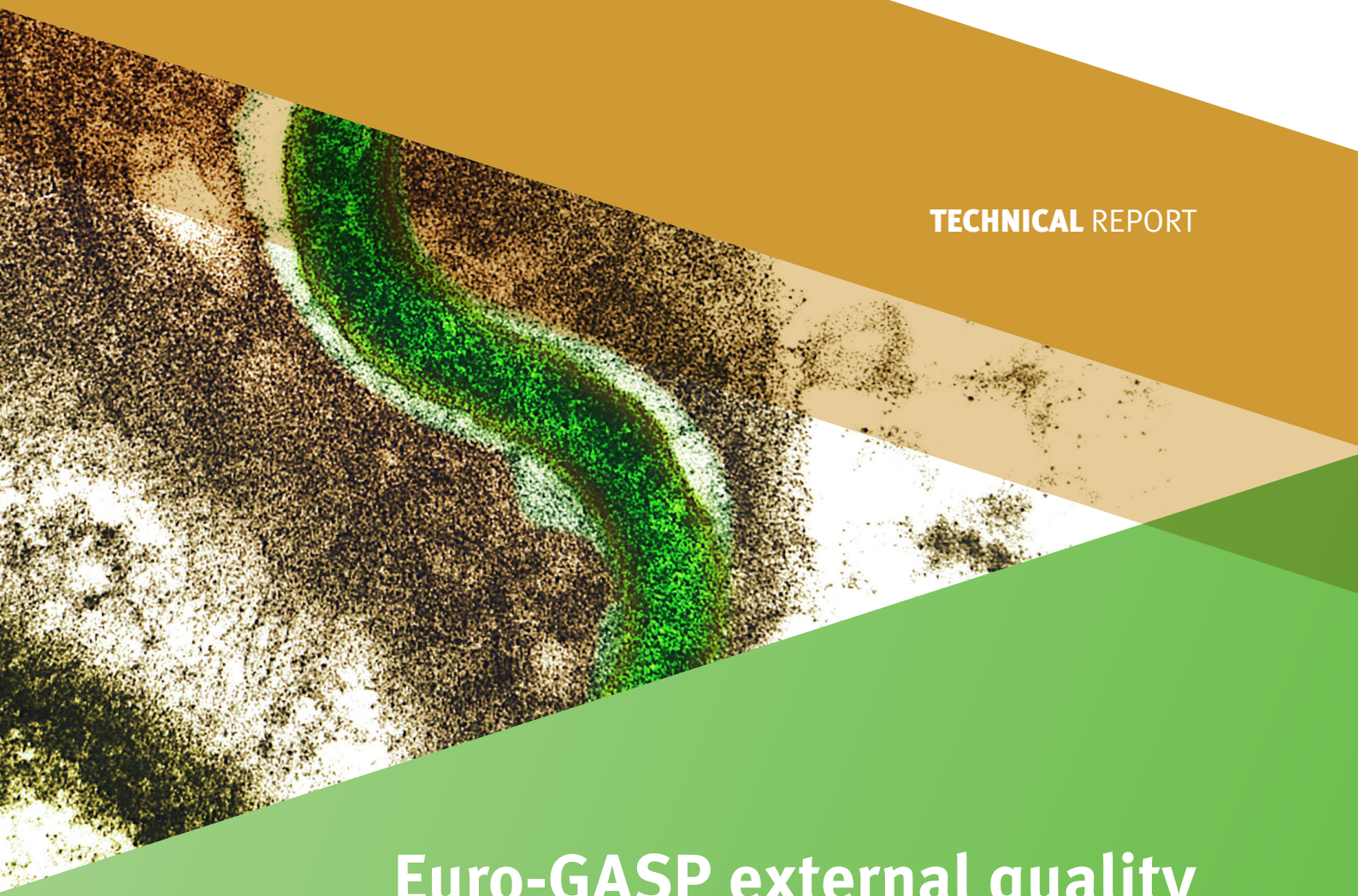

TECHNICAL REPORT

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

2021

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2021

This report was commissioned by the European Centre for Disease Prevention and Control (ECDC), coordinated by Benjamin Bluemel and Marieke J. van der Werf and produced by Michaela Day, Thinushaa Uthayakumaran and Michelle Cole, 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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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
UKHSA	United Kingdom Health Security Agency
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, even when using differing methodologies.

Materials and methods

The EQA specimen panel of 10 gonococcal isolates was selected by UK Health Security Agency (UKHSA) (formerly Public Health England) 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 as singular isolates, 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, O, V and X, and two clinical isolates obtained in the UK in 2020. Participating laboratories were requested to test the EQA panel using their 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 UKHSA, who decoded and analysed the results based on the categories of susceptibility assigned. Susceptibility category concordance (categorical agreement) was assessed using the consensus category (the category most often reported) 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 2021, 28 laboratories in 28 European Union/European Economic Area countries were dispatched 10 gonococcal isolates for antimicrobial susceptibility testing. Only 26 of the 28 participating laboratories (one laboratory was unable to retrieve *N. gonorrhoeae* from the freeze-dried cultures and one did not receive the isolates) returned EQA results to UK NEQAS. Most (96.4%) laboratories used MIC gradient strip tests and all used EUCAST breakpoints. The highest level of categorical agreement was seen with spectinomycin and ceftriaxone (both 100%), while the lowest was seen with ciprofloxacin (92.9%). Compared to the previous distribution, except for ciprofloxacin (92.9% in 2021, 99.3% in 2020), categorical agreement increased for all antibiotics with the largest increase observed for azithromycin (96.4% in 2021, 90.4% in 2020).

Overall, 91.5% and 96.0% of the reported minimum inhibitory concentrations (MICs) were within one (essential agreement) and two doubling dilutions of the modal MIC, demonstrating that the level of essential agreement has decreased since 2020 (93.8%). However, this decrease may also be due to the fact that there were different laboratories participating in the analysis for each year (76% were decentralised testing laboratories in the 2020 report, 67% were decentralised testing laboratories in this report). When comparing the 2021 and 2020 EQA schemes, the level of essential agreement for individual antimicrobials decreased for ciprofloxacin, ceftriaxone, azithromycin, and gentamicin and increased for cefixime and spectinomycin. Of the 26 laboratories, 19 (73%) achieved an intralaboratory MIC concordance percentage score of 95% or higher, with nine laboratories obtaining a score of 100%.

Discussion and conclusion

The harmonisation of susceptibility testing methodologies and breakpoints used by participating laboratories was maintained in 2021, with most laboratories using MIC gradient strip tests and all applying EUCAST breakpoints for interpretation of MIC results. Overall, most laboratories participating in the 2021 EQA scheme performed well and showed good levels of competency in testing *N. gonorrhoeae* isolates of unknown phenotype. When compared with 2020, the level of categorical agreement increased for all tested antibiotics, except ciprofloxacin, with the largest increase for azithromycin. In most cases, the inter- and intralaboratory concordance was high, demonstrating comparability between different testing methodologies and promoting 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 five centres in need of further guidance to help bring them in line with the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) recommended target (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 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 especially for this purpose. ECDC's disease-specific networks organise a series of EQAs for EU/EEA countries. For 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 2021, the number of laboratories participating in the *N. gonorrhoeae* antimicrobial susceptibility testing EQA increased from 18 to 26. In general, the EQAs have 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 using agar dilution and MIC gradient strip tests, agar 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 United Kingdom Health Security Agency (UKHSA), Örebro University Hospital and ECDC 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 UKHSA to demonstrate a range of susceptibility profiles for relevant therapeutic antimicrobial agents and consisted of four WHO reference gonococcal strains, WHO G, O, V and X [3], and two clinical isolates from the UK isolated in 2020. To measure intralaboratory reproducibility, one of these strains was supplied in triplicate (Strain 4 (WHO X), coded in the EQA as 7057/7060/7061), and two strains were supplied in duplicate (Strain 2 (WHO O), EQA codes 7055/7062 and Strain 6 (H20956), EQA codes 7059/7063). The remaining three strains were supplied as individual isolates (Strain 1 (WHO G), EQA code 7054; Strain 3 (WHO V), EQA code 7056 and Strain 5 (20C21), EQA code 7058). Six different strains were therefore 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 'ECDC Instructions, External Quality Assessment v6. European Gonococcal Antimicrobial Surveillance Programme 2018-2021' [4].

2.2 Susceptibility testing methods

Information was requested on the methodology and the clinical breakpoints/guidelines (e.g. European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints (Table 1) [5]) used for determining the category of susceptibility for each antimicrobial tested. 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 MIC 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

** From January 2019, the EUCAST SIR categories were removed for azithromycin and replaced with an epidemiological cut-off (ECOFF) value of 1 mg/L. Since then, isolates with azithromycin MIC>1 mg/L have been referred to as resistant. Please note there are currently no EUCAST interpretive criteria for gentamicin [5].*

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 UKHSA for further collated analysis.

For the analysis, all MIC results that fell between dilutions on 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 were established for each strain.

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 MIC) 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 (a total of six in this distribution; consensus calculated from all isolates in the triplicate or duplicate sets) were calculated once all participating laboratories had reported their results. 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 four) and two duplicate strains (strains two and six). 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 more 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 comparing them 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 2021 EQA scheme (QA21) 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. The consensus category of susceptibility for each strain tested is also shown. The strains tested demonstrated a range of phenotypes, and none of the strains were 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 4; WHO X), and the other had a high-level resistance to azithromycin (MIC >256 mg/L, Strain 3; WHO V).
- One strain had an MIC above the azithromycin ECOFF (1 mg/L) (Strain 5; 20C21).
- Two strains were resistant to ciprofloxacin (Strain 1; WHO G, Strain 6; H20956).
- One strain was resistant to spectinomycin (Strain 2; WHO O).

3.2 Susceptibility testing methods

In July 2021, 28 laboratories in 28 countries were dispatched 10 gonococcal isolates (QA21) for susceptibility testing from UK NEQAS. Only 26 laboratories returned results to UK NEQAS, Latvia was not able to retrieve any *N. gonorrhoeae* from the freeze-dried vials and the Netherlands did not receive the freeze-dried specimens for testing although they were dispatched by UKNEQAS (Figure 1). Results from three EU/EAA countries (Romania, Lithuania and Bulgaria) which do not participate in the Euro-GASP sentinel study but do participate in the EQA, are included in this report. Results from these countries were not included in previous reports. The changes in participants have affected the overall percentage of decentralised Euro-GASP laboratories included in the analysis for 2021 (67% decentralised Euro-GASP participants in 2021 and 76% in 2020). 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 (42%) were the most common testing methodology and medium used, respectively.

Figure 1. Countries participating in the 2021 *N. gonorrhoeae* susceptibility testing EQA scheme

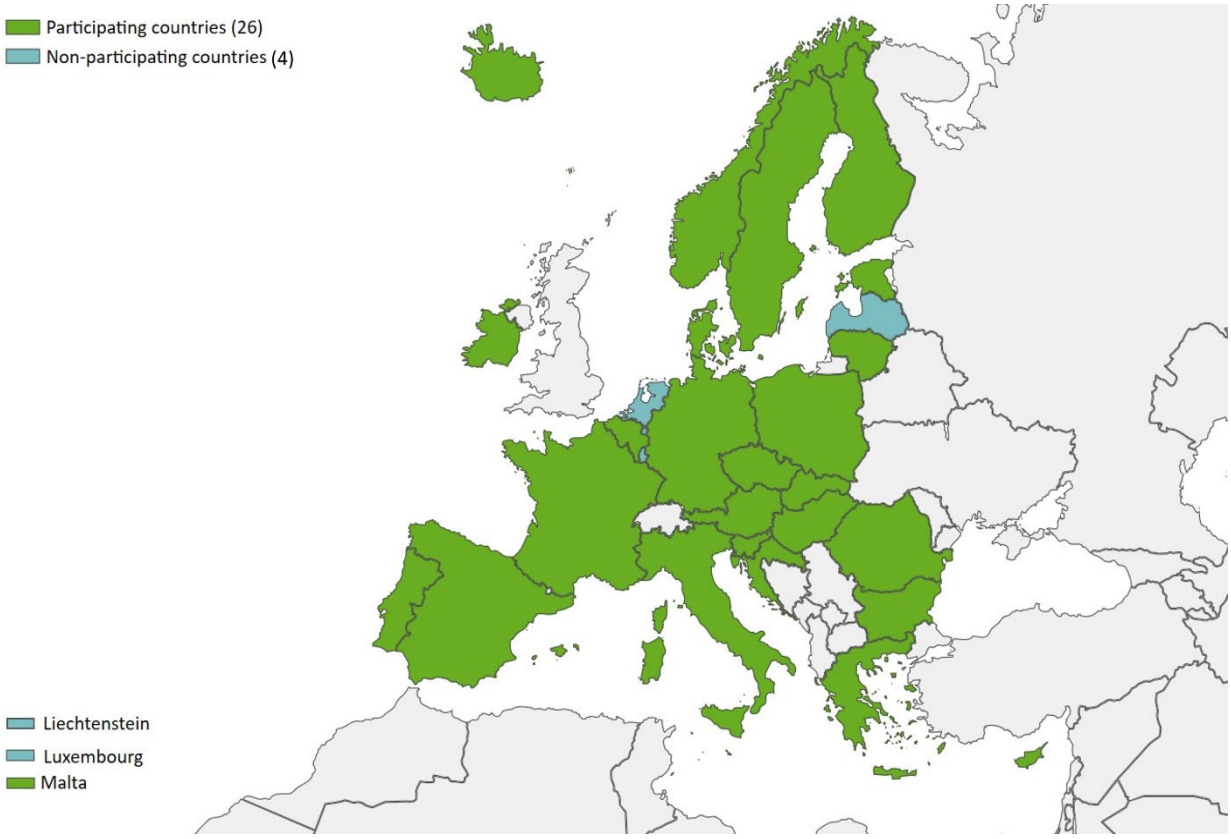


Table 2. Consensus category, modal MIC (range) for MIC gradient strip test and agar dilution (mg/L) and the percentage concordance of susceptibility category for the 2021 EQA panel

Strain		Azithromycin consensus	Cefixime consensus	Ceftriaxone consensus	Ciprofloxacin consensus	Gentamicin consensus	Spectinomycin consensus	Beta-lactamase consensus
Strain 1: 7054 (WHO G [3]) CipR	Consensus category	S	S	S	R	N/A	S	Neg
	Modal MIC (range)	0.25 (≤0.016 - 0.5)	≤0.016 (≤0.016 - 0.032)	0.004 (0.002 - 0.016)	0.064 (0.032 - 0.125)	4 (2 - 8)	16 (2 - 16)	N/A
	Susceptibility category concordance (%)	100	100	100	57.7	N/A	100	100
	Reference MIC [3]	0.25	≤0.016	≤0.016	0.125	4	16	N/A
Strain 2: 7055/7062 (WHO O [3]) BLP, SpcR	Consensus category	S	S	S	S	N/A	R	POS
	Modal MIC (range)	0.25 (≤0.016 - 1)	≤0.016 (≤0.016 - 0.032)	0.016 (≤0.002 - 0.032)	0.008 (0.002 - 0.016)	8 (≤0.016 - 16)	>1024 (1024 - >1024)	N/A
	Susceptibility category concordance (%)	100	100	100	100	N/A	100	93.8
	Reference MIC [3]	0.25	≤0.016	0.032	0.008	4	>1024	N/A
Strain 3: 7056 (WHO V [3]) BLP, Az>256, CipR	Consensus category	R	S	S	R	N/A	S	POS
	Modal MIC (range)	>256 (>32 - >256)	≤0.016 (≤0.016 - 0.032)	0.032 (0.002 - 0.064)	>32 (8 - >32)	8 (1 - 16)	16 (1 - 16)	N/A
	Susceptibility category concordance (%)	100	100	100	100	N/A	100	100
	Reference MIC [3]	>256	≤0.016	0.064	>32	8	16	N/A
Strain 4: 7057/7060/ 7061 (WHO X [3]) CfmR, CroR, CipR	Consensus category	S	R	R	R	N/A	S	NEG
	Modal MIC (range)	0.5 (≤0.016 - 1)	4 (0.032 - 8)	2 (0.25 - 2)	>32 (32 - >32)	4 (1 - 16)	16 (2 - 16)	N/A
	Susceptibility category concordance (%)	100	98.7	100	100	N/A	100	97.2
	Reference MIC [3]	0.5	4	2	>32	4	16	N/A
Strain 5: 7058 (20C21) Az>1 mg/L	Consensus category	R	S	S	S	N/A	S	NEG
	Modal MIC (range)	2 (1 - 4)	≤0.016 (≤0.016 - 0.032)	0.008 (0.004 - 0.032)	0.016 (0.008 - 0.064)	8 (2 - 16)	16 (8 - 32)	N/A
	Susceptibility category concordance (%)	88	100	100	100	N/A	100	100
	Reference MIC*	2	≤0.016	≤0.016	0.032	4	16	N/A
Strain 6: 7059/7063 (H20956) CipR	Consensus category	S	S	S	R	N/A	S	NEG
	Modal MIC (range)	0.5 (0.25 - 2)	0.064 (0.032 - 0.25)	0.032 (0.004 - 0.064)	>32 (2 - >32)	8 (1 - 16)	16 (8 - 16)	N/A
	Susceptibility category concordance (%)	90.5	98	100	100	N/A	100	100
	Reference MIC*	0.5	0.064	0.032	24	4	8	N/A

** 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.
S: susceptible; N/A: not available; MIC: minimum inhibitory concentration; WHO: World Health Organization; BLP: beta-lactamase production; Az: azithromycin; CfmR: cefixime-resistant; CroR: ceftriaxone-resistant; CipR: ciprofloxacin-resistant; SpcR: spectinomycin-resistant; R: resistant; NEG: negative; POS: positive. [3].

3.3 Interpretation of MICs

All 26 laboratories reported adherence to the EUCAST breakpoints (Table 1) [5]. Most laboratories that tested gentamicin did not interpret categories of susceptibility as there are currently no internationally defined interpretive criteria for this antimicrobial. Two laboratories did submit categories of susceptibility for gentamicin, using local interpretive criteria however these data were not analysed in the report.

Table 3. Susceptibility testing methods used by participating laboratories, July 2021 EQA

	Number of participating laboratories (%)	
Type of susceptibility test used	**2020**	**2021**
MIC gradient strip tests	24 (96%)	25 (96%)
Agar dilution	2 (8%)	2 (8%)
Testing guidelines used		
EUCAST	25 (100%)	26 (100%)
Agar base used		
GC agar base	11 (44%)	11 (42%)
Chocolatised blood agar	8 (32%)	9 (35%)
Diagnostic sensitivity agar	2 (8%)	1 (4%)
Thayer-Martin/Mueller-Hinton	2 (8%)	3 (12%)
Other	2* (8%)	2 (8%)

**Includes one unknown (not reported).*
Please note, countries that reported using agar dilution also reported use of gradient strips.

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 annexes (Tables A1.6 – A1.12). Analysis of the breakdown of results has highlighted that twelve laboratories reported isolates with MICs greater than two doubling dilutions different from the modal MIC. Five laboratories reported more than 5% of results greater than two doubling dilutions from the modal MIC; one of these does not currently participate in the Euro-GASP sentinel study, three participate in Euro-GASP via centralised testing and one has very low isolate numbers annually so this will not have an impact on the Euro-GASP data. Nevertheless, the laboratories will be supported to improve the quality of their susceptibility testing.

In the 2020 EQA (QA20), 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 QA21 EQA but still has over 5% of results more than two doubling dilutions from the modal. It should be noted that this laboratory does not test the full panel of antibiotics so instances of MICs outside of essential agreement will have a larger impact on percentage scores than for other laboratories that test against the full panel. This laboratory still participates in the Euro-GASP sentinel study via centralised testing.

3.5 Susceptibility category concordance

Susceptibility category data for azithromycin, ceftriaxone and ciprofloxacin were submitted from all 26 laboratories, cefixime from 25 laboratories, beta-lactamase production from 24 laboratories, and spectinomycin from 18 laboratories. Seven laboratories submitted incomplete susceptibility category results.

Incomplete data were submitted for:

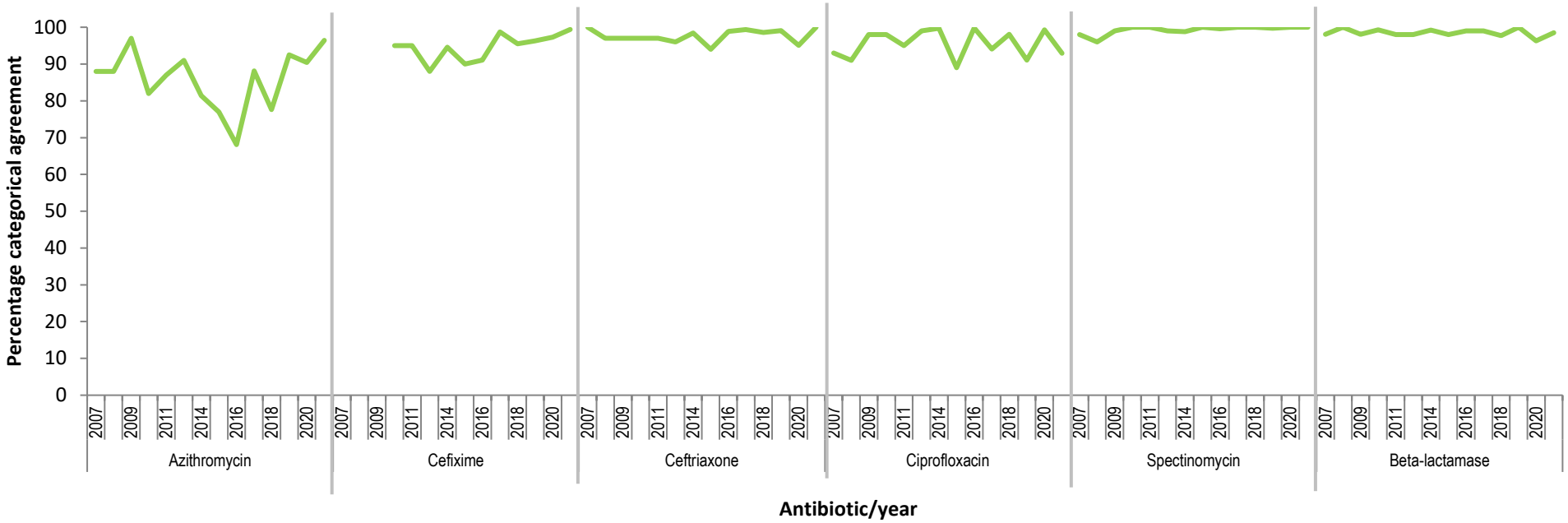
- azithromycin (laboratory 92624, laboratory 92626, laboratory 92630 and laboratory 92784 did not assign an SIR category for isolates with MICs below the ECOFF, laboratory 94938 did not interpret any azithromycin MICs);
- cefixime (laboratory 92626 (isolate 7063 only), laboratory 94602 (isolate 7054 only);
- ciprofloxacin (laboratory 94938 (isolate 7060 only);
- spectinomycin (laboratory 92632 (isolate 7056 and 7059) laboratory 94602 (isolate 7061 only).

Laboratory 92621 did not test for cefixime susceptibility (Table A1.3), laboratories 90969, 90984, 92613, 92621, 93997, 94936, 94938 and 95589 did not test for spectinomycin susceptibility (Table A1.9). Two laboratories (94936 and 95589) did not test for the production of beta-lactamases (Table A1.12).

The highest levels of categorical agreement were seen for spectinomycin and ceftriaxone (both 100%), closely followed by cefixime (99.4%). The lowest level was seen for ciprofloxacin, with 92.9% 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) [6] and ECDC Euro-GASP (QA2010-20) [7-16], there is a slight increase in concordance for most antimicrobials tested (Figure 2). The exception is ciprofloxacin, which displayed a decrease in concordance, (92.9%) compared to 2020 (99.3%). However, concordance for ciprofloxacin fluctuates annually and is still at a higher level in this EQA distribution than was observed in 2019 (91.1%). Spectinomycin concordance remains high at 100% (Figure 2).

Figure 2. Longitudinal comparison of EQA interlaboratory antimicrobial categorical agreement, EU/EEA, 2007-2021



Note: cefixime was added to the EQA scheme in 2010.
ESSTI EQA distributions (2007 – 2009) comprised of 30 isolates (10 strains in triplicate).
The number of laboratories participating in the EQA has 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), 28 laboratories (2019), 25 laboratories (2020), and 26 laboratories (2021).

3.6 MIC concordance

Overall, MIC essential agreement (MIC results within one doubling dilution of the modal MIC) was at 91.5% for all antimicrobials tested (Table 4), which is lower than the level of essential agreement achieved with the previous EQA panel distribution in 2020 (93.8%) [16]. The highest level of essential agreement was seen for cefixime (98.8%) and the lowest for ceftriaxone (84.8%) which is a change from the observations in QA20 when the highest essential agreement was for gentamicin (97.0%) and the lowest for cefixime (90.2%) (Table 4) [16]. For all MICs combined, 96.0% 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 (8.8%), and cefixime had the lowest (0.8%).

When MIC concordance data are compared with previous ECDC Euro-GASP EQA distributions (QA2010–20) [7-16], the proportion of results within two doubling dilutions of the modal MIC has decreased for most antimicrobials tested since the stabilisation observed for the past two distributions in 2019 and 2020. The exception to this is cefixime which remained stable in 2021 (Figure 3).

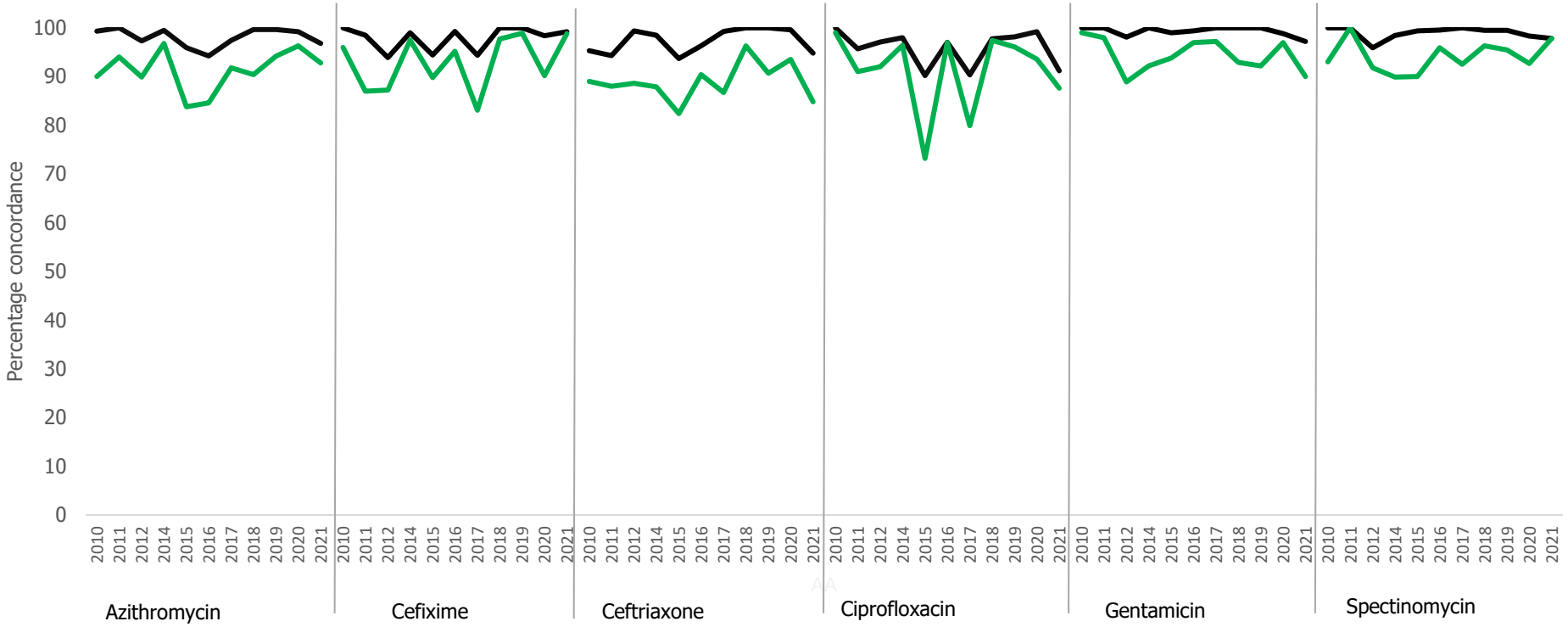
Table 4. Variation from modal MIC for EQA QA21

QA21	Azithromycin		Cefixime		Ceftriaxone		Ciprofloxacin		Gentamicin		Spectinomycin		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Within +/- one doubling dilution	232	92.8	237	98.8	212	84.8	219	87.6	162	90.0	173	96.1	1235	91.5
Within +/- two doubling dilutions	10	4.0	1	0.4	25	10.0	9	3.6	13	7.2	3	1.7	61	4.5
More than +/- two doubling dilutions	8	3.2	2	0.8	13	5.2	22	8.8	5	2.8	4	2.2	54	4.0
Total number of isolates with MIC data	250		240		250		250		180		180		1350	

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, 2010−2021

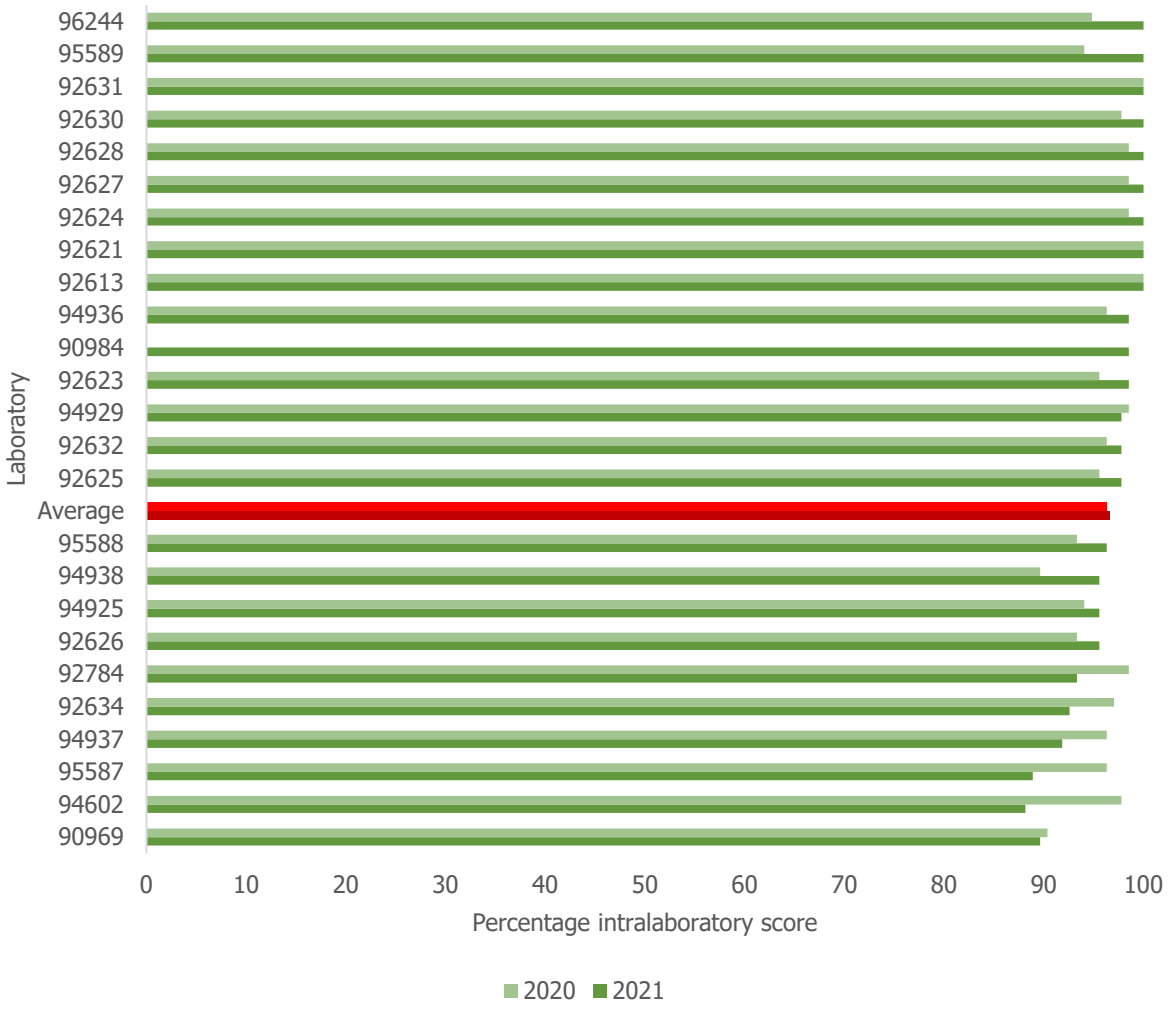


Note: The number of laboratories participating in the EQA has changed over time: 18 laboratories (2010), 20 laboratories (2011), 19 laboratories (2012), 21 laboratories (2014), 26 laboratories (2015), 27 laboratories (2016), 28 laboratories (2017), 27 laboratories (2018), 28 laboratories (2019), 25 laboratories (2020) and 26 laboratories (2021).

3.7 Intralaboratory concordance

Intralaboratory concordance was examined using the triplicate (strain four) and two duplicate strains (strains two and six). Figure 4 shows the results for the 2020 and 2021 concordance scores in comparison with averages scores for 2021 (96.7.%) and 2020 (96.3%). Most laboratories performed well, with 77% of laboratories (20/26) scoring 95% concordance or higher in QA2021, including nine laboratories obtaining a perfect score of 100%. Of the six laboratories scoring less than 95%, only two participate in Euro-GASP via decentralised testing. These laboratories did not have either 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. Only one laboratory with an intralaboratory concordance score below 95% in the 2020 EQA distribution also scored less than 95% concordance in the 2021 distribution, and this laboratory is a non-Euro-GASP participant. Five laboratories with an intralaboratory concordance score of less than 95% in the 2020 EQA improved in the 2021 distribution, scoring over 95% concordance.

Figure 4. Intralaboratory MIC concordance percentage 2020 versus 2021

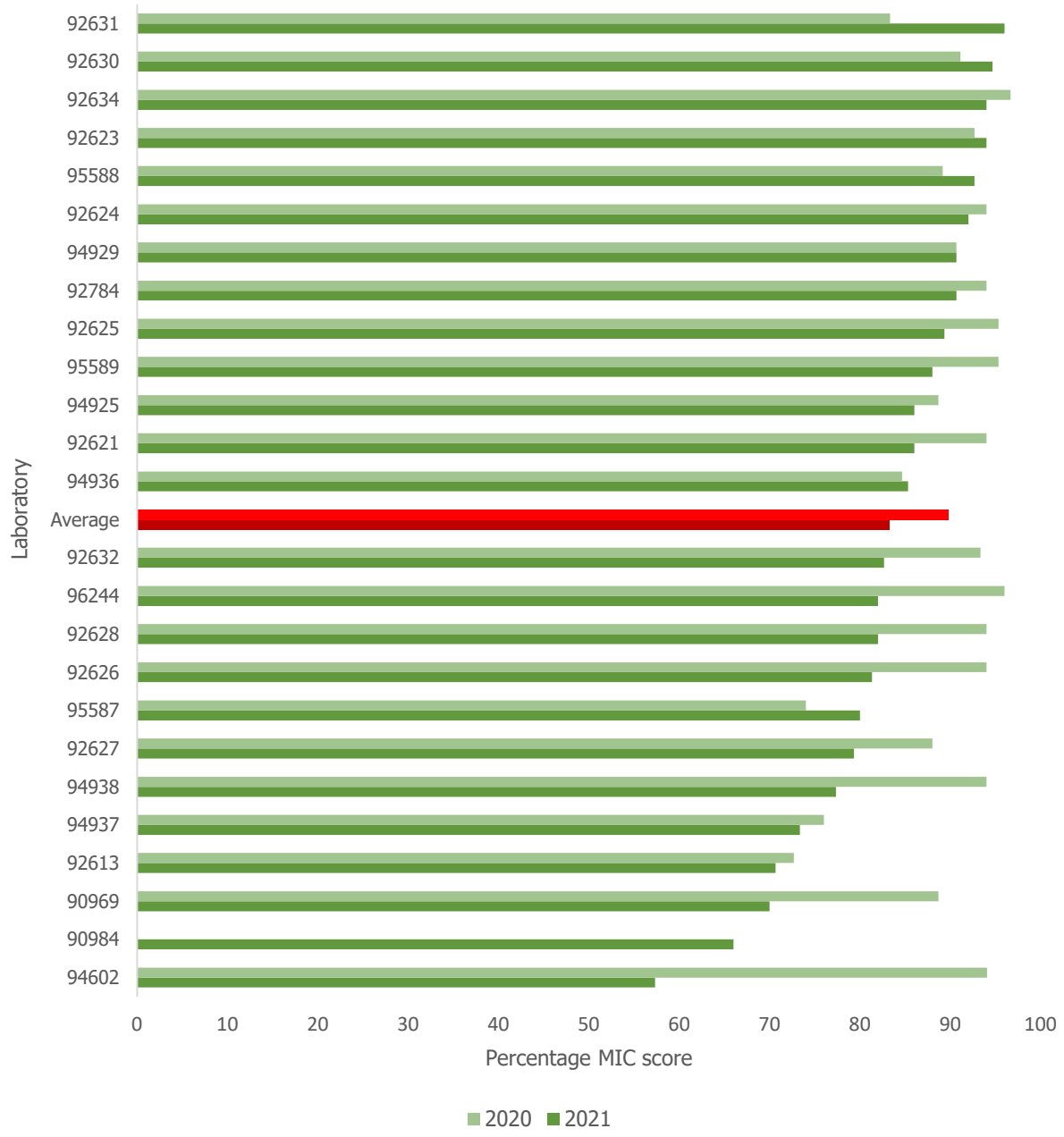


Note: The light red and dark red bars show the average score in 2020 and 2021, respectively.

3.8 Overall EQA scores

Figure 5 shows the overall MIC scores for the 2021 EQA versus the 2020 EQA, with the average score shown in red (2021: 83.3% (dark red); 2020: 89.8% (light red)). For the 2021 EQA, 12 laboratories had a below-average score, five of which had over 5% of results more 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 in terms of minor, major, very major or no faults. The overall percentage score value is shown at the base of each bar.

Figure 5. EQA overall MIC scores, 2020 versus 2021



Note: The light red and dark red bars show the average score in 2020 and 2021, respectively.

Laboratory 93997 is not included in the chart as it did not provide any MIC data for the core antimicrobials in 2021.

Figure 6. EQA overall categorical agreement scores, 2021

Maximum score was 150, unless otherwise specified. The overall percentage score is shown at the base of each bar.

** Maximum score was 95 as azithromycin MICs were not interpreted and MIC of strain 7056 was not interpreted for ciprofloxacin*

~ Maximum score was 110 as an SIR category was not assigned to azithromycin MICs below the ECOFF

4. Discussion

The 2021 Euro-GASP EQA distribution was sent out to 28 laboratories in 28 participating countries, most laboratories (92.9%, 26/28) reported results for all or most of the requested tests. Most laboratories (96%) 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 EU/EEA. The GC agar base continues to be the most frequently-used media, followed by chocolatised blood agar.

In general, the categorical agreement increased for most antimicrobials compared with the previous distribution; the exception was ciprofloxacin, for which categorical agreement decreased (from 99.3% in 2020 to 92.9% in 2021). The highest increase was seen in azithromycin (from 90.4% to 96.4%). For ciprofloxacin, one of the strains had an MIC close to a breakpoint (modal MIC = 0.064 mg/L, reference MIC = 0.125 mg/L, resistance breakpoint MIC>0.06 mg/L) so the lower categorical agreement was not unexpected. The increase in categorical concordance for azithromycin may be due to improvement in interpretation of the azithromycin ECOFF, which was introduced in 2019, and the inclusion of only one strain (strain five) with an MIC one doubling dilution above the ECOFF (modal MIC= 2 mg/L).

Overall, categorical agreement scores were high, with only one laboratory scoring less than 95%, which was due to two major faults (two MIC doubling dilutions difference) in MICs and not due to incorrect interpretation. Five laboratories had a very major fault (designating a resistant isolate as 'susceptible'), which for two of them was due to a minor fault in the ciprofloxacin MIC for strain 7054. For the same isolate, another laboratory interpreted an MIC at the breakpoint (MIC = 0.064 mg/L, breakpoint MIC>0.064 mg/L) as 'susceptible' whereas the majority of other participants that obtained this MIC interpreted it as 'susceptible, increased exposure'. The other very major faults were due to minor faults in the azithromycin MIC for strain 7058 as the strain had a modal MIC one doubling dilution above the ECOFF (2 mg/L). Two of the five laboratories involved participate in Euro-GASP via centralised testing, two are non-participants and one participates via decentralised testing but only reports very low numbers of results annually (n<5). The average categorical concordance for the core antimicrobials was 99.0%, a slight improvement on the 98.1% observed in 2020. Essential MIC agreement was lower than for the 2020 distribution - 91.5% compared to 98.2%. The decrease observed for 2021 is possibly a consequence of different laboratories participating in the distribution, the absence of the UK and the Netherlands, both of which usually have high levels of essential agreement, and the inclusion of non-Euro-GASP participants in the 2021 analysis (Bulgaria, Lithuania and Romania). Concordance of beta-lactamase detection increased slightly in 2021 to 98.5%.

Breakdown of EQA susceptibility testing results by laboratory allowed for detailed analysis of individual laboratory performance. In the 2021 EQA, laboratories performed well in general, with a good level of interlaboratory and intralaboratory concordance of results. Five laboratories reported over 5% of results greater than two MIC doubling dilutions from the modal MIC, an increase on 2020, which may in part be explained by the fact that different laboratories participated in the two EQA exercises, with an increase in the number of non-decentralised testing laboratories. As one of these laboratories does not currently participate in the Euro-GASP sentinel study, three participate in Euro-GASP via centralised testing and one has very low isolate numbers annually, the impact on the quality of the data in TESSy is negligible. The one laboratory reporting more than 5% variation from the modal MIC in QA20 improved its results slightly in the QA21. However, since the laboratory tested a lower number of antibiotics it still had over 5% of results greater than two doubling dilutions from the modal. This laboratory still participates in Euro-GASP via centralised testing.

It should be noted that the methods used for the antimicrobial 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 has been published [17].

5. Conclusion

The laboratories participating in the QA21 EQA scheme for antimicrobial susceptibility testing of *N. gonorrhoeae* showed good levels of competency and capability in recovering and testing strains of unknown phenotype. Intralaboratory essential agreement for the different strains improved compared to the 2020 EQA distribution, showing consistency of testing within laboratories. Although interlaboratory essential agreement decreased in 2021 against 2020, it remains high on average despite the increase in the number of non-decentralised testing laboratories included in the analysis. This promotes confidence in Euro-GASP de-centralised antimicrobial susceptibility testing and the 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 Euro-GASP EQA plays an important role in ensuring that results from different submitting laboratories are comparable and that significant over- and under-reporting of antimicrobial resistance does 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 ensure their own quality assurance in a variety of diagnostic and antimicrobial susceptibility testing methods. Antimicrobial susceptibility results from Euro-GASP contribute to the evidence base for gonorrhoea treatment guidelines and local susceptibility testing can be used for individual patient management, so confidence in reporting is essential.

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Annexes QA21 detailed results

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

		Laboratory codes																													
	Strain	90969	90984	92613	92621	92623	92624	92625	92626	92627	92628	92630	92631	92632	92634	92784	93997	94602	94925	94929	94936	94937	94938	95587	95588	95589	96244	Total	No. S	No. I	No. R	Consensus	Concordance (%)
1	7054	S	S	S	S	S	N	S	N	S	S	N	S	S	S	N	S	S	S	S	S	S	N	S	S	S	S	21	21	0	0	S	100.0
2	7055	S	S	S	S	S	N	S	N	S	S	N	S	S	S	N	S	S	S	S	S	S	N	S	S	S	S	42	42	0	0	S	100.0
	7062	S	S	S	S	S	N	S	N	S	S	N	S	S	S	N	S	S	S	S	S	S	N	S	S	S	S						
3	7056	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	R	25	0	0	25	R	100.0
4	7057	S	S	S	S	S	N	S	N	S	S	N	S	S	S	N	S	S	S	S	S	S	N	S	S	S	S	63	63	0	0	S	100.0
	7060	S	S	S	S	S	N	S	N	S	S	N	S	S	S	N	S	S	S	S	S	S	N	S	S	S	S						
	7061	S	S	S	S	S	N	S	N	S	S	N	S	S	S	N	S	S	S	S	S	S	N	S	S	S	S						
5	7058	R	S	S	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	S	N	R	R	R	R	25	3	0	22	R	88.0
6	7059	R	S	S	S	S	N	S	N	R	S	N	S	S	S	N	S	S	S	S	S	S	N	S	S	S	S	42	38	0	4	S	90.5
	7063	R	S	S	S	S	N	S	N	R	S	N	S	S	S	N	S	S	S	S	S	S	N	S	S	S	S						
																																Total	96.4

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

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

		Laboratory codes																													
	Strain	90969	90984	92613	92621	92623	92624	92625	92626	92627	92628	92630	92631	92632	92634	92784	93997	94602	94925	94929	94936	94937	94938	95587	95588	95589	96244	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
1	7054	0.25	0.25	0.25	0.25	0.5	0.25	0.125	0.25	0.5	0.25	0.25	0.25	0.25	0.25	0.25	N	0.016	0.25	0.5	0.5	0.064	0.25	0.25	0.25	0.25	0.25	0.25	0.016	0.5	1	1
2	7055	0.25	<0.016	0.5	0.5	0.5	0.25	0.25	0.25	1	0.5	0.25	0.25	0.25	0.5	0.25	N	0.016	0.25	0.5	0.5	0.125	0.125	0.5	0.25	0.5	0.25	0.25	0.016	1	3	4
	7062	0.5	<0.016	0.5	0.5	0.5	0.25	0.25	0.125	1	0.5	0.25	0.25	0.25	0.5	0.5	N	0.016	0.25	0.5	0.5	0.064	0.25	0.25	0.25	0.5	0.25					
3	7056	>256	>256	>256	>256	>256	>256	>256	>256	>256	>256	>32	>256	>256	>256	>256	N	256	>256	>256	256	>256	>256	>256	>256	>256	256	>256	>32	>256	0	0
4	7057	0.5	0.5	0.25	0.5	0.5	0.25	0.25	0.5	1	0.5	0.25	0.5	0.5	0.5	0.5	N	0.016	0.25	0.5	0.5	0.125	0.25	0.5	0.25	0.5	0.25	0.5	0.016	1	2	3
	7060	0.5	0.25	0.25	0.5	0.5	0.25	0.25	0.5	1	0.5	0.25	0.5	0.5	0.5	0.5	N	0.5	0.25	0.5	0.5	0.125	0.25	0.5	0.5	0.5	0.25					
	7061	0.5	0.5	0.25	0.5	0.5	0.25	0.25	0.5	1	0.5	0.25	0.5	0.5	1	0.5	N	0.032	0.25	0.5	0.5	0.064	0.25	0.5	0.5	0.5	0.25					
5	7058	2	1	1	2	2	2	2	2	4	2	2	4	2	2	2	N	2	2	4	4	1	1	2	2	2	2	2	1	4	0	0
6	7059	2	0.5	0.25	0.5	1	0.5	0.5	0.5	2	0.5	1	0.5	0.5	1	0.25	N	0.5	0.5	1	1	0.25	0.5	0.5	0.5	0.5	0.5	0.5	0.25	2	4	0
	7063	2	0.5	0.25	0.5	1	0.5	0.5	0.5	2	0.5	1	0.5	0.5	1	0.5	N	0.5	0.5	1	1	0.25	0.5	0.5	0.5	0.5	0.5					

N: no result; not retrieved, not tested or MIC not supplied.

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

		Laboratory codes																													
	Strain	90969	90984	92613	92621	92623	92624	92625	92626	92627	92628	92630	92631	92632	92634	92784	93997	94602	94925	94929	94936	94937	94938	95587	95588	95589	96244	Total	No. S	No. I	No. R	Consensus	Concordance (%)
1	7054	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	24	24	0	0	S	100.0
2	7055	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	50	50	0	0	S	100.0
	7062	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S						
3	7056	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	25	25	0	0	S	100.0
4	7057	R	R	R	N	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	75	1	0	74	R	98.7
	7060	R	R	R	N	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R						
	7061	R	R	R	N	R	R	R	R	R	R	R	R	R	R	R	R	S	R	R	R	R	R	R	R	R	R						
5	7058	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	25	25	0	0	S	100.0
6	7059	S	S	S	N	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	49	48	0	1	S	98.0
	7063	S	S	S	N	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S						
																																Total	99.4

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

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

		Laboratory codes																													
	Strain	90969	90984	92613	92621	92623	92624	92625	92626	92627	92628	92630	92631	92632	92634	92784	93997	94602	94925	94929	94936	94937	94938	95587	95588	95589	96244	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
1	7054	<0.016	<0.016	<0.016	N	<0.016	<0.016	0.016	<0.016	<0.016	<0.016	<0.016	<0.016	<0.016	<0.016	0.032	N	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	0
2	7055	<0.016	<0.016	<0.016	N	0.032	<0.016	0.032	<0.016	<0.016	<0.016	0.016	0.016	<0.016	0.032	0.032	N	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	0
	7062	<0.016	<0.016	<0.016	N	0.016	<0.016	0.032	<0.016	<0.016	<0.016	0.016	0.016	<0.016	0.016	0.032	N	0.016	<=0.016	0.016	0.032	0.016	<0.016	<0.016	<=0.016	0.032	0.016					
3	7056	<0.016	0.032	<0.016	N	0.016	<0.016	0.032	<0.016	<0.016	<0.016	0.016	<0.016	<0.016	0.016	0.032	N	0.016	<=0.016	0.016	0.032	0.016	<0.016	<0.016	<=0.016	<0.016	0.016	<0.016	<0.016	0.032	0	0
4	7057	2	8	4	N	4	4	4	4	4	4	2	4	2	4	8	N	0.5	4	4	4	4	4	4	4	2	2	4	0.032	8	0	2
	7060	2	8	4	N	4	4	4	4	4	4	2	4	4	4	8	N	4	8	8	4	4	4	4	4	2	2					
	7061	2	8	4	N	4	4	4	4	4	4	2	4	4	4	8	N	0.032	8	8	4	4	4	4	4	2	2					
5	7058	<0.016	<0.016	0.032	N	<0.016	<0.016	0.032	<0.016	<0.016	<0.016	<0.016	0.016	<0.016	<0.016	0.032	N	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	0
6	7059	0.032	0.064	0.064	N	0.25	0.125	0.125	0.064	0.064	0.032	0.064	0.064	0.064	0.125	0.125	N	0.064	0.064	0.125	0.125	0.125	0.032	0.032	0.064	0.064	0.064	0.064	0.032	0.25	1	0
	7063	0.032	0.125	0.064	N	0.125	0.125	0.125	0.064	0.064	0.032	0.064	0.064	0.032	0.125	0.125	N	0.064	0.125	0.125	0.125	0.064	0.064	0.032	0.064	0.125	0.064					

N: no result; not retrieved, not tested or MIC not supplied.

Note: Laboratory 92621 did not submit cefixime data.

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

		Laboratory codes																														
	Strain	90969	90984	92613	92621	92623	92624	92625	92626	92627	92628	92630	92631	92632	92634	92784	93997	94602	94925	94929	94936	94937	94938	95587	95588	95589	96244	Total	No. S	No. I	No. R	Consensus	Concordance (%)
1	7054	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	26	26	0	0	S	100.0
2	7055	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	52	52	0	0	S	100.0
	7062	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						
3	7056	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	26	26	0	0	S	100.0
4	7057	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	78	0	0	78	R	100.0
	7060	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						
	7061	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	7058	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	26	26	0	0	S	100.0
6	7059	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	52	52	0	0	S	100.0
	7063	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						
																																Total	100.0

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

		Laboratory codes																													
	Strain	90969	90984	92613	92621	92623	92624	92625	92626	92627	92628	92630	92631	92632	92634	92784	93997	94602	94925	94929	94936	94937	94938	95587	95588	95589	96244	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
1	7054	0.004	0.016	0.004	0.016	0.008	0.008	<0.016	0.004	0.008	0.004	<0.016	0.008	0.004	0.008	0.016	N	0.002	<=0.016	<0.016	0.016	0.004	0.002	0.002	0.004	0.008	0.004	0.004	0.002	0.016	5	0
2	7055	0.008	<0.002	0.008	0.032	0.016	0.016	0.016	0.004	0.016	0.004	0.016	0.032	0.008	0.032	0.016	N	0.002	<=0.016	0.032	0.016	0.008	0.002	0.004	0.008	0.016	0.008	0.016	<0.002	0.032	8	5
	7062	0.004	<0.002	0.008	0.032	0.016	0.016	0.016	0.004	0.016	0.004	0.016	0.032	0.008	0.016	0.016	N	0.002	<=0.016	0.032	0.016	0.008	0.004	0.004	0.008	0.016	0.008					
3	7056	0.002	0.032	0.008	0.064	0.032	0.016	0.032	0.004	0.016	0.008	0.016	0.032	0.008	0.032	0.064	N	0.002	<=0.016	0.032	0.032	0.016	0.004	0.004	0.016	0.032	0.016	0.032	0.002	0.064	3	5
4	7057	0.5	2	1	2	2	1	1	1	2	2	2	2	1	1	2	N	0.25	2	2	1	1	1	1	2	1	1	2	0.25	2	1	2
	7060	1	2	1	2	1	1	1	1	2	2	2	2	1	2	2	N	2	2	2	2	1	1	1	2	1	1					
	7061	1	2	1	2	2	1	1	1	2	2	2	2	1	2	2	N	0.25	2	2	2	1	1	1	2	1	1					
5	7058	0.004	0.032	0.008	0.032	0.008	0.008	0.032	0.008	0.016	0.004	<0.016	0.008	0.008	0.008	0.032	N	0.008	<=0.016	0.016	0.016	0.008	0.004	0.004	0.008	0.016	0.008	0.008	0.004	0.032	4	0
6	7059	0.004	0.032	0.008	0.032	0.032	0.032	0.032	0.016	0.032	0.016	0.032	0.032	0.016	0.016	0.032	N	0.016	0.032	0.064	0.064	0.032	0.016	0.008	0.016	0.032	0.016	0.032	0.004	0.064	4	1
	7063	0.016	0.032	0.008	0.032	0.032	0.032	0.032	0.016	0.032	0.016	0.032	0.032	0.008	0.032	0.032	N	0.032	0.064	0.064	0.064	0.032	0.016	0.016	0.032	0.032	0.016					

N: no result; not retrieved, not tested or MIC not supplied.

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

		Laboratory codes																														
	Strain	90969	90984	92613	92621	92623	92624	92625	92626	92627	92628	92630	92631	92632	92634	92784	93997	94602	94925	94929	94936	94937	94938	95587	95588	95589	96244	Total	No. S	No. I	No. R	Consensus	Concordance (%)
1	7054	R	R	S	I	R	R	I	I	R	R	R	R	I	I	R	R	S	S	R	R	R	I	R	R	I	I	26	3	8	15	R	57.7
2	7055	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	52	52	0	0	S	100.0
	7062	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						
3	7056	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	26	0	0	26	R	100.0
4	7057	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	77	0	0	77	R	100.0
	7060	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	R						
	7061	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	7058	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	26	26	0	0	S	100.0
6	7059	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	52	0	0	52	R	100.0
	7063	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	92.9	

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

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

		Laboratory codes																														
	Strain	90969	90984	92613	92621	92623	92624	92625	92626	92627	92628	92630	92631	92632	92634	92784	93997	94602	94925	94929	94936	94937	94938	95587	95588	95589	96244	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
1	7054	0.064	0.125	0.032	0.064	0.125	0.125	0.064	0.064	0.125	0.064	0.125	0.125	0.064	0.064	0.125	N	0.032	0.064	0.125	0.125	0.125	0.064	0.064	0.125	0.064	0.064	0.064	0.032	0.125	0	0
2	7055	0.004	<0.002	0.004	0.008	0.008	0.016	0.008	0.008	0.016	0.008	0.008	0.008	0.004	0.008	0.016	N	0.002	0.008	0.008	0.008	0.004	0.008	0.008	0.016	0.008	0.004	0.008	0.002	0.016	2	2
	7062	0.004	<0.002	0.004	0.008	0.008	0.016	0.008	0.008	0.016	0.008	0.008	0.008	0.004	0.008	0.008	N	0.002	0.004	0.016	0.008	0.004	0.008	0.004	0.016	0.008	0.004					
3	7056	>32	>32	8	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	N	>32	>32	>32	32	>32	>32	>32	>32	>32	32	>32	8	>32	0	1
4	7057	>32	>32	>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	0	0
	7060	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	N	32	>32	>32	32	>32	>32	>32	>32	>32	32					
	7061	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	>32	N	>32	>32	>32	32	>32	>32	>32	>32	>32	32					
5	7058	0.008	0.016	0.008	0.016	0.032	0.032	0.032	0.016	0.064	0.016	0.032	0.032	0.016	0.016	0.032	N	0.016	0.016	0.032	0.032	0.008	0.016	0.016	0.032	0.032	0.016	0.016	0.008	0.064	1	0
6	7059	8	8	2	16	>32	>32	16	16	>32	8	>32	>32	8	>32	>32	N	32	4	>32	32	8	16	>32	32	8	8	>32	2	>32	6	19
	7063	8	8	2	16	>32	>32	>32	8	>32	8	>32	>32	8	>32	>32	N	32	8	>32	32	>32	16	8	32	8	8					

N: no result; not retrieved, not tested or MIC not supplied.

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

		Laboratory codes																												
	Strain	90969	90984	92613	92621	92623	92624	92625	92626	92627	92628	92630	92631	92632	92634	92784	93997	94602	94925	94929	94936	94937	94938	95587	95588	95589	96244	Total	No. S	No. I	No. R	Consensus	Concordance (%)
1	7054	N	N	N	N	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	S	N	S	18	18	0	0	S	100.0
2	7055	N	N	N	N	R	R	R	R	R	R	R	R	R	R	R	N	R	R	R	N	R	N	R	R	N	R	36	0	0	36	R	100.0
	7062	N	N	N	N	R	R	R	R	R	R	R	R	R	R	R	N	R	R	R	N	R	N	R	R	N	R						
3	7056	N	N	N	N	S	S	S	S	S	S	S	S	N	S	S	N	S	S	S	N	S	N	S	S	N	S	17	17	0	0	S	100.0
4	7057	N	N	N	N	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	S	N	S	53	53	0	0	S	100.0
	7060	N	N	N	N	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	S	N	S						
	7061	N	N	N	N	S	S	S	S	S	S	S	S	S	S	S	N	N	S	S	N	S	N	S	S	N	S						
5	7058	N	N	N	N	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	S	N	S	18	18	0	0	S	100.0
6	7059	N	N	N	N	S	S	S	S	S	S	S	S	N	S	S	N	S	S	S	N	S	N	S	S	N	S	35	35	0	0	S	100.0
	7063	N	N	N	N	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	N	S	N	S	S	N	S						
																																Total	100.0

N – not retrieved or susceptibility category not supplied.

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

		Laboratory codes																													
	Strain	90969	90984	92613	92621	92623	92624	92625	92626	92627	92628	92630	92631	92632	92634	92784	93997	94602	94925	94929	94936	94937	94938	95587	95588	95589	96244	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
1	7054	N	N	N	N	16	16	16	16	16	8	8	16	8	16	16	N	2	16	16	N	8	N	8	16	N	8	16	2	16	0	1
2	7055	N	N	N	N	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	N	>1024	>1024	>1024	N	>1024	N	>1024	>1024	N	1024	>1024	1024	>1024	0	0
	7062	N	N	N	N	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	N	>1024	>1024	>1024	N	>1024	N	>1024	>1024	N	1024					
3	7056	N	N	N	N	16	8	8	8	16	16	8	16	16	8	16	N	1	16	16	N	4	N	8	8	N	8	16	1	16	1	1
4	7057	N	N	N	N	16	16	16	8	16	16	8	16	16	16	16	N	2	8	16	N	8	N	16	16	N	16	16	2	16	2	2
	7060	N	N	N	N	16	16	16	16	16	16	8	16	16	16	16	N	8	16	16	N	4	N	8	16	N	8					
	7061	N	N	N	N	16	16	16	16	16	16	8	16	16	16	16	N	2	16	16	N	4	N	8	16	N	8					
5	7058	N	N	N	N	16	16	16	16	16	8	8	8	16	16	16	N	8	8	16	N	8	N	8	32	N	8	16	8	32	0	0
6	7059	N	N	N	N	16	16	16	8	16	8	8	16	8	16	16	N	8	16	16	N	8	N	8	16	N	8	16	8	16	0	0
	7063	N	N	N	N	16	16	16	8	16	8	8	16	16	16	8	N	8	8	16	N	8	N	8	16	N	8					

Note: Laboratories 90969, 90984, 92613, 92621, 93997, 94936, 94938 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																										Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
	Strain	90969	90984	92613	92621	92623	92624	92625	92626	92627	92628	92630	92631	92632	92634	92784	93997	94602	94925	94929	94936	94937	94938	95587	95588	95589	96244					
1	7054	N	8	N	N	N	8	4	4	4	8	4	4	2	4	4	N	2	4	4	N	2	N	8	4	N	4	4	2	8	0	0
2	7055	N	<0.016	N	N	N	8	4	4	16	8	8	4	2	8	4	N	2	4	8	N	2	N	8	8	N	4	8	<0.016	16	3	3
	7062	N	<0.016	N	N	N	8	4	8	16	8	8	4	4	8	8	N	4	4	8	N	1	N	8	8	N	4					
3	7056	N	8	N	N	N	8	4	8	16	8	8	8	2	4	8	N	4	4	4	N	1	N	8	8	N	4	8	1	16	1	1
4	7057	N	8	N	N	N	8	4	8	8	4	8	4	2	4	8	N	1	4	8	N	2	N	16	8	N	4	4	1	16	3	0
	7060	N	8	N	N	N	8	4	4	8	4	8	4	2	4	4	N	4	8	8	N	2	N	8	4	N	4					
	7061	N	8	N	N	N	8	4	4	8	4	8	4	2	4	4	N	4	4	8	N	1	N	8	4	N	4					
5	7058	N	8	N	N	N	16	4	8	16	8	8	8	2	8	8	N	4	4	8	N	2	N	8	8	N	4	8	2	16	2	0
6	7059	N	8	N	N	N	8	4	4	16	8	8	8	2	4	8	N	4	8	8	N	2	N	8	8	N	4	8	1	16	4	1
	7063	N	8	N	N	N	8	4	4	8	8	8	8	2	4	8	N	4	2	8	N	1	N	16	8	N	4					

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																										Total	No. S	No. I	No. R	Consensus	Concordance (%)
	Strain	90969	90984	92613	92621	92623	92624	92625	92626	92627	92628	92630	92631	92632	92634	92784	93997	94602	94925	94929	94936	94937	94938	95587	95588	95589	96244						
1	7054	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	N	S	24	24	0	0	S	100.0
2	7055	R	S	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	R	R	R	R	N	R	48	3	0	45	R	93.8
	7062	R	S	R	R	R	R	R	R	R	R	R	R	R	R	R	S	R	R	R	N	R	R	R	R	N	R						
3	7056	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	R	R	R	R	N	R	24	0	0	24	R	100.0
4	7057	S	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	N	S	72	70	0	2	S	97.2
	7060	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	R	S	S	S	N	S						
	7061	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	N	S						
5	7058	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	N	S	24	24	0	0	S	100.0
6	7059	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	N	S	48	48	0	0	S	100.0
	7063	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	N	S						
																																Total	98.5

Note: Laboratories 94936 and 9558 did not submit any beta-lactamase testing results.

N: no result; not retrieved or beta-lactamase result not supplied.

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