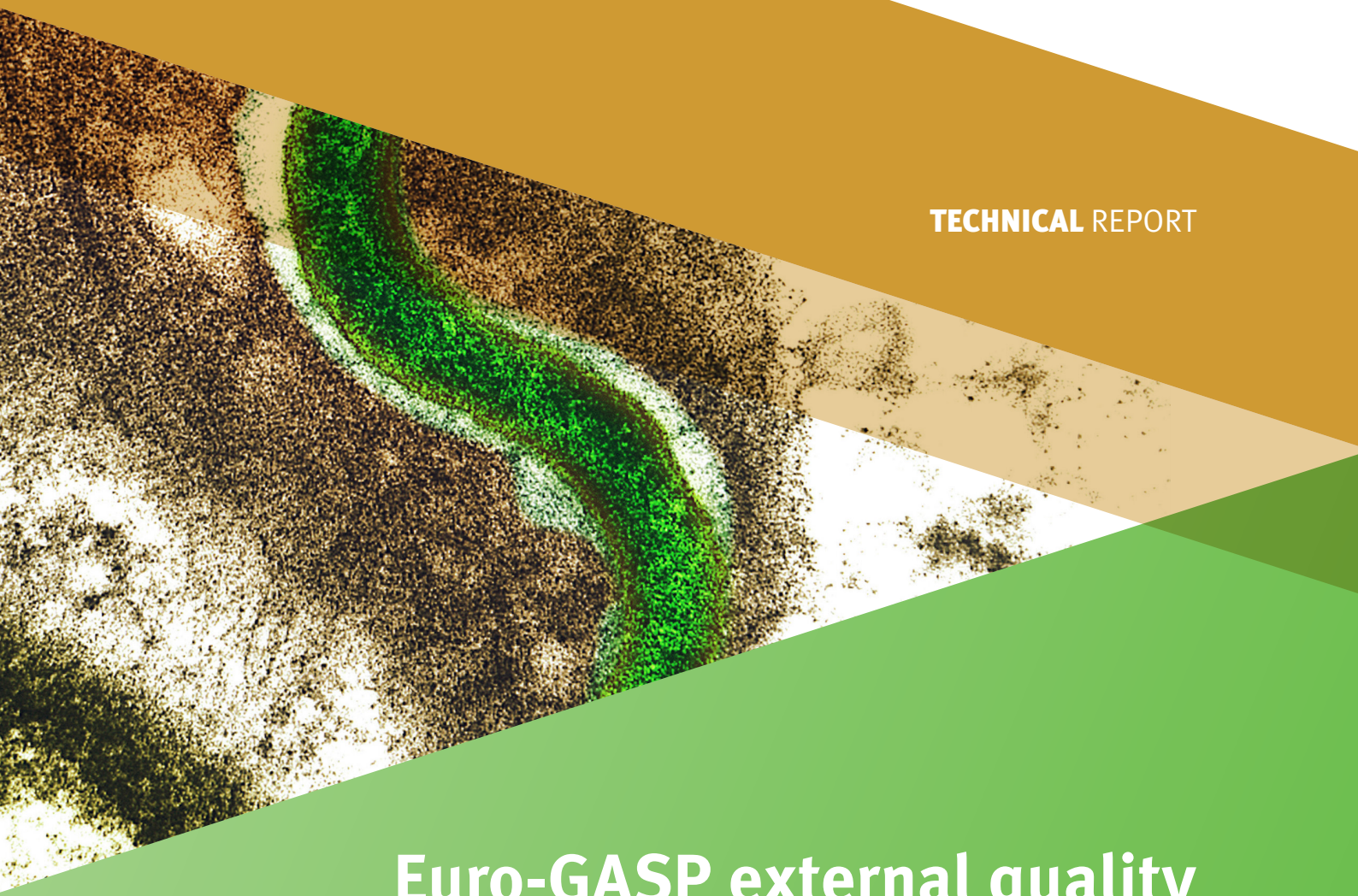

TECHNICAL REPORT

Euro-GASP external quality assessment scheme for *Neisseria gonorrhoeae* antimicrobial susceptibility testing

2019

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2019

This report was commissioned by the European Centre for Disease Prevention and Control (ECDC), coordinated by Gianfranco Spiteri, Benjamin Bluemel, Andrew J Amato-Gauci and Marieke J. van der Werf and produced by Michaela Day and Michelle Cole, Public Health England (now the UK Health Security Agency), London, and Susanne Jacobsson and Magnus Unemo, Örebro University Hospital, on behalf of the EURO-GASP network participants.

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Contents

Figures

Tables

Abbreviations

CLSI	Clinical and Laboratory Standards Institute
ECDC	European Centre for Disease Prevention and Control
ECOFF	Epidemiological cut-off
EEA	European Economic Area
EQA	External quality assessment
ESSTI	European Surveillance of Sexually Transmitted Infections Project
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
Euro-GASP	European Gonococcal Antimicrobial Surveillance Programme
GC	Gonococcal
I	Susceptible, increased exposure
MIC	Minimum inhibitory concentration
PHE	Public Health England
R	Resistant
S	Susceptible
STI	Sexually transmitted infection
UK	United Kingdom
UK NEQAS	United Kingdom National External Quality Assessment Service
WHO	World Health Organization

Executive summary

Introduction

External quality assessment (EQA) is an essential part of any laboratory-based surveillance system, allowing for the monitoring of performance and comparability of results from participating laboratories, identification of potential issues and deployment of resources and training where necessary. An EQA scheme for antimicrobial susceptibility testing in *Neisseria gonorrhoeae* has been available to laboratories participating in ECDC's European Sexually Transmitted Infections (STI) surveillance network since 2010. This EQA scheme has so far shown high levels of inter-laboratory comparability in the presence of differing methodologies.

Materials and methods

The EQA specimen panel of 10 gonococcal isolates was selected by Public Health England (PHE, now UK Health Security Agency (UKHSA)) and distributed by the United Kingdom National External Quality Assessment Service (UK NEQAS). Of the 10 gonococcal isolates provided, one strain was in triplicate and two strains were in duplicate to test intralaboratory concordance. The remaining isolates were all provided singularly, meaning that the *N. gonorrhoeae* antimicrobial susceptibility EQA panel comprised of six different strains in total. The isolates were representative of a range of different antimicrobial susceptibility profiles and consisted of the four WHO reference strains, WHO G, K, N and P, and two clinical isolates obtained in the UK in 2018 and 2019. Participating laboratories were requested to test the EQA panel using local methodology (i.e. MIC gradient strip test, agar dilution, or disc diffusion) and relevant international breakpoints (i.e. EUCAST, CLSI, etc.) against a range of antimicrobial agents. Results were submitted directly to UK NEQAS, who issued individual laboratory reports. The results were then supplied to PHE, who decoded and analysed the results based on the categories of susceptibility assigned. Susceptibility category concordance (categorical agreement) was assessed using the consensus category (most often reported category) of susceptibility for each tested strain. MIC concordance was assessed by examining MIC results within one (essential agreement) and two doubling dilutions of the modal MIC. Intralaboratory concordance was examined using the triplicate and the two duplicate strains.

Results

In July 2019, 28 laboratories in 27 participating countries received 10 gonococcal isolates for antimicrobial susceptibility testing. All laboratories returned EQA results to UK NEQAS. Most laboratories used MIC gradient strip tests and all used EUCAST breakpoints. The highest level of categorical agreement (other than production of beta-lactamase; 100%) was seen with spectinomycin (99.7%) and ceftriaxone (99.1%), while the lowest was seen with ciprofloxacin (91.1%). Compared to the previous distribution, the largest increase for categorical agreement was observed for azithromycin (92.5% in 2019, 77.6% in 2018) and the largest decrease for ciprofloxacin (91.1% in 2019, 98.1% in 2018).

Overall, 94.7% and 99.2% of the reported minimum inhibitory concentrations (MICs) were within one (essential agreement) and two doubling dilutions of the modal MIC, respectively demonstrating essential agreement has remained consistent after the increase observed in 2018 (95.2% in 2018, 87.7% in 2017). No relevant changes in the essential agreement for any one antimicrobial were observed between QA18 and QA19. Of the 28 laboratories, 22 (79%) reached an intralaboratory MIC concordance percentage score of 95% or higher with six laboratories obtaining a score of 100%.

Discussion and conclusion

There has been further harmonisation of susceptibility testing methodologies and breakpoints used by participating laboratories; most laboratories used MIC gradient strip tests and all applied EUCAST breakpoints for interpretation of MIC results. Overall, the laboratories participating in the EQA scheme QA19 performed well and showed good levels of competency in testing *N. gonorrhoeae* isolates of unknown phenotype. Categorical agreement increased in this distribution when compared with 2018, especially for azithromycin. The exception was ciprofloxacin, where a slight decrease was seen. The inter- and intralaboratory concordance was high in most cases, demonstrating comparability between different testing methodologies and allowing confidence in decentralised testing for surveillance purposes. Most susceptibility category discrepancies were attributable to strains with MICs on or close to a breakpoint, which highlights the need to consider the actual MIC as well as susceptibility category when interpreting susceptibility results. Analysis of the individual results submitted by the participating laboratories highlighted one centre in need of further guidance to help bring them into line with the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) recommended target of 95% of MICs within two doubling-dilutions of the modal MICs and beta-lactamase assessment.

1. Introduction

The European Centre for Disease Prevention and Control (ECDC) is a European Union (EU) agency with a mandate to operate the dedicated surveillance networks (DSNs) and to identify, assess, and communicate current and emerging threats to human health from communicable diseases. Within its mission, ECDC shall:

> 'foster the development of sufficient capacity within the Community for the diagnosis, detection, identification and characterisation of infectious agents which may threaten public health. The Centre shall maintain and extend such cooperation and support the implementation of quality assurance schemes.' (Article 5.3, EC 851/2004[1]).

As part of its mandate, ECDC commissions and supports External Quality Assessment (EQA) exercises across public health microbiology laboratories in the EU/European Economic Area (EEA) Member States with the objective of:

- verifying the quality and comparability of surveillance data reported at European level; and
- ensuring threat detection capability for emerging and epidemic disease or drug resistance.

EQAs are conducted within a quality management system and evaluate the performance of laboratories. They are carried out by an outside agency and with materials supplied specially for this purpose. ECDC's disease-specific networks organise a series of EQA for EU/EEA countries. In some networks, ECDC also includes non-EU/EEA countries in its EQA activities. The aim of these EQAs is to identify weak points in the diagnostic capacities of EU/EEA laboratories that are relevant to the surveillance of diseases listed in Commission Implementing Decision (EU) 2018/945; another aim is to ensure comparability of laboratory results from all EU/EEA countries.

The main purposes of EQA schemes include:

- Assessment of the general standard of performance ('state of the art');
- Assessment of the effects of analytical procedures (method principle, instruments, reagents, calibration);
- Evaluation of individual laboratory performance;
- Identification of vulnerabilities;
- Provision of continuing education for participating laboratories; and
- Identification of needs for training activities.

A major aim of the European Sexually Transmitted Infections (STI) surveillance network is to strengthen the surveillance of *Neisseria gonorrhoeae* antimicrobial susceptibility in EU/EEA Member States. An EQA scheme for *N. gonorrhoeae* antimicrobial susceptibility testing was established in 2007 as part of the European Surveillance of STIs (ESSTI) programme funded by the European Commission's Directorate-General for Health and Consumers (DG-SANCO). The EQA has been part of the ECDC STI microbiology project since 2009, with the first ECDC EQA distributed in 2010.

The EQA scheme is available to all laboratories in the STI surveillance network. An EQA scheme is an essential component of the laboratory-based surveillance programme, ensuring comparability of data between and within testing centres, and successful performance in EQA is a requirement for laboratories participating in decentralised testing as part of antimicrobial resistance surveillance across Europe [1, 2].

Between 2010 and 2019, the number of laboratories participating in the *N. gonorrhoeae* antimicrobial susceptibility testing EQA increased from 18 to 28; in general, the EQA revealed high levels of inter-laboratory comparability even in the presence of different antimicrobial susceptibility testing methodologies. Problems identified in previous EQA distributions included reduced comparability of results determined using discs compared with those determined by agar dilution and MIC gradient strip tests, media not suitably supporting gonococcal growth, and reduced comparability of results among laboratories using MIC gradient strip tests from a particular manufacturer.

The United Kingdom National External Quality Assessment Service (UK NEQAS) collaborated with Public Health England (PHE) for the EQA described in this report. UK NEQAS is accredited by the United Kingdom Accreditation Service to ISO 17043 (Conformity Assessment – General Requirements for Proficiency Testing). Participation in this EQA scheme for *N. gonorrhoeae* antimicrobial susceptibility provides a mechanism for laboratories in the network to meet the requirements of these standards.

[1] Regulation (EC) no 851/2004 of the European Parliament and of the Council of 21 April 2004 establishing a European Centre for Disease Prevention and Control

2. Materials and methods

2.1 Antimicrobial susceptibility testing external quality assessment panel

Members of the STI network and Euro-GASP contact points were invited by ECDC to participate in the EQA scheme. All laboratories that expressed interest in the EQA received 10 gonococcal isolates from UK NEQAS. The isolates included in the panel were selected by PHE to demonstrate a range of susceptibility profiles for relevant therapeutic antimicrobial agents and consisted of four WHO reference gonococcal strains, WHO G, K, N and P [3], and two clinical isolates from the UK isolated in 2018 [4] and 2019. To measure intralaboratory reproducibility, one of these strains was supplied in triplicate (Strain 6 (H18-502), coded in the EQA as 5574/5576/5578), and two strains were supplied in duplicate (Strain 4 (WHO K), EQA codes 5572/5575 and Strain 5 (G-401), EQA codes 5573/5577). The remaining three strains were supplied as individual isolates (Strain 1 (WHO G), EQA code 5569; Strain 2 (WHO P), EQA code 5570 and Strain 3 (WHO N), EQA code 5571). Therefore, six different strains were included in the distribution.

Participating laboratories tested the EQA panel of isolates using their own routine methodologies against the following therapeutic antimicrobials where possible:

- Azithromycin
- Cefixime
- Ceftriaxone
- Ciprofloxacin
- Gentamicin
- Spectinomycin

Participating laboratories also tested the EQA panel of isolates for beta-lactamase production where possible.

The antimicrobials listed are those detailed in the *ECDC Instructions, External Quality Assessment v6* [5].

2.2 Susceptibility testing methods

The methodology and the clinical breakpoints/guidelines (e.g. European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints (Table 1) [6]) used for determining the category of susceptibility for each antimicrobial tested was requested. Antimicrobial susceptibility testing results for each isolate were reported as both the category of susceptibility (resistant (R), susceptible, increased exposure (I), susceptible (S)), and the minimum inhibitory concentration (MIC) for the gradient strip and agar dilution methods.

Table 1. European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints

Antimicrobial	MIC breakpoint (mg/L)		
	S ≤	I	R >
Azithromycin	*		*
Cefixime	0.125		0.125
Ceftriaxone	0.125		0.125
Ciprofloxacin	0.03	0.06	0.06
Spectinomycin	64		64

**: The 2019 EUCAST breakpoints were released in January 2019 in which the SIR categories have been removed for azithromycin and replaced with an epidemiological cut-off (ECOFF) value of 1 mg/L. Please note currently there are no EUCAST interpretive criteria for gentamicin [6].*

2.3. Analysis and interpretation of the results

Raw results for the EQA were submitted by each participating laboratory directly to UK NEQAS for the production of individual laboratory reports. The results were also forwarded to PHE for further collated analysis.

For the analysis, all MIC results that fell between the MIC gradient strip full-dilution scale were rounded up to the next full MIC gradient strip dilution, as this was the most commonly used testing method. The minimum, maximum, and modal MIC for each strain was established. The number of MIC measurements within two MIC dilutions of the modal MIC and the number of MIC measurements above or below two MIC dilutions of the modal MIC for each strain were established.

A percentage of overall MIC concordance for each laboratory was calculated for the number of isolates within two doubling dilutions of the modal MIC from the total number of antimicrobials including beta-lactamase from each laboratory. Essential agreement (MICs within one doubling dilution of the modal) was also examined and used as the basis for an overall MIC score for each participating laboratory. The overall MIC score for each laboratory was calculated based on minor and major faults in the MIC for ceftriaxone, azithromycin, and ciprofloxacin. Where the MIC result matched the modal result, a score of five was assigned; a one MIC doubling dilution difference from the modal was considered a minor fault and a score of four was given; a difference of two doubling dilutions from the modal MIC was classed as a major fault and given a score of one. An MIC greater than two doubling dilutions from the modal was classed as a very major fault and a score of zero was given. The total score was then converted into a percentage of the maximum score achievable (150 = (10x5) + (10x5) + (10x5)).

Consensus categories of susceptibility (categorical agreement) for each strain tested (six in total in this distribution; consensus calculated from all isolates in the triplicate or duplicate sets) were calculated once all participating laboratories had reported results back. The 'consensus' was assigned to the category reported most often irrespective of breakpoint criteria used. The overall concordance for each antimicrobial was established by taking the average of each strain's percentage concordance. The total categorical concordance score was calculated by assigning a score of five for results the same as the consensus, four for a minor fault (susceptible or resistant miscategorised as intermediate or vice versa), three for a major fault (susceptible miscategorised as resistant), and one for a very major fault (resistant miscategorised as susceptible).

Intralaboratory concordance was examined using the triplicate (strain six) and two duplicate strains (strains four and five). All MIC results for these strains were assigned a score: five if the same as the other results, four if one MIC doubling dilution different (minor fault), three if two MIC doubling dilutions different (major fault) and zero if greater than two MIC doubling dilutions different (very major fault). These results were then averaged for the total number of results observed and given a percentage error score by comparison to the maximum score possible if there were no faults i.e. 5 = ((5+5+5)/3) + (5+5/2) + (5+5/2))/3). The higher the percentage, the more consistent the laboratory MIC test results were.

3. Results

3.1 QA19 panel strain characteristics

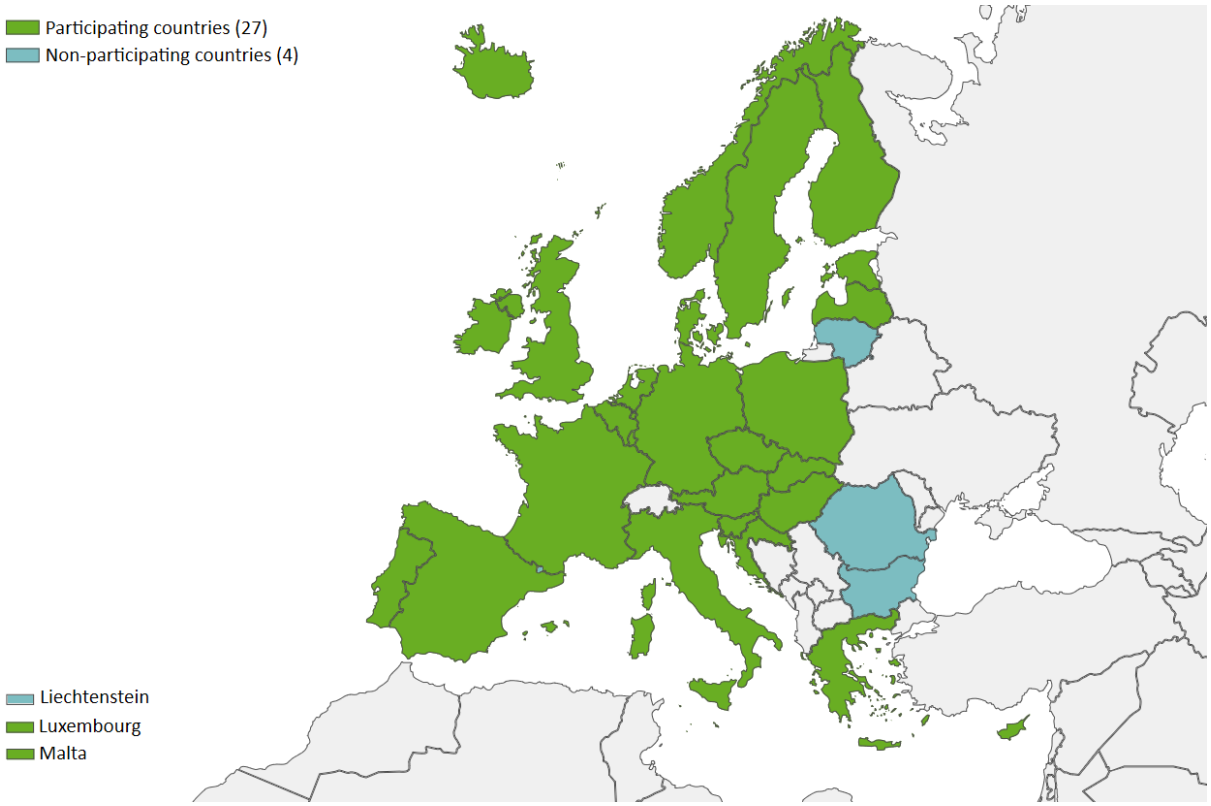
Table 2 shows the overall consensus category, the modal/range MIC for all tests, and the percentage concordance for each strain in the EQA panel. Consensus category of susceptibility for each strain tested are also shown. The strains tested demonstrated a range of phenotypes, and none of the strains was fully susceptible to all antimicrobials tested:

- Two strains were multidrug-resistant with high-level resistance to ciprofloxacin, one also had resistance to ceftriaxone and cefixime (Strain 6; H18-502), and the other had resistance to cefixime (Strain 4; WHO K).
- Two strains had MICs greater than azithromycin ECOFF (1 mg/L), of which one had high-level resistance (Strain 2; WHO P, Strain 5; G-401, MIC ≥256 mg/L).
- One strain was only susceptible, increased exposure and one resistant to ciprofloxacin (Strain 1; WHO G, Strain 3; WHO N).

3.2 Susceptibility testing methods

In July 2019, 28 laboratories in 27 countries received 10 gonococcal isolates (QA19) for susceptibility testing from UK NEQAS. All laboratories returned results to UK NEQAS (Figure 1). This is one country more than in the 2018 EQA, as Norway did not participate that year. All laboratories provided details on the methodology and breakpoints/guidelines (Table 3) used to test the isolates in the EQA. MIC gradient strip tests (96.4%) and GC agar (39.3%) were the most common testing methodology and medium used, respectively.

Figure 1. Countries participating in the 2019 *N. gonorrhoeae* susceptibility testing EQA scheme



Note: 28 laboratories participated in the 2019 EQA scheme; the United Kingdom had two participating laboratories.

Table 2. Consensus category, modal MIC (range) for gradient strip test and agar dilution (mg/L) and the percentage concordance of susceptibility category for the 2019 EQA panel

Strain		Azithromycin consensus	Cefixime consensus	Ceftriaxone consensus	Ciprofloxacin consensus	Gentamicin consensus	Spectinomycin consensus	Beta-lactamase consensus
Strain 1: 5569 (WHO G) (3) CipR	Consensus category	S	S	S	I	NA	S	NEG
	Modal MIC (range)	0.25 (0.064-0.5)	≤0.016 (≤0.016-0.125)	0.008 (0.004-0.064)	0.064 (0.032->32)	4 (2-8)	16 (4-32)	NA
	Susceptibility category concordance (%)	100	100	100	46.4	NA	100	100
	Reference MIC [3]	0.25	≤0.016	≤0.016	0.125	4	16	NA
Strain 2: 5570 (WHO P) (3) Az >1 mg/L	Consensus category	R	S	S	S	NA	S	NEG
	Modal MIC (range)	2 (1-8)	≤0.016 (≤0.016)	0.004 (0.002-0.016)	0.004 (0.002-0.008)	4 (2-8)	16 (4-16)	NA
	Susceptibility category concordance (%)	96.2	100	100	100	NA	100	100
	Reference MIC [3]	4	≤0.016	≤0.016	0.004	4	8	NA
Strain 3: 5571 (WHO N) (3) CipR	Consensus category	S	S	S	R	NA	S	POS
	Modal MIC (range)	0.25 (0.064-0.5)	≤0.016 (≤0.016-0.064)	0.004/0.008 (0.002-0.016)	4 (1->32)	4 (2-16)	16 (8-16)	NA
	Susceptibility category concordance (%)	100	100	100	100	NA	100	100
	Reference MIC [3]	0.25	≤0.016	≤0.016	4	4	16	NA
Strain 4: 5572 /5575 (WHO K) (3) CfmR, CroR, CipR	Consensus category	S	R	S	R	NA	S	NEG
	Modal MIC (range)	0.25 (0.064-1)	0.25 (0.125-0.5)	0.064 (0.016-0.25)	>32 (≥32)	4 (2-8)	16 (2-16)	NA
	Susceptibility category concordance (%)	88.5	77.8	94.6	100	NA	100	100
	Reference MIC [3]	0.5	0.5	0.125	≥32	2	16	NA

Strain		Azithromycin consensus	Cefixime consensus	Ceftriaxone consensus	Ciprofloxacin consensus	Gentamicin consensus	Spectinomycin consensus	Beta-lactamase consensus
Strain 5: 5573/5577 (G-401) Az ≥256 mg/L	Consensus category	R	S	S	S	NA	S	NEG
	Modal MIC (range)	>256 (≥256)	≤0.016 (≤0.016-0.032)	0.004 or 0.008 (0.002-0.016)	0.008 (0.002-0.125)	4 (1-4)	16 (4-32)	NA
	Susceptibility category concordance (%)	100	100	100	100	NA	100	100
	Reference MIC*	>256	≤0.016	≤0.016	0.008	2	16	NA
Strain 6: 5574/5576/ 5578 (H18-502) CfmR, CroR, CipR	Consensus category	S	R	R	R	NA	S	NEG
	Modal MIC (range)	0.5 (0.064-1)	2 (0.5-4)	1 (0.25-4)	>32 (8->32)	4 (1-32)	16 (4-16)	NA
	Susceptibility category concordance (%)	70.1	100	100	100	NA	98.3	100
	Reference MIC*	0.5	1	1	≥32	4	8	NA

** MICs taken from UK NEQAS reference MIC results.*
Note: No consensus category of susceptibility was assigned to gentamicin as there are currently no published breakpoints for this antimicrobial.
NA: not available; MIC: minimum inhibitory concentration; WHO: World Health Organization; Az: azithromycin; CfmR: cefixime-resistant; CroR: ceftriaxone-resistant; CipR: ciprofloxacin-resistant; R: resistant; NEG: negative; POS: positive. [3]: see 3 in reference list.

3.3 Interpretation of MICs

All 28 laboratories reported adherence to the EUCAST breakpoints (Table 1) [6]. Most laboratories that tested gentamicin did not interpret categories of susceptibility as there are currently no internationally defined interpretive criteria for this antimicrobial. However, one laboratory did submit categories of susceptibility for gentamicin, using local interpretive criteria; these data were not analysed in this report.

Table 3. Susceptibility methods used by participating laboratories, July 2019 EQA

	Number of participating laboratories (%)	
Type of susceptibility test used	**2018**	**2019**
MIC gradient strip tests	26 (96.3%)	27 (96.4%)
Agar dilution	1 (3.7 %)	1 (3.6 %)
Testing guidelines used		
EUCAST	27 (100%)	28 (100%)
Agar base used		
GC agar base	9 (33.3%)	11 (39.3%)
Chocolatised blood agar	11 (40.7%)	9 (32.1%)
Diagnostic sensitivity agar	2 (7.4%)	3 (10.7%)
Thayer-Martin/Mueller-Hinton	3 (11.1%)	2 (7.1%)
Other	2 (7.4%)	3 (10.7%)

3.4 Coded breakdown of concordance

Due to the confidential nature of the EQA scheme, only coded laboratory breakdowns for beta-lactamase assessment concordance, category of susceptibility concordance, and MIC values for MIC gradient strip tests and agar dilution method are shown in the Annex (Tables A1.6 – A1.12). Analysis of the breakdown of results has highlighted that six laboratories reported isolates with MICs greater than two doubling dilutions different from the modal MIC. Only one laboratory reported more than 5% of results greater than two doubling dilutions from the modal MIC; this laboratory used chocolatised blood agar. As this laboratory participates in the Euro-GASP sentinel study via centralised testing this will not have an impact on the Euro-GASP data, but the laboratory will be supported to improve the quality of their susceptibility testing.

In the 2018 EQA (QA18), only one laboratory reported more than 5% of results greater than two doubling dilutions from the modal MIC. This laboratory improved its results in the QA19 EQA and had 100% of results within two doubling dilutions of the modal MICs, showing that the problems identified in QA18 have been rectified. This laboratory also still participates via centralised testing.

3.5 Susceptibility category concordance

Susceptibility category data for ceftriaxone and ciprofloxacin were submitted from all 28 laboratories, cefixime from 27 laboratories, azithromycin and beta-lactamase production from 26 laboratories, and spectinomycin from 20 laboratories. Four laboratories submitted incomplete susceptibility category results.

Incomplete data were submitted for:

- Azithromycin (laboratory 92623 (isolate 5573 only) and laboratory 94929 (isolate 5578 only));
- Spectinomycin (laboratory 92636 (isolate 5578 only)); and
- Beta-lactamase production (laboratory 92613 (isolate 5577 and 5578)).

Laboratories 94603 and 94938 did not test for azithromycin susceptibility (Table A1.1) and laboratory 95588 did not test for cefixime susceptibility (Table A1.3). Two laboratories (92629 and 95589) did not test for the production of beta-lactamases (Table A1.12).

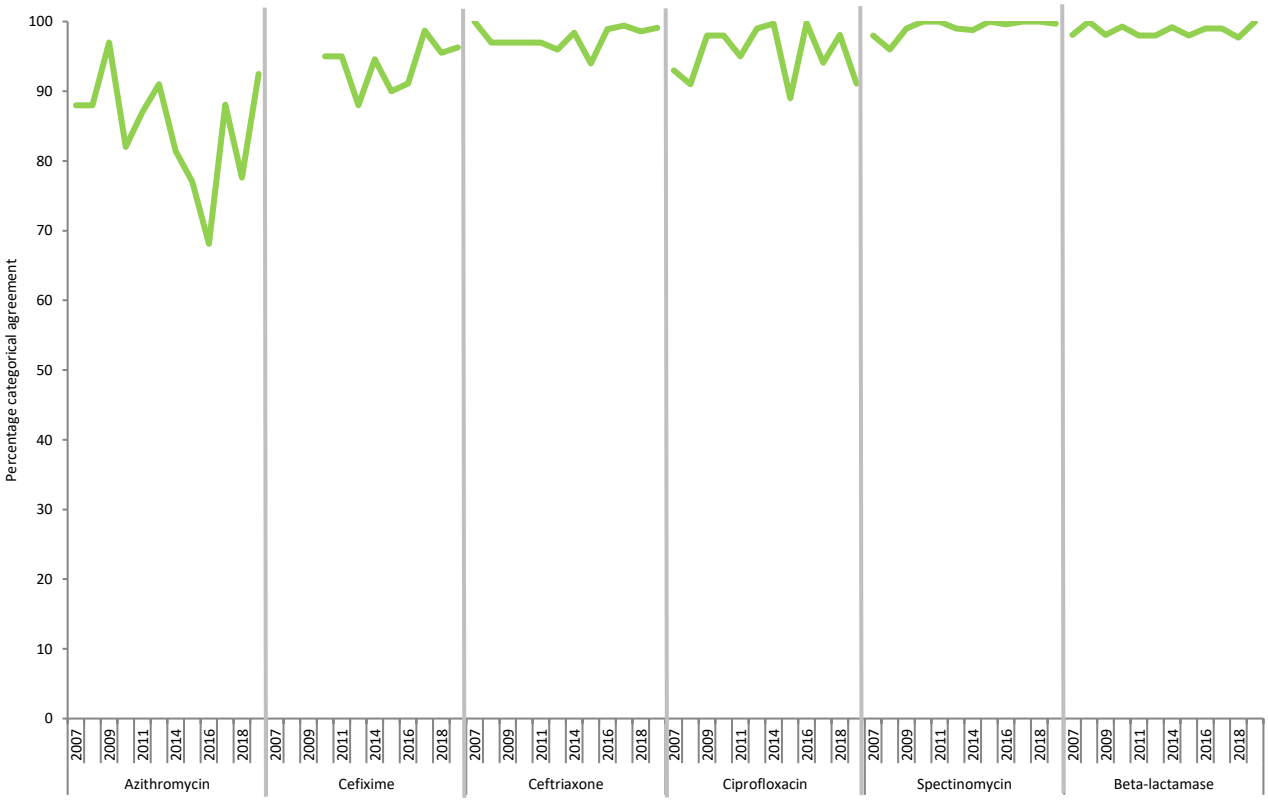
The highest levels of categorical agreement were seen for the production of beta-lactamase (100%) and spectinomycin and ceftriaxone, with 99.7% and 99.1% concordance respectively. The lowest level was seen for ciprofloxacin, with 91.1% concordance (Figure 2 and Tables A1.1, A1.3, A1.5, A1.7, A1.9 and A1.12). Consensus susceptibility categories were not assigned for gentamicin as there are currently no published breakpoints for interpretation of results.

When categorical agreement data are compared with previous EQA distributions from both ESSTI (QA2007, QA2008 and QA2009) [7] and ECDC Euro-GASP (QA2010-18) [8-15], there is a slight increase in concordance for

most antimicrobials tested (Figure 2). The exception is ciprofloxacin, which displayed a decrease in concordance, (91.1%) compared to 2018 (98.1%).

Beta-lactamase result concordance remains high at 100% (Figure 2).

Figure 2. Longitudinal comparison of EQA interlaboratory antimicrobial categorical agreement, EU/EEA, 2007-2019



Note: Cefixime was added to the EQA scheme in 2010.
ESSTI EQA distributions (2007 – 2009) constituted 30 isolates (10 strains in triplicate).
The number of laboratories participating in the EQA changed over time: 19 laboratories (2007 and 2008), 16 laboratories (2009), 18 laboratories (2010), 20 laboratories (2011), 19 laboratories (2012), 21 laboratories (2014), 26 laboratories (2015), 27 laboratories (2016), 28 laboratories (2017), 27 laboratories (2018), and 28 laboratories (2019).

3.6 MIC concordance

Overall, MIC essential agreement (MIC results within one doubling dilution of the modal MIC recorded) was at 94.7% for all antimicrobials tested (Table 4), which is comparable to the level of essential agreement achieved with the previous EQA panel distribution in 2018 (95.4%) [15]. As in the previous QA18 EQA panel, the highest level of essential agreement was seen for cefixime (98.9%), while in a change from azithromycin in QA18, the lowest level of essential agreement was seen for ceftriaxone (90.7%) (Table 4). For all MICs combined, 99.2% were within two doubling dilutions of the modal MIC. Ciprofloxacin had the highest proportion of isolates with an MIC greater than two doubling dilutions of the modal MIC (1.8%), and cefixime and ceftriaxone had the lowest (0.4%).

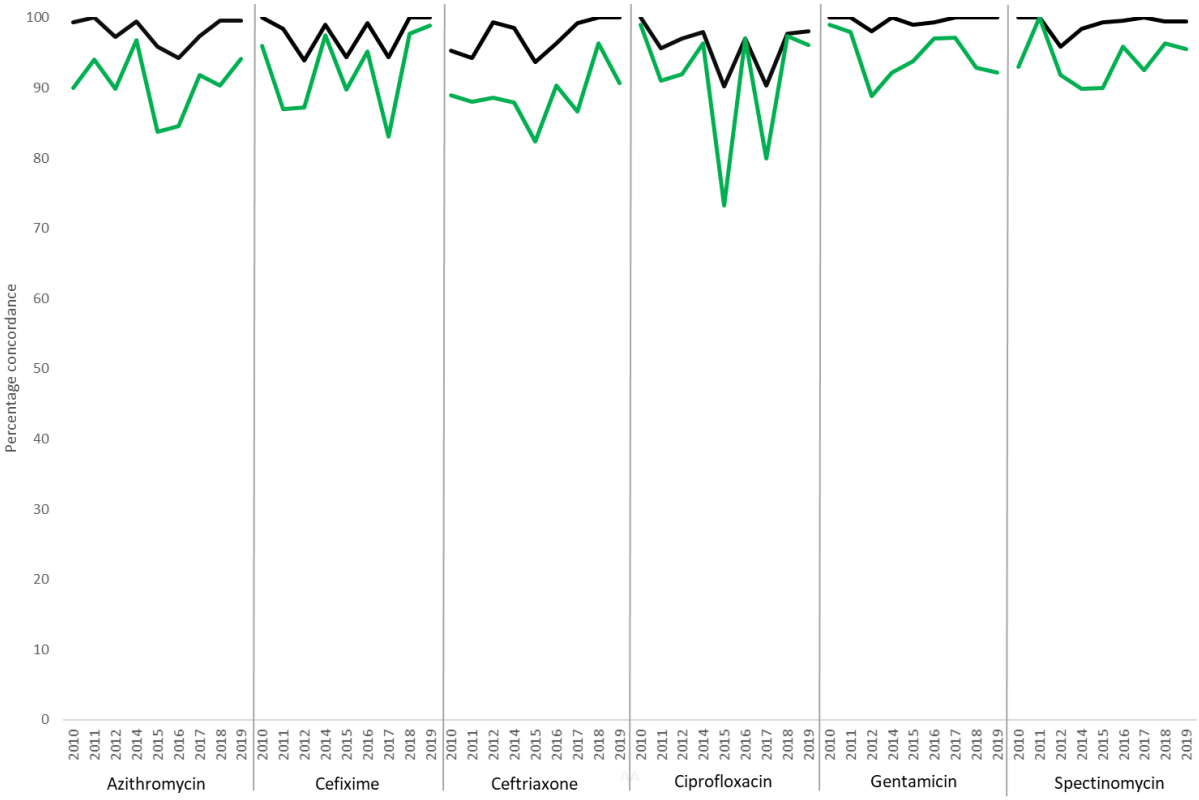
When MIC concordance data are compared with previous ECDC Euro-GASP EQA distributions (QA2010-18) [8-15], the MIC concordance for all antimicrobials tested has stabilised after the slight increase in MIC concordance for most antimicrobials tested in 2018 (Figure 3).

Table 4. Variation from modal MIC for EQA QA19

QA19	Azithromycin		Cefixime		Ceftriaxone		Ciprofloxacin		Gentamicin		Spectinomycin		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Within +/- 1 doubling dilution	243	94.2	267	98.9	254	90.7	269	96.1	166	92.2	190	95.5	1 389	94.7
Within +/- 2 doubling dilutions	12	4.7	2	0.7	25	8.9	6	2.1	13	7.2	8	4.0	66	4.5
More than +/- 2 doubling dilutions	3	1.2	1	0.4	1	0.4	5	1.8	1	0.6	1	0.5	12	0.8
Total no. of isolates with MIC data	258		270		280		280		180		199		1 467	

No.: Number of isolates with MIC data.
Some percentages may not add up to 100% due to rounding.

Figure 3. Longitudinal comparison of EQA interlaboratory MIC concordance, percentage of essential agreement (green line) and percentage of results within two doubling dilutions of the modal MIC (black line), EU/EEA, 2010-2019



Note: The number of laboratories participating in the EQA changed over time: 18 laboratories (2010), 20 laboratories (2011), 19 laboratories (2012), 21 laboratories (2014), 26 laboratories (2015), 27 laboratories (2016), 28 laboratories (2017), 27 laboratories (2018), and 28 laboratories (2019).

3.7 Intralaboratory concordance

Intralaboratory concordance was examined using the triplicate (strain six) and two duplicate strains (strains four and five). Figure 4 shows the results for the 2019 concordance scores. Most laboratories performed well, with 79% of laboratories (22/28) scoring 95% concordance or higher, including six laboratories obtaining a perfect score of 100%. Of the six laboratories scoring less than 95%, only one participates in Euro-GASP via decentralised testing. This laboratory had no major or very major faults and achieved essential agreement for all duplicates and triplicates tested, so there is no issue with the data they provided for the TESSy database. Three laboratories with a percentage error score of greater than 5% in the 2018 EQA distribution also scored less than 95% concordance in the 2019 distribution, only one of which had a major fault in 2019. Two laboratories with a percentage error score of greater than 5% in the 2018 EQA improved in the 2019 distribution and scored over 95% concordance.

Figure 4. Intralaboratory MIC concordance percentage, 2019

3.8 Overall EQA scores

Figure 5 shows the overall MIC scores for the 2019 EQA versus the 2018 EQA, with the average score shown in red (2019: 89.6% (dark red); 2018: 89.9% (light red)). For the 2019 EQA, 10 laboratories scored a below average result, one of which had greater than 5% of results greater than two doubling dilutions from the modal MIC. The scores for overall categorical agreement are shown in Figure 6. The total score achieved by each laboratory out of a potential 150 is shown by the bars, which are coloured to show the composition of the score by none, minor, major, and very major faults.

Figure 5. EQA overall MIC scores, 2018 vs 2019

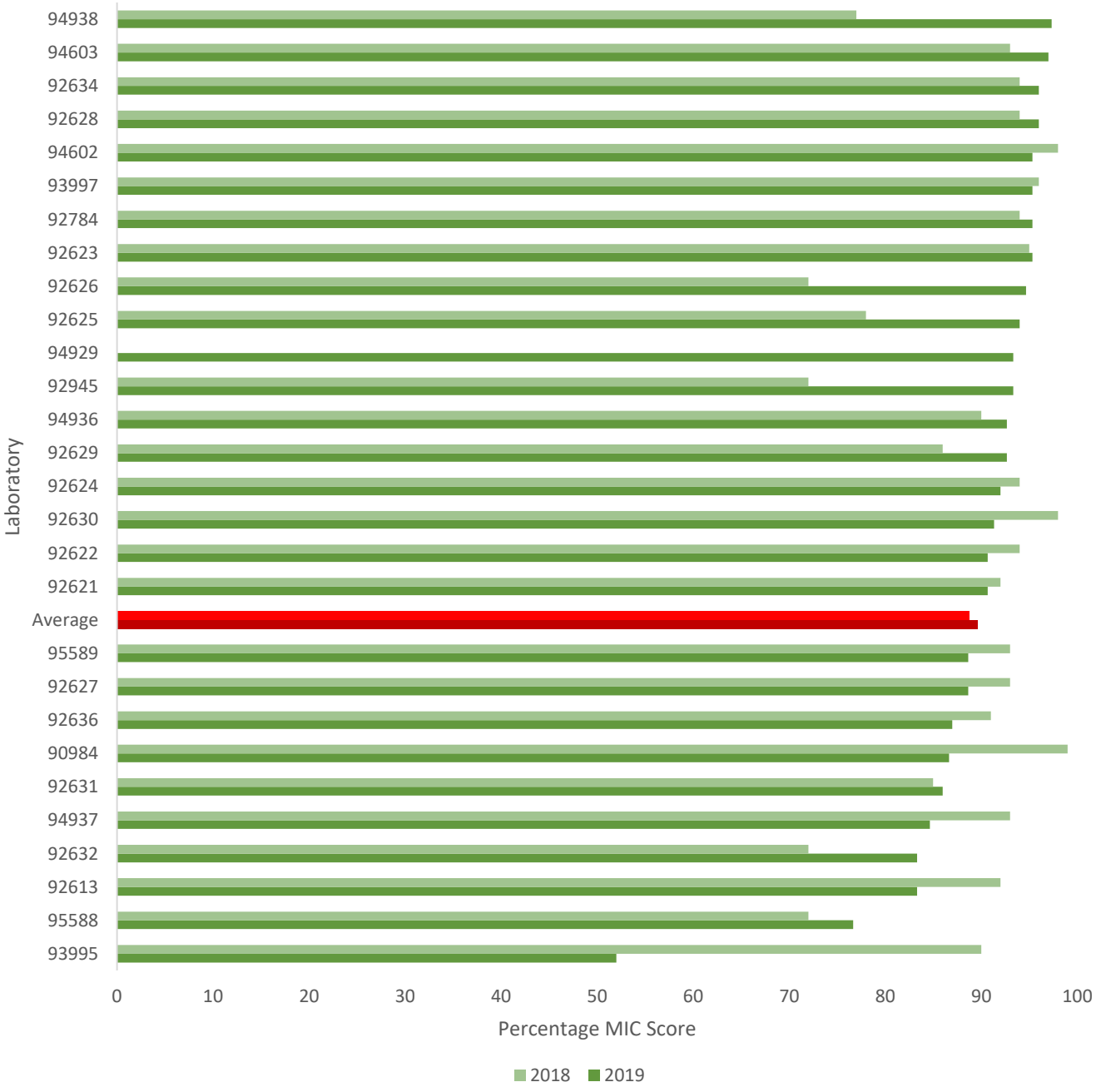
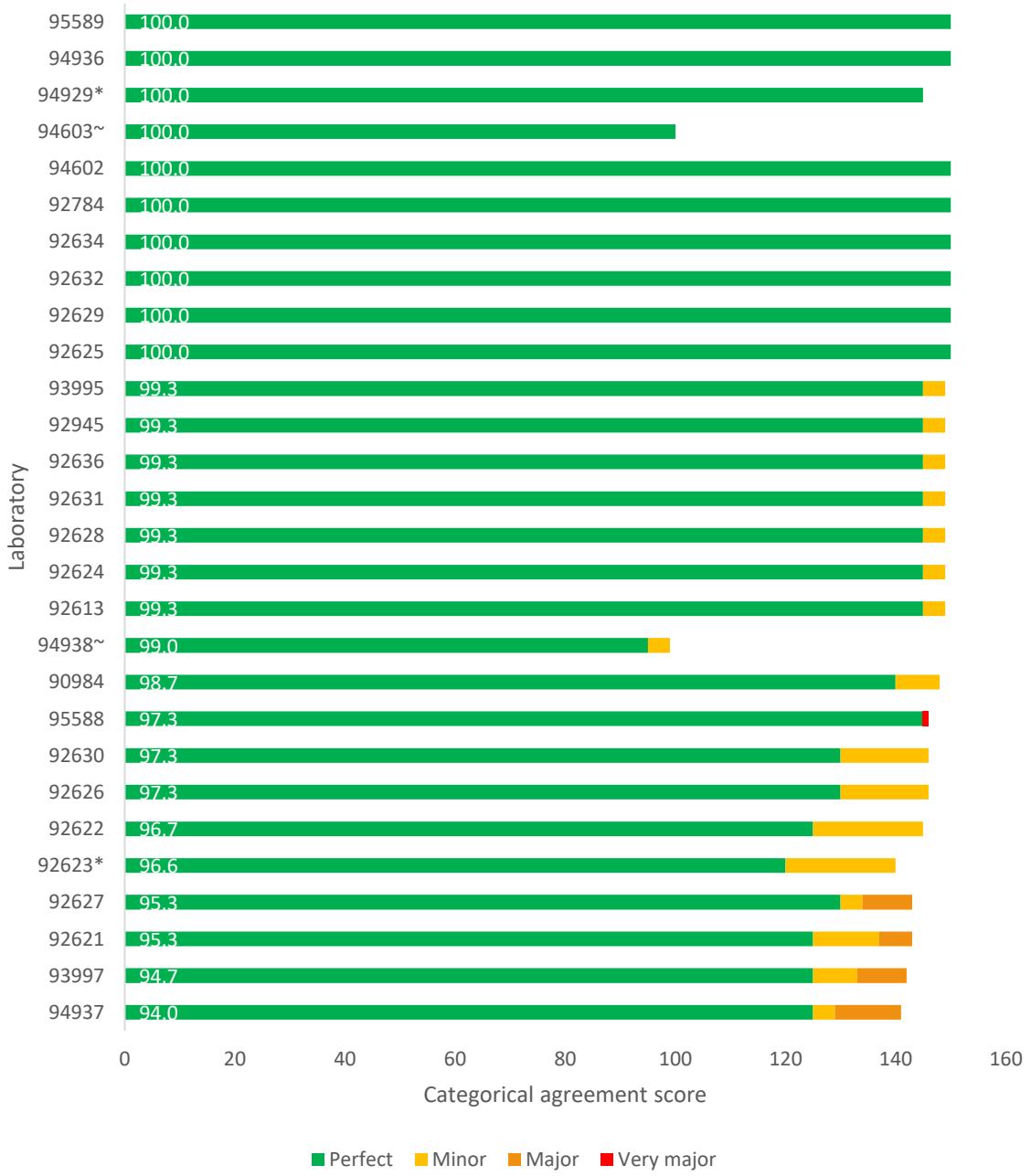


Figure 6. EQA overall categorical agreement scores, 2019



** Maximum score for laboratories 92623 and 94929 was 145 as one resistance category interpretation for azithromycin was not available.*
~ Maximum score for laboratories 94938 and 94603 was 100 as no resistance category interpretations were available for azithromycin

4. Discussion

The 2019 Euro-GASP EQA distribution was sent out to 28 laboratories in 27 participating countries, and all laboratories reported results for all or most of the requested tests. Most laboratories (96.4%) used MIC gradient strip tests to perform antimicrobial susceptibility testing in *N. gonorrhoeae*. EUCAST guidelines were used by all the participating laboratories to interpret MIC results. These results show the continuing implementation of the EUCAST guidelines and of MIC gradient strip tests across the Euro-GASP participating laboratories. The number of laboratories utilising GC agar base previously decreased from 50% to 33% in 2018 largely due to issues with supply. This appears to have improved in 2019 with 39% of laboratories utilising GC agar base with a decrease in the use of chocolatised blood agar from 44% in 2018 to 32% in 2019.

In general, the categorical agreement increased for most antimicrobials in comparison with the previous distribution; the exception was ciprofloxacin, for which categorical agreement decreased (from 98.1% to 91.1%). The highest increase was seen in azithromycin (from 77.6% to 92.5%). For ciprofloxacin, one of the strains had a MIC close to a breakpoint (modal MIC = 0.064 mg/L, reference MIC = 0.125 mg/L, resistance breakpoint >0.06 mg/L) so the lower categorical agreement was not unexpected. The increase in categorical concordance for azithromycin may be due to a lower proportion of strains in this distribution with MICs close to breakpoints (three out of 10 in 2019, six out of 10 in 2018). There was some confusion with the new EUCAST ECOFF for azithromycin, with six laboratories using the old EUCAST susceptible, increased exposure value of 0.5 mg/L, but as this is the first year with the new guidelines some issues as laboratories adjust were to be expected. In September 2019, after the EQA results were completed, a meeting of Euro-GASP collaborators was held in which the new EUCAST guidelines were discussed in detail, and hopefully this clarified how to interpret the azithromycin ECOFF correctly.

Overall categorical agreement scores were high, with only one laboratory scoring less than 95%, which was largely due to misinterpretation of the new azithromycin ECOFF (incorrectly calling an isolate with an azithromycin MIC= 1 mg/L resistant). Only one laboratory had a very major fault (calling a resistant isolate susceptible), which was due to a major fault in the azithromycin MIC for strain 5570. This laboratory participates in Euro-GASP via centralised testing. The average categorical concordance for the core antimicrobials was 98.5%, an improvement on the 96.4% observed in 2018. Essential MIC agreement was high at 94.7%, maintaining the increase observed in the 2018 distribution (95.4%). Concordance of beta-lactamase detection, which was high in previous years, increased to 100% in 2019.

Breakdown of EQA susceptibility testing results by laboratory allowed for detailed analysis of individual laboratory performance. In the 2019 EQA, in general laboratories performed well, with a good level of interlaboratory and intralaboratory concordance of results. Only one laboratory reported more than 5% of results greater than two doubling dilutions from the modal MIC, which was likely due to a change in the culture media used. In previous EQA distributions this laboratory has obtained much better MIC concordance, and the switch of media supplier and type coincides with the discrepancies. As this laboratory participates in Euro-GASP via centralised testing, this change in media and performance will not have affected the TESSy data. In the 2018 EQA, one laboratory reported more than 5% variation from the modal MIC and the issue appeared to be confined to one antibiotic, ciprofloxacin, with lower than expected MICs achieved. The results of the QA19 EQA distribution demonstrate that this laboratory has improved and this year they achieved 100% essential agreement, demonstrating that the problems identified in QA18 have been rectified.

It should be noted that the methods used for the susceptibility testing and the breakpoints used have changed over time, although there has been greater consistency in recent years. A full analysis of the different methods and breakpoints used in Euro-GASP EQAs over the years is publicly available [15].

5. Conclusion

The laboratories participating in the QA19 EQA scheme for susceptibility testing of *N. gonorrhoeae* showed good levels of competency and capability in recovering and testing strains of unknown phenotype. Both inter- and intralaboratory essential agreement for the different strains improved from the QA18 EQA distribution, allowing confidence in Euro-GASP de-centralised susceptibility testing and comparison of surveillance data from the members of the Euro-GASP network. These results indicate that the Euro-GASP antimicrobial surveillance quality is of a good standard. The improvements observed in laboratories with results out of range in previous distributions demonstrate that appropriate troubleshooting and implementation have led to improvements in quality standards.

This Euro-GASP EQA is important to ensure that results from different submitting laboratories are comparable and that significant over- and under-reporting of resistance do not occur. It is also important that reference laboratories have access to appropriate internal quality control (IQC) strains such as the WHO control panel (3) to routinely ensure their own quality assurance in a variety of diagnostic and antimicrobial susceptibility testing. Antimicrobial susceptibility results from Euro-GASP contribute to the evidence base of gonorrhoea treatment guidelines and local susceptibility testing can be used for individual patient management, so confidence in reporting is essential.

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Annex. QA19 detailed results

Table A1.1. Country coded category of susceptibility concordance – azithromycin

		Laboratory codes																																
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94929	94936	94937	94938	95588	95589	Total	No. S	No. I	No. R	Consensus	Concordance (%)
1	5569	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	N	S	S	26	26	0	0	S	100.0
2	5570	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	R	R	R	N	S	R	26	1	0	25	R	96.2
3	5571	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	N	S	S	26	26	0	0	S	100.0
4	5572	S	S	S	S	I	S	S	S	S	S	S	S	S	S	S	S	S	S	S	I	S	N	S	S	S	N	S	S	52	46	5	1	S	88.5
	5575	S	S	S	I	I	S	S	S	S	S	S	S	S	S	S	S	S	S	S	I	S	N	S	S	R	N	S	S						
5	5573	R	R	R	R	N	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	R	R	R	N	R	R	51	0	0	51	R	100.0
	5577	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	R	R	R	N	R	R						
6	5574	S	S	I	I	I	S	S	I	R	S	S	I	S	S	S	S	S	S	S	R	S	N	S	S	R	N	S	S	77	54	14	9	S	70.1
	5576	S	S	S	I	I	S	S	I	R	S	S	I	S	S	S	S	S	S	S	R	S	N	S	S	R	N	S	S						
	5578	S	S	I	I	I	S	S	I	R	S	S	I	S	S	S	S	S	S	S	R	S	N	N	S	R	N	S	S						
																																	Total	92.5

Table A1.2. Country coded MIC values (mg/L) – azithromycin

		Laboratory codes																																
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94929	94936	94937	94938	95588	95589	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
1	5569	0.5	0.25	0.25	0.25	0.25	0.25	0.125	0.25	0.5	0.25	0.25	0.25	0.5	0.5	0.25	0.25	0.25	0.125	0.064	0.25	0.25	N	0.5	0.25	0.125	0.25	0.25	0.25	0.25	0.064	0.5	1	0
2	5570	8	2	4	2	4	2	2	4	4	2	4	2	8	2	2	2	4	1	1	4	4	N	4	2	4	4	1	2	2	1	8	2	0
3	5571	0.5	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.5	0.25	0.25	0.25	0.5	0.25	0.125	0.25	0.25	0.125	0.064	0.25	0.25	N	0.25	0.25	0.25	0.125	0.25	0.125	0.25	0.064	0.5	1	0
4	5572	1	0.25	0.25	0.25	0.5	0.5	0.25	0.25	0.5	0.25	0.25	0.25	1	1	0.25	0.25	0.25	0.125	0.064	0.5	0.5	N	0.5	0.5	0.064	0.25	0.25	0.125	0.25	0.064	1	7	0
	5575	0.5	0.25	0.25	0.5	0.5	0.5	0.25	0.25	0.5	0.25	0.25	0.25	1	1	0.25	0.25	0.25	0.125	0.125	0.5	0.25	N	0.5	0.25	0.5	0.25	0.25	0.125					
5	5573	256	>256	>256	256	>256	>256	>256	>256	>256	>256	>256	>256	>256	>256	>256	>256	≥256	>256	>256	>256	>256	N	>256	256	>256	>256	>256	>256	>256	256	>256	0	0
	5577	256	>256	>256	256	>256	>256	>256	>256	>256	>256	>256	>256	>256	>256	>256	>256	≥256	>256	>256	>256	>256	N	>256	256	>256	>256	>256	>256					
6	5574	0.5	0.25	0.5	0.5	0.5	0.5	0.25	0.5	1	1	0.25	0.5	1	1	0.5	0.5	0.5	0.25	0.064	1	0.5	N	1	0.5	1	0.5	0.5	0.25	0.5	0.064	1	1	3
	5576	1	0.25	0.25	0.5	0.5	0.5	0.5	0.5	1	0.5	0.25	0.5	1	0.5	0.5	0.25	0.5	0.25	0.064	1	0.5	N	0.5	0.5	1	0.5	0.5	0.125					
	5578	0.5	0.25	0.5	0.5	0.5	0.5	0.25	0.5	1	0.5	0.5	0.5	1	0.5	0.5	0.5	0.5	0.25	0.064	1	0.5	N	0.5	0.5	1	0.5	0.5	0.25					

Table A1.3. Country coded category of susceptibility concordance – cefixime

	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94929	94936	94937	94938	95588	95589	Total	No. S	No. I	No. R	Consensus	Concordance (%)
		Laboratory codes																																	
1	5569	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	27	27	0	0	S	100.0
2	5570	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	27	27	0	0	S	100.0
3	5571	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	27	27	0	0	S	100.0
4	5572	R	S	R	S	R	R	R	R	R	S	R	R	R	S	R	R	R	R	S	R	R	S	R	R	R	R	N	R	54	12	0	42	R	77.8
	5575	R	S	R	S	R	R	R	R	R	R	R	R	R	S	R	R	R	R	S	R	R	S	R	R	R	R	N	S						
5	5573	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	54	54	0	0	S	100.0
	5577	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S						
6	5574	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	R	81	0	0	81	R	100.0
	5576	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	R						
	5578	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	R						
																																		Total	96.3

N: no result; not retrieved or susceptibility category not supplied.

Table A1.4. Country coded MIC values (mg/L) – cefixime

	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94929	94936	94937	94938	95588	95589	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
		Laboratory codes																																
1	5569	0.016	≤0.016	0.016	≤0.016	≤0.016	0.016	0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.125	≤0.016	≤0.016	0.016	0.032	≤0.016	≤0.016	≤0.016	≤0.016	0.016	≤0.016	≤0.016	0.016	0.016	≤0.016	N	≤0.016	≤0.016	≤0.016	0.125	0	1
2	5570	0.016	≤0.016	0.016	≤0.016	≤0.016	0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.016	≤0.016	≤0.016	0.016	0.016	≤0.016	N	≤0.016	≤0.016	≤0.016	≤0.016	0	0
3	5571	0.016	≤0.016	0.016	≤0.016	≤0.016	0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.064	≤0.016	≤0.016	≤0.016	0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.016	≤0.016	≤0.016	0.016	0.016	≤0.016	N	≤0.016	≤0.016	≤0.016	0.064	1	0
4	5572	0.5	0.125	0.5	0.25	0.25	0.25	0.5	0.25	0.25	0.125	0.25	0.5	0.25	0.125	0.5	0.25	0.5	0.25	0.125	0.25	0.25	0.125	0.25	0.25	0.25	0.25	N	0.25	0.25	0.125	0.5	0	0
	5575	0.5	0.125	0.5	0.125	0.25	0.25	0.5	0.25	0.25	0.25	0.25	0.25	0.25	0.125	0.25	0.25	0.5	0.25	0.125	0.25	0.25	0.125	0.25	0.25	0.25	0.25	N	0.125					
5	5573	0.016	≤0.016	0.016	≤0.016	0.016	0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.016	≤0.016	0.016	≤0.016	≤0.016	0.032	≤0.016	0.032	≤0.016	≤0.016	0.016	≤0.016	0.016	0.032	0.016	≤0.016	N	0.016	≤0.016	≤0.016	0.032	0	0
	5577	0.016	≤0.016	0.016	≤0.016	0.016	0.016	0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.016	≤0.016	≤0.016	0.032	0.032	0.032	≤0.016	≤0.016	0.016	≤0.016	0.016	0.032	0.032	0.016	N	0.016					
6	5574	4	2	≥2	1	2	2	2	2	2	2	2	2	2	1	2	1	4	2	1	1	2	1	2	2	1	2	N	0.5	2	0,5	4	1	0
	5576	4	2	≥2	1	2	2	2	2	2	2	1	2	2	1	2	1	4	2	1	1	2	1	2	2	2	2	N	1					
	5578	4	2	≥2	1	2	2	2	2	2	1	1	2	2	1	2	1	4	2	1	1	2	1	2	2	1	2	N	2					

Note: Laboratories 95588 did not submit cefixime data.
N: no result; not retrieved, not tested or MIC not supplied.

Table A1.5. Country coded category of susceptibility concordance – ceftriaxone

		Laboratory codes																																
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94929	94936	94937	94938	95588	95589	Total	No. S	No. I	No. R	Consensus	Concordance (%)
1	5569	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	28	28	0	0	S	100.0
2	5570	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	28	28	0	0	S	100.0
3	5571	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	28	28	0	0	S	100.0
4	5572	S	S	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	56	53	1	2	S	94.6
	5575	I	S	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S						
5	5573	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	56	56	0	0	S	100.0
	5577	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S						
6	5574	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	84	0	0	84	R	100.0
	5576	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R						
	5578	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R						
																																		Total	99.1

Table A1.6. Country coded MIC values (mg/L) – ceftriaxone

		Laboratory codes																																
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94929	94936	94937	94938	95588	95589	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
1	5569	0.016	0.004	0.016	0.004	0.008	0.008	0.016	0.004	0.008	0.004	0.008	<0.016	0.004	0.004	0.008	0.016	0.008	<0.016	0.004	<0.016	0.008	<0.016	0.008	0.064	0.008	0.004	0.016	<0.016	0.008	0.004	0.064	0	1
2	5570	0.016	0.002	<0.016	0.002	0.004	0.002	<0.016	0.002	0.004	<0.002	0.004	<0.016	0.002	<0.016	0.004	0.008	0.008	<0.016	0.004	<0.016	0.004	<0.016	0.004	0.004	0.004	0.004	0.008	<0.016	0.004	0.002	0.016	1	0
3	5571	0.008	0.004	<0.016	0.004	0.004	0.008	<0.016	0.004	0.004	0.004	0.008	0.016	0.002	0.002	0.004	0.016	0.008	<0.016	<0.002	<0.016	0.008	<0.016	0.008	0.008	0.008	0.004	0.016	<0.016	0.004 or 0.008	0.002	0.016	3	0
4	5572	0.125	0.032	0.25	0.064	0.064	0.064	0.125	0.032	0.125	0.064	0.125	0.064	0.032	0.032	0.064	0.064	0.064	0.064	0.016	0.125	0.125	0.064	0.125	0.064	0.016	0.064	0.125	0.064	0.064	0.016	0.25	5	0
	5575	0.125	0.032	0.25	0.032	0.125	0.064	0.125	0.064	0.064	0.064	0.125	0.064	0.032	0.032	0.064	0.064	0.125	0.064	0.016	0.125	0.125	0.032	0.125	0.064	0.125	0.064	0.064	0.064					
5	5573	0.004	0.002	<0.016	0.004	0.008	0.004	<0.016	0.002	0.004	0.002	0.008	<0.016	0.002	0.002	0.004	0.008	0.008	<0.016	<0.002	<0.016	0.008	<0.016	0.008	0.008	0.004	0.004	0.016	<0.016	0.004 or 0.008	0.002	0.016	3 or 8	0
	5577	0.004	<0.002	0.016	0.004	0.008	0.004	<0.016	0.004	0.004	0.004	0.008	<0.016	0.002	<0.002	0.004	0.008	0.008	<0.016	<0.002	<0.016	0.008	<0.016	0.008	0.008	0.008	0.004	0.016	<0.016					
6	5574	1	0.5	2	0.5	1	1	1	0.5	1	1	0.5	1	1	0.25	1	1	1	1	0.25	1	1	1	1	0.5	0.5	1	4	0.5	1	0.25	4	8	0
	5576	1	0.5	2	0.5	1	1	1	0.5	1	0.5	0.5	1	1	0.5	1	1	1	1	0.25	1	1	0.5	1	1	1	0.5	4	0.5					
	5578	1	0.5	1	0.5	1	1	1	0.5	1	1	1	1	1	0.25	1	1	1	1	0.25	1	1	0.5	1	1	0.5	1	4	0.5					

Table A1.7. Country coded category of susceptibility concordance – ciprofloxacin

		Laboratory codes																																						
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94929	94936	94937	94938	95588	95589	Total	No. S	No. I	No. R	Consensus	Concordance (%)
1	5569	R	S	R	S	I	R	I	R	R	R	I	R	R	I	I	R	I	R	S	I	I	I	I	I	R	R	I	I	28	3	13	12	I	46.4
2	5570	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	28	28	0	0	S	100.0
3	5571	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	28	0	0	28	R	100.0
4	5572	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	56	0	0	56	R	100.0
	5575	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R						
5	5573	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	56	56	0	0	S	100.0
	5577	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S						
6	5574	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	84	0	0	84	R	100.0
	5576	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R						
	5578	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R						
																																		Total	91.1

Table A1.8. Country coded MIC values (mg/L) – ciprofloxacin

		Laboratory codes																																						
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94929	94936	94937	94938	95588	95589	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
1	5569	0.064	0.032	0.125	0.064	0.064	0.125	0.064	0.125	0.25	0.064	0.064	>32	0.125	0.064	0.064	N	0.064	0.125	0.064	0.064	0.064	0.064	0.064	0.064	0.064	0.064	0.125	0.064	0.064	0.064	0.032	>32	1	1
2	5570	0.004	<0.002	0.004	0.002	0.004	0.008	0.004	0.004	0.008	0.004	<0.002	0.008	0.004	0.004	0.004	N	0.008	<0.004	<0.002	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.008	0.004	0.004	0.002	0.008	0	0
3	5571	4	1	4	4	2	16	8	4	8	8	4	>32	4	4	8	N	4	2	2	4	4	4	4	4	16	4	8	2	4	1	>32	3	1
4	5572	32	>32	>32	32	>32	32	>32	>32	>32	>32.0	>32	>32	>32	>32	>32	N	>32	>32	>32	>32	>32	>32	>32	32	>32	>32	>32	>32	>32	32	>32	0	0
	5575	32	>32	>32	32	>32	32	>32	>32	>32	>32.0	>32	>32	>32	>32	>32	N	>32	>32	>32	>32	>32	>32	>32	32	>32	>32	>32	>32					
5	5573	0.004	0.008	0.008	0.125	0.008	0.008	0.004	0.008	0.016	0.008	0.008	0.008	0.008	0.008	0.004	N	0.008	0.008	0.008	0.008	0.008	0.008	0.008	0.008	0.008	0.008	0.008	0.004	0.008	0.002	0.125	2	1
	5577	0.008	0.002	0.008	0.004	0.008	0.008	0.008	0.004	0.016	0.008	0.008	0.008	0.008	0.008	0.004	N	0.008	0.008	0.002	0.008	0.008	0.008	0.008	0.008	0.016	0.008	0.008	0.004					
6	5574	32	16	>32	32	>32	32	>32	>32	>32	>32	>32	>32	>32	>32	>32	N	>32	>32	>32	>32	>32	>32	>32	32	>32	>32	>32	>32	>32	8	>32	0	2
	5576	32	16	>32	32	>32	32	>32	>32	>32	>32	>32	>32	>32	>32	>32	N	>32	>32	8	>32	>32	>32	>32	32	>32	>32	>32	>32					
	5578	32	16	>32	32	>32	32	>32	>32	>32	>32	>32	>32	>32	>32	>32	N	>32	>32	8	>32	>32	>32	>32	32	>32	>32	>32	>32					

Table A1.9. Country coded category of susceptibility concordance – spectinomycin

		Laboratory codes																																		
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94929	94936	94937	94938	95588	95589	Total	No. S	No. I	No. R	Consensus	Concordance (%)
1	5569	N	N	S	S	S	S	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	N	20	20	0	0	S	100.0
2	5570	N	N	S	S	S	S	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	N	20	20	0	0	S	100.0
3	5571	N	N	S	S	S	S	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	N	20	20	0	0	S	100.0
4	5572	N	N	S	S	S	S	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	N	40	40	0	0	S	100.0
	5575	N	N	S	S	S	S	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	N						
5	5573	N	N	S	S	S	S	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	N	40	40	0	0	S	100.0
	5577	N	N	S	S	S	S	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	N						
6	5574	N	N	S	S	S	S	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	N	59	58	0	1	S	98.3
	5576	N	N	S	S	S	S	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	N						
	5578	N	N	S	S	S	S	S	S	S	S	N	N	S	S	S	N	R	S	S	N	S	S	S	N	S	N	S	N						
																																		Total	99.7

N – not retrieved or susceptibility category not supplied.

Table A1.10. Country coded MIC values (mg/L) – spectinomycin

		Laboratory codes																																		
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94929	94936	94937	94938	95588	95589	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
1	5569	N	N	32	8	16	16	8	16	16	8	N	N	16	8	16	N	16	≤16	4	N	16	4	16	N	4	N	N	N	16	4	32	3	0
2	5570	N	N	16	8	16	16	8	16	16	8	N	N	16	4	16	N	16	≤16	16	N	16	8	16	N	8	N	8	N	16	4	16	1	0
3	5571	N	N	16	8	16	16	8	16	16	8	N	N	16	8	8	N	16	≤16	8	N	16	8	16	N	8	N	8	N	16	8	16	0	0
4	5572	N	N	16	8	16	16	8	16	16	8	N	N	16	16	16	N	16	≤16	8	N	16	8	16	N	2	N	16	N	16	2	16	0	1
	5575	N	N	16	8	16	16	8	16	16	16	N	N	16	16	16	N	16	≤16	8	N	16	8	16	N	8	N	16	N					
5	5573	N	N	16	8	16	16	8	16	32	16	N	N	16	8	16	N	16	≤16	4	N	16	8	32	N	16	N	16	N	16	4	32	2	0
	5577	N	N	16	8	16	16	8	16	32	8	N	N	16	16	16	N	16	≤16	4	N	16	16	32	N	16	N	16	N					
6	5574	N	N	16	8	16	16	8	16	16	8	N	N	16	8	16	N	16	≤16	4	N	16	8	16	N	8	N	16	N	16	4	16	2	0
	5576	N	N	16	8	16	16	8	16	16	16	N	N	16	8	16	N	16	≤16	8	N	16	8	16	N	8	N	16	N					
	5578	N	N	16	8	16	16	8	16	16	8	N	N	16	8	16	N	16	≤16	4	N	16	8	16	N	16	N	16	N					

Note: Laboratories 90984, 92613, 92624, 92629, 92630, 93997, 94936 and 95589 did not submit spectinomycin data.
N: no result; not retrieved, not tested or MIC not supplied.

Table A1.11. Country coded MIC values (mg/L) – gentamicin

		Laboratory codes																																				
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94929	94936	94937	94938	95588	95589	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
1	5569	4	N	8	4	N	4	4	4	8	4	N	8	8	2	N	4	4	N	4	2	4	N	4	N	4	N	N	N	4	2	8	0	0
2	5570	4	N	8	4	N	8	4	8	8	8	N	8	8	2	N	4	4	N	2	2	4	N	4	N	4	N	N	N	4	2	8	0	0
3	5571	8	N	16	4	N	16	4	8	8	4	N	8	8	4	N	4	4	N	2	8	4	N	4	N	8	N	N	N	4	2	16	2	0
4	5572	8	N	8	4	N	4	4	4	8	4	N	8	8	4	N	4	4	N	4	4	4	N	4	N	2	N	N	N	4	2	8	0	0
	5575	4	N	8	4	N	8	4	4	8	8	N	8	8	4	N	4	4	N	4	4	4	N	4	N	4	N	N	N					
5	5573	4	N	4	4	N	4	1	4	4	4	N	4	4	2	N	2	2	N	1	2	2	N	4	N	4	N	N	N	4	1	4	3	0
	5577	2	N	4	4	N	4	2	4	4	2	N	4	4	2	N	2	4	N	1	2	2	N	4	N	4	N	N	N					
6	5574	8	N	16	4	N	8	4	8	32	8	N	16	16	4	N	4	8	N	4	4	8	N	8	N	4	N	N	N	4	1	32	8	1
	5576	8	N	16	8	N	8	4	8	16	8	N	16	16	4	N	4	4	N	4	4	8	N	8	N	8	N	N	N					
	5578	2	N	4	4	N	4	2	4	4	2	N	4	4	2	N	2	4	N	1	2	2	N	4	N	4	N	N	N					

Note: Laboratories 90984, 92613, 92623, 92628, 92629, 92634, 92636, 92945, 94603, and 95589 did not submit gentamicin data.
N: no result; not retrieved, not tested or MIC not supplied.

Table A1.12. Country coded concordance – beta-lactamase

		Laboratory codes																																				
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94929	94936	94937	94938	95588	95589	Total	No. S	No. I	No. R	Consensus	Concordance (%)
1	5569	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	26	26	0	0	S	100.0
2	5570	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	26	26	0	0	S	100.0
3	5571	R	R	R	R	R	R	R	R	R	R	N	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	26	0	0	26	R	100.0
4	5572	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	52	52	0	0	S	100.0
	5575	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N						
5	5573	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	51	51	0	0	S	100.0
	5577	S	N	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N						
6	5574	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	77	77	0	0	S	100.0
	5576	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N						
	5578	S	N	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N						
																																		Total	100.0

Note: Laboratories 92629 and 95589 did not submit any beta-lactamase testing results.
N: no result; not retrieved or beta-lactamase result not supplied.

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