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Widespread implementation of EUCAST breakpoints for antibacterial susceptibility testing in Europe

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The European Committee on Antimicrobial Susceptibility Testing (EUCAST) was established to harmonise clinical antimicrobial breakpoints and to define breakpoints for new agents in Europe. Data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) external quality assessment (EQA) exercises from 2009 to 2012, from the United Kingdom External Quality Assessment Scheme (UK NEQAS) from November 2009 to March 2013 and data collected by EUCAST through a questionnaire in the first quarter of 2013 were analysed to investigate implementation of EUCAST guidelines in Europe. A rapid change to use of EUCAST breakpoints was observed over time. Figures for implementation of EUCAST breakpoints at the end of the studied period were 61.2% from EARS-Net data and 73.2% from UK NEQAS data. Responses to the EUCAST questionnaire indicated that EUCAST breakpoints were used by over 50% of laboratories in 18 countries, by 10 to 50% of laboratories in eight countries and by less than 10% in seven countries. The EUCAST disk diffusion method was used by more than 50% of laboratories in 12 countries, by 10 to 50% of laboratories in ten countries and by less than 10% in eleven countries. EUCAST guidelines implementation is essential to ensure consistent clinical reporting of antimicrobial susceptibility results and antimicrobial resistance surveillance.

Background

The use of common clinical breakpoints for antimicrobial susceptibility testing is important both for consistent clinical reporting of antimicrobial susceptibility and for international surveillance of the antimicrobial susceptibility of microorganisms. The principal objective of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) [1] is to harmonise antimicrobial breakpoints in Europe and to define breakpoints for new agents in collaboration with the European Medicines Agency (EMA) [2] following a standard operating procedure agreed between EUCAST and the EMA [3,4]. EUCAST was established by the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) in 1997 [5]. The committee was restructured in the years 2001 and 2002 with the support and central involvement of the national breakpoint committees that were active in Europe, i.e. those in France, Germany, the Netherlands, Norway, Sweden and the United Kingdom, and has been in operation in its current form since 2002. EUCAST has a General Committee [6], which includes one representative of each country from Europe and any country outside Europe interested in being part of the EUCAST process.

ESCMID has remained the administrative, financial and scientific platform of EUCAST throughout. Principal financial support over the years has been from ESCMID, European Union (EU) grants, a grant from the European Centre for Disease Prevention and Control (ECDC) and currently through a framework contract with the ECDC.

Today, EUCAST is well established as the only pan-European antimicrobial breakpoint committee, with representatives throughout Europe and beyond. It is accepted as the European antimicrobial breakpoint committee by clinicians and clinical microbiologists, by

national breakpoint committees and medicines agencies in Europe, the ECDC, the EMA, the European Food Safety Authority (EFSA), the pharmaceutical industry and diagnostic companies with interests in antimicrobial susceptibility testing. Of note, the EUCAST clinical breakpoints apply to antimicrobial resistance case definition as reportable to the European Union (EU) surveillance network for communicable diseases [7].

The breakpoint harmonisation process for all major groups of antimicrobial agents and organisms was completed in 2008/09. Since then there has been rapid adoption of EUCAST breakpoints and methods in Europe. Complete data on uptake in all European laboratories are not available as in most countries there is no mechanism for collection of information on susceptibility testing guidelines followed. A combination of different data sources needs to be used to obtain this information.

Analysed data sources

Data presented here are taken from three different sources. Firstly, the external quality assessment (EQA) exercise that is part of the European Antimicrobial Resistance Surveillance Network (EARS-Net) [8] organised by ECDC though a framework contract with the UK National External Quality Assessment Scheme (UK NEQAS). Secondly, the international external quality assessment scheme run by UK NEQAS [9]. Thirdly, data collected by EUCAST in the first quarter of 2013 through a questionnaire on guidelines and methods used in different countries.

EARS-Net external quality assessment

The ECDC EARS-Net resistance surveillance programme collects data from all EU countries, two European Economic Area countries (Norway and Iceland) [7], plus Bosnia, Croatia (also EU since 1 July 2014), Israel and Turkey between 2009 and 2011 only. The number of participating laboratories in each country varies, with a total of between 766 and 817 laboratories from 28 to 30 countries participating in the annual EQA exercises between 2009 and 2012 [10–13]. As part of the EQA exercise information is collected on breakpoint guidelines followed and methods used.

UK NEQAS for antimicrobial susceptibility testing

The UK NEQAS EQA scheme [9] includes subscribing laboratories principally from European countries and, as with EARS-Net, the number of participating laboratories in each country is variable. However, the distribution of numbers of laboratories among countries differs from that of EARS-Net, with a total of between 632 and 656 laboratories participating in the EQA scheme between November 2009 and March 2013. In the UK NEQAS for antimicrobial susceptibility testing two organisms of a variety of species are distributed each month. The number of participating laboratories returning results varies with the organism and antimicrobial agent so for consistency the data are based on results returned for *E. coli* isolates tested against ciprofloxacin, one of the most widely tested combinations. For each organism distributed, information is collected on breakpoint guidelines followed and methods used.

EUCAST questionnaire on guidelines and methods used in different countries

In the first quarter of 2013, a questionnaire was distributed to all General Committee members with the objective of collecting information on whether EUCAST breakpoint guidelines were followed, adoption of the EUCAST disk diffusion method and whether the country has a national antimicrobial susceptibility committee (NAC) as recommended by EUCAST [14]. At that time there were 35 countries with national representatives on the EUCAST General Committee, Australia, Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Latvia, Lithuania, Luxemburg, the Netherlands, Norway, Poland, Portugal, Romania, Russia, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom. In most countries there is no official requirement for laboratories to follow any particular breakpoint guidelines and a variety of methods is used. Also most countries have no mechanism for collecting precise information on guidelines and methods used, and this may be continually changing as individual laboratories make decisions to change susceptibility testing guidelines followed or methods used. Therefore, the General Committee representatives were asked to provide estimates of the proportions of laboratories falling into broad categories for use of EUCAST guidelines and the EUCAST disk diffusion method. The categories provided were below 10%, 10 to 50% and above 50% of laboratories.

Results

Data from EARS-Net (Table) show a decline in use of the Clinical and Laboratory Standards Institute (CLSI, United States) breakpoints from 67.5% in September 2009 to 38.4% in May 2012, and an increase in use of EUCAST breakpoints from 22.2% in 2009 to 61.2% in 2012. Some national guidelines such as the British Society for Antimicrobial Chemotherapy (BSAC, United Kingdom) [15] and the Comité de l'Antibiogramme de la Société Française de Microbiologie (CA-SFM, France) [16] have adopted EUCAST MIC breakpoints and initially calibrated their own disk diffusion method to the EUCAST breakpoints, so they were using EUCAST-related methods and are therefore also counted as using EUCAST breakpoints. Both BSAC and CA-SFM are now in the process of changing to the EUCAST disk diffusion method.

Data from UK NEQAS EQA (Table) show a similar decline in use of CLSI breakpoints as seen in EARS-Net, from 58.5% in November 2009 to 26.8% in March 2013 and an increase in use of EUCAST breakpoints, from 36.1% to 73.2% over the same period. As with EARS-Net data, some national guidelines have adopted EUCAST

Table

Antimicrobial susceptibility testing guidelines used by laboratories participating in the EARS-Net EQA exercises, 2009–2012 and UK NEQAS for antimicrobial susceptibility testing, 2009–2013

Data source	Date, number of laboratories	Percentage of laboratories using indicated guidelines		
		CLSI	EUCAST and EUCAST-based	Other[a]/ combined/ not stated
EARS-Net EQA	September 2009 n = 775	67.5	22.2	10.3
	June 2010 n = 766	65.8	28.7	5.5
	May 2011 n = 817	46.8	47.6	5.6
	May 2012 n = 807	38.4	61.2	0.4
UK NEQAS EQA	November 2009 n = 651	58.8	36.1	5.1
	November 2010 n = 656	51.5	42.2	6.3
	November 2011 n = 643	36.8	58.6	4.6
	April 2012 n = 632	31.8	68.2	0
	March 2013 n = 650	26.8	73.2	0

CLSI: Clinical and Laboratory Standards Institute; EARS: European Antimicrobial Resistance Surveillance Network; EQA: external quality assessment; EUCAST: European Committee on Antimicrobial Susceptibility Testing; UK NEQAS: United Kingdom External Quality Assessment Scheme.

[a] Other guidelines are local methods not complying with EUCAST or CLSI recommendations.

MIC breakpoints and are therefore counted as using EUCAST breakpoints.

Questionnaires were completed by 33 of the 35 General Committee representatives. Countries with a NAC are shown in Figure 1. At the time of the survey, 25 of the responding countries had an established NAC, four were in the process of setting up a NAC and four had no NAC. Use of EUCAST breakpoint guidelines is shown in Figure 2. EUCAST breakpoints were used by more than 50% of laboratories in 18 countries, by 10 to 50% of laboratories in eight countries and by less than 10% in seven countries. Use of EUCAST disk diffusion method is shown in Figure 3. The EUCAST disk diffusion method was used by more than 50% of laboratories in 12 countries, by 10 to 50% of laboratories in ten countries and by less than 10% in eleven countries.

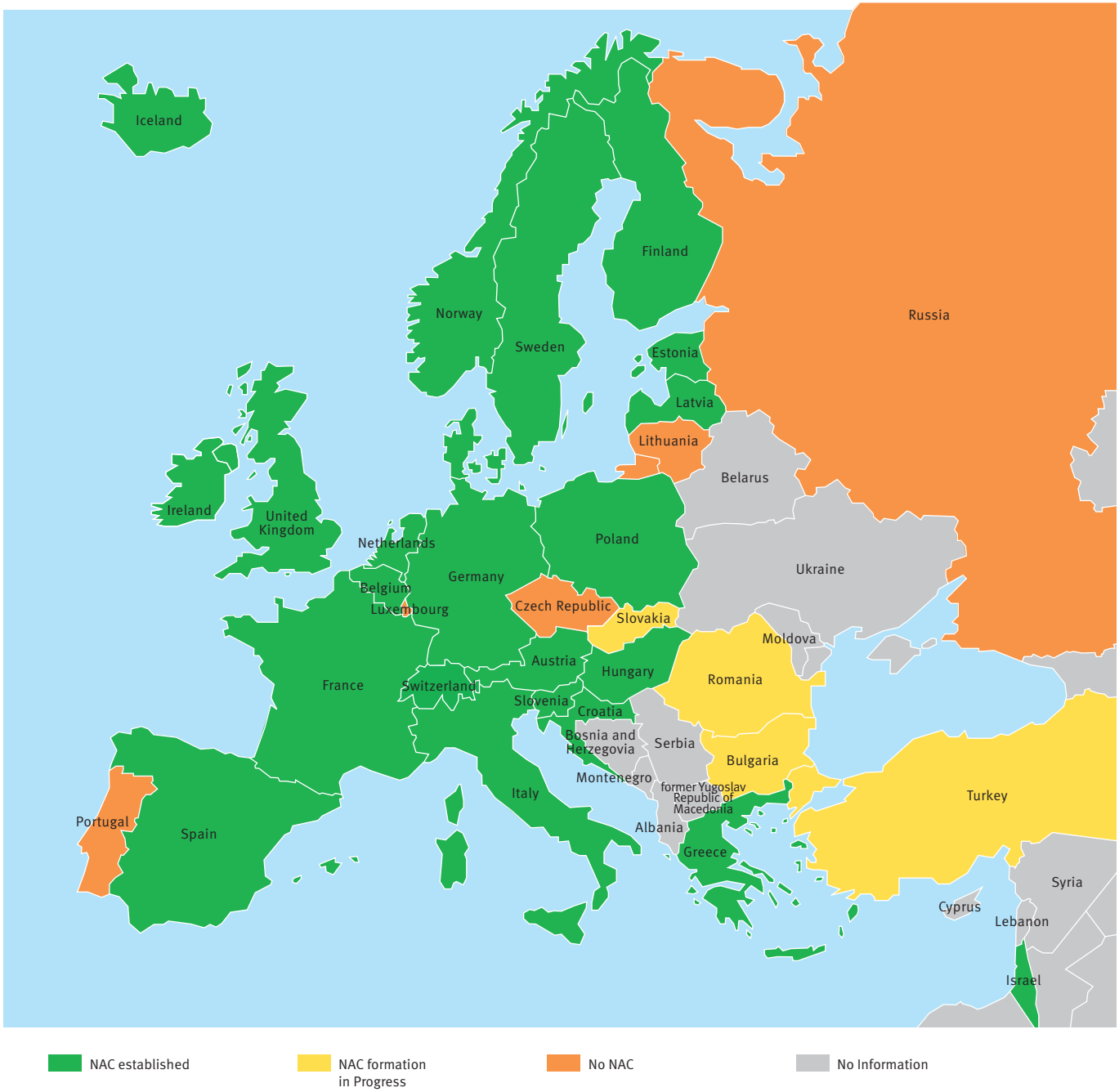
Discussion

Collection of reliable data on use of clinical breakpoint guidelines and methods for antimicrobial susceptibility testing in different countries is difficult because in most countries there is no national requirement to follow particular guidelines or methods, there are no mechanisms in place to collect such data, and the situation may change gradually over time as laboratories decide to change guidelines or methods. However, the findings from three independent data sources presented here consistently show that there has been widespread adoption of EUCAST breakpoints in recent years across clinical laboratories in the majority of European countries. The EQA exercises organised by EARS-Net and UK NEQAS include different but overlapping sets of laboratories covering most European countries. These EQA exercises show similar trends towards adoption of EUCAST breakpoints since 2009, with the UK NEQAS data indicating that over 70% of the laboratories providing data used EUCAST breakpoints in March 2013. The adoption of EUCAST guidelines has been mirrored by a decline in the use of CLSI breakpoints. This process has been fuelled by the adoption of EUCAST breakpoints by EMA in 2005 [3] as part of the official European process for marketing authorisation of antimicrobial agents, the adoption of EUCAST breakpoints by the European Commission Decision on case definition for surveillance of antimicrobial resistance in humans in 2012 [7], as well as the strong support by ESCMID and ECDC for use of EUCAST breakpoints for surveillance. Moreover, in some countries, the position taken by national societies of clinical microbiology and/or infectious diseases has had a positive impact.

The rate of adoption of EUCAST breakpoints has been variable in different countries, as illustrated by the results from the EUCAST survey early in 2013. While in just over half of the countries surveyed the majority of laboratories have adopted EUCAST breakpoints, in others the proportion of laboratories using EUCAST

Figure 1

Countries with National Antimicrobial Susceptibility Testing Committees, EUCAST survey 2013

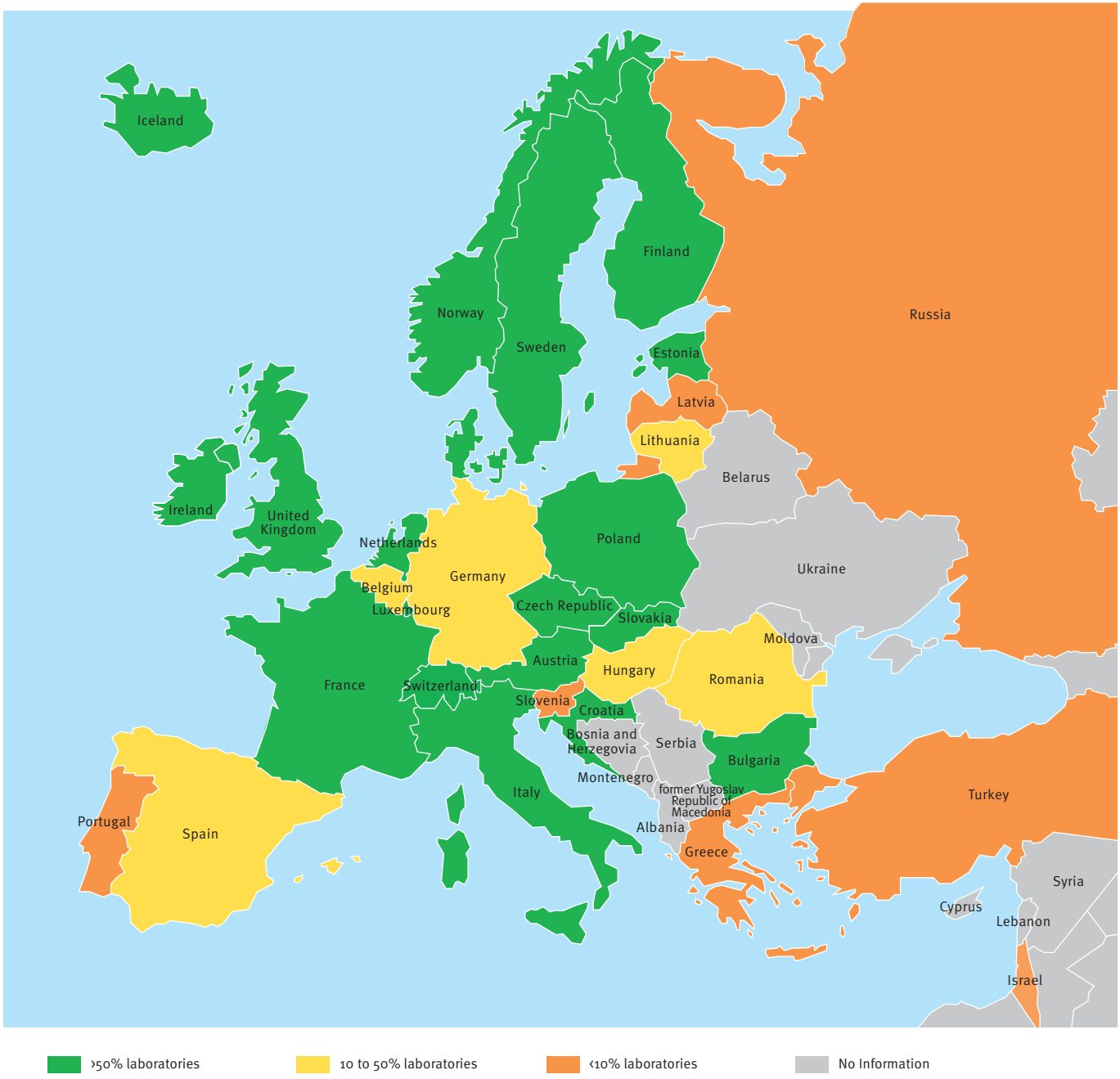


Australia (has NAC) is not on this map.

EUCAST: European Committee on Antimicrobial Susceptibility Testing, NAC: National Antimicrobial Susceptibility Testing Committee.

Figure 2

Use of EUCAST breakpoint guidelines in different countries, EUCAST survey 2013

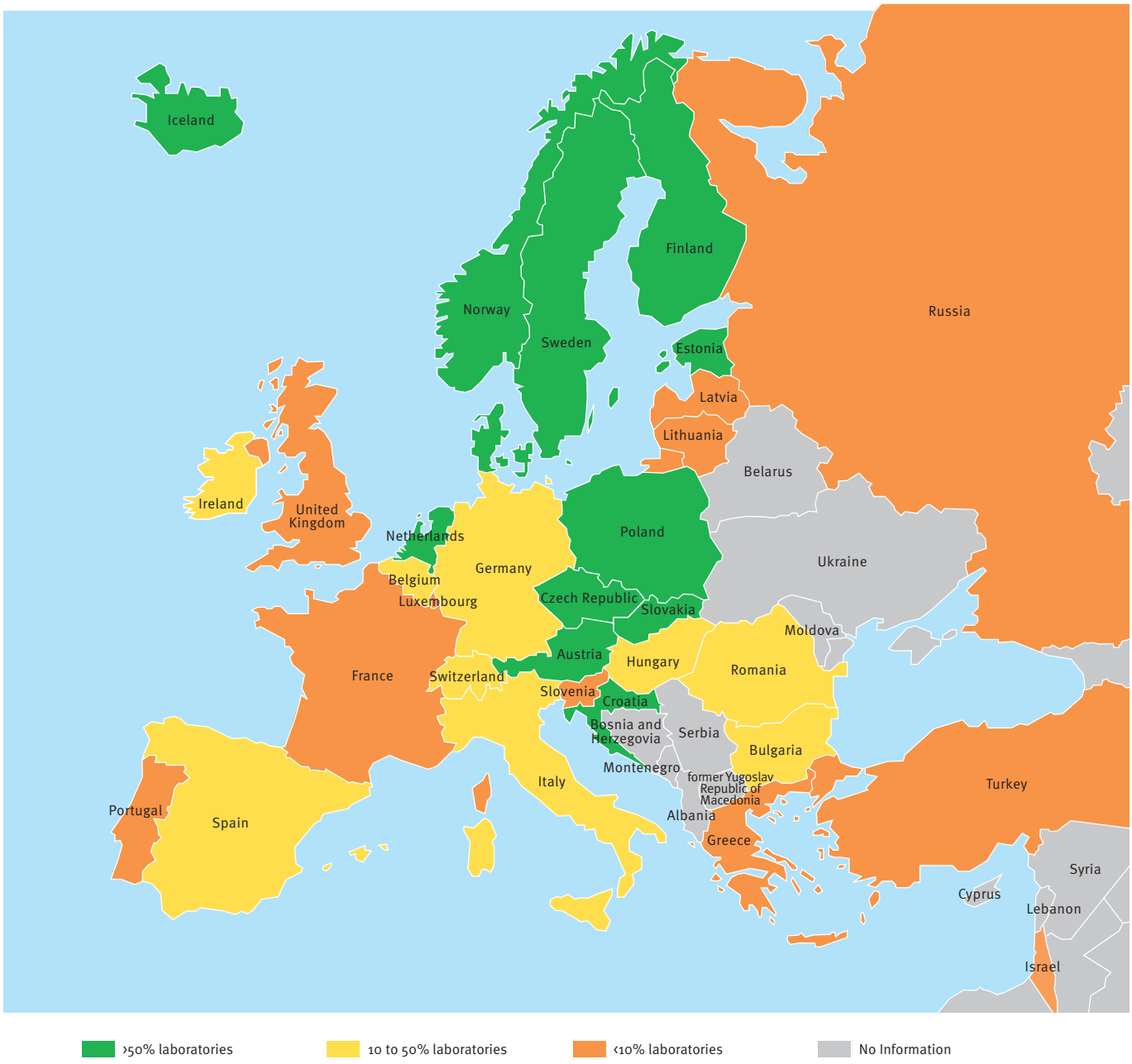


Australia (10 to 50% laboratories) is not on this map.

EUCAST: European Committee on Antimicrobial Susceptibility Testing.

Figure 3

Use of the EUCAST disk diffusion method in different countries, EUCAST survey 2013



Australia (10 to 50% laboratories) is not on this map.
EUCAST: European Committee on Antimicrobial Susceptibility Testing.

breakpoints is still small. It is expected that the uptake of guidelines will be gradual as laboratories make the decision to change breakpoints and incorporate breakpoints into local methods and information systems. The existence of a NAC to provide national guidance on antimicrobial susceptibility testing breakpoints and methods might have a substantial impact on laboratory practices. EUCAST has actively promoted the establishment of NACs in countries where no such group existed. The EUCAST survey shows that most countries now have a NAC or are in the process of setting up a NAC, and it is likely that these committees will positively influence the uptake of EUCAST guidelines. Furthermore, adoption of EUCAST breakpoints by public health microbiology national reference laboratories participating in ECDC-supported external quality assessment programmes will encourage alignment of testing practice across the EU. In addition, free access to EUCAST breakpoint documents via the internet and implementation of EUCAST breakpoints in automatic susceptibility testing devices facilitate the wide adoption of EUCAST guidelines.

Any standardised antimicrobial susceptibility testing method may be calibrated to EUCAST MIC breakpoints and national disk diffusion methods in France and the UK have been calibrated in this way [17,18]. However, there has been widespread demand for a EUCAST disk diffusion method and a EUCAST disk diffusion method was released in 2010 and published in 2014 [19]. The EUCAST 2013 survey has shown that, as with the uptake of EUCAST breakpoints, adoption of EUCAST disk diffusion method has been variable in different countries, but is used in a considerable proportion of laboratories in two thirds of surveyed countries. In many laboratories, the main antimicrobial susceptibility testing method is an automated system and delays in the implementation of EUCAST breakpoints in automated systems have delayed adoption of EUCAST breakpoints in some laboratories. However, the majority of EUCAST breakpoints are now implemented in automated systems [20] and laboratories can choose to use EUCAST breakpoints in their automated systems.

The information on uptake of EUCAST guidelines from EARS-Net and EUCAST relates only to clinical laboratories and the UK NEQAS EQA scheme includes greater than 95% of clinical laboratories. Information on guidelines followed in veterinary and food safety laboratories has not been surveyed by EUCAST but it would be useful to do so in collaboration with veterinary and food safety networks.

It is clear that there has been a rapid change to use of EUCAST breakpoints over the last few years and there are indications that this trend is continuing as EUCAST breakpoints are increasingly referred to in scientific communications. The wide adoption of EUCAST breakpoints will result in increased consistency of reporting of antimicrobial susceptibility testing results in different countries and better comparability of antimicrobial resistance surveillance data among countries. Annual monitoring of progress in implementation of EUCAST breakpoints across clinical and reference laboratories in Europe will be conducted jointly by EUCAST and ECDC as a key public health microbiology performance indicator.

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Conflicts of interest

Derek Brown is Scientific Secretary of EUCAST, chairs the UK NEQAS Specialist Advisory Group on Antimicrobial Susceptibility Testing and advises UK NEQAS on Antimicrobial Susceptibility Testing issues. Rafael Cantón is Chairman of EUCAST and Gunnar Kahlmeter is Clinical Data Coordinator of EUCAST. Derek Brown, Gunnar Kahlmeter, Luc Dubreuil, Sören Gatermann, Christian Giske, Alasdair MacGowan, Luis Martínez-Martínez, Johan Mouton, Robert Skov, Martin Steinbakk and Rafael Cantón are members of the EUCAST Steering Committee. Christine Walton is the organiser of the UK NEQAS for Antimicrobial Susceptibility Testing. Ole Heuer and Liselotte Diaz Högberg administer the ECDC EARS-Net programme and Marc Struelens managed the ECDC service contract with EUCAST.

Authors' contributions

Derek Brown, Rafael Cantón and Gunnar Kahlmeter led the preparation of this manuscript. All members of the EUCAST Steering Committee were involved in the EUCAST survey and reviewed the manuscript. Christine Walton led the UK NEQAS team that organised and, with Derek Brown, analysed the data from the UK NEQAS and EARS-Net EQA distributions and also reviewed this manuscript. Ole Heuer, Liselotte Diaz Högberg and Marc Struelens reviewed and contributed to this manuscript.

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