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NATIONAL INSTITUTE OF PUBLIC HEALTH AND THE ENVIRONMENT

RIVM report 218621001

EARSS:
European Antimicrobial Resistance Surveillance System; data from the Netherlands (1999)

Incidence and resistance rates for *Streptococcus pneumoniae* and *Staphylococcus aureus*

W Goettsch, H de Neeling and the Dutch EARSS laboratories[1]

June 2001

[1]for participating laboratories see page 3

This investigation has been performed by order and for the account of the European Union, DGV, within the framework of project EARSS (V/218621/10/AR).

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Abstract

In a prospective prevalence and incidence survey in the Netherlands in 1999 antimicrobial susceptibility data on invasive *Streptococcus pneumoniae* and *Staphylococcus aureus* infections were collected within the framework of European Antimicrobial Resistance Surveillance System (EARSS). Data on the catchment population and the hospital coverage (in patient-days) indicated that the EARSS project covered approximately 40% of the Dutch population (extramural) and 40% of the total number of patient-days (intramural). Susceptibility data on 767 invasive *S. pneumoniae* isolates and 1259 invasive *S. aureus* isolates were collected from 21 laboratories. Penicillin resistance in *S. pneumoniae* was minimal; only 9 of 767 (1.2%) isolates were non-susceptible. These strains all had MICs between 0.12 and 1 mg/l. Resistance to other antibiotics in *S. pneumoniae* was also low. Resistance to oxacillin in *S. aureus* was low, only 4 (0.3%) isolates were MRSA (mecA positive). Resistance to other antibiotics in *S. aureus* was also low. The incidence of invasive *S. pneumoniae* was 117 cases/1,000,000 person-years; the incidence of invasive penicillin non-susceptible *S. pneumoniae* was 1 case/1,000,000 person-years. The incidence of invasive *S. aureus* infections was 0.25 cases/1000 patient-days; the incidence of invasive MRSA infections was 0.0006 cases/1000 patient-days. EARSS can be concluded to contribute added value to national antimicrobial surveillance in Netherlands, since not only data on susceptibility testing were collected and compared, but also data on susceptibility testing methods, and hospital and community coverage. Integration of these different information sources has led to more insight into the comparability of susceptibility data and the public health relevance of antimicrobial resistance.

Preface

Antimicrobial resistance is an emerging problem across the Member States of the European Union (EU). In order to compare differences in antibiotic resistance in the Member States an European Antimicrobial Resistance Surveillance System (EARSS) was started in the beginning of 1998. This project is funded by the European Commission, DG Sanco, (DG responsible for Health) and accumulates antimicrobial resistance surveillance data from the different Member States as well from Iceland and Norway. EARSS is based on national surveillance systems. Data from these national surveillance systems are collected, aggregated and analysed at the Dutch National Institute of Public Health and the Environment. In this report we present the start up of the Dutch National Part of the EARSS surveillance and the results of one year EARSS surveillance in the Netherlands.

Contents

Samenvatting

Doel: Het verzamelen en analyseren van gevoeligheidsgegevens van invasieve *Streptococcus pneumoniae* and *Staphylococcus aureus* isolaten in Nederland binnen het kader van het European Antimicrobial Resistance Surveillance System (EARSS).
Opzet: Prospectief prevalentie en incidentie onderzoek in de medische microbiologische laboratoria in Nederland in 1999.
Methode: Gegevens over de dekkingsgraad in de open bevolking van het EARSS project werden geschat met behulp van adherentiegegevens van ziekenhuizen, die door de EARSS laboratoria werden bediend. Gegevens over de dekkingsgraad van EARSS over alle Nederlandse ziekenhuizen (in patiëntdagen) werden ontvangen uit de gegevens van het Nederlandse instituut Prismant. Daarnaast werden gegevens over de gebruikte gevoeligheidsbepalingen verzameld om deze te vergelijken met de resultaten van de gevoeligheidsbepalingen. Tenslotte werden de gevoeligheidsgegevens met betrekking tot *S. pneumoniae* and *S. aureus* elektronisch elk kwartaal van de deelnemende laboratoria verzameld.
Resultaten: EARSS had een dekkingsgraad van ongeveer 40% (zowel over de ziekenhuizen als over de open populatie). Gegevens uit de vragenlijsten over de gebruikte testmethoden gaven aan dat de meeste (16/20) Nederlandse laboratoria voor *S. pneumoniae* het EARSS protocol volgden. Daarentegen werd voor *S. aureus* slechts door een aantal laboratoria (10/19) het EARSS protocol gevolgd. Gevoeligheidsgegevens werden verzameld over 767 invasieve *S. pneumoniae* isolaten en 1259 invasieve *S. aureus* isolaten van 21 laboratoria. Penicilline resistentie in *S. pneumoniae* was minimaal; slechts 9 van 767 (1.2%) isolates waren niet gevoelig. Deze stammen hadden allen MICs tussen de 0.12 en 1 mg/l. Resistentie in *S. pneumoniae* tegen andere antibiotica was ook laag. Resistentie tegen oxacilline in *S. aureus* was laag, slechts 4 (0.3%) isolaten waren MRSA (mecA positief). Ook was de resistentie tegen andere antibiotica in *S. aureus* laag. De incidentie van invasieve *S. pneumoniae* was 117 cases/1.000.000 bewoners; de incidentie van invasieve penicilline niet gevoelige *S. pneumoniae* was 1 case/1.000.000 bewoners. De incidentie van invasieve *S. aureus* infecties was 0.25 cases/1000 patiëntdagen; de incidentie van invasieve MRSA infecties was 0.0006 cases/1000 patiëntdagen.
Conclusies: EARSS heeft een toegevoegde waarde voor de nationale surveillance van antimicrobiële resistentie omdat in deze surveillance niet alleen gevoeligheidsgegevens, maar ook gegevens over de gebruikte gevoeligheidstesten en gegevens over de dekkingsgraad van de surveillance worden verzameld. Integratie van deze informatiebronnen heeft geleid tot meer inzicht in de vergelijkbaarheid van de gevoeligheidsdata en in public health relevantie van antibioticumresistentie.

Summary

Objective: The collection and analysis of susceptibility data on invasive *S. pneumoniae* and *S. aureus* isolates in the Netherlands in the framework of the European Antimicrobial Resistance Surveillance System (EARSS).
Design: Prospective prevalence and incidence survey in medical microbiological laboratories in the Netherlands in 1999.
Methods: Data on the catchment population were estimated using adherence population data from hospitals served by the EARSS. Data on the hospital coverage (in patient-days) were derived from Prismant. Laboratories were interviewed for the methods and the interpretative criteria that were used locally for susceptibility testing. Subsequently, test results were compared with the methods and criteria in order to be able to explain discrepancies between laboratories. Finally, susceptibility data on *S. pneumoniae* and *S. aureus* were electronically extracted from local laboratories on a quarterly basis.
Results: Approximately 40% of the Dutch population participated in the EARSS project and 40% of the total number of patient-days were used. Data from the questionnaire on susceptibility methods indicated that most laboratories had followed the EARSS protocol for susceptibility testing for *S. pneumoniae*. However, only a few laboratories strictly followed the EARSS protocol for *S. aureus*. In 1999, susceptibility data on 1259 invasive *S. aureus* isolates and 767 invasive *S. pneumoniae* isolates were collected from 21 laboratories. Penicillin resistance in *S. pneumoniae* was minimal; only 9 out of 767 (1.2%) isolates were non-susceptible. These strains all had MICs between 0.12 mg/l and 1 mg/l. Resistance of *S. pneumoniae* to other antibiotics was also low. Resistance of *S. aureus* to oxacillin was low; only 4 (0.3%) isolates were MRSA (mecA positive). Resistance to other antibiotics in *S. aureus* was also low. Invasive *S. pneumoniae* showed an incidence of 117 cases/1,000,000 inhabitants; the incidence of invasive penicillin non-susceptible *S. pneumoniae* was one case/1,000,000 inhabitants. The incidence of invasive *S. aureus* infections was 0.25 cases/1000 patient-days; the incidence of invasive MRSA infections was 0.0006 cases/1000 patient-days.
Conclusions: EARSS contributes added value to national antimicrobial surveillance in Netherlands, since not only data on susceptibility testing were collected and compared, but also data on susceptibility testing methods, and hospital and community coverage. Integration of these different information sources has led to more insight into the comparability of susceptibility data and the public health relevance of antimicrobial resistance.

1. Introduction

Antimicrobial resistance is an emerging problem across the Member States of the European Union (EU). In order to compare differences in antibiotic resistance in the Member States an European Antimicrobial Resistance Surveillance System (EARSS) started in the beginning of 1998. This project is funded by the European Commission (DG V) and accumulates antimicrobial resistance surveillance data from the different Member States and Iceland and Norway. EARSS is based on national surveillance systems. Data from these national surveillance systems are collected, aggregated and analysed at the Dutch National Institute of Public Health and the Environment.

In most participating countries the EARSS surveillance was set up or based on an already present surveillance system for antimicrobial resistance. In the Netherlands two major surveillance system were already present: the Infectious Diseases Surveillance Information System (ISIS; www.isis.rivm.nl) and the National Public Health Laboratory Resistance Surveillance System. We used those two surveillance systems to start up the EARSS surveillance for *S. pneumoniae* and *S. aureus*. Additionally, a number of other laboratories also participated in EARSS in order to increase the coverage of EARSS in the Netherlands.

In this report, we want to describe the experiences with one year of EARSS surveillance (1999) in the Netherlands. We will give special attention to:

1. How to use different data sets and formats for surveillance?
2. What are the techniques used for antimicrobial susceptibility testing?
3. How can we calculate coverage for hospital- and community-acquired pathogens?
4. Do we find resistance to the most important antibiotics in invasive *S. pneumoniae* and *S. aureus* infections?
5. What is the value of the EARSS network in addition to the existing antimicrobial susceptibility surveillance networks?

2. Material and Methods

2.1 Selection of laboratories

Laboratories were selected on basis of a number of criteria:

a. Coverage of all participating laboratories had to be at least 20% of the Dutch population (for *S. pneumoniae*) and 20% of the total number of patient-days in 1999 in the Netherlands (for *S. aureus*)
b. Coverage had to be nation-wide, no important regions can be missed.
c. All different kinds of hospitals had to be covered; academic and non-academic hospitals
d. Participation in an already existing electronic surveillance network, such as ISIS surveillance network or the Public Health Laboratory Resistance Network (PHLRN). This is not mandatory, laboratories which were not participating in these two projects were also included in the EARSS

2.2 Calculation of the coverage

2.2.1 Hospital coverage

In order to calculate hospital coverage, data on the number of patient-days were derived from a Dutch National Institute, called Prismant, which collects basic data on a yearly basis from all Dutch hospitals[1]. However, in some cases the laboratories did not identify the hospital for every single isolate. So, we were only able to calculate the total hospital coverage for a laboratory, knowing which hospitals were served by an individual EARSS participating laboratory.

2.2.2 Coverage of the community

Data on the catchment population (or coverage) of laboratories were often not present. For that reason we tried to estimate the catchment population of the Dutch laboratories on basis of adherence of the hospitals which were served by these laboratories. Data on the number of admissions from all hospitals in the Netherlands were available for every individual municipality for the year 1996 at the National Institute of Public Health[2]. We assumed that there was a linear relation between the number of admissions and microbiological workload for a laboratory. This seemed a reasonable assumption in case of invasive infections, where the microbiological sample is taken in the hospital where the patient stays. Using this information it was possible to calculate a percentage of laboratory coverage for every municipality (see table 1). Using the percentages, and the number of people living in the municipalities, we could calculate a catchment population for every laboratory (for an example, see table 1). For some laboratories the catchment population, calculated on basis of the adherence of hospitals, could be compared with the catchment population calculated on the basis of geographical background information on the isolates tested by these laboratories. This indicated that the catchment population, calculated on basis of the adherence of the hospital, gave a good indication of the catchment of a laboratory[3].

Table 1. Example of a calculation of catchment population on basis of the adherence of the hospitals in the different municipalities

Name of lab	Location of lab	Municipality	Number of admissions	Total number of admissions	%[1]	Number of citizens	Catchment[2]
St. Jans Gasthuis	Weert	WEERT	4137	5052	82	40695	33324
St. Jans Gasthuis	Weert	NEDERWEERT	1349	1672	81	15506	12511
St. Jans Gasthuis	Weert	STRAMPROY	435	552	79	4961	3909
St. Jans Gasthuis	Weert	BUDEL	858	1375	62	12025	7504
St. Jans Gasthuis	Weert	HUNSEL	379	610	62	5762	3580
St. Jans Gasthuis	Weert	HEYTHUYSEN	471	1179	40	11300	4514
St. Jans Gasthuis	Weert	THORN	122	364	34	2645	887
St. Jans Gasthuis	Weert	MAARHEEZE	320	1011	32	8925	2825
St. Jans Gasthuis	Weert	MEIJEL	106	543	20	5348	1044
St. Jans Gasthuis	Weert	HEEL	125	865	14	8320	1202
		TOTAL					**71300**

[1]=percentage of admissions covered by this laboratory
[2]=catchment is a product of the percentage coverage and the number of citizins

2.3 Collection of data on laboratory testing methods

A questionnaire (annex 2) was developed in order to get information on:
- the participating laboratory
- the hospitals which were served by this laboratory
- laboratory methods which were used to determine *S. pneumoniae* and *S. aureus*
- testing methods which were used to assess the susceptibility of these two micro-organisms (see annex 2). These testing methods were compared to the official EARSS protocol as was defined in the EARSS manual (annex 6).

This questionnaire was sent out to all laboratories. Additionally, some laboratories which were part from ISIS or PHLRN got a similar, but somewhat different, questionnaire.

2.4 Data check of susceptibility testing results from the laboratories

Data from ISIS and PHLRN surveillance were converted into EARSS format (see annex 3) using SAS software, version 6.12 (SAS Institute, Cary, NC, USA). Data from laboratories that did not participate in these two surveillance systems, were mostly received in ASCII format and were converted in EARSS format using SAS software. Data were validated using SAS software; records without any information on the month or year of birth were deleted. Month and year of birth, gender, type of pathogen and laboratory-code were used to specify an unique patient-identifier in order to remove duplicates in every quarter. Validated data were used for the analysis of susceptibility of *S. pneumoniae* and *S. aureus*.

3. Results

3.1 Basic characteristics of participating laboratories

We collected data from 21 laboratories (annex 4). Most of the laboratories were public health laboratories (13), but also general (5) and university hospitals (3) were included. Most regions of the Netherlands were represented in the EARSS surveillance (figure 1).

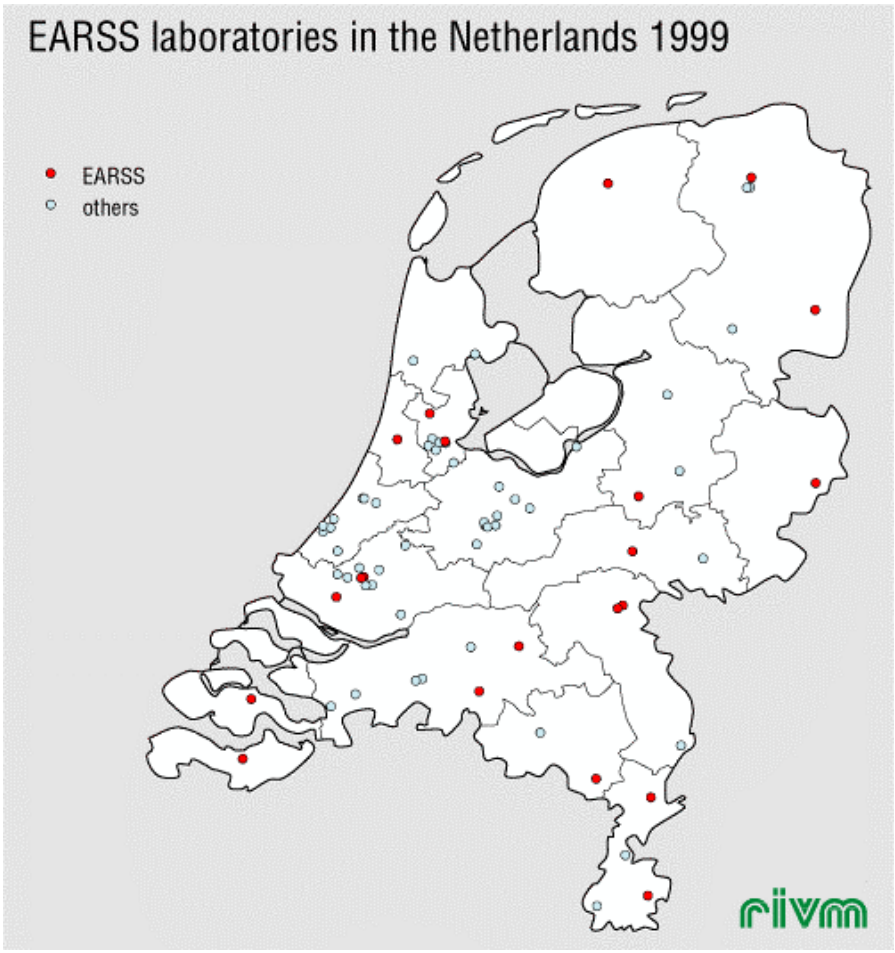

Figure 1. EARSS laboratories in the Netherlands in 1999

3.2 Coverage of EARSS in the Netherlands

Calculation of the hospital catchment indicated that the laboratories covered approximately 40% of the total number patient-days in the Netherlands in 1999 (annex 4).

Calculation of the community catchment based on the admission data of the hospital indicated a coverage of EARSS of approximately 40% of the Dutch population. The catchment data on individual hospitals demonstrated a large variation in coverage (annex 4).

3.3 Methods of antibiotic susceptibility testing

3.3.1 Type of antibiotics tested

We collected information on testing methods from 20 laboratories on *S. pneumoniae* and 19 laboratories on *S. aureus*. A large number of antibiotics was tested by the different laboratories. Table 2 summarises the most important antibiotics tested with *S. pneumoniae* and *S. aureus*. Most antibiotics tested for both pathogens were oxacillin and erythromycin. For *S. pneumoniae* oxacillin was mostly tested in combination with penicillin; when the *S. pneumoniae* strain was non-susceptible after the first oxacillin disk test, the MIC was measured using an E-test (15/20). Other antibiotics, as defined by the EARSS protocol (annex 6), were not tested very frequently, cefotaxime (7/20), ceftriaxone (7/20) and ciprofloxacine (5/20) were only tested in some laboratories. However, in some cases these antibiotics were only tested in the case of a suspected MRSA. For *S. aureus*, mostly oxacillin is used for MRSA testing, additionally sometimes methicillin is used. Also vancomycin is often tested, not only on methicillin resistant *S. aureus* (MRSA) but also on methicillin susceptible *S. aureus* (MSSA).

Table 2. Antibiotics tested for S. aureus and S. pneumoniae

		S. pneumoniae		*S. aureus*	
		always	**resistant**[1]	**always**	**resistant**[2]
Penicillins	Oxacillin	18/20	1/20	15/19	1/19
	Methicillin	--	--	5/19	3/19
	Flucloxacilline	--	--	1/19	0/19
	Penicillin	9/20	8/20	8/19	0/19
	Amoxicillin	6/20	0/20	5/19	0/19
	Amoxicillin/clavulanic acid	4/20	0/20	3/19	1/19
Cefalosporins	Cefotaxime	5/20	2/20	1/19	0/19
	Cefuroxime	6/20	0/20	3/19	0/19
	Ceftriaxone	1/20	6/20	--	--
Macrolides	Erythromycin	19/20	0/20	16/19	0/19
	Claritromycin	3/20	0/20	1/19	0/19
Tetracyclines	Tetracycline	15/20	0/20	7/19	1/19
	Doxycycline	3/20	0/20	1/19	0/19
Aminoglycosides	Gentamicin	2/20	0/20	11/19	2/19
	Tobramycin	1/20	0/20	3/19	3/19
Fluoroquinolones	Ciprofloxacin	3/20	2/20	5/19	4/19
	Ofloxacin	3/20	0/20	5/19	1/19
Others	Clindamycin	3/20	0/20	9/19	0/19
	Trimethoprim/sulfamethoxazol	7/20	1/20	7/19	2/19
	Vancomycin	10/20	6/20	14/19	3/19
	Rifampin	--	--	3/19	2/19
	Fusidic acid	--	--	0/19	3/19
	Mupirocin	--	--	2/19	2/19

[1]resistant=only tested when penicillin non-susceptible *S. pneumoniae* is suspected.
[2]resistant=only tested when methicillin resistant *S. aureus* is suspected

Additionally, we compared data from the questionnaire with real susceptibility data in order to verify whether strains were tested for the antibiotics indicated in the questionnaire. Table 3 indicated that there were large discrepancies between the information from questionnaire and the real data. For instance, oxacillin test results for *S. pneumoniae* and *S. aureus* seemed to be far less common than suggested from the data from the questionnaire. This will be reviewed in more detail in the discussion.

Table 3. Percentage of isolates tested for antibiotics as indicated 'always tested' in the questionnaire

S. pneumoniae	never	<25%	26-50%	51-75%	>75%	always
Oxacillin	11/18	2/18	1/18	1/18	0/18	3/18
Penicillin	0/9	0/9	1/9	0/9	0/9	8/9
Ceftotaxime	0/5	1/5	1/5	1/5	1/5	1/5
Erythromycin	1/19	0/19	0/19	1/19	1/19	16/19
Tetracycline	3/15	1/15	0/15	3/15	5/15	3/15
Ciprofloxacin	0/3	1/3	0/3	0/3	0/3	2/3

S.aureus	never	<25%	26-50%	51-75%	>75%	always
Oxacillin	6/15	1/15	0/15	1/15	0/15	6/15
Methicillin	2/5	1/5	0/5	0/5	0/5	2/5
Penicillin	0/8	0/8	0/8	0/8	1/8	7/8
Erythromycin	1/16	1/16	0/16	0/16	3/16	11/16
Gentamicin	0/11	1/11	0/11	1/11	4/11	5/11
Vancomycin	0/14	1/14	0/14	1/14	2/14	10/14

3.3.2 Type of methods used for antibiotic testing

We analysed the techniques used to perform antimicrobial susceptibility testing; mainly three techniques were used; screen- disk and MIC testing. Data indicated that there was large variation between the techniques used in the different laboratories. For *S. pneumoniae* disks were often used for susceptibility testing. Mostly, Rosco tablets were used, sometimes also Oxoid disks were used (annex 5). Additionally, when a MIC-test was used, mostly E-tests were used, for example for testing penicillin resistance (annex 5). For *S. aureus* MIC testing was more common (annex 5). However, this could be partly attributed to the use of an automated machine, such as the VITEK (annex 5), which does not measure a real MIC, but calculates a MIC on basis of the growth curve of bacteria in media supplemented with antibiotics.

3.3.3 Comparison between susceptibility testing methods as indicated in the questionnaire and the EARSS protocol

We compared the techniques used by the different laboratories with the EARSS protocol (annex 6) at different levels (table 4). For *S. pneumoniae*, it was clear that most laboratories tested the bacteria for oxacillin, using a 1 µg oxacillin disk. In case of a non-susceptible strain additionally a MIC for penicillin was determined (table 4). The agreement with the EARSS protocol was lower when breakpoint were added to comparison (table 4A). For *S. aureus*, the compatibility with the EARSS protocol was low (table 4). When breakpoint were included in the comparison only a few laboratories strictly followed the EARSS protocol

Table 4. Comparison of methods used for antibiotic susceptibility testing for S. aureus and S. pneumoniae and the EARSS protocols.

S. pneumoniae

Method			***Result***
1.	Oxacillin disk		18/20
2.	1 µg or 5 µg oxacillin disk		18/20
3.	1 µg (20 mm S breakpoint) or 5 µg (26 mm S breakpoint) oxacillin disk		13/20
4.	MIC for penicillin		18/20
5.	Combination of 1 and 4	}	16/20
6.	Combination of 2 and 4	}**> adherence to EARSS protocol**	16/20
7.	Combination of 3 and 4	}	11/20

S. aureus

Method			***Result***
1.	Oxacillin disk or oxacillin screen plate		12/19
2.	1 µg or 5 µg oxacillin disk or 6 µg oxacillin screen plate		11/19
3.	1 µg (10 mm S breakpoint) or 5 µg (19 mm S breakpoint) oxacillin disk or 6 µg oxacillin screen plate		3/19
4.	MIC for oxacillin		5/19
5.	PCR mecA test (local or at reference laboratory)		10/19
6.	Combination of 1 and 4 and 5	}	10/19
7.	Combination of 2 and 4 and 5	}**> adherence to EARSS protocol**	10/19
8.	Combination of 3 and 4 and 5	}	2/19

3.4 Susceptibility results

3.4.1 Basic characteristics of the data

Data were collected electronically. Five laboratories delivered the data using the ISIS system; eight laboratories used the format of the PHLRN; seven laboratories delivered data in EARSS format and one laboratory sent on paper. Most of the data, obtained from those laboratories were qualitative data; that means interpretations (S, I, R). In some cases, also data from MIC, E-tests and zone diameters were delivered.

3.4.2 Basic characteristics of the patients and isolates

Susceptibility test results from 767 invasive *S. pneumoniae* and 1259 *S. aureus* isolates were collected from 21 laboratories. Basis statistics on the patients are summarised in annex 7. Information on clinical diagnosis and other conditions was rare. Information on hospital department was reported in approximately 50% of the isolates. Information on the origin of the patient showed that most patients with both infections were admitted (>80% of the 'known' patients). There was a slight overrepresentation of male patients (55-60%) and nearly 50% of the patients was 66 years or older. Most isolates were from blood, only 10% of the strains were isolated from cerebrospinal fluid in case of *S. pneumoniae* infections.

3.4.3 Results from ATCC quality control

Of all participating laboratories four laboratories regularly sent data on the testing of the four quality control ATCC strains. This response was low. Results of these four labs indicated that their testing results were similar to the testing results of the Dutch Reference Laboratory for EARSS (National Institute of Public Health and the Environment).

3.4.4 Antibiotic susceptibility in *S. pneumoniae*

On a total of 767 isolates we found 9 isolates, which were scored as non-susceptible. Eight of those had MICs for penicillin, which were all intermediate (annex 8). Most of these were susceptible for other antibiotics. Overall, in all *S. pneumoniae* isolates resistance to the most antibiotics was low (figure 2A). Only resistance to ciprofloxacine/ofloxacine seemed to be high. This was probably due to the low intrinsic activity of this generation of fluoroquinolones for *S. pneumoniae.* Results for the individual laboratories are presented in annex 9.

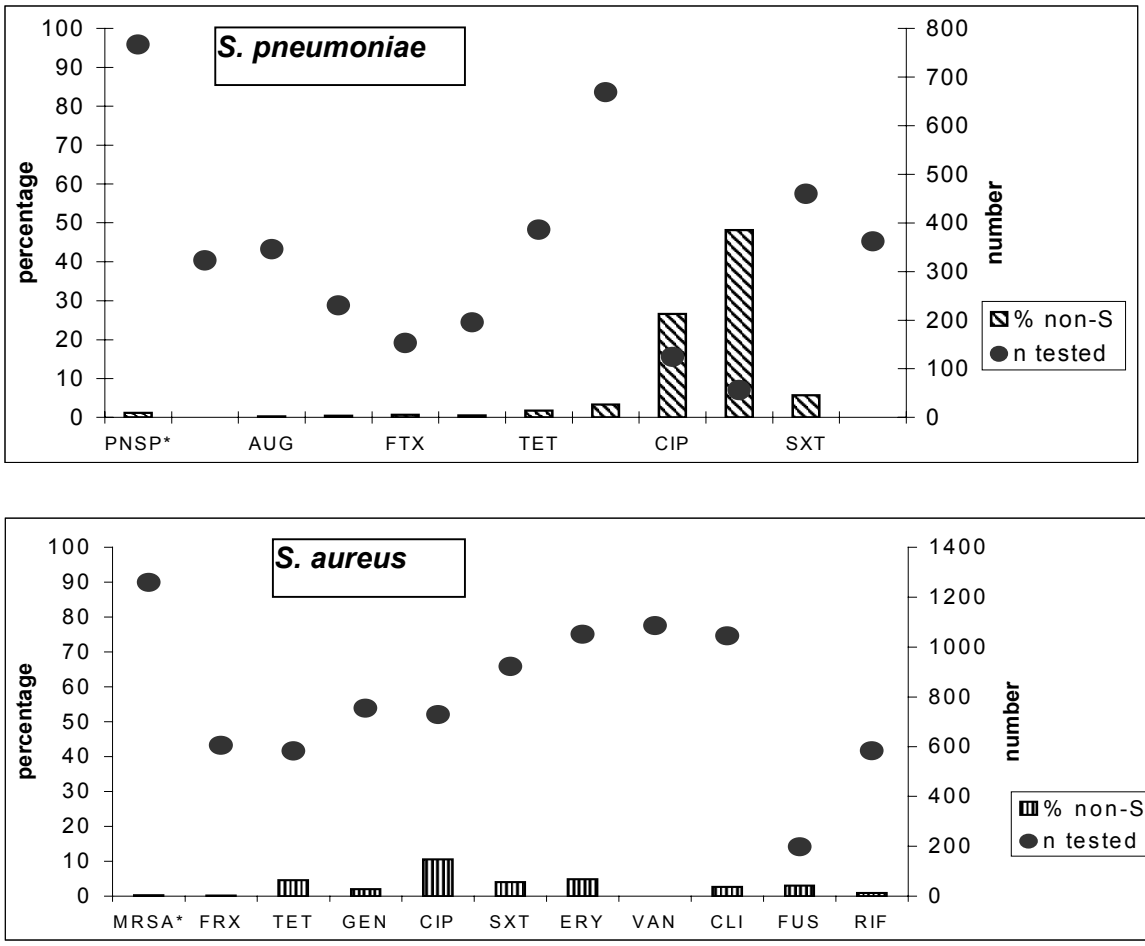

Figure 2. Resistance to most important antibiotics and number of isolates tested in S. pneumoniae and S. aureus. PNSP (penicillin non susceptible S. pneumoniae) is determined by testing of susceptibility for oxacillin in combination with penicillin. MRSA* (methicillin resistant S. aureus) is determined by testing of susceptibility for oxacillin or methicillin.*

3.4.5 Antibiotic susceptibility in *S. aureus*

On a total of 1259 invasive *S. aureus* isolates 4 MRSA were found. All four strains were PCR MecA positive and had high MICs for flucloxacillin and methicillin (annex 8). The strains were susceptible for vancomycin, gentamicin (3/4 tested), cotrimoxazole (3/4 tested). When all *S. aureus* strains were studied, the percentage of non-susceptible strains was low; for most antibiotics the percentage of non-susceptible strains was below 5%. Results for the individual laboratories were presented in annex 9.

3.4.6 Incidence of *S. pneumoniae* and *S. aureus*

Incidences were calculated for invasive *S. pneumoniae* and *S. aureus* infections using the hospital and community coverage data. Data are presented for the individual laboratories in figure 3. Incidence of invasive *S. pneumoniae* infections varied between 0.07 and 0.3 cases per 1000 nursing days and varied between 7 and 20 cases per 100000 person-years. Incidence of invasive *S. aureus* infections varied between 0.1 and 0.5 cases per 1000 nursing days and varied between 10 and 40 cases per 100000 person-years. Incidence of PRP and MRSA was low; only a few hospitals reported 1 or 2 invasive PRP and MRSA infections.

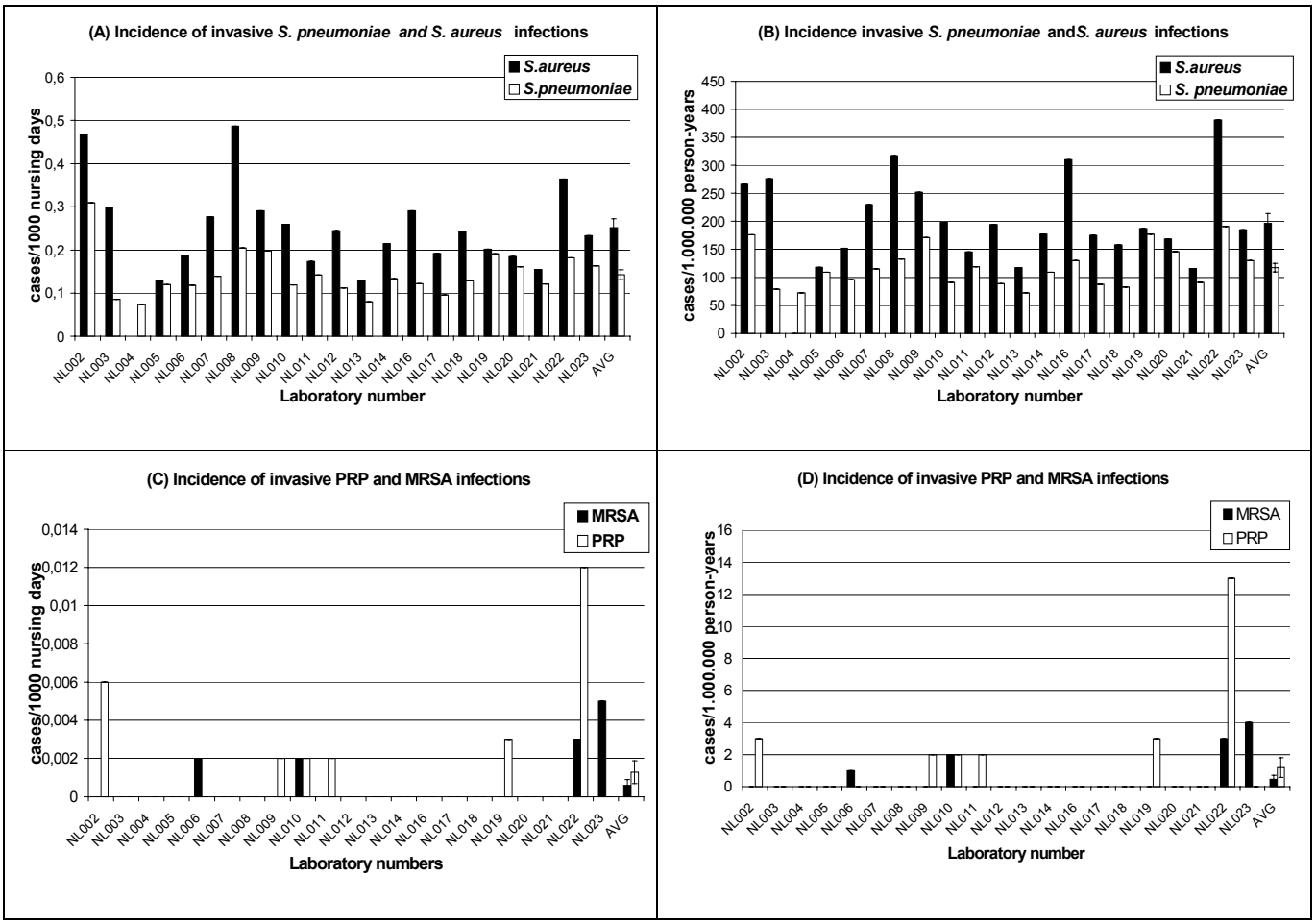

Figure 3. Incidence of invasive S. pneumoniae and S. aureus and in the hospital (A) and community (B) and incidence of invasive PRP and MRSA in the hospital (C) and community (D). AVG=average, which is presented as average of all laboratories + standard error of the mean (SEM).

4. Discussion

The results of 1999 EARSS data collection indicated that it is possible to get data on susceptibility of different pathogens together with information on the testing methods of the participating laboratories. This information is necessary when the validity of a comparison of surveillance data from difference laboratories is estimated.
The data on the coverage indicated that EARSS in the Netherlands covered a reasonable number of laboratories, which served 40% of the community and the hospitals. In the EARSS surveillance different kinds of laboratories were included; not only public health laboratories but also laboratories affiliated to general hospitals and large university hospitals were included. We also demonstrated in figure 1 that EARSS covered all regions of the Netherlands. So, we believe that EARSS gave a representative picture of the Netherlands, concerning the antibiotic susceptibility of invasive *S. pneumoniae* and *S. aureus* infections. However, we decided in 2000 to expand the EARSS system in the Netherlands, because we believe that it is important to involve a larger number of (university) hospitals in order to increase the support for this surveillance system.

A comparison of the information on the testing methods used (as we got from the questionnaire) and the susceptibility results showed some interesting differences. While most laboratories indicated in the questionnaire that they tested oxacillin as a first screening method for *S. pneumoniae* and *S. aureus*, the laboratories often reported results on penicillin (*S. pneumoniae*), methicillin (*S. aureus*) and flucloxacillin (*S. aureus*). The reason for this difference is obvious; results from antibiotic susceptibility testing must guide the clinicians in the hospitals in their choice of therapy. Thus, medical microbiologists will report on penicillin (*S. pneumoniae*) and flucloxacillin (*S. aureus*) which are the first choice for the clinician when the strains are susceptible, but not on oxacillin which is not used for clinical therapy. This result, however, underlines the importance of information on the susceptibility testing methods; on basis of the test data only it could be wrongly assumed that only a few Dutch laboratories use oxacillin as a first screening for PRP and MRSA.

More detailed information on the methods used for susceptibility tested indicated a large variety of different methods used. For penicillin susceptibility testing of *S. pneumoniae*, there was a large agreement in testing method. The use of a 1 µg oxacillin disk, followed by a penicillin E-test, for penicillin susceptibility testing is common and accepted around the world. So, for this pathogen the EARSS protocol was followed by most participating laboratories. However, it must be emphasised that the second step in the EARSS protocol was only partly followed; additional E-test testing for ceftriaxone or cefotaxime and ciprofloxacin were rarely performed (less than 25% of the participating laboratories).
A large variety of methods was used for MRSA testing. In addition to the widely accepted 6 µg oxacillin screen test, 1 and 5 µg oxacillin and methicillin disks were used for MRSA testing. Furthermore, also the VITEK was used often for the susceptibility testing of *S. aureus*. Thus, the EARSS protocol was only utilised by a limited number of participating laboratories (10/19). Results of the external QA can be used in order to estimate whether the use of different testing methods will lead to different test results.

A first analysis of the quality of the testing results indicated that it is difficult for most laboratories to get additional clinical information. Not only information on the clinical diagnosis but also information on the condition of the patient was difficult to obtain. The standard set of data from the susceptibility testing of isolates, which derived from a laboratory information system (LIS), had only limited information on the patient. However, this problem was not limited to the Dutch laboratories, in general in EARSS participating laboratories had no or limited clinical information[4].

Another problem was the availability of quantitative MIC data. Especially MICs on ceftriaxone for *S. pneumoniae* and on vancomycin for *S. aureus* were difficult to obtain. We believe that it is important to collect this information, because it gives additional valuable insight in the susceptibility pattern of non-susceptible *S. pneumoniae* and *S. aureus*.

In the beginning of 1999 we asked the participating laboratories to regularly test 4 ATCC strains in order to get some insight in the comparability of the data. However, only a limited number of laboratories regularly tested these 4 ATCC strains. Contacts with laboratories indicated that, although the workload of monthly testing of the four ATCC strains was not high, incorporation of this protocol within the regular daily testing was difficult. Also in other countries there were problems with incorporation of these QA strains in the daily practice. For that reason, we decided to (temporarily) stop this internal QA with strains with known susceptibility pattern. Instead, an external QA protocol was initialised in co-operation with the NEQAS and executed in September 2000. Participation in this protocol was more than 90% in the Netherlands, but also in average within the whole EARSS program. The results of this QA will be reported in a later stage.

Antibiotic resistance in *S. aureus* and *S. pneumoniae* was low. Penicillin resistance in *S. pneumoniae* was minimal (≈1%). This result was comparable to other results from the Netherlands, which also reported low resistance to penicillin in invasive and non-invasive *S. pneumoniae* strains.[5,6] When compared to other countries in the EARSS, it was clear that this resistance percentage is one of the lowest in the EU (figure 4).[4,7] Resistance to other antibiotics, such as the cefalosporins, tetracycline, erythromycin and cotrimoxazole was also below 6%.
Oxacillin resistance in *S. aureus* was under 1%, which was in line with other results previously reported from the Netherlands[8,9,10]. In comparison to the other EARSS participating countries, the resistance percentage was low (figure 4)[7]. Only four invasive MRSA infections were found, which were mostly susceptible for gentamicin and co-trimoxazole. Nevertheless, the EARSS surveillance for these two pathogens is only representative for invasive infections and resistance percentage in other compartments might be higher[9].

Incidence rates are important in order to estimate the public health relevance of antimicrobial resistance. For that reason, we tried to calculate the incidence of susceptible and resistant *S. aureus* and *S. pneumoniae* infections in two different ways. Firstly, we calculated the number of (resistant) strains in relation to the number of patient-days in order to estimate the public health relevance of resistance for the hospital. Secondly, we also calculated the number of (resistant) strains in relation to the community coverage in order to estimate the public health relevance of resistance for the community. Our data gave an indication on the incidence of invasive *S. aureus* and *S. pneumoniae* infections in the

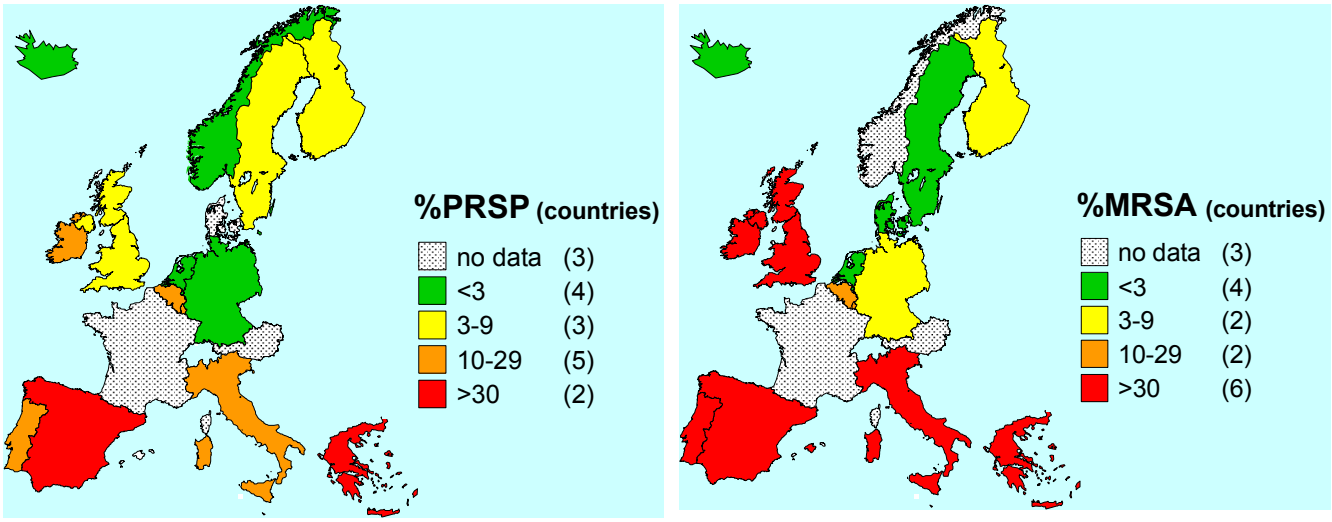

Figure 4. Percentages of invasive PRSP (penicillin resistant S. pneumoniae) and MRSA (methicillin resistant S. aureus) in the different EU countries participating in EARSS (1999)

different hospitals or in the community For *S. pneumoniae* these results were comparable to previous results reported by our institute[11]. These data were difficult to compare to data on specific diagnoses[12], because the information on clinical diagnosis was rarely present in the EARSS database. Nevertheless, the information becomes relevant when it is compared to other countries. In comparison with Swedish data, it is evident that the incidence of invasive PRSP infections in the Netherlands is lower (1 case/1.000.000 pyrs (NL) versus 6 cases/1.000.000 pyrs (SE)). However, in most countries catchment data are still not available, which makes a comparison difficult. We believe that incidence data are important in order to investigate the public health relevance of resistant pathogens and to evaluate the effect of new intervention strategies or control policies directed to decrease the antimicrobial resistance. For that reason, it is important to find methods to calculate the catchment populations for the local laboratories in the different countries. EARSS must be committed to support its participating countries to develop these methods.

In conclusion, we believe that the EARSS surveillance in the Netherlands has an added value to already existing national surveillance systems. Firstly, we collected data in a format which was used in more than 15 countries, which made it easy to compare our national data to data from other countries. Secondly, in addition to SIR interpretations, we also collected quantitative data, which gave us more insight in the susceptibility of non-susceptible *S. aureus* and *S. pneumoniae* strains. Thirdly, by comparing the testing results to the data from the questionnaire it was possible to explain certain differences in testing methods by the different laboratories. However, external QA, as was already performed in September 2000, is essential to estimate whether the use of different techniques can be ignored or is relevant for the interpretation of the test results. Finally, we believe that the calculation of incidences of resistant pathogens will become more common in the near future; the EARSS network in the Netherlands is on the forefront in determining catchment populations in the order to estimate these incidences.

5. Acknowledgements

This study was impossible without the help of the medical microbiologists, laboratory personal and system administrators of the participating laboratories. Additionally, we want to thank Prof dr. J. Degener, dr. U. Buchholz and P. Schrijnemakers from the RIVM for reviewing this report.

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Annex 1 Mailing list

1	Ministerie van VWS, Directeur-Generaal
2	Hoofdinspecteur voor de Gezondheidszorg
3-4	Ministerie van VWS, Directie Gezondheidsbeleid
5-6	Inspectie voor de Gezondheidszorg
7-11	Earss Management Team
12-112	Contactpersonen EARSS project
113	Stichting Zorgonderzoek Nederland
114	Gezondheidsraad
115	Nederlandse Vereniging voor Medische Microbiologie
116	Landelijk Coordinatiestructuur Infectieziektenbestrijding
117	Vereniging voor Infectieziekten
118	Drs. M. Esveld
119	Drs. L. Koole
120	Prof. dr. J. Huisman
121	Prof. dr. J. van der Noordaa
122	Prof. dr. H. Verbrugh
123	Prof. dr. C.M.J.E. Vandenbroucke-Grauls
124	Prof. dr. J. Dankert
125	Prof. dr. J. Verhoef
126	Prof. dr. J.A.A. Hoogkamp-Korstanje
127	Dr. E. Stobberingh
126-186	Nationale coördinatoren EARSS
187	Depot Nederlandse Publicaties en Nederlandse bibliografie
188	Directie RIVM
189	Prof. dr. ir. D. Kromhout, RIVM
190	Hoofd CIE, RIVM
191	Drs. W.J. van Leeuwen, RIVM
192	Dr. J.F.P. Schellekens, RIVM
193	VPR
194	Bureau Rapporten registratie
195-215	Rapportenbeheer
216	Bibliotheek RIVM
217-400	Reserve

ANNEX 2 Questionnaire on susceptibility testing

Questionnaire on *S. pneumoniae* and *S. aureus* susceptibility testing

Introduction

This survey is part of the pilot phase of EARSS (European Antimicrobial Resistance Surveillance System), funded by the EC/DG V and co-ordinated by the RIVM (National Institute of Public Health and Environment) in Bilthoven, the Netherlands.
Comparison of resistance in the different countries of the EU is biased by differences in the antimicrobial agents tested, the samples chosen for testing, the susceptibility test systems used, and the breakpoints adopted. EARSS is an international network of national surveillance systems, which aims to aggregate comparable and reliable antimicrobial resistance data for public health purposes, in Europe.
Taking into account laboratory methods as well as epidemiological principles, EARSS will act as an early warning system, analyse regional differences, assess risk factors, and provide electronic feedback. For the feasibility study of 18 months, microbiologists and epidemiologists, from all western European countries, decided to collect quantitative resistance data on *Streptococcus pneumoniae* and *Staphylococcus aureus*.

In order to come to proper comparisons and have denominator data we ask the laboratories that will participate in the EARSS project to fill out this questionnaire. See the EARSS Manual, for more information. You can also consult the EARSS web-site: www.earss.rivm.nl

Instructions for filling out the questionnaire

Fill out the questionnaire by typing or writing in capital letters in the appropriate space, or ticking the box corresponding to your answer. You may tick several boxes for the same question, except for 'yes/no' questions. This questionnaire consists of three parts:

Part 1: *Questions concerning the participating laboratory in general*
Part 2: *S. pneumoniae* susceptibility testing procedures
Part 3: *S. aureus* susceptibility testing procedures

If you will not forward resistance data on one of the above mentioned pathogens, it is not necessary to fill out the part of the questionnaire concerning that pathogen.

Contact addresses

Any clarifications regarding the questionnaire can be requested from the contact persons listed below; a copy of the questionnaire in **electronic format** can also be acquired from these persons.

Your national co-ordinator
To be filled out by the national coordinator

Project co-ordinator EARSS
Stef Bronzwaer
National Institute of Public Health and Environment (RIVM), the Netherlands
Antonie van Leeuwenhoeklaan 9
PO Box 1, 3720 BA Bilthoven
the Netherlands
Tel. +31(30)274 3911
Fax +31(30)274 4409
e-mail info.earss@rivm.nl

Thank you very much for your very precious collaboration. It will provide you with access to most up-to-date information on resistance in Europe. Please send the completed copy, to your national co-ordinator (see above), by courier, express mail, or electronic mail, before **18 December 1998**.

Part I: Questions concerning laboratory in general

I. 1) Information on laboratory

Name of laboratory: …….

Address: …….

City: …….

Country: …….

Contact person laboratory: …….

Tel: ……. Fax: …… E-mail: …….

Laboratory Code (*to be filled out by national co-ordinator*): ……..

I.2) Which person and institution/ laboratory is to be acknowledged if data of your laboratory will be used for publication?

Title / Name …….

Name Institution/laboratory …….

I. 3) What is the catchment population of your laboratory (coverage)?

The catchment population of my laboratory is (coverage): ……...

Comments: …….

…….

I. 4a) Do you have an automated laboratory information system in which you save isolate information?

❒ Yes
❒ No

If yes, what data-entry program do you use?

❒ WHONET (DOS)
❒ Other: ……

I. 4b) Will you forward EARSS resistance data electronically (on diskette) to your national co-ordinator?

❒ Yes
❒ No

If yes, in what format?

❒ ASCII
❒ DBase

Part II: S. pneumoniae *susceptibility testing procedures*

(Fill out only if you will forward data on S. pneumoniae*)*

II. 1) Which tests do you perform to identify *S. pneumoniae* strains?

- ❒ Optochin
- ❒ Bile solubility test: ❒ Tube
  ❒ Other: …….
- ❒ API - strep
- ❒ Other: …….

II. 2) Do you perform further testing on penicillin non-susceptible *S. pneumoniae* strains?

- ❒ Yes
- ❒ No

II.3) Do you send penicillin non-susceptible *S. pneumoniae* strains to a reference laboratory?

- ❒ Yes
- ❒ No

II. 4) What number of patient isolates did your laboratory process in 1997. Fill out the following table

	1997
Total number of *S. pneumoniae* isolated	
Total number of *S. pneumoniae* from blood + CSF	
Total number of penicillin non-susceptible S. pneumoniae *strains isolated from blood + CSF*	
Total number of cultures from blood + CSF	

II. 5) Please fill out table 1 on susceptibility testing of *Streptococcus pneumoniae*. Fill this out for the antibiotics that are routinely tested and for the methods that are routinely used.

- In the first row (1.a) you tick the antibiotics for which you perform routinely testing. If you test an antibiotic only in case of penicillin resistance tick the row 1.b **pen**.
- In the second row (***screening plate***) specify the final concentration of the antibiotic incorporated into the agar, when you use a screening plate to screen for resistant strains (in mg/l).
- If you use a disk-diffusion test, specify in the third group of rows (***disk-diffusion***) which type of disk you use (specify the manufacturer) and the disk content (µg). Also specify the test procedures, such as inoculum, medium, time of incubation, temperature of incubation and other specific circumstances (for instance incubation with CO_2). In addition, specify the inhibition zone diameter that corresponds with specific breakpoints (use also the signs: =, >, <, ≥, ≤).
- If you use a MIC-method, specify in the fourth group of rows (***MIC-methods)*** which method you use (agar, (micro)broth dilution, E-test, automated methods); in case of automated methods, specify the manufacturer. Also specify the test procedures, such as inoculum, medium, time of incubation, temperature of incubation and other specific circumstances (for instance incubation with CO_2). Indicate which antibiotic concentrations (total range) and breakpoint criteria (in mg/l) are used. Use also the signs: =, >, <, ≥, ≤.
- In the fifth row (**QA**) you can specify about the quality assurance if you use ATCC or in-house control strains. Does your laboratory have the strain ATCC 49619 ❒ Yes
  ❒ No

Part III: S. aureus *susceptibility testing procedures*

(Fill out only if you will forward data on *S. aureus*)

III. 1 If your laboratory is serving more hospitals please copy this page as many times as needed and fill out, as completely as possible, questions III. 1 – III.4 for every hospital:

Name of hospital: …….

Hospital address: …….

Postal Code and Town: …….

Contact person in hospital: …….

Name/ Title …….

Tel: ……. Fax: …… E-mail: …….

Hospital Code (*see EARSS Manual*): ……..

III. 2 How is the hospital best classifiable?

❒ Nursing home
❒ General hospital
❒ Tertiary (academic) hospital

III. 3 Please fill out the following table

Denominator data in 1997	**1997**
Total number of admissions	
Total number of beds	
Average annual bed occupancy rate	
Number of intensive care units (ICU) beds (adult, pediatric, neonatal)	
ICU, total number of admissions	
ICU, total number of patient-days	

III. 4 Is the hospital offering one of the following facilities

❒ Dialysis / CAPD
❒ Transplantation unit (renal, cardiac, liver)
❒ Cardiac surgery
❒ Infectious diseases (e.g. AIDS) department
❒ Chemotherapy (immunosuppresive treatments)
❒ Vascular surgery

III. 5 Which assays do you <u>always</u> use for the determination of *S.aureus*?

❑ coagulase test (direct/indirect)

❑ catalase ❑ mannitol-salt ❑ mannitol ❑ DNAse

❑ commercial agglutination assays, like ……

❑ biochemical identification ❑ Api strip ❑ Vitek

❑ other: …….

III. 6 Do you perform further testing if you find oxacillin/methicillin resistance in *S. aureus*?

❑ Yes Do you perform PCR ❑ Yes
❑ No

❒ No

III.7 Do you send non-susceptible *S. aureus* strains to a reference laboratory?

❒ Yes
❒ No

III. 8 What number of patient isolates did your laboratory process in 1997. Fill out the following table

	1997
Total number of *S. aureus* from blood	
Total number of cultures from blood	
Total number of oxacillin/methicillin resistant *S. aureus* strains isolated from blood	

III. 9 Please fill out table 2 on susceptibility testing of *Staphylococcus aureus*. Fill this out for the antibiotics that are <u>routinely</u> tested and for the methods that are <u>routinely</u> used.

- In the first row (1.a) you tick the antibiotics for which you perform routinely testing. If you test an antibiotic only in case of penicillin resistance tick row 1.b **MRSA**
- In the second row (***screening plate***) specify the final concentration of the antibiotic incorporated into the agar, when you use a screening plate to screen for resistant strains (in mg/l)
- If you use a disk-diffusion test, specify in the third group of rows (***disk-diffusion***) which type of disk you use (specify the manufacturer) and the disk content (µg). Also specify the test procedures, such as inoculum, medium, time of incubation, temperature of incubation and other specific circumstances (for instance incubation with CO_2). In addition, specify the inhibition zone diameter that corresponds with specific breakpoints (use also the signs: =, >, <, ≥, ≤).
- If you use a MIC-method, specify in the fourth group of rows (***MIC-methods)*** which method you use (agar, (micro)broth dilution, E-test, automated methods); in case of automated methods, specify the manufacturer. Also specify the test procedures, such as inoculum, medium, time of incubation, temperature of incubation and other specific circumstances (for instance incubation with CO_2). Indicate which antibiotic concentrations (total range) and the breakpoint criteria (in mg/l) are used. Use also the signs: =, >, <, ≥, ≤.

- In the fifth row (***QA***) you can specify about the quality assurance if you use ATCC or in-house control strains. Does your laboratory have the strains:

ATCC 29213	❒	Yes	ATCC 43300	❒	Yes
	❒	No		❒	No

- In the last row there is space for other tests. For example, if you perform a DNA-test, please specify which kind of test

Table 1: susceptibility testing for Streptococcus pneumoniae

		Oxacillin	Penicillin	Cefotaxime	Ceftriaxone	Ciprofloxacin	Tetracycline	Erythromycin	Vancomycin	.....	.....
Test											
1	a. always										
	b. pen										
Screening plate											
2	Conc. (mg/l)										
Disk-diffusion											
3 **disk type**	a. manufacturer										
	b. load (µg)										
test procedures	c. inoculum										
	d. medium										
Incubation	e. time (hours)										
	f. temp. (°C)										
	g. circumst.										
breakpoint criteria (specify zone diameter)	h. S										
	I										
	R										
MIC-methods											
4 **method**	a. agar										
	b. broth										
	c. E-test										
	d. automated										
test procedures	e. inoculum										
	f. medium										
	g. time (hours)										
incubation	h. temp. (°C)										
	i. circumst.										
	j. testrange(mg/l)										
breakpoint criteria (mg/l)	k. S										
	I										
	R										
QA											
5 **reference strains**	a. ATCC										
	b. internal										
Remarks											

Table 2: susceptibility testing for Staphylococcus aureus

		Oxacillin	Methicillin	Vancomycin	Tetracycline	Erythromycin	Ciprofloxacin	Gentamicin	.....	.....	.....
Test											
1	a. always										
	b. MRSA										
Screening plate											
2	Conc. (mg/l)										
Disk-diffusion											
3 **disk type**	a. manufacturer										
	b. load (µg)										
test procedures	c. inoculum										
	d. medium										
incubation	e. time										
	f. temp.										
	g. circumst.										
breakpoint criteria (specify zone diameter)	h. S										
	I										
	R										
MIC-methods											
4 **method**	a. agar										
	b. broth										
	c. E-test										
	d. automated										
test procedures	e. inoculum										
	f. medium										
	g. time										
incubation	h. temp.										
	i. circumst.										
	j. testrange(mg/l)										
breakpoint criteria (mg/l)	k. S										
	I										
	R										
QA											
5 **reference strains**	a. ATCC										
	b. internal										
Other tests											
6	a. DNA-test										

ANNEX 3 Isolate Record Forms and data exchange format

Isolate Record Form - *Staphylococcus aureus* - Blood isolates

(Please send data on resistant and on susceptible strains; use one form per isolate!)

TO BE FILLED OUT BY LABORATORY

Case definition: Resistance data on the first isolate only of each strain from the **blood** of each patient with a hospital acquired *S. aureus* infection, confirmed by a coagulase test.

Laboratory Data				
Current date	dd/mm/yyyy	_ _ / _ _ / _ _ _ _		
Laboratory Code *	CC000	_ _ _ _ _		
Isolate Data				
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 §	free text	_ _		
Hospital Data				
Name/code of hospital	free text	_ _		
Origin of patient	tick box	❒ Admitted	❒ Outpatient	❒ Unknown
Hospital Department	tick box	❒ Surgery	❒ (Internal) Medicine	❒ Infectious diseases (AIDS)
		❒ Ob/Gyn	❒ ICU	❒ Emergency
		❒ Pedriatics	❒ Pediatric ICU	❒ Other: _ _ _ _ _ _ _ _ _ _

Antibiotic susceptibility testing		**S / R** (fill in S or R)	**Zone diameter** (mm)	**MIC** (in mg/l)
Oxacillin	S/R, zone and/or MIC	|__|	|__||__|	|__||__|
Vancomycin	S/R, zone and/or MIC	|__|	|__||__|	|__||__|
PCR mec-gene		❒ Positive	❒ Negative	
Optional	S/R, zone and/or MIC			
Streptomycin		|__|	|__||__|	|__||__|
Tetracycline		|__|	|__||__|	|__||__|
Gentamicin		|__|	|__||__|	|__||__|
Erythromycin		|__|	|__||__|	|__||__|
Ciprofloxacin		|__|	|__||__|	|__||__|
Rifampin		|__|	|__||__|	|__||__|
Other: ……..		|__|	|__||__|	|__||__|
Other: ……..		|__|	|__||__|	|__||__|
Other: ……..		|__|	|__||__|	|__||__|

* The national co-ordinator will provide a laboratory code, that consists of the ISO-Country Code (CC) followed by 3 numbers.

§ Optional information

Send this form to: ……. (name national co-ordinator) …… (name Institute)

Address: ……..…… Tel: ……. Fax: …… E-mail: ……..

Isolate Record Form - *Streptococcus pneumoniae* - Blood isolates + CSF

(Please send data on resistant and on susceptible strains; use one form per isolate!)

TO BE FILLED OUT BY LABORATORY

Case definition: Resistance data on the first isolate only, of each strain from the **blood or CSF** of each patient with a community acquired S. *pneumoniae* infection, confirmed by an optochin test.

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 §	free text	_ _
Hospital Data		
Origin of patient	tick box	❒ Admitted ❒ Outpatient ❒ Unknown
Hospital Department	tick box	❒ Surgery ❒ (Internal) Medicine ❒ Infectious diseases (AIDS)
		❒ Ob/Gyn ❒ ICU ❒ Emergency
		❒ Pedriatics ❒ Pediatric ICU ❒ Other: _ _ _ _ _ _ _ _ _ _

Antibiotic susceptibility testing		**S / R** (fill in S or R)	**Zone diameter** (mm)	**MIC** (in mg/l)
Oxacillin	S/R, zone and/or MIC	|__|	|__||__|	|__||__|
Penicillin	S/R, zone and/or MIC	|__|	|__||__|	|__||__|
Cefotaxime	S/R, zone and/or MIC	|__|	|__||__|	|__||__|
Ceftriaxone	S/R, zone and/or MIC	|__|	|__||__|	|__||__|
Ciprofloxacin	S/R, zone and/or MIC	|__|	|__||__|	|__||__|
Optional	S/R, zone and/or MIC			
Tetracycline		|__|	|__||__|	|__||__|
Erythromycin		|__|	|__||__|	|__||__|
Rifampin		|__|	|__||__|	|__||__|
Clindamycin		|__|	|__||__|	|__||__|
Vancomycin		|__|	|__||__|	|__||__|
Other: ……..		|__|	|__||__|	|__||__|
Other: ……..		|__|	|__||__|	|__||__|

* The national co-ordinator will provide a laboratory code, that consists of the ISO-country Code (CC) followed by 3 numbers.
§ Optional information

Send this form to: ……. (name national co-ordinator) …… (name Institute)

Address: ……..…… Tel: ……. Fax: …… E-mail: ……..

Data exchange format EARSS
Pilot phase

On the following pages you find a description of the data exchange format between national databases and the central database at the RIVM. The format can be ASCII fixed format or tab separated. We worked out a brief description in a table and an extensive description in which we explain the variables more in detail, and specify the codification.

Motivation

Choosing a format to exchange data is quite complex, because many factors should be considered. The most important factors in this matter for the EARSS project are:

1. Many parties are involved.
2. The parties may not always have easy access to the necessary programming skills.
3. Many computing platforms are involved.
4. The amount of work to produce the data should be minimal and equally distributed between the parties.
5. The data must be easily accessible (so that it can be reviewed/checked).
6. The data infrastructure around it must be maintainable.
7. The format should be unambiguous.

Therefore the format should be as simple as possible, but should allow some flexibility to extend the collection of data (i.e., more antibiotics can be added).
Looking at the choices made:

1. ASCII was chosen in favour of other formats like Dbase, because those formats are usually generated by various tools. Very often the exact Dbase format can not be controlled and it is very hard to write custom made routines to do so.
2. The most simple format is to put everything into columns and thus to reserve columns for every type of antibiotic. Doing so, the lines will get too long (above 254 characters). Many editors and other tools have problems handling very long lines. Therefore every antibiotic gets its own line (instead of a column).
3. Patient, sample and other data are repeated in every line. This is the main drawback. It uses a lot of disk memory (if not compressed). To counter this problem one could introduce some simple database structures, but the integrity of the data is easily compromised.
4. The format is fixed length or tab-separated. Tab-separated data is usually easier to produce. A disadvantage is that the length of the lines is harder to control, but because codes are used this should be no problem.

We ask you to send the files every 3 months to the RIVM on diskette. The name of the file will be composed of 10 characters, as follows: CCQYYYY.txt
CC = Country Code (ISO country code as proposed by EARSS, see also Manual – Annex 4)
Q = number of quarter (i.e. 1, 2, 3, or 4)
YYYY = year (4 characters, e.g., 1999)
The file may be zipped using “pkzip” or a compatible program.

Each line contains test-results for one antibiotic.

Laboratory, Isolate, Patient, Hospital, and Pathogen data are repeated every line.

Field Name: Name of the variable
Field Length: The field length is the total number of characters allowed for that field.
Mandatory Field: All mandatory fields must be entered. In order not to 'lose' isolates for data analysis very few fields are obligatory. Fill out as many fields as possible.
Description: Description/explanation for a field, and in some cases the codification.

In case of fixed format

Field Type: A = Alphanumeric (spaces if unknown) (tabs / special ASCII characters not allowed)
N = Numeric (all numbers, dots, and comma's 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'.

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
- In case a field can not be filled out, one can go to the next column using a tab
- 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.

Remarks

Regarding susceptibility testing results:
- On the Isolate Record Forms there is space to fill out S (susceptible) or R (resistant). In the database also the test result I (intermediate) is allowed.
- For both pathogens the test results for Oxacillin will always be filled out. In case of a *S. pneumoniae* isolate, also the test results for penicillin will always be mentioned.
- Fill out the following test results in the following fields:

- The result of the Oxacillin screen plate (and disk) will be mentioned in the S/I/R field, and in case of the Oxacillin disk, possibly the zone diameter will be filled out (e.g., <= 19 mm).
- Disk diffusion test results in the Zone fields.
- MIC methods (agar, (micro-)broth, automated) in the MIC fields.
- Etest results in the Etest fields (Because some EARSS participating labs will perform next to "conventional" MIC methods also Etests to compare both results, it was necessary to add two fields for the Etest result.)

Clinical diagnosis: To be able to code and store varying answers in the free text space on the Isolate Record Forms, we worked out two fields for this variable. The field "Clinical diagnosis" contains infectious disease diagnosis, and the field "Other conditions" contains mainly immuno-compromising factors. The codification is specified under the extensive description.

Laboratory Code: The laboratory code consists of the ISO-country Code (CC) followed by 3 numbers. The National Co-ordinator assigns a specific number to every EARSS participating laboratory (starting from 001, 002, etc.)

Hospital code: 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 in 4 characters (000X). The first 3 characters are the number-code of the laboratory, and the 4th character is the letter assigned to a hospital (starting from A, B, etc.)

Antibiotic coding: The coding for antibiotics in EARSS is the same as in WHONET4 (DOS version). See table Antibiotic coding EARSS. (*With regards to R. Williams and J. Stelling of WHO/EMC. In WHONET 5 (Windows version), a number of the antibiotic codes will be changed to better conform to existing official WHO codes and to standard codes of diagnostic manufacturers where sufficient consensus exists).*

Duplicates: Exclude duplicate isolates of the same strain (species) from the same patient, and send information only on the first isolate of each strain from each patient.

For comments and questions you can contact:

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Brief description data exchange format EARSS

Field Name	Field type	Initial column	Field length	Mandatory Field
Current date	D	1	8	
Laboratory code	A	9	5	Yes
Isolate sample number (lab)	A	14	12	
Isolate source	A	26	2	
Date of sample collection	D	28	8	
Patient ID / Code	A	36	12	
Sex	N	48	1	
Month of birth	N	49	2	
Year of birth	N	51	4	
Clinical diagnosis	A	55	3	
Other conditions	A	58	3	
Hospital code	A	61	4	
Origin of patient	N	65	1	
Hospital department	A	66	3	
Pathogen code	A	69	3	Yes
PCR mec-gene	N	72	1	
Antibiotic susceptibility testing				
Antibiotic code	A	73	3	Yes
S/I/R	A	76	1	
Zone (> < =)	A	77	2	
Zone (Value in mm)	N	79	2	
MIC (> < =)	A	81	2	
MIC (Value in mg/l)	N	83	5	
Etest (> < =)	A	88	2	
Etest (Value in mg/l)	N	90	5	

Extensive description data exchange format EARSS

Columns: 1-8
Field Length: 8 [D] YYYYMMDD
Field Name: Current date
Description: The date that the Isolate Record Form was filled in.

Columns: 9-13, Mandatory
Field Length: 5 [A] CC000
Field Name: Laboratory code
Description: The laboratory code consists of the ISO-country Code (CC) followed by 3 numbers. The National Co-ordinator assigns a specific number to every EARSS participating laboratory (starting from 001, 002, etc.)

Columns: 14-25
Field Length: max. 12 [A]
Field Name: Isolate sample number (lab)
Description: Number in use in lab to specify isolate

Columns: 26-27
Field Length: 2 [A]
Field Name: Isolate source
Description: The source of the isolate, coded as follows:
bl = Blood sf = CSF ot = other source xx = Unknown

Columns: 28-35
Field Length: 8 [D] YYYYMMDD
Field Name: Date of sample collection
Description: Date when sample was taken

Columns: 36-47
Field Length: max. 12 [A]
Field Name: Patient ID / Code
Description: Patient ID / Code

Columns: 48
Field Length: 1 [N]
Field Name: Sex
Description: Coded as follows: 1 = Male 2 = Female 9 = Unknown

Columns: 49-50
Field Length: 2 [N] MM
Field Name: Month of birth
Description: Month of birth of the patient

Columns: 51-54
Field Length: 4 [N] YYYY
Field Name: Year of birth
Description: Year of birth of the patient

To be able to code and store varying answers in the free text space on the Isolate Record Forms, we worked out two fields for the variable "Clinical diagnosis".

Columns: 55-57
Field Length: 3 [A]
Field Name: Clinical diagnosis
Description: The information regarding clinical diagnosis may vary. You will have to choose the most appropriate code for the infectious disease diagnosis:
1 = Pneumoniae, 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 = subcutaneaous/intramuscular), ot = other, xx = Unknown

Columns: 58-60
Field Length: 3 [A]
Field Name: Other conditions
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 woundinfection, 5 = Drug abuse, 6 = Intravascular procedures (6a = Intraveneous catheters, 6b = Intravascular prosthetic devices, 6c = Dialysis), ot = other, xx = Unknown

Columns: 61-64
Field Length: 4 [A] 000X
Field Name: Hospital code
Description: The code consists in 4 characters. The first 3 characters are the number-code of the lab, and the 4th character is the letter assigned to a hospital (starting from A, B, etc.)

Columns: 65
Field Length: 1 [N]
Field Name: Origin of patient
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 2 = Outpatient 8 = Other (e.g., emergency room) 9 = Unknown

Columns: 66-68
Field Length: 3 [A]
Field Name: Hospital department
Description: The variable permits the general classification of locations by service, as follows:

med = Medicine	ped = Pediatrics	pic = Ped. Intensive Care	in = Inpatient
sur = Surgery	neo = Neonates	mix = Mixed	out = Outpatient
icu = Intensive Care	eme = Emergency	obg = Obstet./Gynec.	com = Community
oth = Other	xxx = Not specified		

Columns: 69-71, Mandatory
Field Length: 3 [A]
Field Name: Pathogen code
Description: This is coded as follows: spn = *S. pneumoniae* sau = *S. aureus*

Columns: 72
Field Length: 1 [N]
Field Name: PCR mec-gene
Description: The outcome of this test is coded as follows: 1 = positive 2 = negative 9 = Unknown

Antibiotic susceptibility testing
Specify the antibiotic in the field "Antibiotic code", making use of the Table Antibiotic coding EARSS (see below). For both pathogens the test results for Oxacillin will always be filled out. In case of a *S. pneumoniae* isolate, also the test results for Penicillin will always be mentioned.

Columns: 73-75
Field Length: 3 [A]
Field Name: Antibiotic code
Description: Coded as follows:

Table Antibiotic coding EARSS Part 1: Most commonly used antibiotics in EARSS

Code	Antibiotic
FTX	CEFOTAXIME
CRO	CEFTRIAXONE
CIP	CIPROFLOXACIN (NCCLS-5ug)
CI1	CIPROFLOXACIN (SWEDISH-10ug)
CLI	CLINDAMYCIN (NCCLS,SFM-2ug)
CL1	CLINDAMYCIN (SFM ana,SWE-15ug)
ERY	ERYTHROMYCIN
GEN	GENTAMICIN (NCCLS-10ug)
GE1	GENTAMICIN (SFM-15ug)
GE3	GENTAMICIN (SWEDISH-30ug)
GEH	GENTAMICIN-HIGH (NCCLS-120ug)
GE5	GENTAMICIN-HIGH (SFM-500ug)
OXA	OXACILLIN (NCCLS,SFM spn-1ug)
OX5	OXACILLIN (SFM-5ug)
PEN	PENICILLIN G
RIF	RIFAMPIN (NCCLS-5ug)
RI3	RIFAMPIN (SFM-30ug)
STR	STREPTOMYCIN
STH	STREPTOMYCIN-HIGH (NCCLS-300ug)
ST5	STREPTOMYCIN-HIGH (SFM-500ug)
TET	TETRACYCLINE
VAN	VANCOMYCIN

(See also Table Antibiotic coding EARSS Part 2)

Columns: 76
Field Length: 1 [A] (S, I, or R)
Field Name: S/I/R
Description: Result of susceptibility testing, differentiating susceptible (S), intermediate (I), and resistant (R)

Columns: 77-78
Field Length: 2 [A] (> < =)
Field Name: Zone (> < =)
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

Columns: 79-80
Field Length: 2 [N]
Field Name: Zone (Value in mm)
Description: Zone diameter in millimetres

Columns: 81-82
Field Length: 2 [A] (> < =)
Field Name: MIC (> < =)
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

Columns: 83-87
Field Length: 5 [N]
Field Name: MIC (Value in mg/l)
Description: The value of the MIC test result that can vary from 0.002 to 1024

Columns: 88-89
Field Length: 2 [A] (> < =)
Field Name: Etest (> < =)
Description: This field can indicate if a value of the Etest is “greater than” (>); “equal to or greater than” (>=); “less than” (<); or “equal to or less than” (< =) the value indicated in the following field

Columns: 90-94
Field Length: 5 [N]
Field Name: Etest (Value in mg/l)
Description: The value of the Etest test result that can vary from 0.002 to 1024

Other antibiotic test results of the same isolate will be mentioned as a new line.

Table Antibiotic coding EARSS
Part 2: Other antibiotics

Code	Antibiotic
ACM	ACETYLMIDECAMYCIN
ASP	ACETYLSPIRAMYCIN
AMD	AMDINOCILLIN
AMK	AMIKACIN
AMX	AMOXICILLIN
AUG	AMOXICILLIN/CLAVULANIC ACID
AXS	AMOXICILLIN/SULBACTAM
AMB	AMPHOTERICIN B
AMP	AMPICILLIN
AMS	AMPICILLIN/SULBACTAM
APA	APALCILLIN
APR	APRAMYCIN
AST	ASTROMICIN
AZI	AZITHROMYCINE
AZL	AZLOCILLIN
ATM	AZTREONAM
BAM	BACAMPICILLIN
BAC	BACITRACIN
CAP	CAPREOMYCIN
CAR	CARBENICILLIN
CAM	CARUMONAM
FAC	CEFACETRILE
CFC	CEFACLOR (NCCLS-30ug)
CF1	CEFACLOR (SFM-10ug)
DRX	CEFADROXIL
RID	CEFALORIDIN
MAN	CEFAMANDOLE
FAP	CEFAPIRINE
FAT	CEFATRIZINE
CFZ	CEFAZOLIN
CEP	CEFCAPENE
DIN	CEFDINIR
DIT	CEFDITOREN
FEP	CEFEPIME
FET	CEFETAMET
FIX	CEFIXIME (NCCLS-5ug)
FI1	CEFIXIME (SFM-10ug)
MEN	CEFMENOXIME
CMZ	CEFMETAZOLE
DIZ	CEFODIZIME
CID	CEFONICID
CFP	CEFOPERAZONE (NCCLS-75ug)
CF3	CEFOPERAZONE (SFM-30ug)
CFS	CEFOPERAZONE/SULBACTAM
CTN	CEFOTETAN
FOT	CEFOTIAM
FOX	CEFOXITIN
PIR	CEFPIROME
POD	CEFPODOXIME (NCCLS-10ug)
PO3	CEFPODOXIME (SWEDISH-30ug)
PRO	CEFPROZIL
SLD	CEFSULODIN
CAZ	CEFTAZIDIME
BUT	CEFTIBUTEN (NCCLS-30ug)
BU1	CEFTIBUTEN (SFM-10ug)
TIO	CEFTIOFUR
ZOX	CEFTIZOXIME
FRA	CEFUROXIME AXETIL (NCCLS-30ug)
FR1	CEFUROXIME AXETIL (SFM-10ug)
FRX	CEFUROXIME SODIUM
ZON	CEFUZONAM
ZOP	CEFUZOPRAN
LEX	CEPHALEXIN
KEF	CEPHALOTHIN
RAD	CEPHRADINE
CHL	CHLORAMPHENICOL
CTE	CHLORTETRACYCLINE
CIN	CINOXACIN (NCCLS-100ug)
CI3	CINOXACIN (SWEDISH-30ug)
CLA	CLARITHROMYCIN
CLN	CLINAFLOXACIN
CLO	CLOTRIMAZOLE
CLX	CLOXACILLIN
COL	COLISTIN (NCCLS-10ug)
CO5	COLISTIN (SFM-50ug)
CCL	CYCLACILLIN
CYC	CYCLOSERINE
DEM	DEMECLOCYCLINE
DIB	DIBEKACIN
DIC	DICLOXACILLIN
DIR	DIRITHROMYCIN
DOX	DOXYCYCLINE
ENX	ENOXACIN
ENR	ENROFLOXACIN
ETH	ETHAMBUTOL
ETI	ETHIONAMIDE
FLE	FLEROXACIN
FLO	FLOMOXEF
FLC	FLUCLOXACILLIN
FLU	FLUCONAZOL
FLM	FLUMEQUINE
FOS	FOSFOMYCIN
FRM	FRAMYCETIN
FUS	FUSIDIC ACID (SFM-10ug)
FU5	FUSIDIC ACID (SWEDISH-50ug)
GRE	GREPAFLOXACIN
IMP	IMIPENEM
ISE	ISEPAMICIN
ISO	ISOCONAZOLE
INH	ISONIAZID
ITR	ITRACONAZOLE
JOS	JOSAMYCIN
KAN	KANAMYCIN
KAH	KANAMYCIN-HIGH
KET	KETOCONAZOLE
KIT	KITASAMYCIN
LEV	LEVOFLOXACIN
LIN	LINCOMYCIN
LOM	LOMEFLOXACIN
LOR	LORACARBEF
MEC	MECILLINAM
MEL	MELEUMYCIN
MER	MEROPENEM
MET	METHICILLIN
MTR	METRONIDAZOLE (SFM-4ug)
ME1	METRONIDAZOLE (SWEDISH-10ug)
MEZ	MEZLOCILLIN
MID	MIDECAMYCINE
MIN	MINOCYCLINE
MOX	MOXALACTAM (LATAMOXEF)
MUP	MUPIROCIN
NAF	NAFCILLIN
NAL	NALIDIXIC ACID
NEO	NEOMYCIN
NET	NETILMICIN
FUR	NITROFURANTOIN (NCCLS-300ug)
FU1	NITROFURANTOIN (SWEDISH-100ug)
NIF	NITROFURAZONE
NIT	NITROXOLINE
NOR	NORFLOXACIN (NCCLS-10ug)
NO5	NORFLOXACIN (SFM-5ug)
NVA	NORVANCOMYCIN
NOV	NOVOBIOCIN
OFL	OFLOXACIN (NCCLS-5ug)
OF1	OFLOXACIN (SWEDISH-10ug)
OLE	OLEANDOMYCIN
OPT	OPTOCHIN
ORN	ORNIDAZOLE
OXO	OXOLINIC ACID
OXY	OXYTETRACYCLINE
PAS	P-AMINOSALICYLIC ACID
PAN	PANIPENEM
PEF	PEFLOXACIN

PNV	PENICILLIN V
PNO	PENICILLIN/NOVOBIOCIN
PPA	PIPEMIDIC ACID
PIP	PIPERACILLIN (NCCLS-100ug)
PI7	PIPERACILLIN (SFM-75ug)
PI3	PIPERACILLIN (SWEDISH-30ug)
PTA	PIPERACILLIN/TAZOBACTAM (NCCLS-100/10ug)
PT7	PIPERACILLIN/TAZOBACTAM (SFM-75ug/6ug)
PT3	PIPERACILLIN/TAZOBACTAM (SWEDISH-30/6ug)
PIL	PIRLIMYCIN
POL	POLYMIXIN B
PRI	PRISTINAMYCIN
PRP	PROPICILLIN
PRT	PROTHIONAMIDE
PZA	PYRAZINAMIDE
QUI	QUINUPRISTIN/DALFOPRISTIN
RIB	RIFABUTIN
ROS	ROSOXACINE
ROX	ROXITROMICIN
SIS	SISOMICIN
SPA	SPARFLOXACIN
SPE	SPECTINOMYCIN
SPI	SPIRAMYCINE
SLB	SULBENICILLIN
SUL	SULFONAMIDES
TEI	TEICOPLANIN
TEM	TEMAFLOXACIN
THA	THIACETAZONE
THI	THIAMPHENICOL
TIA	TIAMULIN
TIC	TICARCILLIN
TIM	TICARCILLIN/CLAVULANIC ACID
TIL	TILMICOSIN
TIN	TINIDAZOLE
TOB	TOBRAMYCIN (NCCLS-10ug)
TO3	TOBRAMYCIN (SWEDISH-30ug)
TMP	TRIMETHOPRIM
SXT	TRIMETHOPRIM/SULFAMETHOXAZOLE
TRL	TROLEANDOMYCIN
TRO	TROSPECTOMYCIN
TRV	TROVAFLOXACIN
VIO	VIOMYCIN
VIR	VIRGINIAMYCINE

ANNEX 4. Characterisation of the EARSS participating laboratories

Code of lab	Catchment population	Patient-days
NL002	290000	164914
NL003	290000	267510
NL004	180000	174999
NL005	110000	99651
NL006	670000	541964
NL007	270000	223685
NL008	300000	195203
NL009	480000	415153
NL010	650000	496064
NL011	580000	484280
NL012	180000	142577
NL013	180000	161928
NL014	220000	180982
NL016	100000	106627
NL017	80000	72994
NL018	120000	78139
NL019	310000	287230
NL020	410000	372251
NL021	320000	239332
NL022	320000	335146
NL023	270000	214975
TOTAL	**6330000**	**5255604**
NL	**15700000**	**12890235**
% coverage	**40,1**	**40,8**

ANNEX 5 Methods used for antibiotic susceptibility testing for *S. aureus* and *S. pneumoniae.*

A. Differentation between MIC, disk and screen test

	S. pneumoniae		***S. aureus***		
	MIC	disk	screen	MIC	disk
Oxacillin	4/19	18/19	6/19	11/19	10/19
Methicillin	--	--	3/7	6/7	3/7
Penicillin	18/19	5/19	--	3/8	5/8
Cefotaxime	3/7	5/7	--	1/1	--
Erythromycin	5/19	16/19	1/16	7/16	10/16
Tetracycline	4/15	13/15	1/8	4/8	4/8
Gentamicin	--	2/2	2/13	6/13	8/13
Ciprofloxacin	4/5	2/5	1/9	4/9	5/9
Vancomycin	6/16	14/16	1/17	8/17	10/17

B. Manufacturer of disk tests

	S. pneumoniae		***S. aureus***	
	Rosco	Oxoid	Rosco	Oxoid
Oxacillin	8/12	4/12	7/9	2/9
Methicillin	--	--	1/3	2/3
Penicillin	4/4	--	4/5	1/5
Cefotaxime	3/3	--	--	--
Erythromycin	7/11	4/11	8/10	2/10
Tetracycline	7/11	4/11	3/4	1/4
Gentamicin	1/2	1/2	6/8	2/8
Ciprofloxacin	2/2	--	5/5	--
Vancomycin	7/10	3/10	8/10	2/10

C. Types of MIC testing

	S. pneumoniae				**S. aureus**			
	agar	broth	e-test	Vitek*	agar	broth	e-test	Vitek*
Oxacillin	1/3	--	2/3	--	1/11	2/11	5/11	3/11
Methicillin	--	--	--	--	--	1/6	4/6	1/6
Penicillin	2/18	1/18	15/18	--	--	2/3	--	1/3
Cefotaxime	--	1/3	2/3	--	--	1/1	--	--
Erythromycin	1/5	2/5	2/5	--	1/7	2/7	1/7	3/7
Tetracycline	1/4	1/4	2/4	--	1/4	1/4	1/4	1/4
Gentamicin	--	--	--	--	--	1/6	2/6	3/6
Ciprofloxacin	1/4	2/4	1/4	--	--	1/4	1/4	2/4
Vancomycin	1/6	2/6	3/6	--	1/8	3/8	1/8	3/8

*=automated method which delivers an interpreted MIC

ANNEX 6 Protocols for susceptibility testing

Protocol *Staphylococcus aureus* testing

Objective:
To study the (methicillin)-resistance of *S. aureus,* in blood isolates in hospitals in Europe.

Case definition
Resistance data on the first isolate only of each strain from the blood of each patient with a hospital acquired *S. aureus* infection (confirmed by a coagulase test).

Indicators
- Proportion of oxacillin (=methicillin) resistant strains (MRSA) divided by total number of *S. aureus* cases in a specific lab/hospital.
- Quarterly incidence of MRSA cases per 100 patients admitted during the period of the study.
- Quarterly incidence of MRSA cases per 1,000 patient-days (and bed-days) during the period of the study.

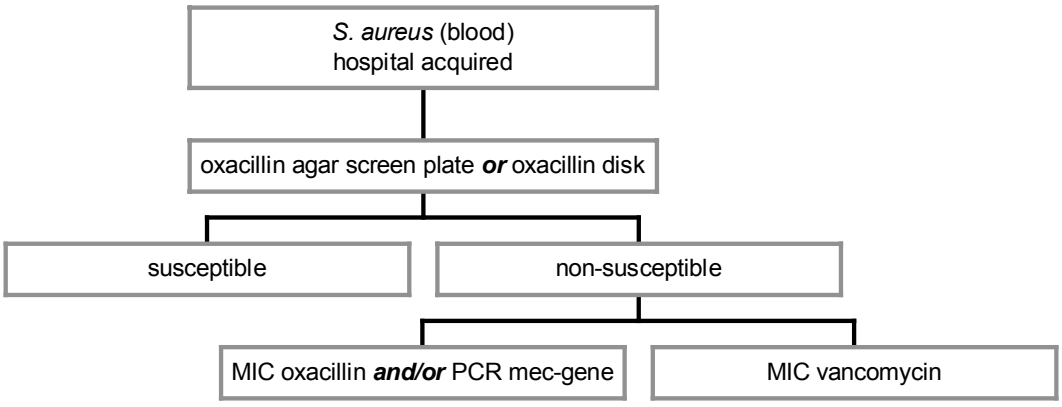
Test procedure: [1]
Oxacillin screen **plate** (6 µg/ml according to NCCLS or other national boards) or oxacillin **disk**[2] (1 µg[3] or 5 µg[4]) will be used.

Output from participating labs: Zone diameter, if possible[5]
Please exclude duplicate isolates of the same strain from the same patient, and send information only on the first isolate, of each strain, from each patient ("patient-isolate").

Oxacillin susceptible and non-susceptible, according to standards in use in your lab:
- register, when possible, the inhibition zone (in case of the disk method). No other tests required.

Oxacillin non-susceptible:[6]
- determine MIC of oxacillin, [7] specifying the method used: microdilution, agardilution or E-test (range of dilutions: 0,016 - 256). [8]
- determine MIC of vancomycin, [9] specifying the method used: microdilution, agardilution or E-test (range of dilutions: 0,016 - 256).

Protocol for testing *S.aureus*



Considerations *S. aureus*

1. For a reliable comparison of resistance against oxacillin in *S. aureus* (SA) the advantage of the use of oxacillin agar screen plates is indisputable. However, results from the questionnaire to the national co-ordinators illustrate that agar screen plates are only used in a few countries. Because one of the key features of EARSS is easy accessibility, the protocol will also accept data from the oxacillin disk diffusion test.

2. Testing of resistance to oxacillin in SA, using disk diffusion tests, may not always lead to comparable results, because of differences in inoculum, medium, time of incubation and temperature, and use of CO_2. Thus, it is important to know what are the test procedures in each individual participating laboratory, in order to check for these differences and to relate these to possible differences in the outcome of resistance testing. An inventory of the test methods in use will be done by means of a questionnaire that will be sent to participating laboratories. As discussed elsewhere (QA), the regular use (monthly) of quality control strains is also necessary to check for the validity of the resistance data from the participating laboratories.

3. If using a disk with a load of 1 µg oxacillin (NCCLS) for oxacillin susceptibility testing, non-susceptibles are strains with a zone size of 10 mm or less (≤ 10 mm).

4. If using a disk with a load of 5 µg oxacillin (e.g. SFM) for oxacillin susceptibility testing, non-susceptibles are strains with a zone size of 19 mm or less (≤ 19 mm).

5. The collection of zone diameters has an additional value. Firstly, zone diameters will give more insight in the distribution of SA strains with different susceptibilities to oxacillin, e.g. high resistance versus intermediate resistance. Secondly, the distribution of zone diameters may be used to study the quality of resistance data from the different participating laboratories. It is acknowledged that laboratories in some participating countries are not able to collect zone diameters.

6. A participating country can decide whether the local laboratory will perform the second step of the protocol or that a ‘reference’ laboratory will collect the non-susceptible strains and perform the MIC for oxacillin (or the PCR for the mec-gene) and vancomycin.

7. The golden standard for confirmation of a MRSA is testing for the presence of a mec-gene. However, when a participating laboratory is not able to perform a PCR, determination of a MIC for oxacillin is important to confirm that a MRSA is not a false positive.

8. It is possible to perform a MIC for oxacillin and vancomycin in one plate using two E-test strips (inoculum is 0.5 McFarland). Regarding the test conditions (medium), discussions are not finalised yet.

9. Testing of MRSA for resistance against vancomycin is very relevant but under debate. Vancomycin-Intermediate SA (VISA) strains, which were first reported in Japan, are often heterogeneously resistant, only a very limited percentage of total population of isolated bacteria is intermediate resistant. The presence of these VISA can be missed measuring a MIC under standard conditions. At this moment there is not an established protocol to test for the VISA. In addition, the relevance of this intermediate resistance to vancomycin for vancomycin therapy of MRSA can be disputed. For that reason, we test the MRSA for vancomycin using the E-test, with a standardised protocol (inoculum is 0.5 McFarland) which is also used testing the oxacillin MIC, realising that some intermediate VISA strains might be missed. The determination of the vancomycin MIC will preferably be done at a central ‘reference’ lab in each country. In case of finding a VISA strain arrangements will be made for further analysis (e.g., sequence analysis).

Protocol *Streptococcus pneumoniae* testing

Objective:
To study the penicillin-resistance of *S. pneumoniae* blood- and CSF-isolates in Europe.

Case definition

Resistance data on the first isolate only, of each strain from the blood or CSF of each patient with a community acquired *S. pneumoniae* infection (confirmed by an optochin test).

Indicators

- Prevalence of oxacillin (penicillin) resistance of *S. pneumoniae* blood and CSF-isolates.
- Quarterly incidence of PRP cases per 1,000,000 persons during the period of study.

Test procedure[1]

Oxacillin disk[2] (1 µg[3] or 5 µg[4]) will be used.

Output from participating labs: Zone diameters, if possible[5]

Please exclude duplicate isolates of the same strain from the same patient, and send information only on the first isolate, of each strain, from each patient ("patient-isolate").

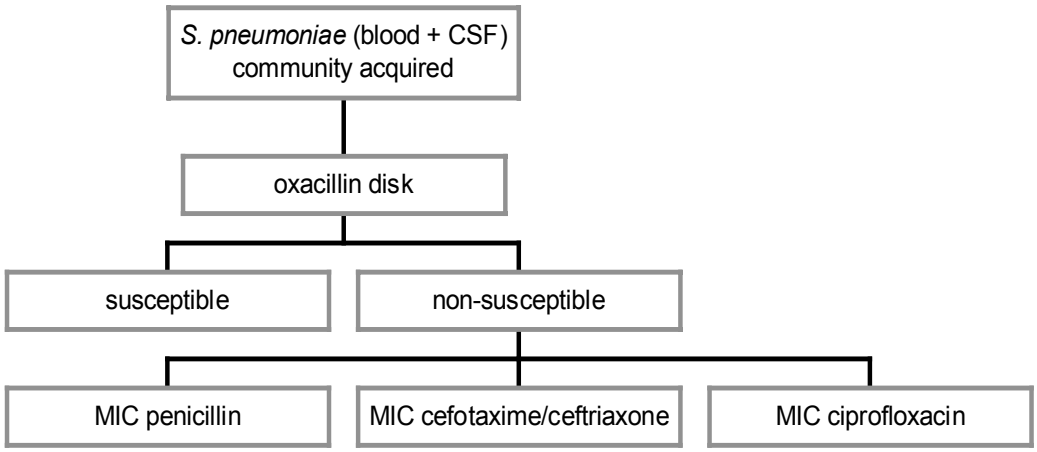
Oxacillin susceptible and non-susceptible, according to standards in use in your lab:

- register, when possible, the inhibition zone (in case of the disk method). No other tests required.

Oxacillin non-susceptible: [6]

- determine MIC of penicillin, specifying the method used: agardilution, microdilution or E-test (range of dilutions: 0,016 - 256).
- determine MIC cefotaxime or ceftriaxone, specifying the method used: agardilution, microdilution or E-test (range of dilutions: 0,002 - 32).
- determine MIC ciprofloxacin, specifying the method used: agardilution, microdilution or E-test (range of dilutions: 0,002 - 32)[7].

Protocol for testing *S. pneumoniae*



Considerations *S. pneumoniae*

1. In this version of the protocol, testing of ciprofloxacin resistance for all strains was not continued, because it was clear from the questionnaires that laboratories in most countries do not perform this testing on a routine basis. In addition, testing for susceptibility of fluoroquinolones in *S. pneumoniae* may be an unwanted incentive. Results from this testing may demonstrate that this pathogen is susceptible for fluoroquinolones, which may lead to unnecessary use of fluoroquinolones for therapy of *S. pneumoniae* infections. For this reason we ask to test for ciprofloxacin resistance only on strains that are non-susceptible to oxacillin.

2. Testing of resistance to oxacillin in *S. pneumoniae* (SP) using a disk diffusion test may not always lead to comparable results, because of differences in inoculum, medium, time of incubation and use of CO_2. Thus, it is important to know what are the test procedures in each individual participating laboratory, in order to check for these differences and to relate these to possible differences in the outcome of resistance testing. An inventory of the test methods in use will be done by means of a questionnaire that will be sent to participating laboratories. As discussed elsewhere (QA), the regular use (monthly) of quality control strains is also necessary to check for the validity of the resistance data from the participating laboratories.

3. Most used in oxacillin susceptibility testing is a disk with a load of 1 µg oxacillin (NCCLS). Non-susceptible penicillin resistant *S. pneumoniae* are strains with a zone size of 20 mm or less (≤ 20 mm).

4. An alternative in oxacillin susceptibility testing is a disk with a load of 5 µg oxacillin (e.g. SFM). Non-susceptible penicillin resistant *S. pneumoniae* are strains with a zone size of 26 mm or less (< 26 mm).

5. It is recognised that the laboratories in some participating countries are not able or willing to collect the zone diameters. However, we believe that the collection of zone diameters has additional value. Firstly, zone diameters will give more insight in the distribution of SP strains with different susceptibilities to oxacillin, e.g. highly resistant versus intermediate resistant. Secondly, the distribution of zone diameters may be used to study the comparability of resistance data from the different participating laboratories

6. A participating country can decide whether the local laboratory will perform the second step of the protocol or that a ‘reference’ laboratory will collect the non-susceptible strains and perform the MIC for penicillin, cefotaxime/ceftriaxone and ciprofloxacin.

7. In case of finding a *S. pneumoniae* strain non-susceptible to ciprofloxacin (the breakpoint will still be defined), arrangements will be made for further analysis.

ANNEX 7 Characteristics of the patients with *S. pneumoniae* and *S. aureus* infections

5.1	5.2	*S. pneumoniae*		*S. aureus*	
		freq	%	freq	%
isolate source					
	blood	695	90,6	1252	99,4
	CSF	72	9,4	7	0,6
age					
	0-4 y	74	9,6	85	6,8
	5-40 y	114	14,9	173	13,7
	41-65y	218	28,4	361	28,7
	>65 y	361	47,1	640	50,8
sex					
	male	431	56,2	733	58,2
	female	336	43,8	526	41,8
diagnosis					
	pneumoniae	43	5,6	6	0,5
	meningitis	12	1,6	1	0,1
	arthritis			6	0,5
	endocarditis			3	0,2
	sepsis without focus in children			12	1,0
	osteomyelitis			2	0,2
	empyema			1	0,1
	skin lesion			8	0,6
	primary peritonitis	1	0,1		
	abcess	1	0,1	17	1,4
	other	31	4,0	87	6,9
	unknown	679	88,5	1116	88,6
condition					
	immunocompromised	6	0,8	5	0,4
	postoperative woundinfection	1	0,1	4	0,3
	drug abuse	1	0,1	2	0,2
	intravascular procedures	1	0,1	16	1,3
	other conditions	2	0,3	22	1,7
	unknown	756	98,6	1210	96,1
origin patient					
	admitted	514	67,0	845	67,1
	outpatient	86	11,2	103	8,2
	other	10	1,3	7	0,6
	unknown	157	20,5	304	24,1
department					
	(internal) medicine	72	9,4	133	10,6
	pediatrics	23	3,0	40	3,2
	ped. intensive care	8	1,0	8	0,6
	inpatient	28	3,7	39	3,1
	surgery	16	2,1	93	7,4
	neonates			14	1,1
	mixed	27	3,5	51	4,1
	outpatients	11	1,4	11	0,9
	intensive care	25	3,3	73	5,8
	emergency	19	2,5	12	1,0
	obstet/gyneacology	1	0,1	6	0,5
	other	131	17,1	158	12,5
	unknown	404	52,8	621	49,3

ANNEX 8. Characterization of resistant *S. pneumoniae* and *S. aureus*

A. S. pneumoniae

Nr	*sex*	*source*	*age*	*PEN*	*CTX*	*CRO*	*ERY*	*TET*	*SXT*	*VAN*
1	m	bl	72	--			S	S	S	S
2	m	bl	60	0,5		S			R	
3	m	bl	71	1,0				S	R	
4	m	bl	78	0,25			S	S	S	S
5	m	bl	71	1	0,125	0,125	S	S	R	S
6	m	bl	0	0,5	S	S	S	S	R	S
7	f	bl	44	0,25			S	S	S	S
8	m	bl	61	0,25			S	S		S
9	f	sf	86	0,5	0,125		S	S		S

B. S. aureus

Nr	*sex*	*age*	*MecA*	*MET*	*FLC*	*VAN*	*ERY*	*GEN*	*SXT*	*CLI*
1	m	72	+		64	S	R	S	S	S
2	m	60	+			0,5	0,5	S	S	S
3	f	71	+	256		1,5		S		
4	m	78	+	256			R		S	R

ANNEX 9 Individual susceptibility results of the laboratories

Invasieve Streptococcus pneumoniae infecties
Resistentie tegen meerdere antibiotica
Resultaten per laboratorium

---------- LA_CODE=NL002 ----------

antibioticum	resistent	aantal_getest	res_perc
penicilline	1	51	2.0
cefuroxime	0	51	0.0
ceftriaxon	0	2	0.0
amoxicilline	0	51	0.0
augmentin	0	51	0.0
tetracycline	1	50	2.0
ciprofloxacine	23	51	45.1
cotrimoxazol	2	51	3.9
erythromycine	0	51	0.0
vancomycine	0	51	0.0
chlooramfenicol	0	2	0.0
rifampicine	0	3	0.0
Tobramycine	34	51	66.7

---------- LA_CODE=NL003 ----------

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	15	0.0
penicilline	0	23	0.0
tetracycline	1	23	4.3
ciprofloxacine	1	1	100.0
erythromycine	1	23	4.3
vancomycine	0	23	0.0
cefpimizole	6	23	26.1

---------- LA_CODE=NL004 ----------

antibioticum	resistent	aantal_getest	res_perc
penicilline	0	13	0.0
cefotaxim	0	8	0.0
amoxicilline	0	1	0.0
augmentin	0	2	0.0
ceftazidime	0	1	0.0
tetracycline	0	12	0.0
gentamicine	1	2	50.0
cotrimoxazol	0	2	0.0
erythromycine	1	13	7.7
vancomycine	0	1	0.0

---------- LA_CODE=NL005 ----------

antibioticum	resistent	aantal_getest	res_perc
penicilline	0	12	0.0
amoxicilline	0	12	0.0
augmentin	0	12	0.0
doxycycline	1	12	8.3
erythromycine	3	12	25.0
cefpimizole	0	2	0.0

---------- LA_CODE=NL006 ----------

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	7	0.0
penicilline	0	64	0.0
amoxicilline	0	64	0.0
augmentin	0	7	0.0
ceftazidime	0	57	0.0
tetracycline	0	57	0.0
doxycycline	0	7	0.0
ciprofloxacine	1	7	14.3
cotrimoxazol	0	64	0.0
erythromycine	3	64	4.7
vancomycine	0	7	0.0
cefpimizole	0	57	0.0

---------- LA_CODE=NL007 ----------

antibioticum	resistent	aantal_getest	res_perc
penicilline	0	31	0.0
tetracycline	0	30	0.0
ciprofloxacine	0	4	0.0
cotrimoxazol	0	3	0.0
erythromycine	0	31	0.0
vancomycine	0	5	0.0
chlooramfenicol	1	30	3.3
rifampicine	0	8	0.0

Invasieve Streptococcus pneumoniae infecties
Resistentie tegen meerdere antibiotica
Resultaten per laboratorium

LA_CODE=NL008

antibioticum	resistent	aantal_getest	res_perc
penicilline	0	40	0
cefotaxim	0	40	0
cefuroxime	0	40	0
amoxicilline	0	40	0.0
augmentin	0	40	0.0
doxycycline	2	40	5.0
ciprofloxacine	6	40	15.0
cotrimoxazol	1	40	2.5
erythromycine	1	40	2.5
vancomycine	0	40	0.0
clindamycine	1	40	2.5
flucoxacilline	0	39	0.0
meticilline	0	1	0.0
cefpimizole	0	40	0.0
chlooramfenicol	0	40	0.0
Tobramycine	40	40	100.0

LA_CODE=NL009

antibioticum	resistent	aantal_getest	res_perc
penicilline	1	82	1.2
cefuroxime	0	82	0.0
ceftriaxon	0	79	0.0
amoxicilline	0	82	0.0
augmentin	0	82	0.0
ceftazidime	0	82	0.0
tetracycline	0	1	0.0
ciprofloxacine	1	1	100.0
cotrimoxazol	6	81	7.4
erythromycine	2	80	2.5
chlooramfenicol	0	79	0.0

LA_CODE=NL010

antibioticum	resistent	aantal_getest	res_perc
penicilline	1	59	1.7
cefotaxim	0	5	0.0
cefuroxime	1	44	2.3
ceftriaxon	0	15	0.0
amoxicilline	0	17	0.0
augmentin	0	42	0.0
ceftazidime	0	18	0.0
tetracycline	0	1	0.0
gentamicine	2	2	100.0
cotrimoxazol	4	44	9.1
erythromycine	0	1	0.0
ofloxacine	0	1	0
chlooramfenicol	0	17	0

LA_CODE=NL011

antibioticum	resistent	aantal_getest	res_perc
penicilline	1	69	1.4
tetracycline	0	52	0.0
doxycycline	1	17	5.9
cotrimoxazol	0	5	0.0
erythromycine	2	69	2.9
vancomycine	0	5	0.0

LA_CODE=NL012

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	16	0.0
tetracycline	0	16	0.0
ciprofloxacine	0	1	0.0
erythromycine	1	16	6.3

LA_CODE=NL013

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	13	0.0
penicilline	0	5	0.0
cefotaxim	1	13	7.7
ceftriaxon	0	13	0.0
tetracycline	0	10	0.0
ciprofloxacine	1	13	7.7
erythromycine	0	13	0.0
vancomycine	0	13	0.0

LA_CODE=NL014

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	1	0
penicilline	0	24	0.0
cefotaxim	0	1	0.0
ceftriaxon	0	4	0.0
amoxicilline	0	22	0.0
augmentin	0	24	0.0
ceftazidime	0	4	0.0
ciprofloxacine	0	4	0.0
cotrimoxazol	0	24	0.0
erythromycine	1	24	4.2
clindamycine	0	24	0.0
cefpimizole	0	24	0.
Tobramycine	2	4	50.0

Invasieve Streptococcus pneumoniae infecties
Resistentie tegen meerdere antibiotica
Resultaten per laboratorium

---------- LA_CODE=NL016 ----------

antibioticum	resistent	aantal_getest	res_perc
penicilline	0	13	0.0
ceftriaxon	0	13	0.0
tetracycline	1	9	11.1
doxycycline	0	13	0.0
erythromycine	0	13	0.0
vancomycine	0	13	0.0
clindamycine	0	13	0.0

---------- LA_CODE=NL017 ----------

antibioticum	resistent	aantal_getest	res_perc
penicilline	0	7	0.0
ceftriaxon	0	7	0.0
amoxicilline	0	5	0.0
augmentin	0	1	0.0
tetracycline	1	7	14.3
cotrimoxazol	1	7	14.3
erythromycine	1	7	14.3
vancomycine	0	7	0.0
clindamycine	1	7	14.3
chlooramfenicol	0	2	0.0

---------- LA_CODE=NL018 ----------

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	3	0.0
penicilline	0	10	0.0
cefotaxim	0	10	0.0
ceftriaxon	0	9	0.0
augmentin	0	1	0.0
tetracycline	0	6	0.0
doxycycline	0	4	0.0
gentamicine	1	4	25.0
ciprofloxacine	0	1	0.0
erythromycine	1	7	14.3
vancomycine	0	9	0.0
clindamycine	0	9	0.0
rifampicine	0	1	0.0

---------- LA_CODE=NL019 ----------

antibioticum	resistent	aantal_getest	res_perc
penicilline	1	55	1.8
cefotaxim	0	54	0.0
augmentin	1	55	1.8
tetracycline	0	51	0.0
doxycycline	0	4	0.0
cotrimoxazol	2	55	3.6
erythromycine	0	55	0.0
vancomycine	0	53	0.0
ofloxacine	27	55	49.1
clindamycine	0	55	0.0
rifampicine	0	1	0.0

---------- LA_CODE=NL020 ----------

antibioticum	resistent	aantal_getest	res_perc
penicilline	0	60	0.0
cefotaxim	0	5	0.0
cefuroxime	0	13	0.0
ceftriaxon	0	34	0.0
erythromycine	2	60	3.3
vancomycine	0	46	0.0
clindamycine	0	5	0.0
cefpimizole	0	8	0.0

---------- LA_CODE=NL021 ----------

antibioticum	resistent	aantal_getest	res_perc
penicilline	0	29	0.0
cefotaxim	0	14	0.0
ceftriaxon	1	16	6.3
amoxicilline	0	29	0.0
augmentin	0	29	0.0
gentamicine	29	29	100.0
ciprofloxacine	0	1	0.0
cotrimoxazol	0	29	0.0
erythromycine	1	29	3.4
vancomycine	0	29	0.0
clindamycine	0	17	0.0
chlooramfenicol	0	29	0.0

---------- LA_CODE=NL022 ----------

antibioticum	resistent	aantal_getest	res_perc
penicilline	4	61	6.6
cefotaxim	0	3	0.0
ceftriaxon	0	3	0.0
tetracycline	3	61	4.9
cotrimoxazol	10	55	18.2
erythromycine	2	61	3.3
vancomycine	0	61	0.0

---------- LA_CODE=NL023 ----------

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	35	0
penicilline	0	1	0

Invasieve Staphylococcus aureus infecties
Resistentie tegen meerdere antibiotica
Resultaten per laboratorium

LA_CODE=NL002

antibioticum	resistent	aantal_getest	res_perc
cefuroxime	0	77	0.0
amoxicilline	55	76	72.4
augmentin	0	77	0.0
cotrimoxazol	0	77	0.0
erythromycine	0	1	0.0
vancomycine	0	77	0.0
clindamycine	2	76	2.6
meticilline	0	77	0.0
rifampicine	0	77	0.0
tobramycine	0	77	0.0

LA_CODE=NL003

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	80	0.0
penicilline	68	79	86.1
augmentin	0	78	0.0
tetracycline	5	79	6.3
gentamicine	3	78	3.8
cotrimoxazol	4	79	5.1
erythromycine	0	80	0.0
vancomycine	0	80	0.0
cefpimizole	0	80	0.0
rifampicine	1	77	1.3
tobramycine	0	1	0.0

LA_CODE=NL005

antibioticum	resistent	aantal_getest	res_perc
penicilline	10	13	76.9
ceftriaxon	0	7	0.0
augmentin	0	13	0.0
ciprofloxacine	1	7	14.3
cotrimoxazol	0	12	0.0
erythromycine	2	13	15.4
vancomycine	0	7	0.0
clindamycine	0	13	0.0
flucoxacilline	0	13	0.0
cefpimizole	0	2	0.0
tobramycine	0	7	0.0

LA_CODE=NL006

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	9	0.0
penicilline	83	94	88.3
amoxicilline	78	94	83.0
augmentin	1	102	1.0
ceftazidime	87	94	92.6
tetracycline	3	94	3.2
doxycycline	0	9	0.0
gentamicine	0	9	0.0
ciprofloxacine	7	102	6.9
cotrimoxazol	1	94	1.1
erythromycine	11	94	11.7
vancomycine	0	9	0.0
clindamycine	6	102	5.9
meticilline	1	94	1.1
cefpimizole	1	94	1.1
tobramycine	94	102	92.2

LA_CODE=NL007

antibioticum	resistent	aantal_getest	res_perc
penicilline	58	62	93.5
cefuroxime	0	62	0.0
tetracycline	0	61	0.0
gentamicine	1	61	1.6
ciprofloxacine	3	62	4.8
cotrimoxazol	0	2	0.0
erythromycine	0	2	0.0
vancomycine	0	62	0.0
clindamycine	1	61	1.6
fusidinezuur	0	1	0.0
meticilline	0	62	0.0
chlooramfenicol	0	1	0.0
rifampicine	0	61	0.0

LA_CODE=NL008

antibioticum	resistent	aantal_getest	res_perc
penicilline	74	95	77.9
cefotaxim	0	95	0.0
cefuroxime	0	95	0.0
amoxicilline	74	95	77.9
augmentin	0	95	0.0
doxycycline	2	95	2.1
ciprofloxacine	20	95	21.1

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LA_CODE=NL008 (continued)

antibioticum	resistent	aantal_getest	res_perc
cotrimoxazol	6	95	6.3
erythromycine	5	95	5.3
vancomycine	0	95	0.0
clindamycine	2	95	2.1
flucoxacilline	0	95	0.0
meticilline	0	95	0.0
cefpimizole	0	95	0.0
chlooramfenicol	4	95	4.2
rifampicine	0	2	0.0
tobramycine	12	95	12.6

LA_CODE=NL009

antibioticum	resistent	aantal_getest	res_perc
penicilline	98	121	81.0
cefuroxime	0	121	0.0
amoxicilline	98	121	81.0
augmentin	0	121	0.0
tetracycline	7	121	5.8
gentamicine	0	121	0.0
ciprofloxacine	4	121	3.3
cotrimoxazol	4	121	3.3
erythromycine	5	121	4.1
vancomycine	0	120	0.0
ofloxacine	3	120	2.5
clindamycine	2	121	1.7
meticilline	0	121	0.0
cefpimizole	0	121	0.0
rifampicine	0	120	0.0

LA_CODE=NL010

antibioticum	resistent	aantal_getest	res_perc
penicilline	102	129	79.1
cefotaxim	0	4	0.0
cefuroxime	0	1	0.0
augmentin	0	129	0.0
gentamicine	5	129	3.9
ciprofloxacine	1	2	50.0
cotrimoxazol	2	129	1.6
erythromycine	10	129	7.8
vancomycine	0	129	0.0
ofloxacine	9	129	7.0
clindamycine	2	129	1.6
flucoxacilline	1	129	0.8

LA_CODE=NL011

antibioticum	resistent	aantal_getest	res_perc
penicilline	67	84	79.8
cefuroxime	0	72	0.0
amoxicilline	57	72	79.2
gentamicine	1	72	1.4
cotrimoxazol	0	12	0.0
erythromycine	0	72	0.0
vancomycine	0	83	0.0
clindamycine	0	84	0.0
meticilline	0	84	0.0
rifampicine	0	15	0.0

LA_CODE=NL012

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	35	0.0
penicilline	30	35	85.7
tetracycline	2	35	5.7
gentamicine	1	35	2.9
ciprofloxacine	1	34	2.9
erythromycine	0	35	0.0
vancomycine	0	35	0.0

LA_CODE=NL013

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	21	0.0
penicilline	13	13	100.0
cefotaxim	13	13	100.0
cefuroxime	0	13	0.0
tetracycline	1	21	4.8
gentamicine	0	12	0.0
ciprofloxacine	1	21	4.8
erythromycine	0	21	0.0
vancomycine	0	21	0.0
tobramycine	0	13	0

Invasieve Staphylococcus aureus infecties
Resistentie tegen meerdere antibiotica
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LA_CODE=NL014

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	39	0.0
penicilline	28	39	71.8
ceftriaxon	0	39	0.0
augmentin	0	38	0.0
ceftazidime	1	39	2.6
ciprofloxacine	3	39	7.7
cotrimoxazol	1	39	2.6
erythromycine	0	39	0.0
vancomycine	0	38	0.0
clindamycine	0	39	0.0
cefpimizole	0	39	0.0
tobramycine	0	39	0.0

LA_CODE=NL016

antibioticum	resistent	aantal_getest	res_perc
penicilline	26	31	83.9
cefuroxime	0	31	0.0
ceftriaxon	0	31	0.0
augmentin	0	31	0.0
ciprofloxacine	0	31	0.0
cotrimoxazol	0	31	0.0
erythromycine	2	31	6.5
vancomycine	0	31	0.0
clindamycine	1	31	3.2
fusidinezuur	2	31	6.5
flucoxacilline	0	31	0.0
rifampicine	0	31	0.0

LA_CODE=NL017

antibioticum	resistent	aantal_getest	res_perc
penicilline	13	14	92.9
cefuroxime	0	14	0.0
ceftriaxon	0	2	0.0
augmentin	0	14	0.0
doxycycline	1	14	7.1
ciprofloxacine	1	14	7.1
cotrimoxazol	1	14	7.1
erythromycine	1	14	7.1
vancomycine	0	2	0.0
clindamycine	1	14	7.1
fusidinezuur	0	2	0.0
flucoxacilline	0	14	0.0
rifampicine	1	2	50.0

LA_CODE=NL018

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	19	0.0
penicilline	8	13	61.5
cefotaxim	0	1	0.0
ceftriaxon	0	1	0.0
tetracycline	2	15	13.3
gentamicine	0	19	0.0
ciprofloxacine	0	2	0.0
cotrimoxazol	0	2	0.0
erythromycine	2	20	10.0
vancomycine	0	12	0.0
clindamycine	1	1	100.0
flucoxacilline	0	5	0.0
meticilline	0	2	0.0
rifampicine	1	5	20.0

LA_CODE=NL019

antibioticum	resistent	aantal_getest	res_perc
penicilline	47	58	81.0
cefotaxim	0	1	0.0
amoxicilline	1	3	33.3
augmentin	0	5	0.0
tetracycline	1	57	1.8
gentamicine	1	58	1.7
ciprofloxacine	0	51	0.0
cotrimoxazol	0	58	0.0
erythromycine	0	58	0.0
vancomycine	0	58	0.0
ofloxacine	0	58	0.0
clindamycine	0	58	0
flucoxacilline	0	8	0
rifampicine	0	6	0

LA_CODE=NL020

antibioticum	resistent	aantal_getest	res_perc
penicilline	59	69	85.5
augmentin	0	1	0.0
erythromycine	2	69	2.9
vancomycine	0	66	0.0
clindamycine	0	69	0.0
fusidinezuur	1	66	1.5
flucoxacilline	0	69	0.0
cefpimizole	0	69	0.0
rifampicine	1	66	1.5

Invasieve Staphylococcus aureus infecties
Resistentie tegen meerdere antibiotica
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---------- LA_CODE=NL021 ----------

antibioticum	resistent	aantal_getest	res_perc
oxacilline	0	24	0.0
penicilline	32	37	86.5
ceftriaxon	0	27	0.0
amoxicilline	32	37	86.5
augmentin	0	37	0.0
gentamicine	3	37	8.1
ciprofloxacine	2	27	7.4
cotrimoxazol	0	37	0.0
erythromycine	0	37	0.0
vancomycine	0	37	0.0
clindamycine	0	31	0.0
meticilline	0	13	0.0
chlooramfenicol	4	37	10.8

---------- LA_CODE=NL022 ----------

antibioticum	resistent	aantal_getest	res_perc
oxacilline	1	122	0.8
penicilline	101	121	83.5
cefuroxime	1	119	0.8
tetracycline	6	100	6.0
gentamicine	0	122	0.0
ciprofloxacine	33	120	27.5
cotrimoxazol	19	120	15.8
erythromycine	12	120	10.0
vancomycine	0	122	0.0
clindamycine	9	120	7.5
fusidinezuur	3	98	3.1
rifampicine	1	122	0.8

---------- LA_CODE=NL023 ----------

antibioticum	resistent	aantal_getest	res_perc
oxacilline	1	50	2
gentamicine	0	1	0
vancomycine	0	1	0