entry is required; however, if you enter data that does not meet the requested combination of "Pathogen", "Specimen" and "Antibiotic", the record is ignored. Coded Value BLOOD = blood; CSF = cerebrospinal fluid	
VariableName Description Required (what happens if not submitted) Data type Code	11 - PatientCounter Numeric code for each patient, unique within laboratory; anonymous code by laboratory to specify patient Yes (Error) Numeric (integer) Required that laboratories anonymize the PatientCounter	
VariableName Description Required (what happens if not submitted) Data type Code	12 - Gender Gender Yes (Warning) Coded Value M = Male; F = Female; O = Other; UNK = Unknown	
VariableName Description Required (what happens if not submitted) Data type Code	13 - Age Age of the patient when the sample was taken Yes (Warning) Numeric Integer	
VariableName Description Required Data type	14 - IsolateId Isolate ID; code for each isolate, unique within laboratory and year Text code assigned by laboratory to specify isolate Yes (Warning) Text	

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VariableName Description Required (what happens if not submitted) Data type Code	15 - Hospitalld Unique identifier for the hospital within each laboratory Yes (Warning) Text Unique identifier for the hospital within each laboratory; recommended format: [LaboratoryCode]-[letter assigned to a hospital – starting from A, B, C, etc.]
VariableName Description Required (what happens if not submitted) Data type Code	 16 - PatientType Origin of patient: is the patient at the moment the isolate is taken admitted in a hospital (inpatient) or not. Patients who go to the hospital for dialysis, other day hospital care and to the emergency room should be classified as "0" for the field "PatientType". All other patients who are admitted in the hospital as inpatients should be classified as "INPAT". Yes (Warning) Coded Value INPAT= Admitted (Inpatient); OUTPAT= Outpatient; O =Other (e.g. emergency room); UNK=Unknown
VariableName Description Required (what happens if not submitted) Data type Code	 17 - HospitalUnitType Hospital department (at sample collection) Yes (Warning) Coded Value INTMED =Internal Medicine; PEDS =Paediatrics/neonatal; PEDSICU=Paediatrics/neonatal ICU; SURG =Surgery; ONCOL=Haematology/ Oncology; OBGYN=Obstetrics/Gynaecology; ICU=Intensive Care Unit; ED=Emergency Department; URO=Urology Ward; INFECT=Infectious Disease Ward; O =Other; UNK=Unknown
VariableName Description Required (what happens if not submitted) Data type Code	 18 - Pathogen Pathogen species and genus of the pathogen that has been isolated from the sample Yes (Error) Coded Value STRPNE=Streptococcus pneumoniae STAAUR=Staphylococcus aureus ENCFAE=Enterococcus faecalis ENCFAI=Enterococcus faecium ESCCOL=Escherichia coli KLEPNE=Klebsiella pneumoniae PSEAER=Pseudomonas aeruginosa ACISPP= Acinetobacter species
VariableName Description Required Data type Code	19 - DateOfHospitalisation Date of admission in hospital No Date Exact date only, "YYYY-MM-DD"
VariableName Description Required Data type Code Validation rule	20 - ResultPCRmec Detection of PCR mecA-gene No Coded Value POS=positive; NEG=negative; UNK=unknown To be reported only if Pathogen=STAAUR
VariableName Description Required Data type Code Validation rule	21 - ResultPbp2aAggl Detection of PBP2a-agglutination No Coded Value POS=positive; NEG=negative; UNK=unknown To be reported only if Pathogen=STAAUR

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Epidemiological variables at isolate level

VariableName Description Required Data type Code Validation rule	22 - Serotype Serotype/group of the pathogen isolated from the sample. Reference: Danish Kauffman-Lund scheme from the WHO Collaborating Centre for Reference and Research on Pneumococci at the Danish Serum Institute. No Coded Value See Annex 6 To be reported only if Pathogen=STRPNE
VariableName Description Required Data type Code Validation rule	23 - ESBL Detection of ESBL No Coded Value POS=positive; NEG=negative; UNK=unknown To be reported only if Pathogen= ESCCOL or KLEPNE
VariableName Description Required Data type Code Validation rule	24 - ResultCarbapenemases Detection of carbapenemases; this refers to phenotypic test for carbapenemase activity (e.g. the modified Hodge test - MHT). No Coded Value POS=positive; NEG=negative; UNK=unknown To be reported only if Pathogen= ESCCOL or KLEPNE or PSEAER.

VariableName Description Required Data type Code	25 - Antibiotic Antibiotic code Yes (Ignore): data entry is required; however, if you enter data that does not meet the requested combination of "Pathogen", "Specimen" and "Antibiotic", the record is ignored. By ignored, we mean that data on these combinations will not be reported Coded Value See Annex 4	
VariableName	26 - SIR	
Description	Final interpretation result of all different susceptibility tests performed	
Required	Yes	
(what happens if not submitted)	(Error)	
Data Type	Coded Value	
Code	S=susceptible; I=intermediate; R=resistant	
VariableName Description Required Data type Code	<pre>27 - ResultZoneSign Zone (> < =); this field can indicate if a value of the zone diameter of the disk test is «less than» (<); "equal to or less than" (< =); «equal to» (=); "equal to or greater than" (>=); or «greater than» (>) the value indicated in the following field. No Coded Value <; <; =; =>; =></pre>	
VariableName	28 - ResultZoneValue	
Description	Zone (Value in mm)	
Required	No	
Data type	Numeric	
Code	Integer	
VariableName	29 - ResultZoneSIR	
Description	Interpretation of the zone test	
Required	No	
Data type	Coded Value	
Code	S=susceptible; I=intermediate; R=resistant	

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VariableName Description Required Data type Code	30 - ResultMICSign MIC (> < =); this field can indicate if a value of the zone diameter of the MIC test is «less than» (<); "equal to or less than" (< =); «equal to» (=); "equal to or greater than" (>=); or «greater than» (>) the value indicated in the following field. No Coded Value <; <; =; = >; = >
VariableName	31 - ResultMICValue
Description	MIC (Value in mg/l)
Required	No
Data Type	Numeric
VariableName	32 - ResultMICSIR
Description	Interpretation of the MIC test.
Required	No
Data type	Coded Value
Code	S=susceptible; I=intermediate; R=resistant
VariableName Description Required Data type Code	<pre>33 - ResultEtestSign Gradient strip test (> < =); this field can indicate if a value of the zone diameter of the gradient strip test is "less than" (<); "equal to or less than" (< =); "equal to" (=); "equal to or greater than" (>=); or "greater than" (>) the value indicated in the following field. No Coded Value <; <; =; = >; = ></pre>
VariableName	34 - ResultEtestValue
Description	Gradient strip test MIC (Value in mg/l)
Required	No
Data type	Numeric
Code	If <1 then float, if >=1 then integer; the value 1.5 is also allowed
VariableName	35 – ResultEtestSIR
Description	Interpretation of the gradient strip test
Required	No
Data Type	Coded Value
Code	S=susceptible; I=intermediate; R=resistant
VariableName Description Required Data type Code	36 - DiskLoad Disk content (only if Zone); this field can be used to mention the load of the antibiotic disk used. Please mention the value and the Units (e.g. mcg, Units or IU). No Text Value and units: i.e. UI, mcg
VariableName Description Required Data type Code	37 - ReferenceGuidelinesSIR To differentiate use of CLSI and EUCAST guidelines for breakpoints No Coded Value EUCAST = European Committee on Antimicrobial Susceptibility Testing CLSI = Clinical and Laboratory Standards Institute NAT = National O = Other

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Denominator questionnaire

CAESAR laboratory and hospital questionnaire

When analysing AMR surveillance data, it is important to have background information of the laboratories and hospitals. This information provides a better understanding of the patient population from which the resistance data are collected and enables calculation of incidence. When a country starts to participate in CAESAR, the AMR focal point is asked to distribute a small questionnaire to the participating laboratories and hospitals. Every year a request will be sent out to update the information provided.

Which questions and why?

The AMR focal point is asked to provide an estimate of the catchment population/population coverage of the laboratories participating in the national AMR network providing data to CAESAR.

Laboratories are asked to provide the following information.

- 1. The town and postal code in order to determine the geographic distribution of the laboratories participating in the network.
- 2. The CAESAR hospital codes for the hospitals served by the laboratory. This information enables the anonymous determination of the proportion of resistance per hospital and the diversity of resistance between hospitals in a country (especially for the mainly hospital-acquired infections, such as MRSA or *P. aeruginosa*).
- 3. If available, provide the total number of blood culture sets used in the past year. One request/set consists of any number of blood culture bottles that are taken from one patient on a single occasion for diagnostic purposes. The total number of blood culture sets in relation to the total number of hospital beds or patient days (of all hospitals the laboratory serves) gives an indication of the blood culturing habits. For example, if the number of blood culture sets taken per hospital beds/patient days is very low, this could mean that blood cultures are only taken in cases of therapeutic failure. The chance of an isolate being resistant increases with therapeutic failure. Therefore, the proportion of resistance would be overestimated if blood cultures are only taken in cases of therapeutic failure.

Hospitals are asked to provide:

- 1. level of care to determine the patient mix;
- 2. number of hospital beds;
- 3. number of hospital intensive care beds;
- 4. number of hospital patient days, or if not available the annual occupancy rate of beds; and
- 5. number of hospital admissions.

Laboratory questionnaire 20.. (please complete the questionnaire for each laboratory participating in CAESAR)

- 1. CAESAR laboratory code: (e.g. BR001)
- 2. Postal code of the laboratory:
- 3. City:
- 4. The total number of blood culture requests (sets)^{11 12} in 20..:
- 5. Please provide the CAESAR hospital codes for all hospitals served by your laboratory and, if available, specify the total number of blood culture requests (sets) in 20.. per hospital served:

No.	CAESAR hospital code	Hospital-specific number of blood culture requests (sets)
1	(for example BR001A)	
2	(for example BR001B)	
3	(for example BR001C)	
4		
5		
6		
7		

11 One request/set consists of any number of blood culture bottles that are taken from one patient on a single occasion for diagnostic purposes.

12 If not available, please calculate by dividing the total number of blood culture bottles processed, by the total number of bottles per blood culture request (set).



Hospital questionnaire 20.. (please complete the questionnaire for each hospital participating in CAESAR)

1.	CAESAR hospital code:	(for example BR001A)
2.	CAESAR laboratory code:	(for example BR001)
3.	Postal code of the hospital:	
4.	City of the hospital:	
5.	The level of care of the hospital : (Important: check definitions)	 Primary level¹³ Secondary level¹⁴ Tertiary level¹⁵ Different, please specify:
6.	Best estimate of catchment population of your hospital in 20 ¹⁶ :	(contact hospital administration)
7.	Hospital size in beds in 20:	(number of beds)
8.	Number of intensive care beds in 20:	(number of beds)
9.	Total number of patient days ¹⁷ in 20:	(number of patient days)
	OR (if not available at all)	
10.	The average occupancy rate in 20:	(%)
11.	Total number of patient admissions in 20:	(number of admissions)

13 Primary level, often referred to as a district hospital or first-level referral. The hospital has few specialities, mainly internal medicine, obstetrics-gynaecology, paediatrics, and general surgery, or only general practice; limited laboratory services are available for general, but not for specialized pathological analysis; bed capacity ranges from 30 to 200 beds.

14 Secondary level often referred to as a provincial hospital. Highly differentiated by function with five to ten clinical specialities; bed capacity ranging from 200 to 800 beds.

15 Tertiary level often referred to as central, regional or tertiary-level hospital. Highly specialized staff and technical equipment, e.g. cardiology, ICU and specialized imaging units; clinical services are highly differentiated by function; may have teaching activities; bed capacity ranges from 300 to 1,500 beds.

17 Patient days: the number of patient days is the number of days spent in the institution for all patients occupying a bed. A day is measured at midnight, and the day of discharge is not counted as an extra day. This means that a patient admitted today and discharged tomorrow will have one patient day. Day patients will have zero patient days as they do not stay past midnight and must not be included in the total count.

¹⁶ We realise that university/teaching hospitals may also serve as district hospitals, thereby actually serving two different populations. If this is the case for your hospital, please provide the catchment population for the university/tertiary care service.



Letter of Agreement

Letter of Agreement

Between the WHO Regional Office for Europe, on behalf of the Central Asian and Eastern European Surveillance on Antibiotic Resistance (CAESAR) network (WHO/Europe and/or the CAESAR network, as the case may be)

and

....., on behalf of, being the national AMR focal point in [Country]

The CAESAR network is an initiative of the WHO/Europe undertaken in collaboration with the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the National Institute of Public Health and the Environment (RIVM) in the Netherlands. The CAESAR network collaborates closely with the European Centre for Disease Control (ECDC). The CAESAR network aims to collect and aggregate comparable and reliable antibiotic resistance data for public health purposes. NAMRSS wishes to cooperate with the CAESAR network, through the sharing of quantitative resistance data on:

- □ Streptococcus pneumoniae
- □ Staphylococcus aureus
- 🗆 Klebsiella pneumoniae
- 🗆 Escherichia coli
- □ Enterococcus faecium/faecalis
- □ Pseudomonas aeruginosa

 \Box Acinetobacter spp.

WHO/Europe Member States are encouraged to collect and share the data of the pathogens mentioned above, as they represent clinically and epidemiologically relevant antibiotic resistance traits. In addition, national surveillance on other relevant pathogens is encouraged.

The parties agree as follows:

- 2. will collect the individual data from the participating laboratories and forward such data to the CAESAR network through WHO/Europe.
- 3.shall ensure that it has the full legal right to share the data with the CAESAR network through WHO/Europe for the purpose of this Letter of Agreement and that such data does not violate any intellectual property rights of any third party.
- 4. WHO/Europe will accept no liability or responsibility on the grounds that the data is a violation of the above warranty. WHO/Europe will transfer any claims to made by third parties concerning

the use of the data by WHO/Europe and the CAESAR network and will deal directly with such thirdparty claims.

- 5. The transfer of the data to WHO shall not convey any intellectual property rights in the data to WHO/ Europe.
- 6. will share collated data on antibiotic resistance collected through the CAESAR network with the participating laboratories in [Country]. shall keep the participating laboratories informed on the progress of the CAESAR network.
- WHO/Europe shall make the collected data available through the Internet on a dedicated platform. Data will be anonymized to a level where individual laboratories or hospitals are not identifiable. WHO/Europe shall keep the informed on the progress of the CAESAR network, related activities and annual reports.
- 8. Both parties intend to provide comparable and correct data, but none of the parties hereto warrants that the data it provides hereunder are complete and correct; nor shall have any liability to the other for any errors or omissions in such data, or the results from the use thereof.
- 9. Participating national institutions to the CAESAR network will be acknowledged as the source in any publication derived from their data contribution. In peer-reviewed papers, will, depending on the journal, either be included as author, be part of the working group or mentioned in the acknowledgement.
- 10. The use of one Party's emblem or name by the other Party is subject to prior approval in writing.
- 11. The Parties will resolve any difference of interpretation or application of this Letter of Agreement by the appointment of representatives from each Party through consultations or negotiations.
- 12. Nothing contained herein shall be construed as a waiver of any of the privileges and immunities enjoyed by WHO/Europe under national or international law and/or as submitting WHO/Europe to any national court or jurisdiction.

Institution:	Institution: WHO Office for Europe o Division of Communicable Disease Health Security , and Environment	
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Date:	Date:	
Signature:	Signature:	







Isolate record forms

Kindly provided by EARS-Net, ECDC

Isolate record forms are now available as Microsoft-Excel-based data entry forms, enabling the electronic capture of CAESAR data at local laboratory level without the need for a dedicated laboratory information system. Data are stored in .xls spreadsheet format and are readily exported in the required CAESAR data format. Additionally, the data entry form automatically checks for completeness, and it ensures sensible data. The data form can be configured to show only the pathogens and antibiotics tested in the laboratory, and can be translated into any language. The required configuration and translation can be made by any user, without the need for programming skills. The data entry form and instructions for configuration, translation and use can be obtained from the international data manager by email (caesar@rivm.nl).



Isolate Record Form S. pneumoniae

Instructions: Please send data of the first **blood and/or cerebrospinal fluid (CSF)** - isolate of every patient with an invasive *S. aureus* infection. Send data on resistant and susceptible isolates; use 1 form per isolate

Laboratory Code "LaboratoryCode"			
Isolate sample number "Isolateld" max. 12 characters	Isolate source "Specimen" Blood CSF	Date of sample collection "DateUsedForStatistics" (yyyy-mm-dd)	
Patient ID / Code max. 12 characters	Gender □ Man □ Female □ Other □ Unknown	Year of birth (yyyy)	
Code of hospital "Hospitalld"	Origin of patient "PatientType" Inpatient I Outpatient Other I Unknown	Date of admission "DateOfHospitalisation" (yyyy-mm-dd)	
Hospital Department "HospitalUnitType" Internal medicine I Paediatrics/neonatal I Paediatrics/neonatal ICU I Surgery I Haematology/Oncology Obstetrics/Gynaecology I Intensive care unit I Emergency department I Urology department Infectious disease ward I Other I Unknown			

Antibiotic susceptibility testing (S/I/R, zone and/or MIC)

Antibiotic	SIR (final interpretation result of all different susceptibility test performed) Fill in S, I or R	Zone diameter (ResultZoneValue) (mm)	Zone diameter interpretation (ResultZoneSIR) Fill in S, I or R	MIC (ResultMICValue) (mg/l)	MIC interpretation (ResultMICSIR) Fill in S, I or R	E-test (ResultEtestValue) (mg/l)	E-test interpretation (ResultEtestSIR) Fill in S, I or R
Oxacillin Disk load:							
Penicillin							
Erythromycin Clarithromycin Azithromycin							
Cefotaxime Ceftriaxone							
Norfloxacin Levofloxacin Moxifloxacin							
Serotype:							

Isolate Record Form S. aureus

To be filled out by laboratory

Instructions: Please send data of the first **blood** - isolate of every patient with an invasive *S. aureus* infection. Send data on resistant and susceptible isolates; use 1 form per isolatee

Laboratory Code "LaboratoryCode"						
Isolate sample number "Isolateld" max. 12 characters	Isolate source "Specimen" ☐ Blood	Date of sample collection "DateUsedForStatistics" (yyyy-mm-dd)				
Patient ID / Code max. 12 characters	Gender Man Female Other Unknown	Year of birth (yyyy)				
Code of hospital "Hospitalld"	Origin of patient "PatientType" Inpatient Uutpatient Other Unknown	Date of admission "DateOfHospitalisation" (yyyy-mm-dd)				
Hospital Department "HospitalUnitType" Internal medicine I Paediatrics/neonatal I Paediatrics/neonatal ICU I Surgery Haematology/Oncology Obstetrics/Gynaecology I Intensive care unit Emergency department Urology department Infectious disease ward Other Unknown						

Antibiotic susceptibility testing (S/I/R, zone and/or MIC)

	SIR (final interpretation result of all different susceptibility test performed)	Zone diameter (ResultZoneValue)	Zone diameter interpretation (ResultZoneSIR)	MIC (ResultMICValue)	MIC interpretation (ResultMICSIR)	E-test (ResultEtestValue)	E-test interpretation (ResultEtestSIR)
Antibiotic	Fill in S, I or R	(mm)	Fill in S, I or R	(mg/l)	Fill in S, I or R	(mg/l)	Fill in S, I or R
Cefoxitin Disk load:							
Oxacillin Methicillin Flucloxacillin Cloxacillin Dicloxacillin							
Ciprofloxacin Ofloxacin Levofloxacin Norfloxacin							
Rifampicin							
Linezolid							
Vancomycin							
Daptomycin							

Isolate Record Form \Box *E. faecium* \Box *E. faecalis*

To be filled out by laboratory

Instructions: Please send data of the first **blood** - isolate of every patient with an invasive *E. faecium* and *E. faecalis* infection (please specify by ticking relevant box above). Send data on resistant and susceptible isolates; use 1 form per isolate

Laboratory Code "LaboratoryCode"						
Isolate sample number "Isolateld" max. 12 characters	Isolate source "Specimen" ☐ Blood	Date of sample collection "DateUsedForStatistics" (yyyy-mm-dd)				
Patient ID / Code max. 12 characters	Gender □ Man □ Female □ Other □ Unknown	Year of birth (yyyy)				
Code of hospital "HospitalId"	Origin of patient "PatientType" Inpatient I Outpatient Other I Unknown	Date of admission "DateOfHospitalisation" (yyyy-mm-dd)				
Hospital Department "HospitalUnitType" Internal medicine I Paediatrics/neonatal I Paediatrics/neonatal ICU I Surgery I Haematology/Oncology Obstetrics/Gynaecology I Intensive care unit Emergency department Urology department Infectious disease ward Other Unknown						

Antibiotic susceptibility testing (S/I/R, zone and/or MIC)

Antibiotic	SIR (final interpretation result of all different susceptibility test performed) Fill in S, I or R	Zone diameter (ResultZoneValue) (mm)	Zone diameter interpretation (ResultZoneSIR) Fill in S, I or R	MIC (ResultMICValue) (mg/l)	MIC interpretation (ResultMICSIR) Fill in S, I or R	E-test (ResultEtestValue) (mg/l)	E-test interpretation (ResultEtestSIR) Fill in S, I or R
Amoxicillin	П		П		П		П
Ampicillin							
Gentamicin High Disk load							
Vancomycin							
Teicoplanin							
Linezolid							

Isolate Record Form E. coli

To be filled out by laboratory

Instructions: Please send data of the first **blood and/or cerebrospinal fluid (CSF)** - isolate of every patient with an invasive *E. coli* infection. Send data on resistant and susceptible isolates; use 1 form per isolate

Laboratory Code "LaboratoryCode"					
Isolate sample number "Isolateld" max. 12 characters	Isolate source "Specimen" □ Blood □ CSF	Date of sample collection "DateUsedForStatistics" (yyyy-mm-dd)			
Patient ID / Code max. 12 characters	Gender □ Man □ Female □ Other □ Unknown	Year of birth (yyyy)			
Code of hospital "HospitalId"	Origin of patient "PatientType" Inpatient Uutpatient Other Unknown	Date of admission "DateOfHospitalisation" (yyyy-mm-dd)			
Hospital Department "HospitalUnitType" Internal medicine I Paediatrics/neonatal ICU Surgery Haematology/Oncology Obstetrics/Gynaecology Intensive care unit Emergency department Urology department Infectious disease ward Other Unknown					

Antibiotic susceptibility testing (S/I/R, zone and/or MIC)

	SIR (final interpretation result of all different susceptibility test performed)	Zone diameter (ResultZoneValue)	Zone diameter interpretation (ResultZoneSIR)	MIC (ResultMICValue)	MIC interpretation (ResultMICSIR)	E-test (ResultEtestValue)	E-test interpretation (ResultEtestSIR)
Antibiotic	Fill in S, I or R	(mm)	Fill in S, I or R	(mg/l)	Fill in S, I or R	(mg/l)	Fill in S, I or R
Amoxicillin Ampicillin							
Amoxicillin clavulanic acid Piperacillin- Tazobactam							
Gentamicin Tobramycin Amikacin Netilimicin							
Ciprofloxacin Ofloxacin Levofloxacin Moxifloxacin							
Cefotaxime Ceftriaxone Ceftazidime							
Cefipime							
lmipenem Meropenem Doripenem Ertapenem							
Colistin Polymixin B							
Tigecycline							

Isolate Record Form K. pneumoniae

To be filled out by laboratory

Instructions: Please send data of the first **blood and/or cerebrospinal fluid (CSF)** - isolate of every patient with an invasive *K. pneumoniae* infection. Send data on resistant and susceptible isolates; use 1 form per isolate

Laboratory Code "LaboratoryCode"					
Isolate sample number "Isolateld" max. 12 characters	Isolate source "Specimen" Blood CSF	Date of sample collection "DateUsedForStatistics" (yyyy-mm-dd)			
Patient ID / Code max. 12 characters	Gender Man Female Other Unknown	Year of birth (yyyy)			
Code of hospital "Hospitalld"	Origin of patient "PatientType" Inpatient Uutpatient Other Unknown	Date of admission "DateOfHospitalisation" (yyyy-mm-dd)			
Hospital Department "HospitalUnitType" Internal medicine I Paediatrics/neonatal ICU Surgery Haematology/Oncology Obstetrics/Gynaecology Intensive care unit Emergency department Urology department Infectious disease ward Other Unknown					

Antibiotic susceptibility testing (S/I/R, zone and/or MIC)

Antibiotic	SIR (final interpretation result of all different susceptibility test performed) Fill in S, I or R	Zone diameter (ResultZoneValue) (mm)	Zone diameter interpretation (ResultZoneSIR) Fill in S, I or R	MIC (ResultMICValue) (mg/l)	MIC interpretation (ResultMICSIR) Fill in S, I or R	E-test (ResultEtestValue) (mg/l)	E-test interpretation (ResultEtestSIR) Fill in S, I or R
Amoxicillin clavulanic acid Piperacillin- Tazobactam							
Gentamicin Tobramycin Amikacin Netilimicin							
Ciprofloxacin Ofloxacin Levofloxacin Moxifloxacin Nalidixic acid							
Cefotaxime Ceftriaxone Ceftazidime							
Cefipime							
lmipenem Meropenem Doripenem Ertapenem							
Colistin Polymixin B							
Tigecycline							

Isolate Record Form P. aeruginosa

To be filled out by laboratory

Instructions: Please send data of the first **blood and/or cerebrospinal fluid (CSF)** - isolate of every patient with an invasive *P. aeruginosa* infection. Send data on resistant and susceptible isolates; use 1 form per isolate

Laboratory Code "LaboratoryCode"						
Isolate sample number "Isolateld" max. 12 characters	Isolate source "Specimen" Blood CSF	Date of sample collection "DateUsedForStatistics" (yyyy-mm-dd)				
Patient ID / Code max. 12 characters	Gender Man Female Other Unknown	Year of birth (yyyy)				
Code of hospital "HospitalId"	Origin of patient "PatientType" Inpatient I Outpatient Other I Unknown	Date of admission "DateOfHospitalisation" (yyyy-mm-dd)				
Hospital Department "HospitalUnitType" Internal medicine I Paediatrics/neonatal ICU Surgery Haematology/Oncology Obstetrics/Gynaecology Intensive care unit Emergency department Urology department Infectious disease ward Other Unknown						

Antibiotic susceptibility testing (S/I/R, zone and/or MIC)

	SIR (final interpretation result of all different susceptibility test performed)	Zone diameter (ResultZoneValue)	Zone diameter interpretation (ResultZoneSIR)	MIC (ResultMICValue)	MIC interpretation (ResultMICSIR)	E-test (ResultEtestValue)	E-test interpretation (ResultEtestSIR)
Antibiotic	Fill In S, I or R	(mm)	Fill In S, I or R	(mg/l)	Fill In S, I or R	(mg/l)	Fill In S, I or R
Piperacillin Piperacillin							
tazobactam							
Gentamicin Tobramycin							
Amikacin Netilimicin							
Ciprofloxacin Levofloxacin							
Ceftazidime Cefipime							
lmipenem Meropenem Doripenem							
Colistin Polymixin B							

Isolate Record Form Acinetobacter spp

To be filled out by laboratory

Instructions: Please send data of the first **blood and/or cerebrospinal fluid (CSF)** - isolate of every patient with an invasive *Acinetobacter* spp infection. Send data on resistant and susceptible isolates; use 1 form per isolate

Laboratory Code "LaboratoryCode"						
Isolate sample number "Isolateld" max. 12 characters	Isolate source "Specimen" Blood CSF	Date of sample collection "DateUsedForStatistics" (yyyy-mm-dd)				
Patient ID / Code max. 12 characters	Gender Man Female Other Unknown	Year of birth (yyyy)				
Code of hospital "HospitalId"	Origin of patient "PatientType" Inpatient I Outpatient Other I Unknown	Date of admission "DateOfHospitalisation" (yyyy-mm-dd)				
Hospital Department "HospitalUnitType" Internal medicine Paediatrics/neonatal Paediatrics/neonatal ICU Surgery Haematology/Oncology Obstetrics/Gynaecology Intensive care unit Emergency department Urology department Infectious disease ward Other Unknown						

Antibiotic susceptibility testing (S/I/R, zone and/or MIC)

Antibiotic	SIR (final interpretation result of all different susceptibility test performed) Fill in S, I or R	Zone diameter (ResultZoneValue) (mm)	Zone diameter interpretation (ResultZoneSIR) Fill in S, I or R	MIC (ResultMICValue) (mg/l)	MIC interpretation (ResultMICSIR) Fill in S, I or R	E-test (ResultEtestValue) (mg/l)	E-test interpretation (ResultEtestSIR) Fill in S, I or R
Ciprofloxacin Levofloxacin							
Gentamicin Tobramycin Amikacin Netilimicin							
lmipenem Meropenem Doripenem							
Colistin Polymixin B							





List of EARS-Net/CAESAR pathogens

Code	Name
ENCFAE	Enterococcus faecalis
ENCFAI	Enterococcus faecium
ESCCOL	Escherichia coli
KLEPNE	Klebsiella pneumoniae
PSEAER	Pseudomonas aeruginosa
STAAUR	Staphylococcus aureus
STRPNE	Streptococcus pneumoniae
ACISPP	Acinetobacter spp.





List of *S. pneumoniae* serotypes (Kauffman-Lund scheme)

Code	Description	Code	Description	Code	Description
1	Type 1	15A	Type 15A	28F	Type 28F
2	Type 2	15B	Type 15B	29	Type 29
3	Туре 3	15C	Type 15C	31	Туре 31
4	Type 4	15F	Type 15F	32	Group 32
5	Туре 5	16	Group 16	32A	Type 32A
6	Group 6	16A	Type 16A	32F	Type 32F
6A	Туре 6А	16F	Type 16F	33	Group 33
6B	Type 6B	17	Group 17	33A	Туре 33А
6C	Туре 6С	17A	Type 17A	33B	Type 33B
6D	Type 6D	17F	Type 17F	33C	Type 33C
7	Group 7	18	Group 18	33D	Type 33D
7A	Type 7A	18A	Type 18A	33F	Type 33F
В	Type 7B	18B	Type 18B	34	Туре 34
7C	Type 7C	18C	Type 18C	35	Group 35
7F	Type 7F	18F	Type 18F	35A	Type 35A
8	Туре 8	19	Group 19	35B	Type 35B
9	Group 9	19A	Туре 19А	35C	Туре 35С
9A	Туре 9А	19B	Type 19B	35F	Type 35F
9L	Type 9L	19C	Туре 19С	36	Туре 36
9N	Type 9N	19F	Type 19F	37	Type 37
9V	Type 9V	20	Туре 20	38	Туре 38
10	Group 10	21	Type 21	39	Туре 39
10A	Type 10A	22	Group 22	40	Type 40
10B	Type 10B	22A	Type 22A	41	Group 41
10C	Type 10C	22F	Type 22F	41A	Type 41A
10F	Type 10F	23	Group 23	41F	Type 41F
11	Group 11	23A	Type 23A	42	Type 42
11A	Type 11A	23B	Type 23B	43	Туре 43
11B	Type 11B	23F	Type 23F	44	Type 44
11C	Type 11C	24	Group 24	45	Type 45
11D	Type 11D	24A	Type 24A	46	Type 46
11F	Type 11F	24B	Type 24B	47	Group 47
12	Type 12	24F	Type 24F	47A	Type 47A
12A	Type 12A	25	Group 25	47F	Type 47F
12B	Type 12B	25A	Type 25A	48	Type 48
12F	Type 12F	25F	Type 25F	UNK	Unknown
13	Type 13	27	Type 27	NA	Not applicable
14	Type 14	28	Group 28		
15	Group 15	28A	Type 28A		

The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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