



EARSS Manual 2005

It is the remit of EARSS to maintain a comprehensive surveillance and information system that links national networks by providing comparable and validated data on the prevalence and spread of major invasive bacteria with clinically and epidemiologically relevant antimicrobial resistance in Europe (www.earss.rivm.nl)

This document has been prepared by the EARSS Management Team in collaboration with the advisory board of EARSS. The protocols on susceptibility testing were agreed upon by the national EARSS representatives during plenary meetings.

Bilthoven (NL), July 2005

Table of contents

Chapter		Page
1	Introduction: How to read this EARSS manual 2005	3
2	List of abbreviations and acronyms	5
3	The objectives, methodology and organisation of EARSS	7
4	Steps in setting up a national network for EARSS	11
5	EARSS protocol for testing of <i>Streptococcus pneumoniae</i>	15
6	EARSS protocol for testing of <i>Staphylococcus aureus</i>	18
7	EARSS recommendation on how to detect VISA/VRSA	21
8	EARSS protocol for testing of <i>Enterococcus faecalis</i> and <i>Enterococcus faecium</i>	23
9	EARSS protocol for testing of <i>Escherichia coli</i>	25
10	EARSS protocol for testing of <i>Klebsiella pneumoniae</i>	27
11	Protocol for ESBL reporting	29
12	EARSS protocol for testing of <i>Pseudomonas aeruginosa</i>	30
13	Steps in routine data collection	31
14	Data exchange format	33
15	Denominator Information	41
Annex 1.	Memorandum of Understanding	42
Annex 2	Isolate Record Form <i>S. pneumoniae</i>	43
Annex 3	Isolate Record Form <i>S. aureus</i>	44
Annex 4.	Isolate Record Form VISA/VRSA	45
Annex 5.	Isolate Record Form <i>E. coli</i>	46
Annex 6.	Isolate Record Form <i>E. faecium/faecalis</i>	47
Annex 7:	Isolate Record Form <i>K. pneumoniae</i>	48
Annex 8	EARSS protocol for testing of <i>Pseudomonas aeruginosa</i>	50
Annex 9	Laboratory/Hospital questionnaire	51
Annex 10	EARSS country codes	56
Annex 11.	Table antibiotic coding EARSS	57
Annex 12	<i>S. pneumoniae</i> serotype codes	60

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1. Introduction: How to read this EARSS manual 2005

EARSS is an evolving network of national surveillance systems. Since its foundation in 1998, countries have continued to join. Therefore we tailored this manual to the needs of “old” and “new” participants.

For the “old” participants already reporting to EARSS, please note the following important updates and new items compared to the EARSS manual 2001:

***S. aureus* protocol (Chapter 6, page 18):** This protocol has been adapted and should be implemented in the first quarter of 2004. The new items are:

1. the recommended use of a cefoxitin disk diffusion test for MRSA screening
2. the addition of PBP2a agglutination as confirmation test
3. the preference to perform a PBP2 or PCR as confirmation test (instead of a MIC)
4. to test for rifampin and linezolid in case of a MRSA
5. the inclusion of fusidic acid as an optional antibiotic

EARSS recommendation for the detection of VISA/VRSA (Chapter 7, page 21): In 2003 a technical guideline has been developed for the detection of VISA/VRSA. We recommend following this technical guide in case a laboratory wants to further characterise MRSA isolates with reduced susceptibility to vancomycin identified by the routine protocol. Please be informed that this technical guide is not mandatory! However, if you have detected a VISA/VRSA confirmed isolate, we ask you to report this result to EARSS. Please use the reporting form that contains the requested information (Annex 4, page 45).

***S. pneumoniae* protocol (Chapter 5, page 15):** Already since 2002, it was decided to collect and report erythromycin AST data routinely for *S. pneumoniae*. The protocol has now been adapted accordingly. As discussed on the plenary meeting 2003 and on advice of the advisory board and EUCAST routine testing against fluoroquinolones is now recommended using norfloxacin/ciprofloxacin for sensitive identification of reduced susceptibility.

***S. pneumoniae* serotyping (Chapter 5, page 15):** Starting in 2004, EARSS collects serotype data for the invasive *S. pneumoniae* isolates that are routinely reported.

***K. pneumoniae* and *P. aeruginosa* protocol (Chapter 10 and 12, page 27-28 and 30):** These pathogens are new in 2005.

Isolate Record Forms (Annex 2 to 8, page 43-50): The isolate record forms for *S. aureus* and *S. pneumoniae* (annex 2 and 3) have been adapted in line with the changes summarised above. The isolate record forms of *K. pneumoniae* and *P. aeruginosa* (annex 7 and 8) are added.

ESBL protocol (Chapter 11, page 29): This protocol has been renewed starting in 2003.

Data exchange format (Chapter 14, page 33): The data exchange format has been modified. New data fields for ‘PBP2a-agglutination’, ‘Serotype’, and additional antibiotics have been added and updates of the software for data entry (DEFS or WHONET) and updated tables/codes are available.

Laboratory/hospital questionnaire (Annex 9, page 51): This questionnaire has been sent out in 2005.

For the “new” participant: If you are at the beginning of setting up a national surveillance system, you may find it helpful to read chapter 4 “Steps in setting up a national network for EARSS”.

For participating laboratories especially the protocols in chapters 5 to 12 and isolate record forms in annexes 2 to 8 are of interest, since they contain all details on what information should be reported.

For national data managers and data managers of the participating laboratories the most relevant information can be found in chapter 13 “Steps in routine data collection” and chapter 14 “Data Exchange Format EARSS”.

2. List of abbreviations and acronyms

AMR	Antimicrobial resistance
ARMed	Antibiotic resistance surveillance and control in the Mediterranean region
AST	Antimicrobial susceptibility testing
BAClink	Microbiology Data Conversion Software from WHONET
CA-SFM	Comité de l'Antibiogramme de la Société Française de Microbiologie
CSF	Cerebrospinal Fluid
DCFP	Data check and feedback program
DEFS	Data Entry and Feedback Software
DG SANCO	Directorate General Health and Consumer Protection
EARSS	European Antimicrobial Resistance Surveillance System
EARSS-MT	EARSS Management Team
EC	European Commission
ESAC	European Surveillance of Antimicrobial Consumption
ESBL	Extended spectrum beta-lactamase
ESCMID	European Society for Clinical Microbiology and Infectious Diseases
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
EQA	External Quality Assurance
ICU	Intensive care unit
ICM	Intersectorial Coordinating Mechanism
IDM	International data manager
ISA	Iso Sensitest Agar
IT	Information Technology
LIS	Laboratory Information System
MIC	Minimal inhibitory concentration
MH	Mueller Hinton
MoH	Ministry of Health
MRSA	Methicillin resistant <i>S. aureus</i>
NAB	National advisory board
NCC	National corresponding centre
NCCLS	National Committee for Clinical Laboratory Standards
NDM	National data manager
NMT	National Management Team
Patient-ID	Unique identifier of a patient
PBP2a-a	Penicillin Binding Protein2a-agglutination
PCR	Polymerase Chain Reaction
PNSP	Penicillin non-susceptible <i>S. pneumoniae</i>
PYR	Pyrolidonyl- β -naphthylamide
RIVM	Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment)
SAR	Self-medication with antibiotics and resistance
S/I/R	Susceptible/Intermediate/Resistant
SFM	Société Française de Microbiologie
UK-NEQAS	UK National External Quality Assessment Scheme for Microbiology; London, UK
VISA	Vancomycin intermediate <i>Staphylococcus aureus</i>
VRE	Vancomycin resistant enterococci

VRSA	Vancomycin resistant <i>Staphylococcus aureus</i>
WHO	World Health Organization
WHONET	Microbiology laboratory database software

3. The objectives, methodology and organisation of EARSS

3.1. Objectives

It is the public health purpose of EARSS to assist in the control of antimicrobial resistance, therefore the following objectives have been set:

- to collect comparable and validated antimicrobial resistance data
- to analyse trends in time and place (among different European countries)
- to provide official national AMR data that constitute a basis for policy decisions
- to provide feedback to ‘those who need to know’
- to provide information on clinically and epidemiologically relevant antimicrobial resistance and evaluate interventions

Furthermore, EARSS aims to:

- encourage the implementation, maintenance and improvement of national antimicrobial resistance surveillance programmes to provide timely information for national policy decisions.
- link antimicrobial resistance data to factors influencing the emergence and spread of antimicrobial resistance, in particular to antibiotic use data in close co-operation with the European Surveillance of Antimicrobial Consumption (ESAC)
- initiate, foster and complement scientific research in Europe in the field of antimicrobial resistance

3.2. The approach of EARSS

It is the remit of EARSS to maintain a comprehensive surveillance and information system that links national networks by providing comparable and validated data on the prevalence and spread of major invasive bacteria with clinically and epidemiologically relevant antimicrobial resistance in Europe. The pathogens that successively became object of surveillance within EARSS were selected according to epidemiological (community vs. hospital-acquisition) and ecological (transmission vs. selection) paradigms. At the same time the focus was set on a selected number of clinically and epidemiologically relevant antibiotic resistance traits. The decision to collect routine data meant that no changes to the regular diagnostic process should be necessary. Therefore, the participation of a large number of laboratories has become feasible, and allows sampling of a substantial part of the population in the participating countries. Reporting of the pathogens was and is restricted to invasive (blood culture and CSF) isolates, which are in most laboratories routinely tested for antimicrobial susceptibility. This avoids bias introduced by different sampling habits such as routine screening on regular sampling of ICU patients in different hospitals and health care settings. After a pilot phase (1998), collection of routinely generated antimicrobial susceptibility test (AST) data started in 1999 for *S. pneumoniae* and for *S. aureus*. Since 2001 the surveillance has been extended to include *E. coli* and enterococci (*E. faecium* and *E. faecalis*). In order to be able to interpret the ecological impact of vaccination with newly introduced polyvalent conjugate vaccines on the population structure of *S. pneumoniae*, EARSS has decided to start collecting complete serotype data for invasive *S. pneumoniae* isolates from 2004 onwards.

3.3. Organisation of the EARSS network

Each participating country has appointed one or two national representatives. These consist of a medical microbiologist and/or an infectious diseases epidemiologist. Moreover, each country has a national data manager. The main task of the national representatives is to connect the EARSS-specific activities of the participating laboratories (data collection, reporting, questionnaire completion, EQA strain and results distribution) with the EARSS

central database, which is continuously maintained and updated by the EARSS Management Team (EARSS-MT). The national representatives also ensure that the laboratories generate their AST data according to the EARSS protocols, as published in this manual. The main task of the national data manager is to collect, approve and forward resistance data each quarter and to assist the national representative. Protocols (chapter 5 to 12) for standardisation of data collection have been developed with the professional help from the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and WHO-NET. To assess the quality and comparability of AST data, each year an External Quality Assurance (EQA) exercise is carried out in collaboration with the United Kingdom National External Quality Assessment Scheme (UK-NEQAS).

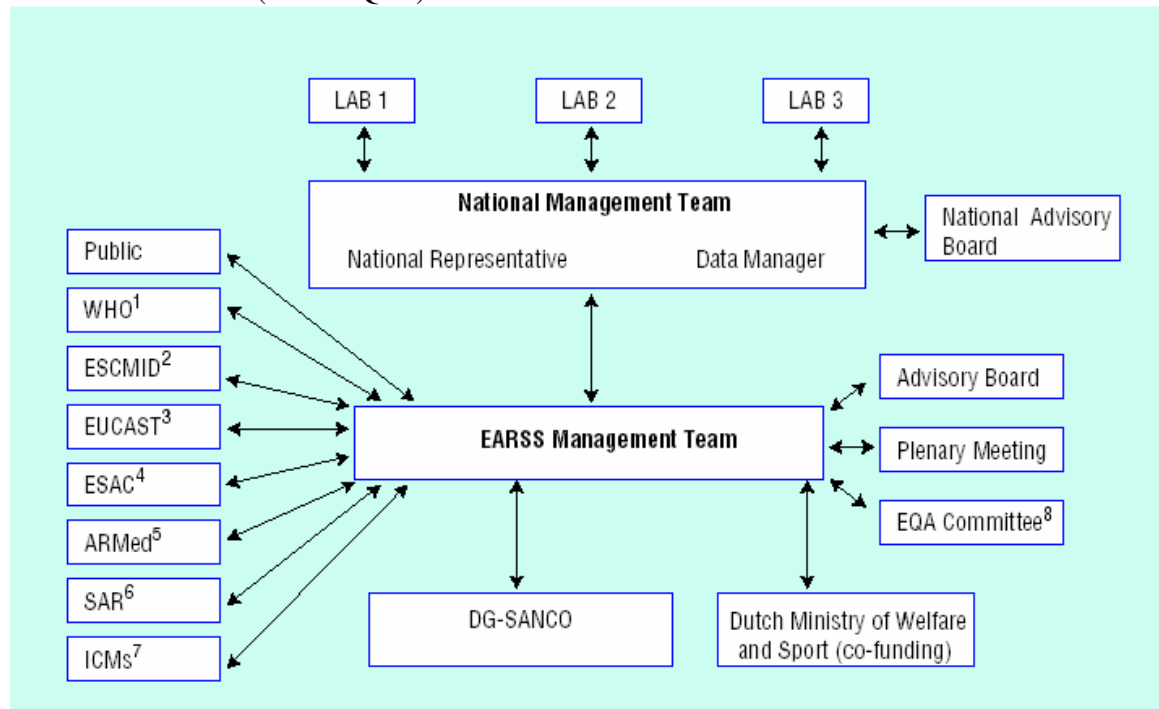


Figure 1. Structure of the EARSS network

1 World Health Organisation, 2 European Society for Clinical Microbiology and Infectious Diseases, 3 European Committee on Antimicrobial Susceptibility Testing, 4 European Surveillance of Antimicrobial Consumption, 5 Antibiotic Resistance Surveillance & Control in the Mediterranean region, 6 Self-medication of antimicrobial and resistance levels in Europe, 7 Intersectoral coordinating mechanisms, 8 External Quality Assurance Committee

3.4. The national networks

As part of the strategy for the prevention of infections and containment of resistant pathogens, the Council of the European Union stipulates the establishment of accurate surveillance systems in all member states throughout the Community¹. It is the role of the national representative and national data manager to lead the national surveillance system on antimicrobial resistance. In this function they shall encourage the participation of laboratories and hospitals whereby a good representation of the population should be achieved. Coverage should exceed 20% of the national population, health care systems should be represented with respect to the mix of academic/tertiary care hospitals, general hospitals, rehabilitation centers and nursery-homes and geographic distribution should be even and include urban and rural catchment areas. EARSS also collects denominator information from the national networks, through laboratory/hospital questionnaire on a regular basis. More detailed information is given in chapter 15 and the full questionnaire is attached in annex 9.

¹ Council and Parliament Decision 2119/98/EU of September 1998 setting up a Community Network for the surveillance and control of communicable diseases

3.4.1. Collecting and processing data

EARSS routinely collects susceptibility test results of invasive isolates and background information about patients. Laboratories are asked to report the first isolate from blood or cerebrospinal fluid per patient per quarter. According to the specifications of the EARSS exchange format (Chapter 14 of this EARSS manual) the system requires: 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, hospitalised, etc.), bacterial species and antibiotic susceptibility testing results as specified in the protocols. Furthermore, optional data are collected: clinical diagnosis, other conditions, susceptibility data for other antibiotics, **and in 2004 EARSS starts to collect the serotype of the reported *S. pneumoniae* strains.**

3.4.2. Laboratories

Participating laboratories can opt for one of two methods of data submission: electronically (by e-mail) or on conventional isolate record forms (paper). EARSS provides different free software tools for electronic data handling, downloadable from the website at www.earss.rivm.nl; 1) WHONET, the microbiology laboratory software, modified for EARSS by John Stelling, and 2) DEFS (Data Entry & Feedback Software), which is tailored for EARSS. Laboratories are asked to collect and forward all AST data specified by the standard EARSS protocols in this manual to the national data manager on a quarterly basis. Before submission, laboratories are asked to check their data for:

- adherence to the EARSS protocol
- microbiological consistency / plausibility
- consistency with clinical S/I/R breakpoints according to the respective guideline issued by an appropriate board or committee (e.g. National guideline, NCCLS, etc..)

3.4.3. National representative & national data manager

At national level the data are processed by the national data manager in consultation with the national representative, in a stepwise procedure:

- Recording of data from all participating laboratories (completeness).
- Manual data entry in case Isolate Records Forms are used.
- Merging of data from all participating laboratories into one single file.
- Removal of duplicate reports. Only primary isolates per patient per quarter shall be reported.
- Conversion of data in EARSS exchange format (EARSS manual 2005)
- Revision of data with the Data Check and Feedback Program (DCFP)
- Approval of data by the national representative (adherence to EARSS protocol, check for microbiological consistency, and check if S/I/R interpretations are in agreement with the minimal inhibitory concentrations (MICs) reported).
- Data transfer to EARSS-MT on a quarterly basis

3.4.4. Feedback from EARSS/RIVM

Accurate and timely feedback is essential for surveillance systems. Once made available to EARSS-MT, data are analysed and returned as a standard feedback report to the national representative. This feedback contains information on pathogens with important (MRSA, PNSP, VRE) and unusual resistance patterns, and contains information on the validity & completeness of the data. Subsequently, the national coordinator is asked to confirm the correctness of the results. With his/her approval, the data will be added to the EARSS database and will become immediately available on the interactive EARSS web-site at www.earss.rivm.nl, where they can be displayed in various formats, such as tables, figures, and topographical maps.

Furthermore, the data from the EARSS database are used to prepare annual reports, newsletters and publications, that are disseminated to the participants, policy makers and to a broader public.

4. Steps in setting up a national network for EARSS

4.1. Agreement with the Ministry of Health

The main objective of EARSS is to supply reliable information on antimicrobial resistance in participating countries. One of the main parties interested in this information is the Ministries of Health (MoH). Therefore it is essential to involve the MoH when setting up a national surveillance network on AMR and gain their support. In the Council and Parliament Decision 2119/98/EU² it is specified that national on-going surveillance systems (for resistance and consumption of antibiotics) that feed into a European-wide system should be in place in every Member State. The national Ministries are expected to act according to legislation, which would mean that National governments have to allocate sufficient resources to sustain surveillance and control-activities. In 2001, at a follow-up conference in Visby, Sweden, it was concluded that all Member States of the European Union (EU) should join the EARSS initiative as a minimum requirement of national surveillance programmes (the Visby recommendations³). In order to set up a national surveillance system on AMR one of the first steps should be to:

4.2. Contact the EARSS Management Team (project leader: Hajo Grundmann) to discuss details of joining EARSS. He will also be happy to send out a letter to the respective MoH to inform about the mission of EARSS, its European role and the importance of the Ministry's support on the national level.

4.3. Appointment of national representative

In every country one (or two) person(s) should be appointed to represent their country. Usually a well respected microbiologist and/or microbiologist epidemiologist is identified, who can lead the national network. In case two national representatives are appointed they do not need to work in the same institute, but good communication between them is essential.

4.4. Appointment of the national EARSS data manager

The national data manager (appointed with agreement of the national representative) should be a person with experience in information technology (IT), and ideally also in microbiology. The detailed tasks of the national data manager are laid out in section 13.4 ("Procedure for handling AMR data at national level"). Briefly, his/her tasks are:

to collect data from participating laboratories on a quarterly basis,

- to perform a data check and, with the help of the microbiologist, a plausibility check,
- to communicate with the participating laboratories,
- to merge the data files of the participating laboratories
- to forward this file on a quarterly basis, before the deadlines, to the RIVM.

4.5. Formation of a "national management team"

The national management team consists of the national representative(s) and the national data manager. Since members of the national management team may work in different institutes, one Institute should be identified in each country, that will be acting as the EARSS "national corresponding centre" (NCC).

4.6. Selection of laboratories and hospitals participating in EARSS

² Council and Parliament Decision 2119/98/EU of September 1998 setting up a Community Network for the surveillance and control of communicable diseases

³ Progress Reports on Antimicrobial Resistance, Visby, Sweden, June 2001.

To ensure sufficient representativeness of AST data within each country, attention should be given to the following minimum criteria for the selection of laboratories.

1) Laboratories from diverse regions

The laboratories that are selected should cover different regions and thereby represent the geographical diversity in terms of population density, socio-economic, ethnical and confessional mix of each country.

2) Reasonable coverage of population and hospital bed-days

Laboratories should be encouraged to participate in order to obtain a sufficiently large catchment area with a coverage which should exceed 20% of the national population.

3) Representative sample of hospitals

The laboratories selected should represent the distribution of both academic and non-academic hospitals i.e. tertiary as well as secondary care (general) hospitals. Furthermore, in some countries other health care facilities like nursing homes deliver a substantial part of health care (to the elderly) and should also be included in the institutions under surveillance if possible.

An important requirement for enrolment as a laboratory for AMR surveillance is the involvement in primary microbiological diagnostic service for any number of hospitals or primary care groups (family doctors). Results reported to the national surveillance network (and to EARSS) must be based on routine clinical samples. To base the data collection on strains sent to specialist laboratories for reference purposes (reference centres) would grossly bias the results! If a participating laboratory asks the reference laboratory to conduct a MIC, for example of oxacillin or vancomycin for a MRSA strain, then these MICs should be included in the report from this participating laboratory.

4.7. “Synchronisation of laboratories”

It may be helpful to invite the laboratories expressing an interest in national surveillance to a meeting with the national management team (NMT). The following topics should be covered during this meeting:

- Presentation of the NMT
- Presentation of EARSS (could be done on request by a member of EARSS MT)
- Presentation of EARSS AST protocols
- Possibilities to store resistant invasive strains at -80°C or send them to reference laboratory
- Layout and requirement to complete the Isolate record forms
- Delivery of data from laboratories to the NCC. Data should arrive at the NCC either on paper using the isolate record forms (one isolate per form), or by email in a data format that is compatible with the required EARSS format (see chapter 14).
- Capabilities of the data check and feedback program (DCFP), that is developed by John Stelling (of the WHO Collaborating Centre for Surveillance of AMR) and EARSS MT. This software provides immediate feedback on the quality of the data and provides also some basic analytical feedback and is very easy to handle (please see details in section 4). DCFP is available for every national data manager and can be distributed to laboratories.

4.8. Assignment of laboratory and hospital codes

The NMT assigns laboratory and hospital codes to the (potential) EARSS participants. Laboratory codes consist of the first two letters of the country code (for example FR for France) + 3 characters (for example 001), resulting in codes, such as: FR001, FR002, FR003, etc.

Hospital codes consist of 4 characters: the 3 characters of the laboratory plus one letter, for example: 001A, 001B, 002A, 003A, etc.

4.9. Data management at the participating laboratories

The participating laboratories will in general follow two different practices to report data: i) either electronically, ii) or by sending isolate record forms to the national data manager. For electronic reporting, please read chapter 13 (steps in routine data collection) and chapter 14 (data exchange format). For reporting on paper, please find the isolate record forms in annexes 2 to 8. It is important on the level of the individual laboratories to check that the S/I/R interpretations and the MIC results are consistent with the breakpoints used in the laboratory and in accordance with the guidelines published by an appropriate committee.

4.10. 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 EARSS protocols and for microbiological plausibility:

- Do the AST data reported follow the EARSS protocol? For example: Are MRSA strains reported with an oxacillin MIC and a vancomycin MIC?
- Do the data make sense microbiologically? For example: a methicillin susceptible *S. aureus* strain with a vancomycin MIC of 16 reflects probably a data entry error.
- Are the S/I/R interpretations consistent with the breakpoints used by the laboratory? To check this, the national data manager needs to know if the individual laboratories follow national guidelines or NCCLS. This information is known from the annual external quality assurance exercises (EARSS/UK-NEQAS EQA). For example: a laboratory uses NCCLS guidelines for the testing of *S. pneumoniae* with penicillin. Reporting a "S" for a result of a MIC of 1,0 would be inconsistent with NCCLS.
- The data also need to be checked for adherence with the EARSS data exchange format. For more information, please read chapter 13 (steps of routine data collection) and 14 (data exchange format).

4.11. Finalisation of the list of participating laboratories

When both the laboratories and the NMT have agreed on the participation in EARSS, a memorandum of understanding shall be signed (annex 1). The final list of participating laboratories should be checked again for the criteria laid out in paragraph 4.6. If the national representatives think there is a certain imbalance in the selection of laboratories, they should attempt to recruit additional laboratories to render a more representative sample.

4.12. Laboratory/Hospital Questionnaire

After the finalisation of the laboratory list, the NMT needs to ensure that laboratories provide some details on the laboratory and hospital characteristics and population denominator using the questionnaire in annex 9. If one laboratory serves for example 2 hospitals, then also 2 Laboratory/Hospital Questionnaires need to be filled (the laboratory information will be repeated in the second questionnaire). More detailed information on the questionnaire is given in chapter 15 and the questionnaire is displayed in annex 9.

4.13. Test phase data

National data managers are encouraged to submit a first complete (merged) data set to EARSS MT which can then be checked for consistency and adherence with the EARSS data exchange format. The main tool at the EARSS MT level is the DCFP. At this point, the international data manager of EARSS MT and the national data manager will communicate frequently to improve the quality of the data should that be necessary.

4.14. Start of regular reporting to EARSS

Full data reporting to EARSS should preferably start with the full (all participating laboratories) data set of one entire quarter. See chapter 13 for the time scheme of sending in data.

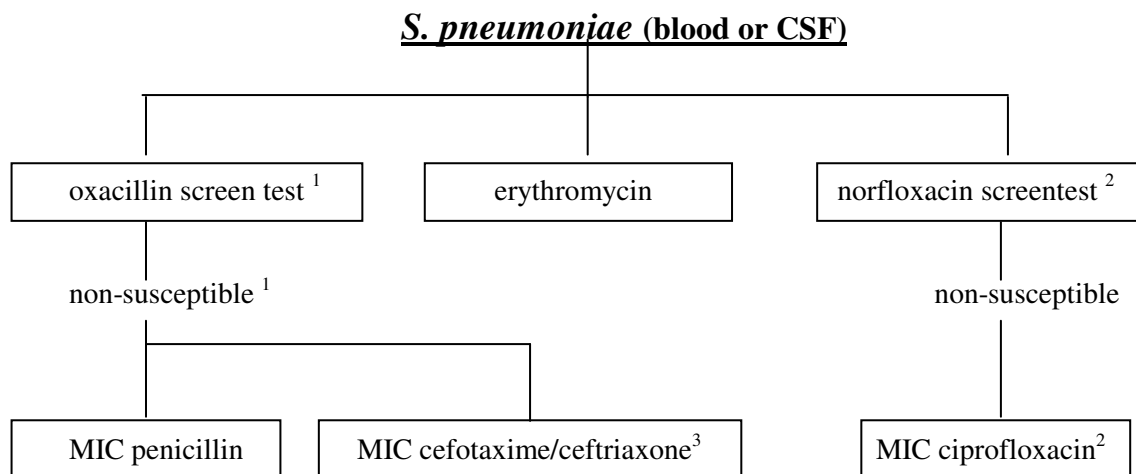
5. EARSS protocol for testing of *Streptococcus pneumoniae*

Objective: To determine the proportion of *S. pneumoniae* resistant to β -lactam-, macrolide- and fluoroquinolone antibiotics in blood and CSF isolates.

5.1. EARSS requirement

Report antimicrobial susceptibility test (AST) results for any primary isolates of *S. pneumoniae* from blood and/or CSF cultures (per patient). See paragraph 5.3 for further clarification.

5.2. Test procedure



β -lactam susceptibility:

Several national boards or committees recommend the use of an oxacillin 1 μ g disk or a 5 μ g disk. The method is validated for a specified medium containing horse or sheep blood, inoculum, temperature etc. Be sure to follow the recommendations of an appropriate board or committee.¹

Oxacillin non-susceptible: ¹

determine MIC of **penicillin**, specifying the method used: agar dilution, microdilution or E-test (range of dilutions: 0,015 - 256).

determine MIC of **cefotaxime** or **ceftriaxone**, specifying the method used: agar dilution, microdilution or E-test (range of dilutions: 0,003 - 32)³.

Macrolide susceptibility:

EARSS requires (since 1999) testing of erythromycin susceptibility. EARSS identified increasing macrolide resistance in Europe. Since macrolides are frequently used to treat lower respiratory tract infections, accurate monitoring of macrolide resistance has become important to guide empirical clinical treatment.

Fluoroquinolone susceptibility:²

Fluoroquinolone resistance (FQR) in *S. pneumoniae* is still rare in Europe (<1 % in EARSS database 2001 and 2002). In order to identify changes in fluoroquinolone susceptibility in *S. pneumoniae*, EARSS encourages susceptibility testing.

In collaboration with EUCAST (the European Committee on Antimicrobial Susceptibility Testing), EARSS recommends the use of a norfloxacin 10 µg disc to **screen for fluoroquinolone resistance**. The disc can be used on either Mueller Hinton- or ISA-medium (appropriately supplemented for the growth of *Streptococcus pneumoniae* and incubated in CO₂ for 16 – 20 hours). Isolates with a zone diameter of **10 mm or less** (breakpoint valid for both media and methods) should be subjected to a ciprofloxacin MIC-test (E-test or other). The use of other discs (ciprofloxacin 1 and 5 µg) may fail to reliably detect strains with ciprofloxacin MICs of 4 mg/L but will most often detect higher MICs (accepted as a poster at ECCMID, Copenhagen 2005). Please report² “fluoroquinolone S or R” on the basis of the screen test and please report ciprofloxacin MIC-values for strains which by the screen procedure were labeled non-susceptible.

Optional antibiotics:

EARSS also welcomes AST data for additional antibiotics in case a participating laboratory routinely tests for them. For *S. pneumoniae* these ‘optional’ antibiotics are: clindamycin, rifampicin, tetracycline, vancomycin, levofloxacin, and moxifloxacin.

5.3. Report from participating laboratories

Reporting of S/I/R interpretation is required and we ask the MIC or inhibition zone diameter (if possible). The first invasive *S. pneumoniae* isolate from blood or CSF per patient per quarter should be reported. If on the first day of sample collection both a blood and CSF isolate are taken please report both. In this case, only the susceptibility pattern of the CSF isolate will be added to the database, and the results of the blood isolates will only be used to study perceived differences in the susceptibility patterns between CSF and blood isolates. Subsequent isolates need not be reported.

5.4. Reporting of serotypes

EARSS encourages laboratories to report the serotype of the isolated strain. See annex 12 for serotype codes (Danish Kauffman-Lund scheme from the WHO Collaborating Centre for Reference and Research on Pneumococci at the Danish Serum Institute).

Comments

¹⁾ Screen for penicillin resistance using oxacillin disks with 1 µg (BSAC, SRGA, CLSI (Clinical and Laboratory Standards Institute - formerly NCCLS) or 5 µg (CA-SFM). Isolates categorized as penicillin non-susceptible by the screen test should be subjected to a penicillin (and if possible cefotaxime or ceftriaxone) MIC-test. Isolates with penicillin MIC<0.064 mg/L are considered susceptible to penicillin and cefotaxime/ceftriaxone. Isolates with penicillin MIC>0.064 mg/L should be categorized as S, I or R to penicillin (and if possible to cefotaxime or ceftriaxone) according to the appropriate MIC breakpoint table. Please report MIC-values when performed.

²⁾ The screening for fluoroquinolone resistance using a norfloxacin 10 µg disc, either on MH agar with lysed sheep blood with a confluent inoculum (0.5 McFarland) or on Isosensitest with defibrinated horse blood, is designed to detect low-level fluoroquinolone resistance. Isolates with zone diameters <10 mm should be reported as resistant to ciprofloxacin and if possible with a ciprofloxacin MIC-value (most commonly between 4 – 64 mg/L). EUCAST and EARSS do not promote the use of norfloxacin or ciprofloxacin for the treatment of respiratory tract infections; their use is recommended only because they increase

the sensitivity of the fluoroquinolone resistance screen method. Laboratories are advised not to report norfloxacin or ciprofloxacin susceptibility testing results to clinicians. However, we believe that, with the introduction of a new generation of fluoroquinolones for the therapy of respiratory tract infections it is important to identify early occurrence of FQ resistance in *S. pneumoniae*.

³⁾ In January 2003, the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) finalised new susceptibility breakpoints for *S. pneumoniae* isolates (Table 1). The change aimed to optimise therapy in the individual patient. The change in breakpoints may affect the proportion of cephalosporin intermediate and resistant *S. pneumoniae* since many European laboratories use CLSI recommendations. To avoid confusion in the EARSS database we ask laboratories to always use the meningitis breakpoints (≤ 0.5 mg/L and $R \geq 2$ mg/L) for cefotaxime and ceftriaxone and to always supply either a cefotaxime or ceftriaxone MIC-value in *S. pneumoniae* with reduced beta-lactam susceptibility.

Table 1. Former and new CLSI (NCCLS) criteria for S, I and R-characterization of cefotaxime and ceftriaxone susceptibility in *S.pneumoniae* isolates from blood and CSF.

Former breakpoints (mg/L)	S	I	R
All isolates	≤ 0.5	1	≥ 2
New breakpoints (mg/L)	S	I	R
Isolates from patients with meningitis	≤ 0.5	1	≥ 2
Isolates from other patients	≤ 1	2	≥ 4

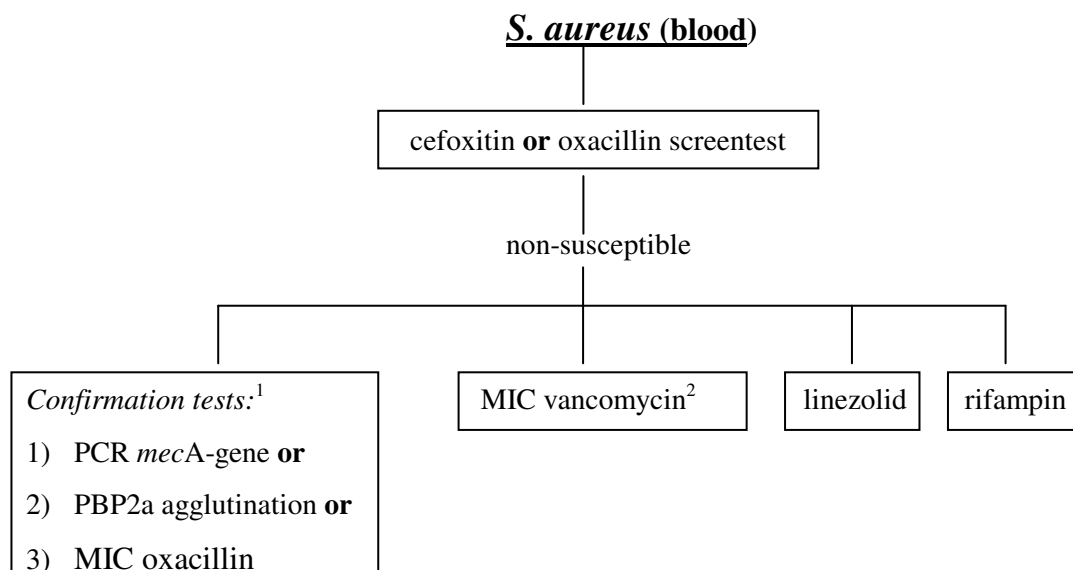
6. EARSS protocol for testing of *Staphylococcus aureus*

Objective: To determine the proportion of *S. aureus* resistant to methicillin in blood isolates.

6.1. EARSS requirement

Report antimicrobial susceptibility test (AST) results for the primary isolate of *S. aureus* from blood-cultures (per patient) positive for coagulase positive Staphylococci (*S. aureus*).

6.2. Test procedure



Methicillin susceptibility:

For reliable detection of MRSA the protocol recommends the use of a cefoxitin disk diffusion test. Alternatively the oxacillin agar screen plates or the oxacillin disk diffusion test (least reliable) can still be used.

Alternative 1. Cefoxitin disk

- Iso-Sensitest agar (ISA) or Mueller Hinton agar (25 ml per 9 cm plate) is prepared according to the instructions of the manufacturer (no salt).
- Plates are incubated over night (16-20 h) at 35 C and inhibition zones read to the nearest mm (inner edge of the zone).
- If a standard European semiconfluent inoculum and cefoxitin disk load of 10 µg is used on ISA or MH agar use the tentative breakpoints in Table A. If a CLSI (formerly NCCLS) confluent inoculum and cefoxitin disk load of 30 µg is used on MH agar, use the tentative breakpoints in Table B.

Table A	Semiconfluent inoculum – Cefoxitin 10 µg disc	
	S	R
Isosensitest medium	≥22 mm	<22 mm
MH agar	≥18 mm	<18 mm

Table B	Confluent inoculum – Cefoxitin 30 µg disc	
	S	R
MH agar	≥20 mm	≤19 mm

Alternative 2. Oxacillin screen plate

Several national boards or committees recommend the use of an oxacillin screen plate. The screen plate has often been validated with certain media, additives, inocula etc. Be sure to follow the appropriate recommendations.

Alternative 3. Oxacillin disk

Several national boards or committees recommend the use of a 1 µg disk or a 5 µg disk. The method is validated for a specified medium containing salt, inoculum, temperature etc. Be sure to follow the appropriate recommendations. However, the oxacillin disk test screen method is inferior (poorer sensitivity) than the cefoxitin disk test and oxacillin screen plate mentioned above.

Cefoxitin/Oxacillin non-susceptible:¹

- If in doubt (close to the breakpoint) confirm the result with either a PCR *mecA*-test or PBP2a agglutination. Oxacillin MIC-determination is less reliable as an MRSA confirmation method than PCR *mecA*- or PBP2a-detection.
- Determine MIC of vancomycin,² specifying the method used: microdilution, agar dilution or E-test.
- Determine the susceptibility to rifampicin and linezolid as two of the most important alternative treatment options for MRSA.

Optional antibiotics:

EARSS also welcomes AST data for additional antibiotics in case a participating laboratory routinely tests for them. For *S. aureus* these 'optional' antibiotics are: ciprofloxacin, erythromycin, clindamycin, gentamicin, tetracycline and fusidic acid.

6.3. Report from participating laboratories

Reporting of S/I/R interpretation is required and we ask the MIC or inhibition zone diameter (if possible). The first invasive *S. aureus* isolate from blood per patient per quarter should be reported. A second isolate shall not be reported even if the susceptibility pattern is different than that of the first isolate.

Comments

¹⁾ A participating country can decide whether the local laboratories or a central laboratory will perform the second step ("confirmation step") of the protocol and then also perform typing and vancomycin AST.

²⁾ Few of the MRSA isolates, may be heterogeneously (not uncommon) or homogeneously intermediate resistant (rare) to vancomycin. The presence of the heterogeneously resistant *S. aureus*, so called VISAs or GISAs (for glycopeptide-resistant *S. aureus*), can be missed when measuring MICs under standard conditions. See the recommendation for the detection of *S. aureus* with reduced susceptibility to vancomycin (Chapter 7).

References

1. Felten A, Grandry B, Lagrange PH, Casin I. Evaluation of Three Techniques for Detection of Low-Level Methicillin-Resistant *Staphylococcus aureus* (MRSA). J Clin Microbiol (2002) 40: 2776
2. Skov R, Smyth R, Clausen M et al. Evaluation of a cefoxitin 30 mcg disc on IsoSensitest

Agar for detection of MRSA. *J Antimicrob Chemother* (2003) 52: 204-207

3. Skov, R., Smyth R, Larsen, A., Frimodt-Møller N, Kahlmeter G. Evaluation of ceftiofur 5 and 10 µg disks for the detection of methicillin resistance in staphylococci. *J Antimicrob Chemother* (2005) 55:157-161.

7. EARSS recommendation on how to detect VISA/VRSA

Objective: If a laboratory wants to characterise MRSA isolates with reduced susceptibility to vancomycin identified by the routine protocol further, the following procedure is recommended by EARSS. Please be informed that this technical guide is not mandatory!

Step 1. VISA/VRSA screening

VISA screening should be undertaken by growing the bacteria, from an original inoculum, overnight in brain heart infusion broth. 10µL of the stationary phase culture should then be plated onto a Mueller Hinton agar plate containing 5µg/mL teicoplanin. The plates must incubate for 48hrs. Growth, of one or more colonies, may indicate reduced susceptibility and the isolate should be screened using the E-test method (Step 2).

Table 1. Step 1; VISA/VRSA screening

Method	Result	Result
Muller Hinton Agar (MHA) plates + 5 µg/mL teicoplanin	No growth = negative	Growth = positive
Interpretation	No suspected VISA/VRSA	Suspected VISA/VRSA, perform E-test → Step 2

Step 2. VISA/VRSA E-test

The E-test inoculum should be prepared in Brain Heart Infusion broth to a density of 2 MacFarland. 200 µl of this suspension is then pipetted onto a 90 mm Brain Heart Infusion agar (BBL (Beckton Dickinson and Comp. Cockeysville, MD, USA)) plate and spread evenly with a swab. The plate is then left to stand ensuring the inoculum has soaked into the plate; and the E-test strip should be carefully applied according to the manufacturer's instructions (AB biodisk, Solna, Sweden). The plates should be read after 48hrs. The plates must be read carefully (using a magnifying glass) observing small colonies or a double zone of inhibition that will grow in the E-test ellipse. The interpretation of a positive result is (i) teicoplanin $\geq 12\mu\text{g/mL}$ OR (ii) teicoplanin $\geq 8\mu\text{g/mL}$ AND vancomycin $\geq 8\mu\text{g/mL}$. Please note that this is just a cut-off level and SHOULD NOT be interpreted as the MIC.

Step 3. Further action

Any VISA/VRSA suspected strains meeting the criteria of steps 1 and 2 should be forwarded onto a reference laboratory where population analysis should be undertaken with appropriate controls i.e. Mu3 (ATCC 700698), Mu50 (700699) and Oxford strain or an alternative suitable control.

Table 2. Step 2; VISA/VRSA E-test and Step 3; Further action

Methods	CUT-OFF result	CUT-OFF result¹
i. E-test macromethod: BHI/ 2 McF/ 48 h	< 8 µg/mL vanco and teico	≥ 8 µg/mL vanco and teico
ii. E-test macromethod: BHI/ 2 McF/ 48 h	< 12 µg/mL teico	≥ 12 µg/mL teico
Interpretation	Susceptible	VISA/VRSA
Further action	In case of doubt send strain to reference lab.	a. Send VISA/VRSA strain to reference lab for (external) confirmation. b. Report VISA/VRSA after external confirmation to EARSS2

¹Do not convert 6 µg/mL to 8 µg/mL.

²On the EARSS website a VISA/VRSA detection form is available to report your invasive VISA/VRSA strain(s) to EARSS.

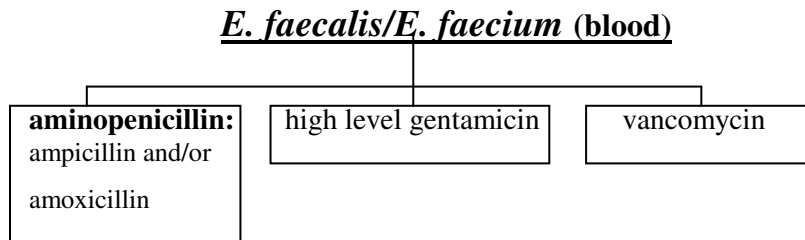
8. EARSS protocol for testing of *Enterococcus faecalis* and *Enterococcus faecium*

Objective: to determine the proportion of *E. faecalis* and *E. faecium* resistant to ampicillin, aminoglycoside and glycopeptide in blood isolates.

8.1. EARSS requirement

Report antimicrobial susceptibility test (AST) results for the primary isolates of *E. faecalis*/*E. faecium* from blood cultures (per patient).⁴ It is essential to differentiate *E. faecalis* from *E. faecium*.^{1, 2}

8.2. Test procedure



High level gentamicin resistance:

The laboratory should detect the presence of high level resistance and report it as resistant (R) to “gentamicin high”. High level resistance can be detected in several ways:

- Follow an official guideline.
- Determine the gentamicin MIC of any *E. faecalis*/*E. faecium* strain without any measurable zone around a disk containing gentamicin 30 – 120 µg, Report as high-level resistant if MIC > 128 mg/L (EUCAST recommended breakpoint).
- *E. faecalis*/*E. faecium* strains that grow in a broth screen test with an appropriate amount of gentamicin (at least 128 mg/L): perform a gentamicin MIC-test. Report as high-level resistant if MIC > 128 mg/L (EUCAST recommended breakpoint).

Optional antibiotics:

EARSS also welcomes AST data for additional antibiotics in case a participating laboratory routinely tests for them. For *E. faecalis*/*faecium* the ‘optional’ antibiotics are: teicoplanin, linezolid.

8.3. Report from participating laboratories

Reporting of S/I/R interpretation is required and we ask the MIC or inhibition zone diameter (if possible). The first invasive *E. faecalis* or *E. faecium* isolate from blood per patient per quarter should be reported. A second isolate shall not be reported even if the susceptibility pattern is different than that of the first isolate.

Comments

¹⁾ To facilitate the differentiation between hospital and community onset, laboratories are encouraged to record the date of admission on the isolate record form.

²⁾ Because of the differences in resistance characteristics and its possible implications for treatment decisions it is mandatory to differentiate between these two species. After differentiating enterococci from other streptococci, e.g. by means of the pyrrolidonyl- β -naphthylamide (PYR) test, *E. faecium* can be differentiated from *E. faecalis* by a number of phenotypic tests, such as tellurite tolerance, pyruvate utilisation and acid formation from arabinose (see Murray P.R. et al. Manual of Clinical Microbiology. ASM PRESS 2003. Chapter 18).

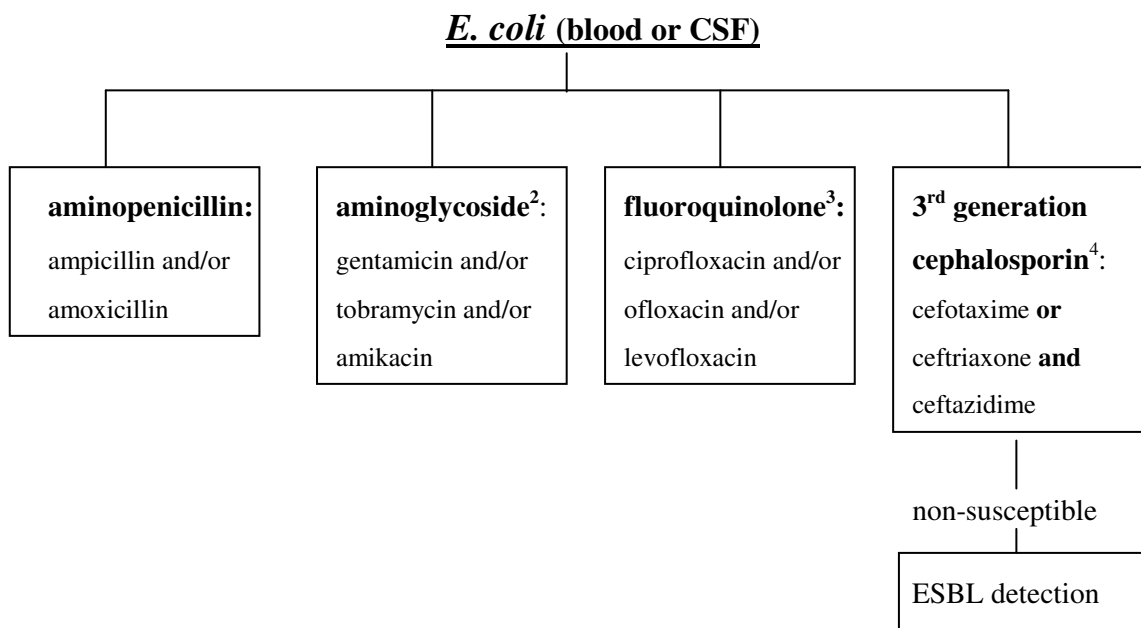
9. EARSS protocol for testing of *Escherichia coli*

Objective: to determine the proportion of *E. coli* resistant to aminopenicillins, aminoglycosides, fluoroquinolones, and 3rd generation cephalosporins in blood and CSF isolates.

9.1. EARSS requirement

Report antimicrobial susceptibility test (AST) results for the primary isolates of *E. coli* from blood and/or CSF cultures (per patient).¹ See paragraph 9.3 for further clarification.

9.2. Test procedure



3rd Generation cephalosporin susceptibility:⁴

For reliable detection of ESBLs the protocol requires laboratories to test for cefotaxime **or** ceftriaxone **and** ceftazidime susceptibility. **If 'I' or 'R' is reported for one or more of these agents please investigate ESBL production should be investigated by proceeding according to the ESBL-protocol (chapter 11).**

Optional antibiotics:

EARSS also welcomes AST data for additional antibiotics in case a participating laboratory routinely tests for them. For *E. coli* these 'optional' antibiotics are: imipenem/meropenem, piperacillin+tazobactam, co-trimoxazole.

9.3. Report from participating laboratories

Reporting of S/I/R interpretation is required and we ask the MIC or inhibition zone diameter (if possible). The first invasive *E. coli* isolate from blood or CSF per patient per quarter should be reported. If on the first day of sample collection both a blood and CSF isolate are taken please report both. In this case, only the susceptibility pattern of the CSF isolate will be added to the database, and the results of the blood isolates will only be used to study perceived differences in the susceptibility patterns between CSF and blood isolates. Subsequent isolates need not be reported.

Comments

- ¹⁾ To facilitate the differentiation between hospital- and community onset infections, laboratories are encouraged to record the date of admission on the isolate record form.
- ²⁾ For consistency purposes, EARSS prefers laboratories to report gentamicin susceptibility results (as the majority already does), but also accepts amikacin or tobramycin.
- ³⁾ Most EARSS participating laboratories test FQ resistance by determining ciprofloxacin susceptibility. Although not ideal as a screening test we would encourage laboratories to continue and adopt this as a routine for reporting consistent data to EARSS.
- ⁴⁾ EARSS prefers to collect data on cefotaxime or ceftriaxone and ceftazidime, in order to optimise the detection of ESBL producing *E. coli* and *K. pneumoniae*. The use of only ceftazidime may fail to detect CTX-M enzymes, the importance of which has been rapidly increasing in hospitals and in the community.

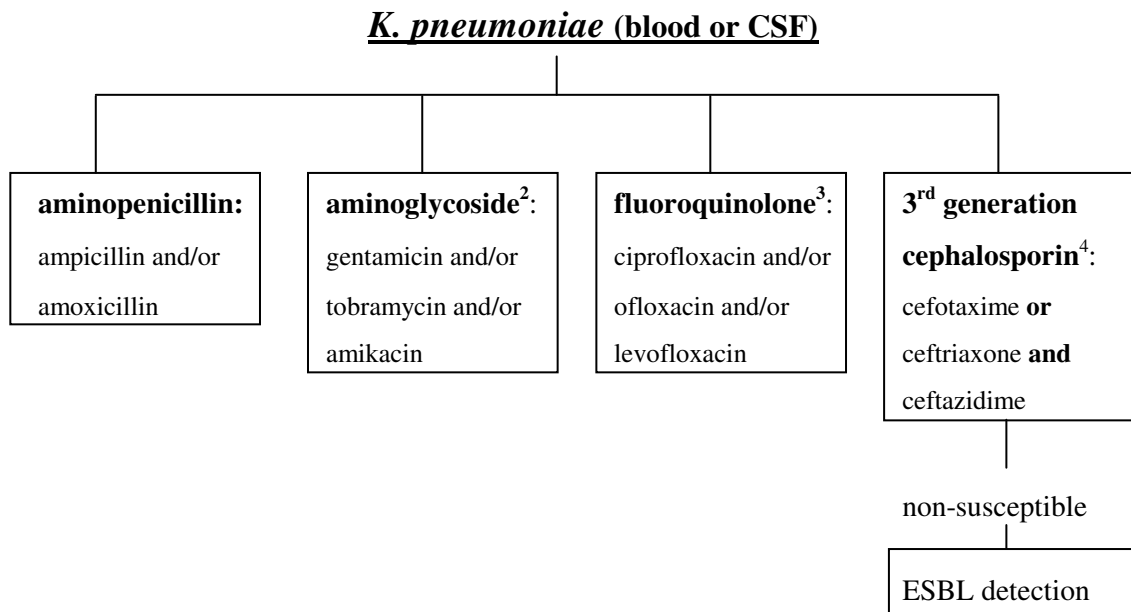
10. EARSS protocol for testing of *Klebsiella pneumoniae*

Objective: to determine the proportion of *E. coli* resistant to aminopenicillins, aminoglycosides, fluoroquinolones, and 3rd generation cephalosporins in blood and CSF isolates.

10.1. EARSS requirement

Report antimicrobial susceptibility test (AST) results for the primary isolates of *K. pneumoniae* from blood and/or CSF cultures (per patient).¹ See paragraph 10.3 for further clarification.

10.2. Test procedure



Species identification:

K. pneumoniae are non-motile capsule-forming short gram-negative rods. They ferment glucose and lactose and therefore appear as red colonies on media such as McConkey. They can be differentiated from other members of the Enterobacteriaceae family by the biochemical assimilation profile (Table 1).

Table 1. Biochemical reactions of named species ^a

Test/substrate	<i>K. pneumoniae</i> ^b	<i>K. oxytoca</i> ^b	<i>E. coli</i> ^b
Indole	0	99	98
Methylred	10	20	99
Voges Proskauer	98	95	0
Citrate	98	95	1
Ornithine decarboxylase	0	0	65

^a adapted from Manual of Clinical Microbiology by Murray PR et al (Chapter 27).

^b each number is the percentage of positive reactions after 2 days of incubation at 36°C.

3rd Generation cephalosporin susceptibility: ⁴

For reliable detection of ESBLs the protocol requires laboratories to test for cefotaxime or ceftriaxone and ceftazidime susceptibility. **If 'I' or 'R' is reported for one or more of these agents, ESBL production should be investigated by proceeding according to the ESBL-protocol (chapter 11).**

Optional antibiotics:

EARSS also welcomes AST data for additional antibiotics in case a participating laboratory routinely tests for them. For *K. pneumoniae* optional antibiotics are: imipenem/meropenem, piperacillin+tazobactam, co-trimoxazole.

10.3. Report from participating laboratories

Reporting of S/I/R interpretation is required and we ask the MIC or inhibition zone diameter (if possible). The first invasive *K. pneumoniae* isolate from blood or CSF per patient per quarter should be reported. If on the first day of sample collection both a blood and CSF isolate are taken please report both. In this case, only the susceptibility pattern of the CSF isolate will be added to the database, and the results of the blood isolates will only be used to study perceived differences in the susceptibility patterns between CSF and blood isolates. Subsequent isolates need not be reported.

Comments

¹⁾ To facilitate the differentiation between hospital- and community-acquired infections, laboratories are encouraged to record the date of admission on the isolate record form.

²⁾ For consistency purposes, EARSS prefers laboratories to report gentamicin susceptibility results (as the majority already does), but also accepts amikacin or tobramycin.

³⁾ Most EARSS participating laboratories test FQ resistance by determining ciprofloxacin susceptibility. Although not ideal as a screening test we would encourage laboratories to continue and adopt this as a routine for reporting consistent data to EARSS

⁴⁾ EARSS prefers to collect data on cefotaxime or ceftriaxone and ceftazidime, in order to optimise the detection of ESBL producing *E. coli* and *K. pneumoniae*. The use of only ceftazidime may fail to detect CTX-M enzymes, the importance of which has been rapidly increasing in hospitals and in the community.

11. Protocol for ESBL reporting

Objective: to study the production of Extended Spectrum β -lactamase (ESBL) by *E. coli* and *K. pneumoniae*, in blood and CSF isolates, in Europe.

Note: report the MIC-values of all 3rd generation cephalosporins you tested!

Step 1. Protocol ESBL screening test

Start by determining the MIC-value of the bacterium (*E.coli*, *Klebsiella spp.*) to cefotaxime (or ceftriaxone) and ceftazidime. If the MIC >1 mg/L for any of the three cephalosporins, the strain should be suspected of ESBL production and tested using a combination of clavulanic acid and the drug(s) to which it exhibited an elevated MIC. ^{1,2}

Methods 4	Calculation of result	
	ESBL negative isolate Report all penicillins, cephalosporins and aztreonam as tested.	ESBL positive isolate: Report all cephalosporins, penicillins and aztreonam as R irrespective of test result.
First choice: ESBL E-test	$\left(\frac{\text{MIC cephalosporin}}{\text{MIC cephalosporin + clav acid}} \right) < 8$	$\left(\frac{\text{MIC cephalosporin}}{\text{MIC cephalosporin + clav acid}} \right) \geq 8$
Second choice: MAST- DD	$\left(\frac{\text{zone cephalosporin + clav acid}}{\text{zone cephalosporin}} \right) < 1.5$	$\left(\frac{\text{zone cephalosporin + clav acid}}{\text{zone cephalosporin}} \right) \geq 1.5$
Third choice: Oxoid combination disk	(zone cephalosporin+clav acid) – (zone cephalosporin) < 5mm	(zone cephalosporin+clav acid) – (zone cephalosporin) \geq 5mm

Comments:

¹⁾ Preferably, also test the cephalosporins without elevated MIC in combination with clavulanic acid.

²⁾ ESBL production is not always determinable, e.g. if both the cephalosporin and the cephalosporin+clav acid produce MICs or zone diameter outside the test range, or there is no clavulanate synergy. These strains probably have other mechanisms of resistance, such as *AmpC*. If ESBL production is indeterminable, send the strain to a reference laboratory (see under footnote 1).

³⁾ If you do not have the possibility to confirm ESBL production in your laboratory, please send suspected strains to a reference laboratory and do not report the isolates to EARSS until you receive results from the reference laboratory. After receiving the test results, report these to EARSS and, if necessary, manually change results for cephalosporins, penicillins and aztreonam to R (i.e. interpretive reading; see Step 2,).

⁴⁾ The choice of method 1 – 3 is decided by the laboratory.

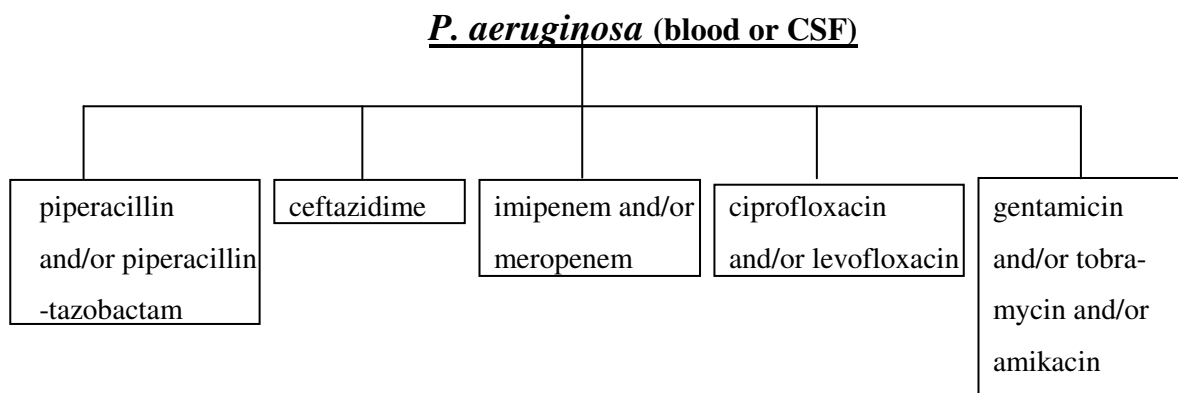
12. EARSS protocol for testing of *Pseudomonas aeruginosa*

Objective: to determine the proportion of *P. aeruginosa* resistant to piperacillin, ceftazidime, carbapenems, fluoroquinolones and aminoglycosides in blood and CSF isolates.

12.1. EARSS requirement

Report antimicrobial susceptibility test (AST) results for the primary isolates of *P. aeruginosa* from blood and/or CSF cultures (per patient). See paragraph 12.3 for further clarification.

12.2. Test procedure



12.3. Report from participating laboratories

Reporting of S/I/R interpretation is required and we ask the MIC or inhibition zone diameter (if possible). The first invasive *P. aeruginosa* isolate from blood or CSF per patient per quarter should be reported. If on the first day of sample collection both a blood and CSF isolate are taken please report both. In this case, only the susceptibility pattern of the CSF isolate will be added to the database, and the results of the blood isolates will only be used to study perceived differences in the susceptibility patterns between CSF and blood isolates. Subsequent isolates need not be reported.

13. Steps in routine data collection

In this chapter you will find the steps and procedures for the parties involved in the collection of AST data from laboratory level through national level to European level

Laboratory level → National level

13.1. Collecting data at laboratory level

- **Manually**; by filling out the corresponding Isolate Records Forms per pathogen (see annex 2-8)
- **Electronically**; it is recommended to follow the specifications of the EARSS data exchange format (see chapter 14) and to create a file with AMR data that can be forwarded from the laboratory to the national level.

Methods/tools that can be used for electronic exchange of data:

- **DEFS** (Data Entry & Feedback Software) is a very simple and ‘ready for use’ data entry tool that is specially developed for EARSS. It supports routine data entry for EARSS and converts data directly in EARSS exchange format. The software and manual can be downloaded at: www.earss.rivm.nl.
- **WHONET** (Microbiology Laboratory Database Software) is a useful tool for processing and analysis of your own laboratory data and supports the data collection for EARSS. It provides a routine procedure to perform data entry and to export data in EARSS exchange format. The software and manual can be downloaded from the EARSS website (www.earss.rivm.nl).
- **BacLink** (Microbiology Data Conversion Software from WHONET) enables you to convert and download AMR data from your Laboratory Information System (LIS). The downloaded file can then be exported by WHONET and converted into EARSS data exchange format.
- Use an export module that has been (or can be) developed by the supplier of the software to download data from your LIS. This module should export routinely generated data from LIS directly into EARSS data exchange format, decreasing the work-load for a participating laboratory substantially.

13.2. Microbiological ‘clearance’ of data

Before sending the data to the national level it is essential to check the output for:

- the microbiological consistency
- consistency of S/I/R interpretation with breakpoints used
- adherence with EARSS protocol

13.3. Forward data from laboratory level → national level

Laboratories are asked to collect AMR data on a routine basis and to forward it to the national level each quarter (preferably within four weeks before the end of a quarter). It is recommended that the national data manager keeps a list with officially participating laboratories, to be able to remind them quarterly of possible missing reports.

National level → European level

13.4. Procedure for handling AMR data at National level

At national level the AMR data from participating laboratories have to be processed, the steps to be performed by national data managers are:

- Collect data from all participating laboratories.
- Get clearance from the microbiologist in the national management team for the microbiological quality of the data (adherence to EARSS protocol, check of microbiological consistency, and check of S/I/R interpretations in relation to the MICs reported)
- Perform data entry if necessary.
- Combine data from all participating laboratories into one file.
- Remove duplicates. Only the first isolate per patient per quarter should be reported.
- Put data in EARSS exchange format (see chapter 14)
- Perform data check (using DCFP) and take corrective action if necessary.
- Send data quarterly to RIVM by e-mail (jos.monen@rivm.nl), following the time schedule given in chapter 13.
- National data managers can send updates on data (containing additional information on AMR results) regularly to RIVM.

EARSS MT supports national data managers in performing these tasks, by:

- organising workshops for national data managers
- appointment of 2 international data managers, responsible for handling of data at European level and giving support (helpdesk) to national data managers:

Jos Monen

jos.monen@rivm.nl

tel. +31 274 3956

13.5. Feedback from RIVM and approval from national level

After receiving files from a country we make a summary report of the results at RIVM, and send this report back to the national level. The EARSS Management Team will add the results to the central database within 2 weeks after sending the summary report to the national level. We ask the national level to confirm that the results are correct within these 2 weeks. Results will be used for reports, newsletters, publications and they will be accessible through our dynamic website (www.earss.rivm.nl).

14. Data exchange format

Brief description of data exchange format

Table 14.1. Brief description of data exchange format

Field Name	Field type	Initial column	Field length	Mandatory /Required /Optional
Current date	D	1	8	O
Laboratory code	A	9	5	M
Isolate sample number	A	14	12	R
Isolate source	A	26	2	R
Date of sample collection	D	28	8	M
Patient ID / Code	A	36	12	M
Sex	N	48	1	R
Month of birth	N	49	2	M
Year of birth	N	51	4	M
Clinical diagnosis	A	55	3	O
Other conditions	A	58	3	O
Hospital code	A	61	4	R
Origin of patient	N	65	1	R
Hospital department	A	66	3	R
Pathogen code	A	69	3	M
PCR mec-gene	N	72	1	O
Antibiotic code	A	73	3	M
S/I/R	A	76	1	M
Zone (> < =)	A	77	2	O
Zone (Value in mm)	A	79	2	O
MIC (> < =)	A	81	2	O
MIC (Value in mg/l)	A	83	5	O
E-test (> < =)	A	88	2	O
E-test (Value in mg/l)	A	90	5	O
Date of admission	D	95	8	O
ESBL present	N	103	1	O
Disk load	N	104	12	O
PBP2a-agglutination	N	116	1	O
Serotype	A	117	4	O

Field Name: Name of the variable, **Field type:** D= Date field, N=Numeric field, A=Alphabetic field, **Initial column:** First position of data field in case a fixed format is being used, **Field Length:** The field length is the total number of characters allowed for that field, **Mandatory:** Mandatory information to be included in the EARSS database, **Required:** Required to fit the EARSS protocols, **Optional:** Optional information is interesting to collect but not always available.

14.2. Extensive description data exchange format EARSS

Field Name: Current date

Columns: 1-8, Optional

Field Length: 8 [D] YYYYMMDD

Description: The date that the Isolate Record Form was filled in.

Field Name: Laboratory code

Columns: 9-13, Mandatory

Field Length: 5 [A] CC000

Description: The laboratory code consists of the country Code (CC) followed by a code of 3 characters. The National Co-ordinator assigns a specific code to every EARSS participating laboratory.

EARSS Country Codes (CC):

AT=Austria	HR= Croatia	PL=Poland
BE=Belgium	HU=Hungary	PT=Portugal
BG=Bulgaria	IS=Iceland	RO=Romania
CZ=Czech Republic	IE=Ireland	SI=Slovenia
DK=Denmark	IL=Israel	SK=Slovakia
FI=Finland	IT=Italy	ES=Spain
FR=France	LU=Luxembourg	SE=Sweden
DE=Germany	MT=Malta	UK=United Kingdom
EE=Estonia	NL=Netherlands	
GR=Greece	NO=Norway	

The laboratory code consists of the EARSS Country Code (CC) followed by 3 characters. The National Co-ordinator assigns a specific code to every EARSS participating laboratory. *Example: NL001 = laboratory 001 in the Netherlands.*

Field Name: Isolate sample number

Columns: 14-25, Required

Field Length: max. 12 [A]

Description: Number assigned by lab to specify isolate

Field Name: Isolate source

Columns: 26-27, Required

Field Length: 2 [A]

Description: The source of the isolate, coded as follows:

bl = Blood sf = CSF ot=other source xx= Unknown

Field Name: Date of sample collection

Columns: 28-35, Mandatory

Field Length: 8 [D] YYYYMMDD

Description: Date when sample was taken

Field Name: Patient ID / Code

Columns: 36-47, Mandatory**

Field Length: max. 12 [A]

Description: Patient ID / Code

****Mandatory: Patient-ID or (month+year) of birth** : If patient ID is not available

each isolate needs to be reported with month + year of birth.

We perform a check for duplicates (over a period of one year), for which we need a patient-identifier (patient-ID). Please be aware that the patient-ID needs to be specific enough. *For example: a patient-ID consisting of two letters is not discriminatory enough.* If the patient-ID is not available it is mandatory to report both month + year of birth, which enables us to generate an identification number. We ask national data managers also to unduplicate data at national level. Please send information only on the first isolate of each species from each patient. If the same species was identified from two different samples (possible for *S. pneumonia* or *E. coli*), or if the same species had different antibiotic susceptibility patterns, please send only the susceptibility test results for the first isolate.

Field Name: Sex

Columns: 48, Required

Field Length: 1 [N]

Description: Coded as follows: 1 = Male 2 = Female 9 = Unknown

Field Name: Month of birth

Columns: 49-50, Mandatory**

Field Length: 2 [N] MM

Description: Month of birth of the patient

Field Name: Year of birth

Columns: 51-54, Mandatory**

Field Length: 4 [N] YYYY

Description: Year of birth of the patient

****Mandatory: Patient-ID or (month+year) of birth:** If patient ID is not available each isolate needs to be reported with month + year of birth.

Field Name: Clinical diagnosis

Columns: 55-57, Optional

Field Length: 3 [A]

Description: The information regarding clinical diagnosis may vary. You will have to choose the most appropriate code for the infectious disease diagnosis:

1 = Pneumonia	2 = Meningitis
3 = Arthritis	4 = Endocarditis
5 = Primary Peritonitis	6 = Sepsis without focus in children
7 = Complicated Otitis Media	8 = Complicated Sinusitis
9 = Osteomyelitis	10 = Empyema
11 = Skin lesion	(11a = Furuncle
11b = Carbuncle)	12 = Abscess
(12a = breast	12b = cerebral
12c = lung	12d = renal
12e = subcutaneous/intramuscular)	ot = other, xx = Unknown

We realise that collection of this information is often not feasible. However to not disrupt the data format it was kept in the exchange format as an optional data field. To be able to code and store varying answers in the free text space on the Isolate Record Forms, there are two fields for this variable. The field “Clinical diagnosis” contains infectious disease diagnosis, and the field “Other conditions” contains mainly immuno-compromising factors.

Field Name: Other conditions

Columns: 58-60, Optional

Field Length: 3 [A]

Description: The information regarding other conditions may vary. You will have to choose the most appropriate code:

1 = Immunocompromised	2 = Following splenectomy
3 = Infected burn wounds	4 = Postoperative wound infection
5 = Drug abuse	6 = Intravascular procedures
(6a = Intravenous catheters	6b = Intravascular prosthetic devices
6c = Dialysis)	ot = other, xx = Unknown

Field Name: Hospital code

Columns: 61-64, Required

Field Length: 4 [A] 000X,

Description: The code consists of 4 characters. The first 3 characters are the code of the lab, and the 4th character is the letter assigned to a hospital (starting from A, B, etc.)

Because one laboratory may serve more hospitals it is very important to specify in which hospital the isolate was taken. The national co-ordinator assigns a letter to all the hospitals that are served by one laboratory. The code consists of 4 characters (000X). The first 3 characters are the code of the laboratory, and the 4th character is the letter assigned to a hospital (starting from A, B, etc.).

Example: 001A = the hospital A that is served by the Dutch laboratory 001.

Field Name: Origin of patient

Columns: 65, Required

Field Length: 1 [N] ,

Description: Is the patient at the moment the isolate is taken admitted in a hospital (inpatient), or not. This is coded as follows:

1 = Admitted(Inpatient)	2 = Outpatient
8= Other(e.g. emergency room)	9 = Unknown

Field Name: Hospital department

Columns: 66-68, Required

Field Length: 3 [A] ,

Description: The variable permits the general classification of locations by service, as follows:

med = Internal Medicine	pdn = Pediatrics/neonatal
pni = pediatrics/neonatal ICU	sur = Surgery
hao = Haematology/Oncology	obg = Obstet./Gynec
icu = Intensive Care	eme = Emergency
uro = Urology	inf = Infectious Diseases
oth = Other	xxx = Unknown

Field Name: Pathogen code

Columns: 69-71, Mandatory

Field Length: 3 [A]

Description: This is coded as follows:

spn = *S. pneumoniae*sau = *S. aureus*efm = *E. faecium*efa = *E. faecalis*eco = *E. coli*kpn = *K. pneumoniae*pae = *P. aeruginosa***Field Name: PCR *mecA*-gene**

Columns: 72, Optional

Field Length: 1 [N]

Description: The result of this test is coded as follows:

1 = positive 2 = negative 9 = Unknown

Field Name: Antibiotic code

Columns: 73-75, Mandatory

Field Length: 3 [A]

Description: specify the antibiotic in the field "Antibiotic code", making use of the Table Antibiotic coding EARSS (annex 11).

The coding for antibiotics in EARSS is the same as in WHONET53 (Windows version), see Annex 11 'Table antibiotic coding EARSS'..

Field Name: S/I/R

Columns: 76, Mandatory

Field Length: 1 [A] (S, I, or R)

Description: Final interpretation result of all different susceptibility tests performed, coded as follows: S = susceptible, I = intermediate, R = resistant.

In this data field the final susceptibility S (Susceptible), I (Intermediate) or R (Resistant) should be reported, which is the final interpretation that is based on one or more test results. EARSS-MT recommends the following rule to determine the final interpretation: E-test result goes over MIC result goes over Zone-diameter

Example: *it may happen that a pathogen is identified as being non-susceptible for a specific antibiotic by a disk-method, whereas by an MIC-method (e.g. at the same lab or at the reference lab) it is shown to be susceptible to this specific antibiotic. In this case mention 'S' as the final result in the S/I/R data field.*

Field Name: Zone (> < =)

Columns: 77-78, Optional

Field Length: 2 [A] (> < =)

Description: This field can indicate if a value of the zone is "greater than" (>); "equal to or greater than" (>=); "less than" (<); or "equal to or less than" (<=) the value indicated in the following field.

Field Name: Zone (Value in mm)

Columns: 79-80, Optional

Field Length: 2 [A]

Description: Zone diameter in millimetres or if the zone diameter is not available the S/I/R interpretation of the disk test.

Field Name: MIC (> < =)

Columns: 81-82, Optional

Field Length: 2 [A] (> < =)

Description: This field can indicate if a value of the MIC is “greater than” (>); “equal to or greater than” (>=); “less than” (<); or “equal to or less than” (<=) the value indicated in the following field.

Field Name: MIC (Value in mg/l)

Columns: 83-87, Optional

Field Length: 5 [A]

Description: Numeric value of the MIC test result that can vary from 0.002 to 1024, or if the numeric value is not available the S/I/R interpretation of the MIC.

Field Name: E-test (> < =)

Columns: 88-89, Optional

Field Length: 2 [A] (> < =)

Description: This field can indicate if a value of the E-test is “greater than” (>); “equal to or greater than” (>=); “less than” (<); or “equal to or less than” (<=) the value indicated in the following field

Field Name: E-test (Value in mg/l)

Columns: 90-94, Optional

Field Length: 5 [A]

Description: The value of the E-test test result that can vary from 0.002 to 1024, or if the numeric value is not available the S/I/R interpretation of the E-test.

Fields MIC (value in mg/l) and Etest (value in mg/l) for quantitative susceptibility test results:

We ask you to report quantitative results in the column that corresponds with the method (*zone value*, *MIC*, *E-test*) that was used. However, if quantitative results are not available, please report the S/I/R result in the column that corresponds with the method used. Note that it is mandatory to report the final interpretation in the S/I/R data field.

Zone (value in mm) to report disk diffusion quantitative results (diameter) or the interpretation (S/I/R) on the disk diffusion test.

MIC to report MIC quantitative results (agar, (micro-)broth) or the interpretation (S/I/R) of the MIC.

Etest to report Etest quantitative results or the interpretation (S/I/R) of the E-test.

The results of an oxacillin screen plate can be considered as a breakpoint MIC with only one concentration. In that case, we ask you to put the concentration of the oxacillin screen plate (or the S/I/R interpretation) in the MIC value field. (e.g. <= concentration used , or > concentration used).

Field Name: ESBL

Columns: 103, Optional

Field Length: 1 [N]

Description: This field indicates if Extended Spectrum β -lactamase is present

The result of this test is coded as follows:

1 = positive 2 = negative 9 = Unknown

Field Name: Disk load

Columns: 104-115, Optional

Field Length: 12 [N]

Description: This field can be used to mention the load of the gentamicin disk used, the field can be used for the disk load of other antibiotics too (optional). Please mention the value and the Units (e.g. mcg, Units or IU).

Field Name: PBP2agglutination

Columns: 116, Optional

Field Length: 1 [A]

Description: The result of this test is coded as follows:

1 = positive 2 = negative 9 = Unknown

Field Name: Serotype

Columns: 117-120, Optional

Field Length: 4 [A]

Description: For the codelist of serotypes see Annex 12.

14.3. Data structure

Each record should contain test-results for one antibiotic: Laboratory, Isolate, Patient, Hospital, and Pathogen data are repeated on every line. Every record is terminated with a carriage return, line feed. We prefer to receive files in tab separated format, since this is easy to handle. As an alternative fixed format can be used. If the last records are empty, in both formats it is not necessary to fill out with empty fields: it is sufficient to truncate the line.

14.3.1. In case of tab separated format

Field Type: A = Alphanumeric (tabs or special characters not allowed)

N = Numeric (all numbers, dots, and comma's allowed)

D = Date format: YYYYMMDD

- No trailing spaces in fields allowed
- A field can be left empty, BUT always use a tab-separator to go to the next column
- In case the last fields of the line do not have to be filled out, records may be truncated to omit trailing tabs. Records are terminated with a carriage return, line feed.

14.3.2. In case of fixed format

Field Type: A = Alphanumeric (spaces if unknown) (tabs / special ASCII characters not allowed)

N = Numeric (all numbers, dots, and commas allowed, spaces if unknown)

D = Date format: YYYYMMDD (spaces if unknown)

Initial column: the number of the first column where the field starts. It is very important to follow exactly this format since it is a 'fixed format', therefore: fields are filled out with spaces, empty fields are completely filled with spaces.

14.4 Preparing the files and sending them to RIVM

14.4.1. Summary

We ask you to send the combined files of all individual labs participating to EARSS in your country every 3 months to RIVM into one file by e-mail to RIVM.

14.4.2. Combining files

Before combining files please make sure that the data structure of the files are identical. If you use WHONET, you can refer to the 'WHONET manual for EARSS' for details on how to export the combined data into EARSS-structured data files. **Warning:** you should only combine files in WHONET for those laboratories who use the same set of antibiotics and set of (species-specific) breakpoints (as specified in the individual laboratory configuration files). In case the different laboratories are using different antibiotics and (species-specific) breakpoints, you should use another method, like a simple DOS command, to combine files. **Example:** Suppose you want to combine 2 files from labs 001 and 002 with filenames NL12001.001 and NL12001.002. **The DOS command** to combine them into the new file NL12001.txt (CCQYYYY.txt) is: **Copy NL12001.001 + NL12001.002 NL12001.txt**

14.4.3. Time scheme for sending data

<u>Date of susceptibility tests</u>	<u>Deadline at RIVM</u>
Jan 1-March 31, 2005	July 1, 2005
April 1 - June 30, 2005	October 1, 2005
July 1 – September 30, 2005	January 1, 2006
October 1 – December 31, 2004	April 1, 2006
and so on.....	

14.4.4. Name of the files

The name of this file will have the following format: CCQYYYY.txt
CC = Country Code (country code as proposed by EARSS)
Q = number of quarter (i.e. 1, 2, 3, or 4)
YYYY = year (4 characters, e.g., 2005)

14.4.5. Sending the files

The file may be zipped using "Winzip, pkzip" or another compatible program and send by e-mail to jos.monen@rivm.nl

15. Denominator Information

EARSS collects 'reference' information of the national networks through laboratory/hospital questionnaires. These questionnaires serve two main purposes;

1) to collect denominator information for the estimation of incidence rates, i.e. the frequency with which resistant bacteria were ascertained in a population. Unlike resistance proportions, incidence rates may improve comparisons between hospitals, regions and countries.

2) to collect information about the representativeness of EARSS results to understand if the reported data should only be applied to regions or can be generalised at country level.

In annex 9 the laboratory/hospital questionnaire for 2004, that was sent out to all participating countries in 2005 is shown.

15.1. Collecting Laboratory/hospital background information

15.1.1. Laboratory level

The laboratories will receive a request from their national EARSS representative to fill in the questionnaires on an electronic form or on paper by mail. Each laboratory is asked to complete one laboratory questionnaire form and a hospital questionnaire form for each hospital they serve (annex 9), repeating the specific laboratory code on each form. Laboratories should forward this information to the national level.

15.1.2. National level

At national level the Laboratory/Hospital questionnaires (annex 9) from participating laboratories have to be processed, steps to be performed by national data managers are:

- Collect the forms of all participating laboratories
- If necessary get the information more complete
- (Enter this information in a database that will be supplied by the EARSS-MT)
- Forward the information to RIVM.

Annex 1. Memorandum of Understanding

MEMORANDUM OF UNDERSTANDING



between the national EARSS representative(s) (Name) of the EARSS project in (country), and the participating laboratory in the EARSS project (Name of laboratory), (Name of contact person).

Both parties wish to collaborate in the European Antimicrobial Resistance Surveillance System (EARSS) project. This project, co-ordinated by the RIVM (Dutch National Institute of Health and the Environment) has been approved by the European Commission, and is funded by Directorate General SANCO. EARSS is a European network of national surveillance systems, which aims to aggregate comparable and reliable antimicrobial resistance data for public health purposes.

The participating laboratory wishes to cooperate with the EARSS project, through the sharing of quantitative resistance data on:

- | | |
|--|---|
| <input type="checkbox"/> <i>Streptococcus pneumoniae</i> | <input type="checkbox"/> <i>Escherichia coli</i> |
| <input type="checkbox"/> <i>Staphylococcus aureus</i> | <input type="checkbox"/> <i>Enterococcus faecium / faecalis</i> |
| <input type="checkbox"/> <i>Klebsiella pneumoniae</i> | <input type="checkbox"/> <i>Pseudomonas aeruginosa</i> |

The parties agree as follows:

1. The participating laboratory shall make individual data available to the national representative of the EARSS project, who shall share with the participating labs collated data on antimicrobial resistance collected through the EARSS project. EARSS shall undertake to make these data available through Internet. Data will be anonymised to a level where individual hospitals are not identifiable.

2. Both parties intend to provide comparable and correct data, but neither party 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.

3. The national representative of the EARSS project shall keep the participating laboratory informed on the progress of the EARSS project.

4. The participating laboratory will participate in EARSS Quality Assurance exercises.

5. This Memorandum of Understanding shall extend the previous memorandum (terminated 31 December 2003) unless renewed or extended by mutual agreement.

National representative(s) EARSS

Participating laboratory

BY: _____

BY: _____

(date) _____

(date) _____



Annex 4. Isolate Record Form VISA/VRSA

EARSS laboratory code:

Postal/ZIP-code of the laboratory:

Type of patient/isolate

1. Was the patient treated with glycopeptides?: yes no unknown
2. Was the patient suffering from a systemic infection?: yes no unknown
if yes, what kind of systemic infection?:
3. Was the patient admitted to the ICU?: yes no unknown

Step 1. VISA/VRSA screening

4. Result of VISA screening after 24hrs incubation on a MHA + 5µg/ml teicoplanin plate:
Growth (one or more colonies): positive negative
5. Did you use another method for screening?: yes no
If yes, what kind of method did you use:
With an incubation time of (hrs):
Growth (one or more colonies): positive negative

Step 2. VISA confirmation

6. Result of the E-test macromethod after 48 hrs:
CUT-OFF result for teicoplaninµg/mL
or
CUT-OFF result for teicoplaninµg/mL **and** vancomycinµg/mL
7. The interpretation according to the CUT-OFF result:
VISA*
Susceptible
* teicoplanin ≥12 µg/ml **or** teicoplanin ≥8µg/ml **and** vancomycin ≥8 µg/ml = VISA

Further action:

8. Was the strain send to a reference lab?: yes no
If yes, to which reference lab?:.....
.....
Was the VISA strain confirmed by the reference lab?: yes no
What method did the reference lab use?.....
.....
Did the reference lab perform the PAP-AUC method?: yes no
If yes, what was the result?:.....
.....

Thank you very much for reporting your VISA strain to EARSS!



Annex 5. 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 Data

Current date dd/mm/yyyy ___ / ___ / ____

Laboratory Code * CC000 -----

Isolate Data

Isolate sample number (lab) max. 12 characters -----

Isolate source tick box Blood CSF

Date of sample collection dd/mm/yyyy ___ / ___ / ____

Patient Data

Patient ID / Code max. 12 characters -----

Sex tick box Male Female Unknown

Month + Year of birth mm/yyyy ___ / ____

Clinical diagnosis (optional) free text

Hospital Data

Name/code of hospital** 000X -----

Origin of patient tick box Admitted Outpatient Unknown

Date of admission dd/mm/yyyy ___ / ___ / ____

Hospital Department tick box Surgery (Internal) Medicine Infectious diseases

Ob/Gyn ICU Emergency

Urology Haematology/oncology Pediatrics/neonatal

Pediatric/neonatal ICU Other: -----

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

Amoxicillin AND/OR S / I / R Zone diameter MIC

(fill in S, I or R) (mm) (in mg/l)

Ampicillin AND/OR -----

Gentamicin AND/OR -----

Tobramycin AND/OR -----

Amikacin AND/OR -----

Ciprofloxacin AND/OR -----

Ofloxacin AND/OR -----

Levofloxacin AND/OR -----

Cefotaxime AND/OR -----

Ceftriaxone AND/OR -----

Ceftazidime AND/OR -----

ESBL present Yes No Not tested

Optional

Co-trimoxazole S / I / R Zone diameter MIC

(fill in S, I or R) (mm) (in mg/l)

Imipenem -----

Meropenem -----

Piperacillin+tazobactam -----

Other: -----

Other: -----

Other: -----

Other: -----

* The national co-ordinators provide the laboratory code, consisting of a Country Code (CC) followed by 3 numbers.

** Consists of three numbers of the laboratory code, followed by a letter identifying the hospital.

Send this form to:	(Name/Institute)
Address: Tel: Fax: E-mail:	



Annex 6. 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 Data

Current date dd/mm/yyyy ___ / ___ / ____
 Laboratory Code * CC000 -----

Isolate Data

Isolate sample number (lab) max. 12 characters -----
 Isolate source tick box Blood CSF
 Date of sample collection dd/mm/yyyy ___ / ___ / ____

Patient Data

Patient ID / Code max. 12 characters -----
 Sex tick box Male Female Unknown
 Month + Year of birth mm/yyyy ___ / ____

Clinical diagnosis (optional) free text

Hospital Data

Name/code of hospital** 000X -----
 Origin of patient tick box Admitted Outpatient Unknown
 Date of admission dd/mm/yyyy ___ / ___ / ____

Hospital Department tick box

Surgery (Internal) Medicine Infectious diseases
 Ob/Gyn ICU Emergency
 Urology Haematology/oncology Pediatrics/neonatal
 Pediatric/neonatal ICU Other: -----

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

	S / I / R (fill in S, I or R)	Zone diameter (mm)	MIC (in mg/l)
<input type="checkbox"/> Amoxicillin AND/OR			-----
<input type="checkbox"/> Ampicillin			-----
<input type="checkbox"/> Gentamicin AND/OR			-----
<input type="checkbox"/> Tobramycin AND/OR			-----
<input type="checkbox"/> Amikacin			-----
<input type="checkbox"/> Ciprofloxacin AND/OR			-----
<input type="checkbox"/> Ofloxacin AND/OR			-----
<input type="checkbox"/> Levofloxacin			-----
<input type="checkbox"/> Cefotaxime AND/OR			-----
<input type="checkbox"/> Ceftriaxone			-----
Ceftazidime			-----
ESBL present	<input type="checkbox"/> Yes <input type="checkbox"/> No		<input type="checkbox"/> Not tested

Optional

	S / I / R	Zone diameter	MIC
Co-trimoxazole			-----
Imipenem			-----
Meropenem			-----
Piperacillin+tazobactam			-----
Other:			-----
Other:			-----
Other:			-----
Other:			-----
Other:			-----

* The national co-ordinators provide the laboratory code, consisting of a Country Code (CC) followed by 3 numbers.

** Consists of three numbers of the laboratory code, followed by a letter identifying the hospital.

Send this form to: (Name/Institute) Address: Tel: Fax: E-mail:



Annex 7. Isolate Record Form *E. faecium/faecalis*

To be filled out by laboratory

Instructions: please send data of the first **blood**-isolate of every patient with invasive *E. faecium/faecalis* infection. It is essential to differentiate between *E. faecium* and *E. faecalis*. Send data on resistant and on susceptible isolates; use 1 form per isolate.

Laboratory Data

Current date dd/mm/yyyy ___ / ___ / ____
 Laboratory Code * CC000 _____

Isolate Data

Pathogen *E. faecium* *E. faecalis* *Enterococcus (not specified)*
 Isolate sample number (lab) max. 12 characters _____
 Date of sample collection dd/mm/yyyy ___ / ___ / ____

Patient Data

Patient ID / Code max. 12 characters _____
 Sex tick box Male Female Unknown
 Month + Year of birth mm/yyyy ___ / ____
 Clinical diagnosis (optional) free text _____

Hospital Data

Name/code of hospital** 000X _____
 Origin of patient tick box Admitted Outpatient Unknown
 Date of admission dd/mm/yyyy ___ / ___ / ____
 Hospital Department tick box
 Surgery (Internal) Medicine Infectious diseases
 Ob/Gyn ICU Emergency
 Urology Haematology/oncology Pediatrics/neonatal
 Pediatric/neonatal ICU Other: _____

Antibiotic susceptibility testing

S/I/R, zone and/or MIC
 Amoxicillin AND/OR S / I / R Zone diameter MIC
 (fill in S, I or R) (mm) (in mg/l)
 Ampicillin _____ [][] _____
 Gentamicin HIGH Disk-load [][] _____
 Vancomycin [][] _____

Optional

Linezolid [][] _____
 Teicoplanin [][] _____
 Other: [][] _____
 Other: [][] _____
 Other: [][] _____
 Other: [][] _____
 Other: [][] _____

* The national co-ordinators provide a laboratory code, consisting of a Country Code (CC) followed by 3 numbers.
 ** Consists of three numbers of the laboratory code, followed by a letter identifying the hospital.

Send this form to: (Name/Institute) Address: Tel: Fax: E-mail:



Annex 8. Isolate Record Form *P. aeruginosa*

To be filled out by laboratory

Instructions: Please send data on the **first blood and/or cerebrospinal fluid (CSF)** isolate of every patient with a *P. aeruginosa* infection.

Please send data on resistant and on susceptible isolates; use 1 form per isolate.

Laboratory Data

Current date dd/mm/yyyy
 Laboratory Code * CC000

__ / __ / ____

Isolate Data

Isolate sample number (lab) max. 12 characters
 Isolate source tick box
 Date of sample collection dd/mm/yyyy

 Blood CSF
 __ / __ / ____

Patient Data

Patient ID / Code max. 12 characters
 Sex tick box
 Month + Year of birth mm/yyyy
 Clinical diagnosis free text

Male Female Unknown
 __ / ____

Hospital Data

Name/code of hospital** 000X
 Origin of patient tick box
 Date of admission dd/mm/yyyy
 Hospital Department tick box

 Admitted Outpatient Unknown
 __ / __ / ____
 Surgery (Internal) Medicine Infectious diseases
 Ob/Gyn ICU Emergency
 Urology Haematology/oncology Pediatrics/neonatal
 Pediatric/neonatal ICU Other: _____

Antibiotic susceptibility testing

S/I/R, zone and/or MIC

- Piperacillin AND/OR
- Piperacillin-tazobactam
- Ceftazidime
- Ciprofloxacin AND/OR
- Levofloxacin
- Imipenem AND/OR
- Meropenem
- Gentamicin AND/OR
- Tobramycin AND/OR
- Amikacin

S / I / R (fill in S, I or R)	Zone diameter (mm)	MIC (in mg/l)
<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	-----
<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	-----
<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	-----
<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	-----
<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	-----
<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	-----
<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	-----
<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	-----
<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	-----
<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	-----
<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	-----
<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	-----

Optional

Other:
 Other:
 Other:
 Other:

* The national co-ordinators provide the laboratory code, consisting of a Country Code (CC) followed by 3 numbers.
 ** Consists of three numbers of the laboratory code, followed by a letter identifying the hospital.

Send this form to:	(name/Institute)
Address: Tel: Fax: E-mail:	

Annex 9. Laboratory/Hospital questionnaire



Reference information about the populations for which laboratories provide their services is essential for understanding the validity, i.e. representativeness and generalisability of antimicrobial resistance data collected by EARSS. A similar questionnaire which asked for laboratory and hospital information was sent in 2001 and 2003. The information extracted from these questionnaires is displayed among other information in the country summary sheets, regularly published in the EARSS annual report and accessible on the website. This year another questionnaire is sent out, and again the information that we ask for will serve a double purpose;

- **collection of denominator information:** to calculate incidence rates (i.e. the frequency with which certain resistant bacteria are isolated from blood cultures in your hospital population over time). Unlike resistance proportions, incidence rates reflect the relative risk of blood-stream infections with resistant bacteria among your patients and can be used to estimate the burden of antimicrobial resistance in a country¹.
- **collection of information about the representativeness of EARSS results**, which will improve our understanding about the characteristics of the population which you serve and thus provide an indication if your data can be applied to the country as a whole.

The specific purposes of this new questionnaire are;

- Firstly, to gather **up-to-date reference information** from the laboratories and hospitals.
- Secondly, to get **reference information that will be readily applicable**. From previous experience we rephrased, deleted and added some questions.

This year the laboratory questionnaire contains only seven questions. We ask for the same service characteristics, but to get a more comprehensive picture on sampling rates, we added two simple questions about culture habits. Furthermore four other questions were included, with respect to the new protocol for antimicrobial susceptibility testing of *Klebsiella pneumoniae*, the new internet-based information system EARSS-*ibis* and a study that could calculate additional costs incurred by resistant organisms in your hospital. The hospital questionnaire contains 11 questions. A few questions were added to get a more comprehensive picture of the hospital population. In addition, a question was included about participation in EARSS sister projects.

We will make the collected background information available on the EARSS website and in the next annual report.

Any clarifications regarding the questionnaire can be requested from the EARSS management team; a copy of the questionnaire in **digital format** can also be requested from our team, or downloaded directly from the EARSS website at www.earss.rivm.nl.

Detailed instructions on how to complete the questionnaire follow on the next pages.

Please send the completed laboratory and hospital questionnaires to your national contact person, by mail, fax, or electronic mail, before the 15th of May.

Contact addresses

Your national contact person

EARSS project epidemiologist

Marlieke de Kraker
National Institute of Public Health and
Environment (RIVM)
PO Box 1, 3720 BA Bilthoven, The Netherlands
Tel. +31(30)2743834
Fax +31(30)274 4409
e-mail Marlieke.de.Kraker@RIVM.nl

Instructions for completion of the questionnaire

General

The **laboratory questionnaire** ('LabcodeLABQ2005.doc') should be completed by the **EARSS – participating laboratory**, the **hospital questionnaire** ('HoscodeHOSQ2005.doc') should be completed for **ALL** hospitals served by this laboratory. This can be done by the laboratory itself (by contacting the hospital administration for some questions) or by someone in the hospital administration (best option if your laboratory is serving several hospitals).

*The questionnaires should be completed **before the 15th of May**.*

How to use the paper form:

1. Fill in the questionnaire for your laboratory and all respective hospitals by writing in the appropriate box, or ticking the box corresponding to your answer.
2. Please send **all** your completed questionnaires back to your national contact person by regular mail / fax.

How to use the electronic form

1. Open the Excel document 'LABQ2005.xls' or 'HOSQ2005.xls'. Save the document with <Save as> and add your EARSS laboratory or hospital code to the filename, like this: 'LA01LABQ2005.xls' or 'HO01HOSQ2005.xls'. If your laboratory serves more than one hospital, save 'HOSQ2005.xls' with the specific EARSS hospital code added to the filename for all hospitals served.
2. Fill in the laboratory questionnaire on the 'lab_q' sheet, and the hospital questionnaire(s) on the 'hosp_q' sheet. Fill in all orange boxes, these will then become white. If you enter text where a number is asked for or vice versa, the specific box will turn red to indicate a typing error. For some questions pre-coded answers are given behind the answer-box(es). For these questions please fill in the code corresponding to your answer. Save the Excel files with your completed questionnaires again and send them to your national contact person by e-mail.

Explanation of individual data fields

In the following we have included an explanation, field by field, why we are interested in the information requested in each of the data fields.

Laboratory Questionnaire (Characteristics 2004)
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- **EARSS Laboratory code** *Mandatory field that is needed to link the questionnaire information to the EARSS database. The laboratory code consists of the country code followed by a 3-digit number. Use the code that has been assigned to your laboratory by the national representative!*
- **Postal code and city** *identifies the geographical location of your laboratory, which can be used to break down the data to a regional level to describe the regional distribution of EARSS laboratories in your country.*
- **Number of hospitals served and EARSS hospital codes** are needed to link EARSS laboratory information to hospitals that you serve.
- **1.a Total number of blood culture requests (sets) in 2004** This information allows us to find out how frequently blood cultures are used in your hospital, and provide us with the denominator of all following questions. This is also important because blood culturing practices vary between centres^{2,3} and we find a positive association between the number of blood cultures and the number of ascertained bloodstream infections. If you do not know the number of sets requested in 2004 try to answer question 1.b and 1.c, which allows some ‘back calculation’.
- **1.b The total number of blood culture bottles in 2004** and
1.c The total number of bottles per blood culture request If you could not answer question 1.a., please try to answer question 1.b. and 1.c. With this information we can still determine the difference in investigation densities between different laboratories/hospitals.
- **2. The total number of blood culture requests (sets) reported positive for all bacterial pathogens (Try to exclude contamination if that is possible)** In combination with the total number of blood culture requests, this will tell us something about the diagnostic practice in your hospitals. Please, check the box if you could exclude contaminations, such as single bottles positive for coagulase-negative Staphylococci in a patient with no clinical suspicion of blood stream infection.
- **3. How many sets per patient do you collect during a normal diagnostic investigation?** In combination with question 1 this will tell us for how many patients blood cultures were requested. This gives us a better trust in the comparison of investigation densities between centres and countries.
- **4. Which system/test-kit is used in your laboratory to identify *Klebsiella pneumoniae* at the species level?** At the plenary meeting in 2004 it was decided that EARSS will collect data on *Klebsiella pneumoniae* as well. Speciation of *Klebsiella*, however, may cause problems depending on the methods used. We are therefore interested in the methods used to specify *Klebsiella* at the species level.
- **5. With respect to EARSS-ibis please provide us with the type of internet connection of your laboratory:** With this information EARSS-MT will know the availability of EARSS-ibis for every laboratory as to estimate potential coverage and actual utilisation of the system.
- **6. Would you be interested in contributing to a study that measures the burden and cost of antibiotic resistance in your hospital?** In addition to the standard questions above, we would also like to explore if you would be interested to contribute to a possible future study on the burden and costs of antibiotic resistance in your hospital. In that case, we would be able to calculate these costs for your hospital provided you could give us the information requested in the next question.
- **7. If yes, which additional information would you be able to provide on the patients that developed positive blood cultures (for example for patients with *S. aureus* or *E. coli* septicaemia)?** We would like to know if you or your clinical colleagues would be able to provide information through a structured questionnaire concerning the seven pertinent items indicated in this question. This would probably include a visit to the patients’ ward and five minutes to complete the questionnaire as well as collecting information when the patients are being discharged.

<i>Hospital Questionnaire (Characteristics 2004)</i>

- **EARSS Hospital code** *Mandatory field that is needed to link the questionnaire information to the EARSS database. Please use the hospital code that you also use when reporting antimicrobial susceptibility test results to EARSS!*
- **EARSS Laboratory code** *Mandatory field that is needed to link your hospital to the EARSS-participating laboratory.*
- **Postal code and city** *identifies the geographical location of the hospital, which can be used to break down the data to describe the regional distribution of EARSS laboratories in your country.*
- **1. Type of hospital** *is necessary to stratify resistance rates by hospital type. It is known⁴ that antibiotic resistance rates differ between hospitals according to specialities and case mix. Please tick only one box. If the hospital provides both secondary and tertiary care, please tick the box 'University/tertiary care hospital'. We realise that there may be hospitals that are highly specialised, so called single specialty hospitals, such as paediatric or TB-clinics. In these cases, please tick the category 'other' and indicate the relevant single specialty.*
- **2. Which of the specialties below were available in your hospital in 2004?** *This information gives us an indication for the treatment of severely susceptible patients. Hospitals with for example burns units or those performing complex organ transplantations are usually faced with higher antibiotic resistance rates. Please tick **all** appropriate boxes. If the hospital has other super-regional specialties than mentioned in the list, please tick the category 'other super-regional specialties' and indicate the relevant specialty.*

The following items may be made available through hospital administration office:

- **3. Best estimate of catchment population of your hospital.** *This is the denominator for calculating incidence rates for community acquired infections^{1,5}. If the catchment population is not exactly known, please give your best estimate.*
We realise that university/tertiary care hospitals may also serve as district hospitals, thereby actually serving two different populations. If this is the case for your hospital, please provide us with the catchment population for the university/tertiary care service.
- **4.a Hospital size in beds** *is needed to group hospitals by size.*
- **4.b Does this include beds in psychiatry and/or long term care?** *This information is important, because these patients are staying for much longer than average patients in acute care hospitals. We need to take this information into consideration when calculating the average length of stay. If there are beds for psychiatry or long term care patients in the hospital, please fill in question 4.c.*
- **4.c If yes, what is the total number of beds in psychiatry and long term care?** *With this number, hospital size can be adjusted for the number of psychiatry and long term care beds, so that hospitals with and without psychiatry and long term care facilities can be compared.*
- **5. Number of intensive care beds** *Provides information on the number of hospital beds that are actually ICU beds, and thus, about the expected case mix of the hospital. Please include paediatric and neonatal ICU beds in this number as well.*
- **6.a Total number of patient-days** *This is the sum of all patient admission episodes in your hospital and is the best denominator needed to calculate incidence rates⁴ for positive blood cultures. Please try to get this figure as it is much better than any estimate. If, however, this information is not available at all, please fill in question 6.b.*
- **6.b The average occupancy rate** *If the number of patient-days is not available, we can estimate number of patient days by multiplying the number of beds with the annual average occupancy. However, this estimate is rather crude!*
- **7. Total number of patient admissions** *This number is needed to calculate the average length of stay per patient.*
- **8.a Were patient transfers between departments counted as new admissions?**
8.b Were patients counted as new admissions the Monday they returned? *This information will give a more clear view of the total number of patient admissions and is required for reliable comparison of*

the total number of patient admissions between hospitals.

- 9. Did your hospital participate in: This information will be used for future linkage of EARSS and ESAC and/or IPSE data.
- 10 & 11 Positive and negative impact of EARSS These questions give the possibility to state any positive or negative effect of participating in EARSS and will be helpful to improve EARSS methods and understand if and to what degree EARSS improves health care delivery.

Thank you in advance for filling in the questionnaire, we are looking forward to your response!

References:

1. Monnet, DL. Only percentage within species; neither incidence, nor prevalence: demographic information and representative surveillance data are urgently needed to estimate the burden of antimicrobial resistance. Letters to the Editor / Int. J. Antimicrob. Agents 2004; 24: 622-623.
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4. Tiemersma EW, Bronzwaer SL, Lyytikäinen O, Degener JE, Schrijnemakers P, Bruinsma N, Monen J, Witte W, Grundman H; European Antimicrobial Resistance Surveillance System Participants. Methicillin-resistant *Staphylococcus aureus* in Europe, 1999-2002. Emerg. Infect. Dis. 2004; 10:1627-34.
5. WHO. Surveillance standards for antimicrobial resistance. Geneva: World Health Organization. WHO/CDS/CSR/DRS/2001.5, 2002.

Annex 10. EARSS country codes

for countries participating or intending to participate in EARSS.

Looking for standardisation in using country-codes within EARSS, we follow the ISO-country code (International Organisation for Standardisation). These codes are also used in web site addresses indicating the country at the end of the address (alpha-2 code elements from ISO 3166-1; also called country code top-level domain identifiers).

Austria	AT
Belgium	BE
Bulgaria	BG
Croatia	HR
Cyprus	CY
Czech Republic	CZ
Denmark	DK
Estonia	EE
Finland	FI
France	FR
Germany	DE
Greece	GR
Hungary	HU
Iceland	IS
Ireland	IE
Israel	IL
Italy	IT
Latvia	LV
Lithuania	LT
Luxembourg	LU
Malta	MT
Netherlands	NL
Norway	NO
Poland	PL
Portugal	PT
Rumania	RO
Russia	RU
Slovakia	SK
Slovenia	SI
Spain	ES
Sweden	SE
Switzerland	CH
Turkey	TR
United Kingdom	UK

Annex 11. Table antibiotic coding EARSS (from WHONET 5.3)

CODE	ANTBIOTIC	CODE	ANTBIOTIC
FCT	5-Fluorocytosine	CID	Cefonicid
ACM	Acetylmidecamycin	CFP	Cefoperazone
ASP	Acetylspiramycin	CSL	Cefoperazone/Sulbactam
AMK	Amikacin	CND	Ceforanide
AMX	Amoxicillin	CTX	Cefotaxime
AMC	Amoxicillin/Clavulanic acid	CTC	Cefotaxime/Clavulanic acid
AXS	Amoxicillin/Sulbactam	CTS	Cefotaxime/Sulbactam
AMB	Amphotericin B	CTT	Cefotetan
AMP	Ampicillin	CTF	Cefotiam
SAM	Ampicillin/Sulbactam	CHE	Cefotiam hexetil
AMR	Amprolium	FOX	Cefoxitin
APL	Apalcillin	ZOP	Cefozopran
APR	Apramycin	CFZ	Cefpimizole
ARB	Arbekacin	CPM	Cefpiramide
APX	Aspoxicillin	CPO	Cefpirome
AST	Astromicin	CPD	Cefpodoxime
AVI	Avilamycin	CPX	Cefpodoxime proxetil
AVO	Avoparcin	CPR	Cefprozil
AZM	Azithromycin	CRD	Cefroxadine
AZL	Azlocillin	CFS	Cefsulodin
ATM	Aztreonam	CSU	Cefsumide
BAM	Bacampicillin	CAZ	Ceftazidime
BAC	Bacitracin	CCV	Ceftazidime/Clavulanic acid
BIA	Biapenem	CEM	Cefteram
BCZ	Bicozamycin	CTB	Ceftibuten
BDP	Brodimoprim	TIO	Ceftiofur
BUT	Butoconazole	CZX	Ceftizoxime
CAP	Capreomycin	CRO	Ceftriaxone
CRB	Carbenicillin	CXA	Cefuroxime axetil
CAR	Carumonam	CXM	Cefuroxime sodium
CAC	Cefacetrile	ZON	Cefuzonam
CEC	Cefaclor	LEX	Cephalexin
CFR	Cefadroxil	CEP	Cephalothin
RID	Cefaloridin	HAP	Cephapirin
MAN	Cefamandole	CED	Cephradine
CTZ	Cefatrizine	CTO	Cetocycline
CZD	Cefazedone	CHL	Chloramphenicol
CZO	Cefazolin	CTE	Chlortetracycline
CFB	Cefbuperazone	CIC	Ciclacillin
CCP	Cefcapene	CIN	Cinoxacin
CDR	Cefdinir	CIP	Ciprofloxacin
DIT	Cefditoren	CLR	Clarithromycin
FEP	Cefepime	CLA	Clavulanic acid
CAT	Cefetamet	CLX	Clinafloxacin
CPI	Cefetamet pivoxil	CLI	Clindamycin
CCL	Cefetecol (Cefcatacol)	CTR	Clotrimazole
CZL	Cefetizole	CLO	Cloxacillin
CFM	Cefixime	COL	Colistin
CMX	Cefmenoxime	CYC	Cycloserine
CMZ	Cefmetazole	DFX	Danofloxacin
CNX	Cefminox	DAP	Daptomycin
CDZ	Cefodizime	DEM	Demeclocycline (Demethylchlortetracycline)

CODE	ANTBIOTIC	CODE	ANTBIOTIC
DKB	Dibekacin	LOM	Lomefloxacin
DIC	Dicloxacillin	LOR	Loracarbef
DIF	Difloxacin	MEC	Mecillinam (Amdinocillin)
DIR	Dirithromycin	MEL	Meleumycin
DOX	Doxycycline	MEM	Meropenem
ECO	Econazole	MES	Mesulfamide
ENX	Enoxacin	MET	Methicillin
ENR	Enrofloxacin	MTP	Metioprim
EPE	Eperozolid	MXT	Metioxate
EPP	Epiroprim	MTR	Metronidazole
ETP	Ertapenem	MEZ	Mezlocillin
ERY	Erythromycin	MSU	Mezlocillin/Sulbactam
ETH	Ethambutol	MCZ	Miconazole
ETI	Ethionamide	MCR	Micromomicin
ETO	Etopabat	MID	Midecamycin
FAR	Faropenem	MIL	Miloxacin
FLA	Flavomycin	MNO	Minocycline
FLE	Fleroxacin	MON	Monensin sodium
FLO	Flomoxef	MOX	Moxalactam (Latamoxef)
FLR	Florfenicol	MFX	Moxifloxacin
FLC	Flucloxacillin	MUP	Mupirocin
FLU	Fluconazole	NAF	Nafcillin
FLM	Flumequine	NAL	Nalidixic acid
FOS	Fosfomycin	NAR	Narasin
FMD	Fosmidomycin	NEO	Neomycin
FRM	Framycetin	NET	Netilmicin
FRZ	Furazolidone	NIC	Nicarbazin
FUS	Fusidic acid	NIF	Nifuroquine
GAT	Gatifloxacin	NIT	Nitrofurantoin
GEM	Gemifloxacin	NIZ	Nitrofurazone
GEN	Gentamicin	NTR	Nitroxoline
GEH	Gentamicin-High	NOR	Norfloxacin
GRX	Grepafloxacin	NVA	Norvancomycin
GRI	Griseofulvin	NOV	Novobiocin
HAB	Habekacin	NYS	Nystatin
HET	Hetacillin	OFX	Ofloxacin
HYG	Hygromycin	OLE	Oleandomycin
IPM	Imipenem	OPT	Optochin
ISE	Isepamicin	ORS	Ormetropim/Sulfamethoxine
ISO	Isoconazole	ORN	Ornidazole
INH	Isoniazid	OXA	Oxacillin
ITR	Itraconazole	OXO	Oxolinic acid
JOS	Josamycin	OXY	Oxytetracycline
KAN	Kanamycin	PAS	P-Aminosalicylic acid
KAH	Kanamycin-High	PAN	Panipenem
KET	Ketoconazole	PAR	Paromomycin
KIT	Kitasamycin (Leucomycin)	PEF	Pefloxacin
LAS	Lasalocid	PEN	Penicillin G
LVX	Levofloxacin	PNV	Penicillin V
LIN	Lincomycin	PNO	Penicillin/Novobiocin
LSP	Linco-spectin	PIM	Pentisomicin
LNZ	Linezolid	PTZ	Pentizidone

CODE	ANTBIOTIC	CODE	ANTBIOTIC
PPA	Pipemidic acid	SDM	Sulfadimidine (Sulfaisodimidine ?)
PIP	Piperacillin	SZO	Sulfamazone
PIS	Piperacillin/Sulbactam	SUM	Sulfamethazine
TZP	Piperacillin/Tazobactam	SMX	Sulfamethoxazole
PRC	Piridicillin	SNA	Sulfasuccinamide
PRL	Pirlimycin	SUT	Sulfathiazole
PIR	Piromidic acid	SOX	Sulfisoxazole
POL	Polymixin B	SSS	Sulfonamides
PRX	Premafloxacine	TLP	Talmetoprim
PRM	Primycin	TAZ	Tazobactam
PRI	Pristinamycin	TEC	Teicoplanin
PRP	Propicillin	TLT	Telithromycin
PKA	Propikacin	TMX	Temafloxacine
PTH	Prothionamide	TEM	Temocillin
PZA	Pyrazinamide	TCY	Tetracycline
QDA	Quinupristin/Dalfopristin	TET	Tetroxoprim
RAC	Ractopamine	THA	Thiacetazone
RIB	Rifabutin	THI	Thiamphenicol
RIF	Rifampin	TIA	Tiamulin
ROK	Rokitamycin	TIC	Ticarcillin
ROS	Rosoxacin	TCC	Ticarcillin/Clavulanic acid
RXT	Roxithromicin	TBQ	Tilbroquinol
SAL	Salinomycin	TIL	Tilmicosin
SAR	Sarafloxacine	TIN	Tinidazole
SRX	Sarmoxicillin	TDC	Tiodonium chloride
SIS	Sisomicin	TXC	Tioxacin
SPX	Sparfloxacine	TOB	Tobramycin
SPT	Spectinomycin	TFX	Tosufloxacine
SPI	Spiramycin	TMP	Trimethoprim
STR	Streptomycin	SXT	Trimethoprim/Sulfamethoxazole
STH	Streptomycin-High	TRL	Troleandomycin
SUL	Sulbactam	TRO	Trospectomycin
SBC	Sulbenicillin	TVA	Trovafloracin
SUC	Sulconazole	TYL	Tylosin
SUP	Sulfachlorpyridazine	VAN	Vancomycin
SDI	Sulfadiazine	VIO	Viomycin
SUD	Sulfadimethoxine	VIR	Virginiamycine

Annex 12 *S. pneumoniae* serotype codes

<i>S. pneumoniae</i>	<i>S. pneumoniae</i> type
Type 1	1
Type 2	2
Type 3	3
Type 4	4
Type 5	5
Group 6	6A
Group 6	6B
Group 7	7A
Group 7	7B
Group 7	7C
Group 7	7F
Type 8	8
Group 9	9A
Group 9	9L
Group 9	9N
Group 9	9V
Group 10	10A
Group 10	10B
Group 10	10C
Group 10	10F
Group 11	11A
Group 11	11B
Group 11	11C
Group 11	11D
Group 11	11F
Group 12	12A
Group 12	12B
Group 12	12F
Type 13	13
Type 14	14
Group 15	15A
Group 15	15B
Group 15	15C
Group 15	15F
Group 16	16A
Group 16	16F
Group 17	17A
Group 17	17F
Group 18	18A
Group 18	18B
Group 18	18C
Group 18	18F
Group 19	19A
Group 19	19B
Group 19	19C
Group 19	19F
Type 20	20
Type 21	21

<i>S. pneumoniae</i>	<i>S. pneumoniae</i> type
Group 22	22A
Group 22	22F
Group 23	23A
Group 23	23B
Group 23	23F
Group 24	24A
Group 24	24B
Group 24	24F
Group 25	25A
Group 25	25F
Type 27	27
Group 28	28A
Group 28	28F
Type 29	29
Type 31	31
Group 32	32A
Group 32	32F
Group 33	33A
Group 33	33B
Group 33	33C
Group 33	33D
Group 33	33F
Type 34	34
Group 35	35A
Group 35	35B
Group 35	35C
Group 35	35F
Type 36	36
Type 37	37
Type 38	38
Type 39	39
Type 40	40
Group 41	41A
Group 41	41F
Type 42	42
Type 43	43
Type 44	44
Type 45	45
Type 46	46
Group 47	47A
Group 47	47F
Type 48	48

Reference: Danish Kauffman-Lund scheme from the WHO Collaborating Centre for Reference and Research on Pneumococci at the Danish Serum Institute.