GLASS-EAR
Simulation Exercise Report

16-30 November 2017

Contents

Background

The Emerging Antimicrobial Resistance Reporting (EAR) component and associated risk assessment components within Global AMR Surveillance System (GLASS) was developed at the request of Member States to support the detection, early warning and risk assessment capacities of national AMR surveillance programmes. EAR module is embedded in the GLASS IT platform and provides a space where experts can share information regarding potential EAR events (as defined in the EAR framework) to assess their importance, facilitate early information sharing, and stimulate epidemiological and microbiological discussion for coordinated actions. The EAR module is targeted directly to those in charge of national AMR surveillance system and constituencies that might discover new types of AMR in bacteria and fungi with potential relevance to public health. The GLASS-EAR community is ideally constituted by all Member States, regardless their GLASS enrolment status, WHO Collaborating Centres, AMR surveillance networks and research institutions producing quality AMR data, and WHO IHR focal points. The EAR component of GLASS implements a workflow process for notifying a diverse range of stakeholders on a timely basis, and in compliance with agreements such as the International Health Regulations (IHR). To increase awareness of EAR, validate the processes in this workflow, and identify strengths and areas for improvement, a simulation exercise was conducted from 16-30 November 2017. The exercise focused on data reporting and sharing component of the workflow. The risk assessment component will be addressed more substantially in the next simulation exercise planned in 2018.

Exercise methodology

Different types of exercises were reviewed, and a functional exercise format was chosen. In a functional exercise, an exercise control group (in this case the GLASS-EAR team at WHO) sends information, referred to as injects, to participants, who act on the information as they normally would, using the GLASS-EAR IT module, from their normal work locations. The exercise took place in real time to allow time for reflection and analysis by those receiving injects and to provide time for other participants to view and comment on events. As all exercise events were simulated, no actual interventions or laboratory actions were included in the exercise.

During the time available, the exercise development team chose to focus on the specific functions of assessing reported events, identification of unusual resistance, initial risk assessment (for a sampling of countries among the participants), creation and updating of an event in the EAR IT module, and the subsequent notifications to GLASS EAR members. Working within these functions, the broad objective of the exercise was to increase awareness of and to validate the processes implemented in the GLASS-EAR component, with the specific objectives of:

- Increasing awareness of the utility of GLASS-EAR and appreciation of reporting emerging AMR events

- Identifying strengths and opportunities for improvement in WHO inter-departmental risk assessment processes

- Validating the usability and efficiency of processes implemented in the reporting, limited elements of risk assessment, notification and updating of events at the country level

- Identifying needs for additional documentation of the EAR component

- Ensuring that notifications through the system reach stakeholders as intended

- Building relationships among stakeholders at all levels

Participant recruitment

Exercise participants were solicited through emails sent to GLASS national focal points, WHO Collaborating Centres and other key individuals in AMR surveillance and response. For those requesting further information, an information sheet was prepared (Annex 1 and 2).

Pre-exercise briefings and support during the exercise

A password protected web site was developed (screen shots and link in Annex 3) to consolidate information needed to participate in the exercise. The website included links to the GLASS-EAR user manual, a handbook on participating in the exercise and links to self-paced training both on the EAR module and the exercise (screenshots and links in Annex 4).

Exercise conduct

To simulate the actual processes for obtaining access to the GLASS-EAR IT module, selected participating GLASS focal points received a scenario for assessment and entering for notification in the EAR IT module (Annex 5). Those receiving scenarios were expected to examine the information, if necessary, discuss with other relevant stakeholders, and determine if the event should be entered into GLASS-EAR and to do so. Events were then examined by WHO and acted on further as if the event were real. These actions included requests for further details, risk assessments, etc.

Exercise documentation

Three documents were provided to the participants to support their work in the simulation. The first document was the current draft *Emerging AMR reporting framework and risk assessment*, explained the purpose and processes of the GLASS-EAR. The second document, *Emerging AMR reporting (EAR): Guide for EAR event sharing*, provided instructions for GLASS-EAR users to guide the creation, submission and editing of events. The final document provided to participants was an exercise handbook. The handbook served as a guidance document for simulation participants on how to participate in the simulation including dates, communications guidelines, and information on how the exercise will be reported. All documentation was made available on the password protected exercise web-site.

Exercise evaluation

Following the conclusion of the exercise, a web-based survey link was sent to participants to gather feedback on their experience and solicit suggestions for improvement. Ten participants responded to the survey. The results of this survey are included in Annex 6.

Exercise Results and Recommendations

A total of 25 users from 15 countries and 10 WHO Collaborating Centres, WHO Regional Offices and headquarters logged into the system over the exercise period from 16-30 November 2017. Eight events were posted to the GLASS-EAR module, representing simulated events in five WHO regions. Forty-three comments were made on the events. The comments ranged in nature from questions on the market authorization of certain medicines in the reporting country to IHR notification questions and risk assessments.

All scenarios sent to GLASS-EAR contact points were registered in the platform within the two-week period suggested in the draft EAR framework. Email notifications of events being entered, published and commented in the system were sent and received as expected.

The process of logging into the system, completing profile information, entering, publishing, and commenting on events notified by the GLASS-EAR component via email identified both strengths in

the system and opportunities for improvement. These findings are detailed in the following categories:

- Documentation and training
- Access to the component and navigation.
- Entering and editing events
- Commenting on events
- Email notifications and
- Overall component features

Documentation and training

Most participants responding to the feedback survey indicated that they had accessed the documentation and training at least once either before or during the simulation. On a scale of 1-10, with the lowest rating being 1 and the highest 10, all respondent rated the documentation and training at 5 and above, with 7 rating the materials at 7 or higher.

Following the finalization of the GLASS-EAR module, the content of the training module should be reviewed, updated, and made available to the GLASS-EAR community. Proactively providing self-paced training can reduce the support needs of users and allows new users to orient themselves to the system as they join.

No suggestions were put forward by participants for improvements to the *Guide for EAR event sharing*, however during the conduct of the simulation some issues emerged which could be addressed in the guide. Suggestions for points to review in the guide are listed in specific topic recommendations below.

While none of the respondents to the survey indicated any specific suggestions for revision of the *Emerging AMR reporting framework and risk assessment*, some feedback indicated that additional information on events such as a *travel* history or detailed phenotypic testing of resistance should be included. This can be an effect of the artificiality of the simulation, as the normal investigation and verification steps that would take place in an actual event were not part of the exercise. However, both the framework and the user manual should be reviewed to ensure that both state the level of detail desired in event entries.

Access and navigation

The issuing of login and password information to participants was a very smooth process. No participants reported issues with accessing the component. Among respondents to the feedback survey, all rated the ease of login between 6 and 10.

After gaining access to the component, participants were asked to complete basic profile information for their account, which did present some challenges. It is not possible in the absence of direct feedback to determine if participants encountered challenges in locating where to complete the information or if they simply forgot. As the completion of this information is reflected in the details of posted events and impacts email notifications from the component, multiple measures are suggested to ensure that profile data is completed.

- Explore if a redirect to the profile page is possible on the first login to the component. This would directly send users to the profile for completion.

- Explore the viability of a check within the EAR IT module to display a pop-up or on-screen reminder to fill in the profile information if that information is blank.

- Review the user guide for the EAR IT module to include more emphasis on the completion of the profile.

Entering and editing events

Participants who entered events gave favorable feedback to the experience, with all respondents rating the experience at least 5 and most at 9 or 10. One area that was identified for careful observation in the event entry process during the simulation was how participants would use the options to save an event as a draft, or to save and submit the event. In the final version of the IT module, only the submitting country will be able to view draft events, however to monitor if this choice created issues during the simulation, viewing draft events was enabled for the exercise control team. One event was unintentionally saved as a draft when the intention was to submit.

No issues arose during the exercise in editing of events or in submitting a draft event.

While one instance of accidentally saving an event as draft rather than submitting does not indicate a significant issue in usability, the user guide should be reviewed to ensure that the difference between the two options is given adequate emphasis.

As indicated earlier, some participants desired additional information to be included in the event information, such as a travel history or additional diagnostic information. In an actual event this information would be available and would likely be either included in the initial report or in follow up questions during the risk assessment. Both the framework and the user guide should reflect the type of information that would be asked for during a risk assessment.

One user reported challenges in finding the export as PDF option during the simulation via the comment features of the related event. He was later able to locate the option, but the user guide should be reviewed to give visibility to the feature.

Commenting on events

The commenting feature was rated as easy to use by participants, with survey feedback rating the experience between 7 and 10. One participant noted that when attempting to comment on an entry the comment box seemed to disappear, after which the participant re-started the comment process and when finally posted the previous draft comments appeared. This should be investigated by the developers to determine if this may have been a browser issue or if the user guide may need further details on the commenting process. As this phenomenon was only reported by one participant, this could also have been an isolated incident.

Email notifications

The EAR module sends notifications to relevant users for different actions:

- To the user entering an event when it is saved as draft or submitted

- To other users from the country when an event is entered

- To all users from the country when a confidential event is edited or commented

- To all users of the EAR module when a non-confidential event is published, edited or commented.

During the simulation, no notifications were sent to inappropriate participants, validating a key feature of the component and its ability to maintain confidentiality of events.

Participants indicated a link directly to the event indicated in the email notification rather than to the GLASS-EAR home page would be helpful, even though the current text of notifications provides detailed instructions to access the event. The possibility of changing the link in notifications to direct the reader to the relevant event should be explored with the developers. One possibility would be to generate a link to the event number for each email. If a direct link in email notifications is not possible, then the user guide should provide further detail when explaining notifications that the link goes to the home page and how to locate the event.

The notifications from the system contain a great deal of information about the event (Annex 7), which raised concerns among some participants about confidentiality issues. Although notifications are only sent to all GLASS-EAR community members for non-confidential events, and to members in the same country for confidential events, there is a significant amount of information that could be compromised in the event of an unauthorized individual gaining access to the community member's email. The amount of information required for notifications to be useful should be weighed against the need for security of the information in the system.

Overall component features

The GLASS-EAR module was seen by participants as already serving as an excellent and highly functional platform for EAR reporting. Moreover, it became clear that, in addition to data sharing, the module could be a tool for sharing experience and providing practical advice to other countries. A good example is the very useful description of IPC measures provided by Malta for the (simulated) first case of *Candida auris* candidemia, or the experience in laboratory detection shared by the UAE for this case.

One suggestion for improvement of the functionality of the module was the implementation of an advanced search feature:

"This form currently does not allow you to perform an advanced search. It would be useful to be able to search all published events and comments. A keyword search - a search for a word, words or phrase in the title or description of a published event would be a practical option. Keyword searches are the quickest and easiest way to search for records on a particular subject"

The addition of a keyword option to the event filter could be an easy means to implement this functionality.

Next steps

The component was viewed by participants as being ready to deploy in its current state and considered to be an easy to use tool for emerging antimicrobial resistance notification. In order to maintain awareness of and buy-in to the use of the component, periodic exercises should be conducted. As the basic functionality of the component has been validated, further simulations could exercise the decision-making process for notification and risk assessment.

Conclusion

The simulation exercise to validate the processes implemented in the GLASS-EAR component, conducted from 16-30 November 2017, brought together a geographically diverse group of stakeholders in EAR reporting. Over the two weeks of the simulation, no significant issues were

reported either with the usability of the documentation for the reporting framework or the system itself. Although there is always room for improvement, the component as it is currently configured was seen to be in a ready to deploy state and could be put into wider use as is, although the GLASS-EAR team may wish to review the documentation and component against the recommendations in this report to evaluate the feasibility of the minor improvements suggested.

Annex 1. Participant recruitment email

The following text was used a basis for participant recruitment emails which were sent to existing members of the GLASS system, WHO Collaborating Centres, and other key entities in AMR surveillance and response.

> The Emerging Antimicrobial Resistance Reporting (EAR) and associated risk assessment framework within Global AMR Surveillance System (GLASS) aims at supporting the detection, early warning and risk assessment capacities of the national AMR surveillance programmes. The framework is supported by the EAR IT module which, embedded in the GLASS-IT platform, provides a space where information regarding potential EAR events (as defined in the EAR framework) can be shared to assess their importance, facilitate timely information sharing, and stimulate technical discussion for coordinated actions.

> You are being invited to participate in a simulation exercise using the GLASS-EAR component to validate the processes implemented for the entry, assessment and communication about emerging antimicrobial resistance events identified in countries.

> You are being invited to participate in this exercise because of your role as a key participant in the GLASS platform, as a member of a WHO Collaborating Center, or other key partner. The exercise is planned to take place 16-30 November, 2017, however participation will not involve a major time commitment. Please contact glass-ear@who.int with any questions you may have about participation or to confirm your interest.

Annex 2. Participant information sheet

The Emerging Antimicrobial Resistance Reporting (EAR) and associated risk assessment framework within Global AMR Surveillance System (GLASS) aims at supporting the detection, early warning and risk assessment capacities of the national AMR surveillance programmes. The framework is supported by the EAR IT module which, embedded in the GLASS-IT platform, provides a space where information regarding potential EAR events (as defined in the EAR framework) can be shared to assess their importance, facilitate timely information sharing, and stimulate technical discussion for coordinated actions. To increase awareness of GLASS-EAR, validate the processes in this workflow, and identify strengths and areas for improvement, a simulation exercise will be conducted from 16-30 November 2017.

This will be a functional exercise, sometimes referred to as a command post exercise. In this type of exercise, participants are in their usual locations, and communicate through normal channels, in this case, via the GLASS-EAR component, email, and other regular communication channels. Participants will receive scenarios and act upon them based on the information provided. No actual interventions or laboratory tests will be carried out.

The broad objective of the exercise is to increase awareness of and to validate the processes implemented in the GLASS-EAR, with the following specific objectives:

- Increase awareness of the utility of GLASS and GLASS-EAR and appreciation of reporting emerging AMR events

- Identify strengths and opportunities for improvement in WHO inter-departmental risk assessment processes

- Validate the usability and efficiency of the GLASS-EAR processes proposed, including the use of the EAR IT module in the reporting and limited elements of risk assessment of EAR events.

- Identify needs for additional documentation of the EAR component.

- Ensure that notifications through the system reach stakeholders as intended.

- Build relationships among stakeholders at all levels

The exercise is validating the processes related to the GLASS-EAR framework and not the participants implementing these processes. A series of WebEx meetings will be scheduled to gather feedback from the participants on their experience and suggestions for improvement.

As a key stakeholder in the implementation of the GLASS-EAR platform, your participation in the exercise would provide valuable feedback on the component and contribute to process improvements. Please contact glass-ear@who.int if you would like the participate, or if you have any questions.

Annex 3. Screen shot of exercise web page
The web page is located at: https://phexercise.com/glass-ear, password: glass-ear

GLASS-EAR Simulation Exercise
16-30 November

The Emerging Antimicrobial Resistance Reporting (EAR) and associated risk assessment framework within Global AMR Surveillance System (GLASS) aims at supporting the detection, early warning and risk assessment capacities of the national AMR surveillance programmes. The framework is supported by the EAR IT module which, embedded in the GLASS-IT platform, provides a space where information regarding potential EAR events (as defined in the EAR framework) can be shared to assess their importance, facilitate timely information sharing, and stimulate technical discussion for coordinated actions. All constituencies that might discover new types of AMR of potential relevance to public health, are expected to contribute to the GLASS-EAR. This includes all Member States, regardless their GLASS enrolment status, WHO Collaborating Centres, AMR surveillance networks and research institutions producing quality AMR data, and, when necessary, WHO IHR focal points. To increase awareness of GLASS-EAR, validate the processes in this workflow, and identify strengths and areas for improvement, a simulation exercise will be conducted from 16.30 November 2017.

Documents for participants

Click here to access the participant handbook

Click here for the DRAFT Emerging AMR reporting framework and risk assessment March 2017

Click here for EAR-module user manual

Click here for the self-paced training material

Annex 4. Screen shots of self-paced training and links

The training consisted of two modules. The first was an overview of the GLASS-EAR IT platform, and the second was a guide to participating in the exercise. The module can be accessed at: http://glass-ear.s3.amazonaws.com/story_html5.html and the Articulate Storyline files used to produce the material have been provided to the GLASS-EAR team.

Annex 5. Simulation scenarios

Scenario details such as city or hospital location were customized to be more relevant to the recipient.

1. First case of infection with VRSA in [country X]

Initial input

Report from Hospital A (located in [the capital of country X] to the [national authorities]

A 74-year-old woman with diabetes mellitus, chronic renal failure requiring haemodialysis, and peripheral vascular disease conditioning critical limb ischaemia underwent endovascular revascularisation and amputation of two gangrenous toes. Cultures of the wound amputation site revealed *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* susceptible to vancomycin, for which the patient was treated with vancomycin and amikacin. On November 16, 2017, a MRSA was isolated from pus of the toe amputation wound. The minimum inhibitory concentrations for vancomycin and teicoplanin were >256 µg/mL and 24 µg/mL, respectively. The strain was resistant also to erythromycin, clindamycin, gentamicin, and ciprofloxacin, and susceptible to co-trimoxazole, tetracycline, tygecycline, linezolid, daptomycin, quinupristin/dalfopristin, fusidic acid, cloramphenicol, rifampicin, and mupirocin. Vitek 2 system detected VRSA. Vancomycin-resistant *Enterococcus faecalis* (VRE) and *P. aeruginosa* were also isolated from the same wound.

The patient is clinically well, and is being treated with daptomycin, rifampicin, and amikacin, and aggressive wound care.

Inject

At the national reference lab, MALDI-TOF analyses confirmed the identification of *S. aureus*. The strain was sequence type ST105, SCC*mec* type II, and harboured the *mec*A and *van*A genes, the latter was also identified in the VRE. The genetic background of the strain is similar to that of VRSA isolated in the USA[1].

At the hospital A IPC precautions were reinforced. An epidemiological investigation is ongoing, but so far transmission of VRSA from this patient to contacts at home, other patients or health-care workers from the dialysis unit was not detected. No epidemiological link with the USA of the patient was identified. The attending physician and several other doctors at the Hospital A participated in a two weeks training course in Pennsylvania in October 2017.

2. Clinical isolate of pan-resistant *Klebsiella pneumoniae* in [country X]

Initial input

Report from Hospital A (located in [the capital of country X] to the [national authorities]

On November 13, 2017, hospital A reported an isolate of carbapenem-resistant *Klebsiella pneumoniae* isolated from a wound specimen collected on October 19, 2017. The patient was a 76-year-old man admitted to the hospital A on October 18, 2017 with a primary diagnosis of systemic inflammatory response syndrome, likely resulting from an infected left hip seroma. In May-June 2017 the patient was hospitalized in India in relation to a hip replacement surgery.

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[1]VN Kos, CA Desjardins, A Griggs, et al. Comparative genomics of vancomycin-resistant Staphylococcus aureus strains and their positions within the clade most commonly associated with methicillin-resistant S. aureus hospital-acquired infection in the United States. MBio, 3 (2012), p. e00112

The isolate was resistant to 26 antibiotics tested, including all aminoglycosides and polymyxins, and intermediately resistant to tigecycline. The fosfomycin MIC was 16 μg/mL.

Inject

The isolate was sent to the national reference laboratory where the AST results were confirmed and the presence of bla_{NDM-1} detected. Because of resistance to colistin, the isolate was tested also for the mcr-1 gene, the results were negative.

Fosfomycin is not registered in [country X].

After the CRE was identified, the patient was placed in a single room under contact precautions. No secondary transmission from the case has been reported. The patient developed septic shock and died.

3. Outbreak of infections caused by carbapenem- and colistin-resistant *Klebsiella pneumoniae* in a hospital in [Country X]

Initial input

Report from Hospital A located in the [capital of country X] to the [national authorities]

From September to November 2017, five clinical isolates of *Klebsiella pneumoniae* resistant to carbapenems and colistin were collected from five patients with healthcare associated bloodstream infection (BSI), admitted in the intensive care unit (ICU) in the hospital A. All patients had undergone various surgical procedures and had received multiple antimicrobial agents. Specifically, all patients received fluoroquinolones, three of them received b-lactam/b-lactamase inhibitor combinations, two of them a carbapenem and one received colistin. All isolates were collected from blood.

Bacterial identification and antibiotic susceptibility testing were performed in the hospital laboratory using the VITEK-2 automated system. Minimum inhibitory concentrations (MICs) of imipenem (IMP), meropenem (MEM) and ertapenem (ERT) were also determined using the broth microdilution method. The MICs for IMP, MEM and ERT of all *K. pneumoniae* isolates were >32 μg/mL. For colistin, the MICs ranged from 12 to 128 μg/mL and the isolates were characterised as resistant. For tigecycline, the MIC of the five isolates was 1 μg/mL and they were considered to be susceptible. Susceptibility to other antimicrobial agents was assessed by the disc diffusion method.

The isolates were resistant to all β-lactams and β-lactam/β-lactamase inhibitor combinations (ampicillin, ampicillin/sulbactam, amoxicillin/clavulanic acid, cephalosporins, piperacillin, piperacillin/tazobactam, ticarcillin, ticarcillin/clavulanic acid, aztreonam), ciprofloxacin, co-trimoxazole and aminoglycosides (amikacin, netilmicin, tobramycin) except gentamicin. The isolates were sent to the national reference laboratory.

Inject

In the reference laboratory, phenotypic screening for the presence of metallo-β-lactamases (MBL) was performed using the synergy test between EDTA-impregnated discs and IMP. In addition, ESBL production was tested with the double disc synergy test (DDST) between amoxicillin/clavulanic acid, third generation cephalosporins, cefepime and aztreonam. The EDTA-IMP synergy test was negative, suggesting the absence of MBL production. In contrast, the phenotypic test for ESBL production based on the synergy between third generation cephalosporins and amoxicillin/clavulanic acid was positive in all isolates that were identified as possible *K. pneumoniae* carbapenemases (KPC) producers.

The isolates were subjected to PCR using specific primers for bla_{KPC}, bla_{SHV}, bla_{TEM} and bla_{CTX-M}. DNA sequencing was performed on both strands of PCR amplification products. Results were compared and aligned with reference sequences using the online BLAST database and CLUSTAL W software. PCR analysis and sequencing revealed that all isolates carried the bla_{KPC-2} gene. In all isolates an SHV type ESBL enzyme was revealed. Sequencing analysis of amplicons identified bla_{SHV-12} in all cases.

At the hospital, after the isolation of the KPC-producing *K. pneumoniae*, the patients were treated with high doses of colistin (1 000 000 units every 4 h) together with tigecycline and/or gentamicin due to limited treatment options. Three patients died within a 14 day period and two survived. In all fatal cases the death was directly attributed to the bloodstream infection.

4. Detection of the optrA gene in two isolates of *Enterococcus faecalis* resistant to vancomycin from humans and food in [Country X]

As part of a research project, all enterococci collected from humans, food, and animals by the national AMR surveillance have been tested for linezolid susceptibility. Among these, four linezolid resistant isolates were detected. The four isolates included two *E. faecium* isolates obtained in 2015 from local broiler meat, one *E. faecalis* obtained in 2016 from domestically produced veal meat, and one *E. faecalis* obtained from a gastric aspirate specimen from a 47-years-old man who was admitted to the emergency room with multiple injuries after a car accident. The patient had a medical history of gastric bypass surgery, performed one year before.

Whole genome sequence (WGS) analysis for resistance mechanisms was performed. Both *E. faecium* isolates had the optrA gene (encoding resistance to oxazolidinones and phenicols), in addition to aph(3')-III, aadE (encoding aminoglycoside resistance), erm(B), msr(C), and lnu(B) (encoding macrolide-lincosamide-streptogramin resistance). The *E. faecalis* isolated from veal meat was positive for optrA, fexA (encoding phenicols oxazolidinones resistance), str (encoding aminoglycoside resistance), erm(B), lsa(A) (encoding macrolide-lincosamide-streptogramin resistance), tet(M) and tet(L) (encoding tetracycline resistance). The *E. faecalis* isolated from the patient was resistant to vancomycin (MIC=16 μg/ml) and, in addition to optrA, fexA, str, erm(B), lsa(A), tet(M) and tet(L), harbored vanD (encoding resistance to vancomycin).

5. Cluster of *Staphylococcus aureus* isolates resistant to all classes of β-lactam antibiotics in [Country X]

Initial input

Report from Hospital A located in the [capital of country X] to the [national authorities]

From October to November 2017, five clinical isolates of *Staphylococcus aureus* resistant to all classes of β-lactams including anti-MRSA cephalosporins, ceftobiprole and ceftaroline, were collected from four ICU patients with healthcare associated bloodstream infection (BSI) and a healthcare worker in the hospital A.

Isolate	Source	MIC of β-lactam antibiotics* (mg/L)											
		PEN	OXA	TMC	FOX	CTX	CAZ	FEP	CBP	CRL	ETP	IPM	MEM
ABC123	Blood, patient V, ICU 1	8	128	>128	64	>64	>128	>32	2	1	>2	8	4
DEF456	Blood, patient	8	>128	>128	64	>64	>128	>32	4	2	>2	4	8

Isolate	Source	MIC of β-lactam antibiotics* (mg/L)											
		PEN	OXA	TMC	FOX	CTX	CAZ	FEP	CBP	CRL	ETP	IPM	MEM
	W, ICU 1												
GHI789	Blood, patient X, ICU 2	16	>128	>128	128	>64	>128	>32	8	2	>2	>16	8
GHI101	Blood, patient Y, ICU 2	16	>128	>128	64	>64	>128	>32	4	2	>2	>16	8
JKL121	Nasal swab, nurse Z, ICU 2	16	>128	>128	128	>64	>128	>32	8	2	>2	>16	8

*PEN, benzylbenicillin; OXA, oxacillin; TMC, temocillin; FOX, cefoxitin; CTX, cefotaxime; CAZ, ceftazidime; FEP, cefepime; CBP, ceftobiprole; CRL, ceftaroline; ETP, ertapenem; IPM, imipenem; MEM, meropenem

Inject

As part of ongoing collaboration, the isolates were sent to the University of B. for confirmation and further identification. The novel *mec*D gene, recently discovered in methicillin-resistant *Macrococcus caseolyticus* strains from bovine and canine origins[2], was identified in all five isolates.

6. First case of *Candida auris* candidemia in [Country X]

Initial input

Report from Hospital A located in the [capital of country X] to the [national authorities]

On October 9, 2017, a 31-year-old man with a long history of chronic renal failure was admitted to the intensive care unit of the Hospital A with symptoms of septic shock secondary to pneumonia and complicated by acute renal failure. The patient was known to have immotile cilia syndrome and bronchiectasis with recurrent episodes of sinusitis. Beginning on day 1, the patient received treatment with different courses of a wide range of broad-spectrum antimicrobial drugs. However, despite treatment, the patient's condition continued to deteriorate. On day 12 after admission, a blood culture yielded yeast growth that was identified with 99% probability as *Candida haemulonii* by using the Vitek 2 yeast identification system. The isolate was sent to the national reference laboratory for further identification and antifungal susceptibility testing. The isolate was resistant to fluconazole (MIC >256 μg/mL) and susceptible to amphotericin B (MIC 0.064 μg/mL), voriconazole (MIC of 0.38 μg/mL), and caspofungin (MIC of 0.064 μg/mL) by using gradient strips.

On MAST ID CHROMagar Candida the isolate formed pink colonies, which grew well at 42°C but not at 45°C. The isolate did not grow on BBL Mycosel Agar containing 0.4 g/L cycloheximide. The isolate assimilated N-acetyl glucosamine. The isolate was further characterized by sequencing of internal transcribed spacer and D1/D2 domains of ribosomal DNA. Genomic sequences for the internal transcribed spacer and D1/D2 regions (EMBL accession numbers LN624638 and LN626311) shared

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[2]VN Kos, CA Desjardins, A Griggs, et al. Comparative genomics of vancomycin-resistant Staphylococcus aureus strains and their positions within the clade most commonly associated with methicillin-resistant S. aureus hospital-acquired infection in the United States. MBio, 3 (2012), p. e00112
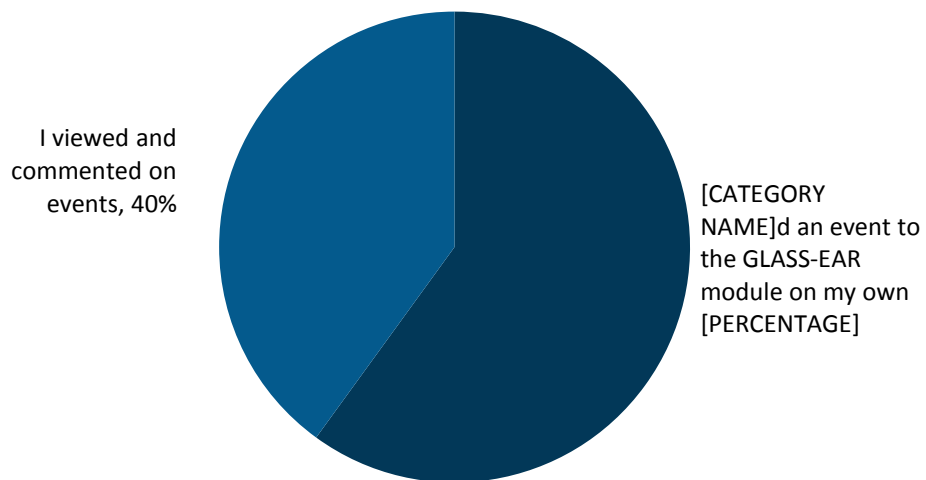
99%-100% identity with sequences for corresponding regions of several *C. auris* strains (CBS 12874, CBS 12875, CBS 12876, CBS 12880, CBS 12882, CBS 12886, and CBS 12887).

Annex 6. Participant feedback survey results

Response Statistics

Status	Count	Percent
Complete	10	100
Partial	0	0
Disqualified	0	0
Totals	10	

How did you participate in the simulation?

I viewed and commented on events, 40%

[CATEGORY NAME]d an event to the GLASS-EAR module on my own [PERCENTAGE]

Did you review any of the self-paced training materials before, or at any time during the simulation?

No 30%

Yes 70%
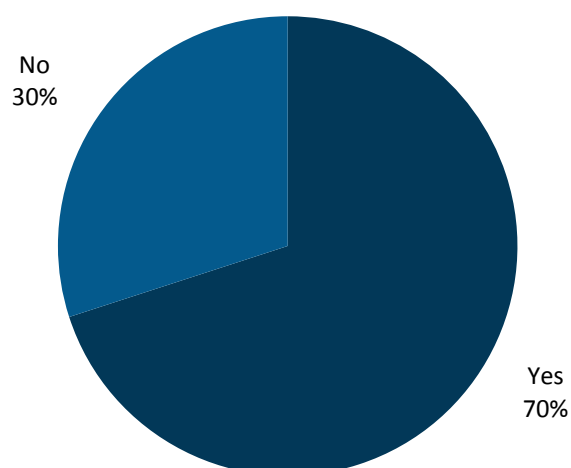
**How would you rate the quality of the training materials?**
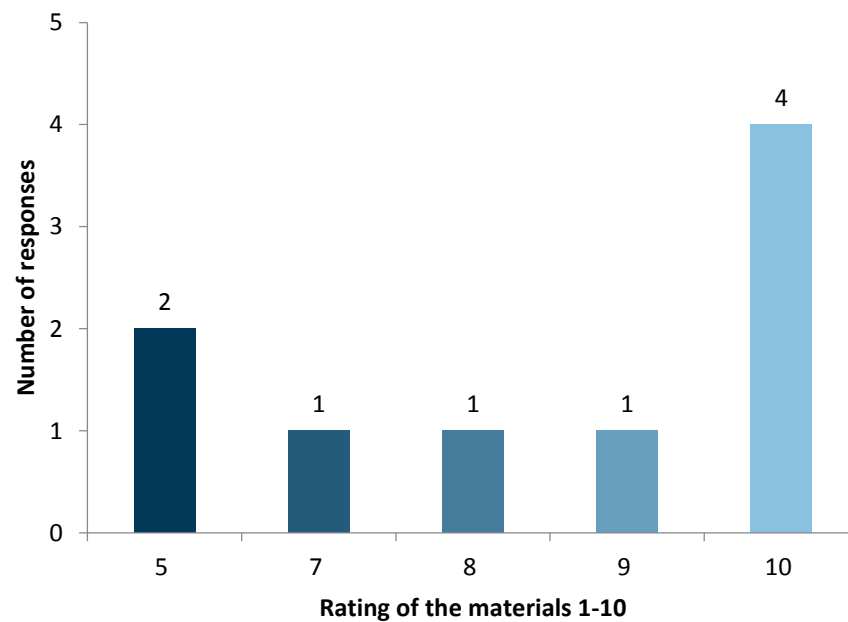
What changes or further clarifications would you suggest in the user manual for the GLASS-EAR module?

- No changes/clarifications

- To have chance to develop own case

- I did not use the manual

- Sorry, I must have missed it. I did not receive the manual or other training materials. However, it would be a good idea to provide access to the manual in the module.

**Rate your experience with process of logging in to GLASS-EAR module**
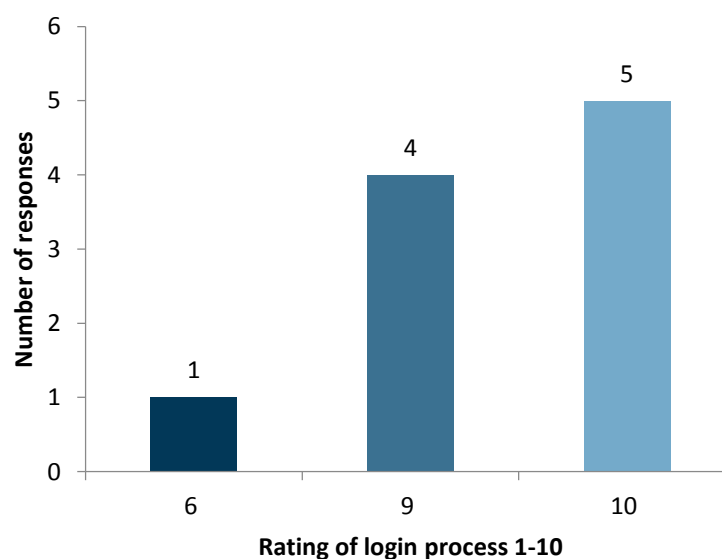
How often did you log in to the EAR module during the simulation?

Daily
30%

A few times
during the
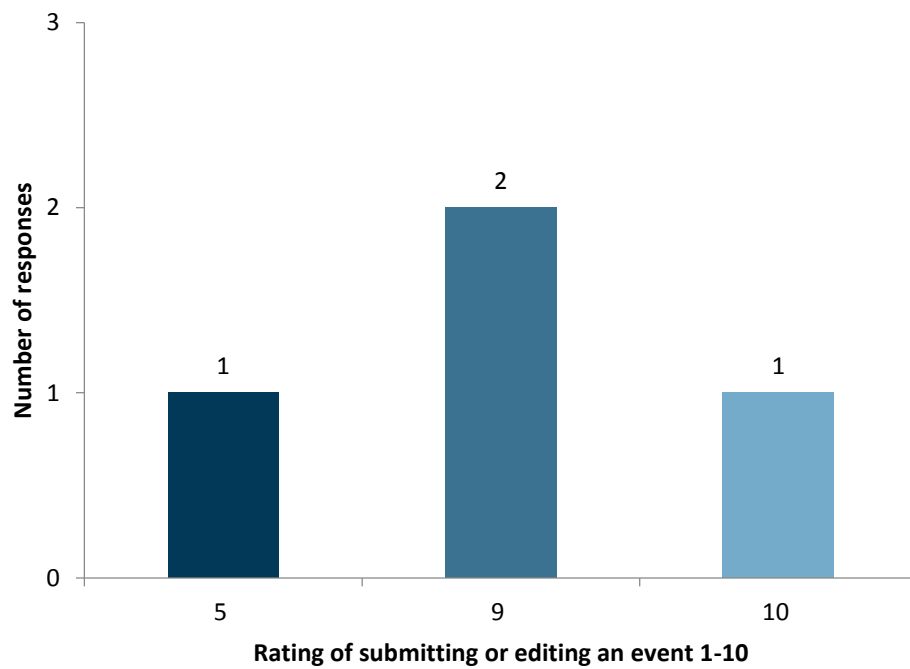simulation
60%

3-5 times per
week
10%
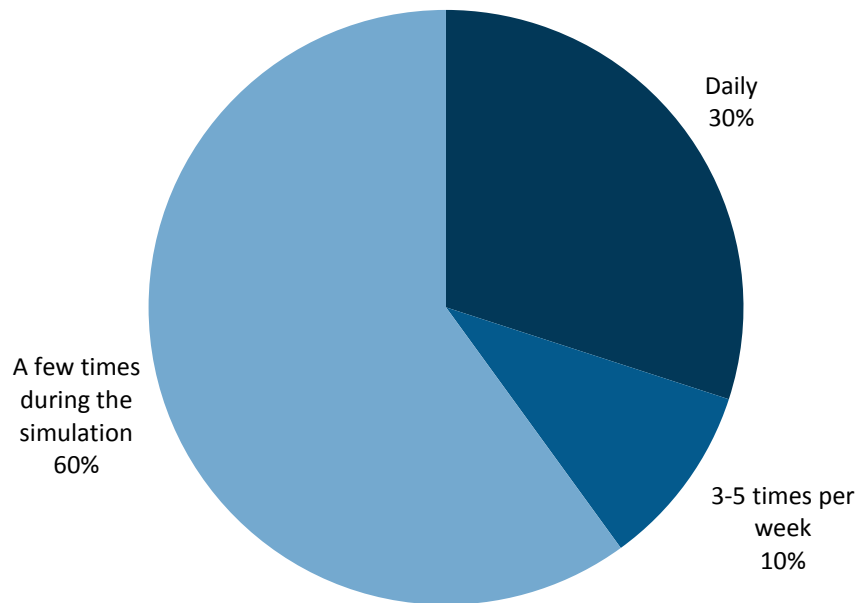
Describe any challenges you encountered logging in to the EAR module.

- No challenges reported.

Rate your experience with navigating through the EAR module

Number of responses

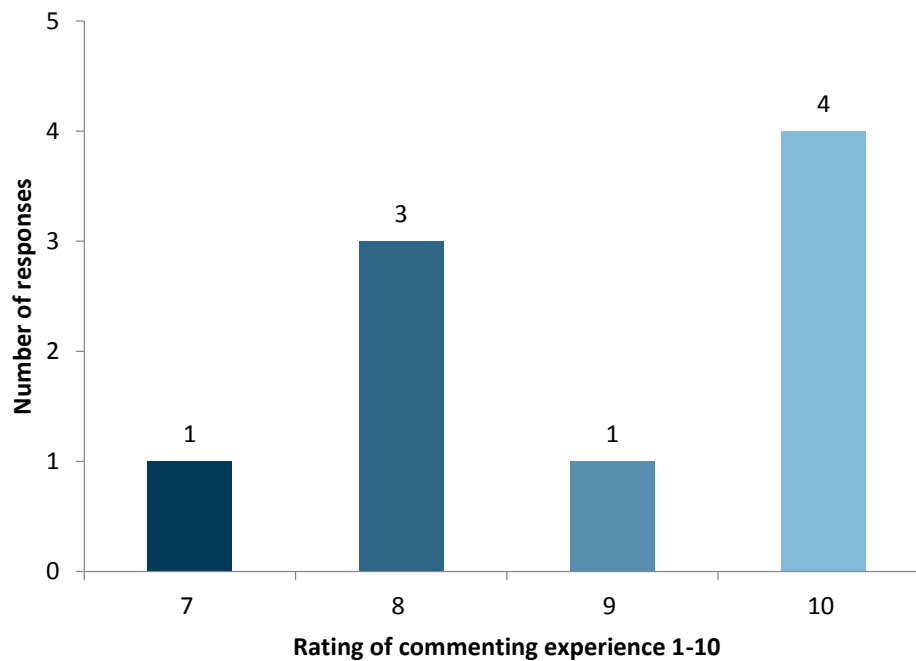| Ease of navigation 1-10	7	8	9	10
Number of responses	1	2	4	3
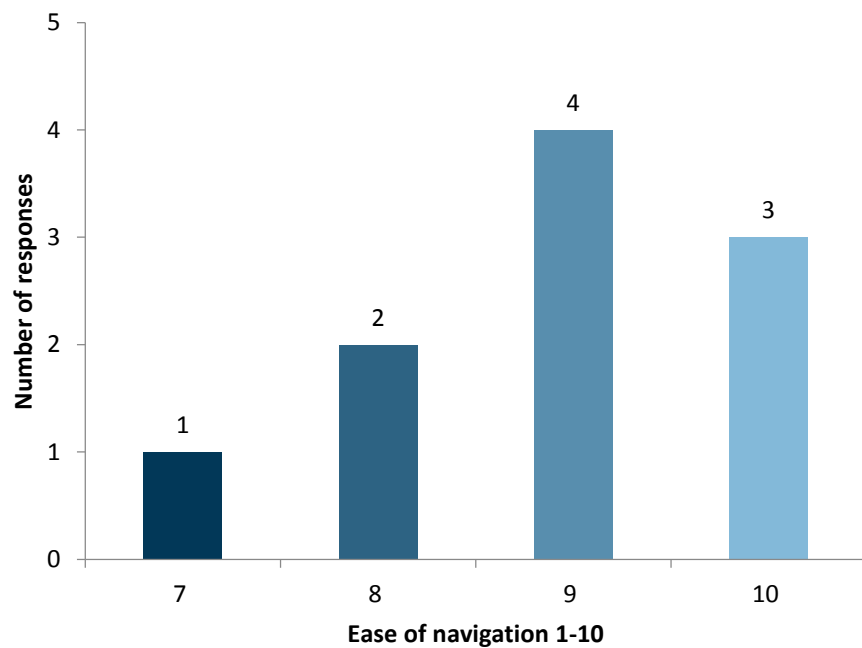
Rate your experience entering and submitting a new event or editing an existing event

Please describe any challenges you encountered entering and submitting or editing an event.

- No challenges reported

**Rate your experience of viewing and/or commenting on events**

Please describe any challenges you encountered commenting on an event.

- Straightforward. rapid email afterwards, highlighting the new comment. Hyperlink in email to go directly to the record would be useful. Tricky to refer to the record while adding a comment. In this situation, the comment box seemed to disappear, I couldn't find it and had to start again. However, when I posted, several draft comments appeared.

- No challenges encountered.

- I viewed only the emails received and did not comment.

Do you feel that the event form includes all the relevant information, or would you suggest modification or addition of some areas?

- Consulted with GLASS leads in UK; we could think of no changes. reports are clear

- I think the form includes all the relevant information

- Form includes all relevant information

- Some of the events lack detailed phenotypic testing of resistance (ESBL testing, Carba NP, MHT, MBD for colistin, ...) which are usually done prior to genotypic techniques.

- Adding geographic location (i.e. region, city, etc.) of initial sampling may be helpful. Location may be approximate.

- I felt in some cases an assessment of the importance and relevance of the reported event would provide more added value. E.g. if PDR is detected for the first time in a country or region (or even hospital if we want to be inclusive). Another similar example was the case of the optR detection.

How would you rate the frequency of email notifications and the rationale behind the notifications?


Too many
40%

About right
60%
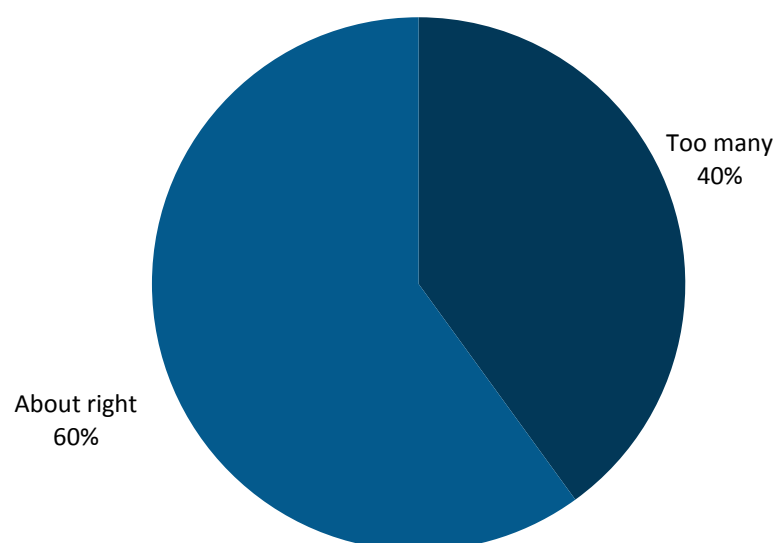
How could notifications issued by the system be modified to be more useful to you?

- Hyperlink in email to go directly to the record would be useful, rather than just to main site. For simplicity, the record rating to the most recent email notification should appear at top of list in GLASS-EAR.

- Travel history of patients should be available routinely, so that users from other countries could better assess potential risk of transmission and relevance for their respective countries.

- Notification on the comments should be categorized based on the added value of the comments (e.g. further testing required, missing information completed, observer, ...)

- Notifications issued by the system are practical.

- Just right

- The notifications are very useful. However, I was wondering if including all information in an e-mail could risk confidentiality.

Tell us about elements of the GLASS-EAR module and the simulation that you find work well?

- Very rapid; simple to use; would be easy to populate; provide a nice portal for exchange opinions and expertise

- GLASS-EAR module is working well

- It is a highly effective and fast way of communicating EAR events

- Notifications issued by the system

- Adding an event is clear as fields are available for each step for information required

- The aim of notification and information exchange is successfully accomplished.

Are the roles and flow of information through the module clear?

No
10%

Yes
90%
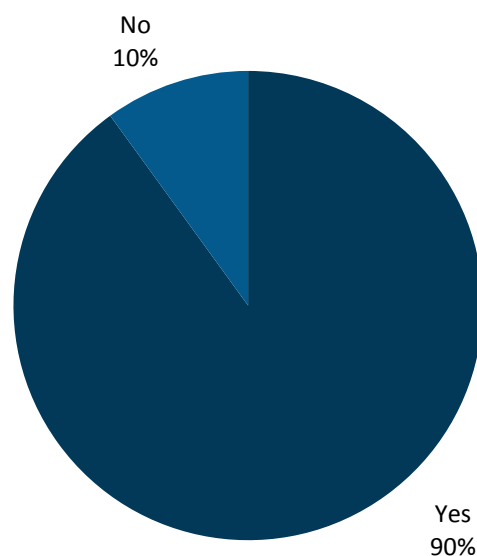
Do you have any suggestions to improve the roles and flow of information in the module?

- No

- Did not have much time to check the roles and flow

Where would you like to see changes or improvements in the module?

- I think no changes and improvements are needed

- Travel history of patients

- This form currently does not allow you to perform an advanced search. It would be useful to be able to search all published events and comments. A keyword search - a search for a word, words or phrase in the title or description of a published event would be a practical option. Keyword searches are the quickest and easiest way to search for records on a particular subject (for example "mcr 1").

- Not applicable

- One point that could be improved is that in the list of notifications the topic is very general. So if I want to add information from my country on optR, it would not be easy to see that other countries have done so already and perhaps comment on the same flow. The title or some keywords could be included in the list of notifications and a filter or search function could help find relevant reports. Another idea is to be able to attach or otherwise relate a new report to older ones on the same resistance determinant, e.g. with tags. Hope it makes sense.

Annex 7 Sample email notification

Subject: EAR event published

Dear GLASS-EAR member,
A new EAR event has been published.
A summary of the event is available below. The full report is also available on the GLASS IT platform.

Click the following link from your computer: https://glass.voozanoo.net/ear/
Type your username and password.
Click on the EAR button
Then Click on the "Published events" button. The identification number of the event is: **231**

If you have problem accessing the platform please contact the GLASS Secretariat at glass-ear@who.int.
The GLASS-team

****

Event ID: **231**
Title: **First case of Candida auris candidemia in Malta**
Reporting Country: **292**

Date of reporting to GLASS: **22/11/2017**
Date of last edit: **22/11/2017**
Date of last comment:

Date of first identification of the event: **21/10/2017**
Level of confidentiality: **Not-confidential**

Reason for reporting: **Other**
Event Confirmed: **Yes**
National reporting: **Yes**
International reporting other than GLASS: **Yes**

Involved microorganism(s): **Fungi**
Name(s) of the involved microorganism(s) : **Candida auris**
Phenotypic R details (including original MICs or zone diameters) : **The isolate was resistant to fluconazole (MIC >256 µg/mL) and susceptible to amphotericin B (MIC 0.064 µg/mL), voriconazole (MIC of 0.38 µg/mL), and caspofungin (MIC of 0.064 µg/mL) by using gradient strips**
Genotypic R details (molecular mechanism(s)) : **Genomic sequences for the internal transcribed spacer and D1/D2 regions (EMBL accession numbers LN624638 and LN626311) shared 99%-100% identity with sequences for corresponding regions of several C. auris strains (CBS 12874, CBS 12875, CBS 12876, CBS 1288**
Source(s) of the microorganism(s): **Human**

Summary: **Report from Hospital A located in Msida to the national authorities**
On October 9, 2017, a 31-year-old man with a long history of chronic renal failure was admitted to the intensive care unit of the Hospital A with symptoms of septic shock secondary to pneumonia and complicated by acute renal failure. The patient was known to have immotile cilia syndrome and bronchiectasis with recurrent episodes of sinusitis. Beginning on day 1, the patient received treatment with different courses of a wide range of broad-spectrum antimicrobial drugs. However, despite treatment, the patient's condition continued to deteriorate. On day 12 after admission, a blood culture yielded yeast growth that was identified with 99% probability as Candida haemulonii by using the Vitek 2 yeast identification system. The isolate was sent to the national reference laboratory for further identification and antifungal susceptibility testing. The isolate was resistant to fluconazole (MIC >256 µg/mL) and susceptible to amphotericin B (MIC 0.064 µg/mL), voriconazole (MIC of 0.38 µg/mL), and caspofungin (MIC of 0.064 µg/mL) by using gradient strips.

On MAST ID CHROMagar Candida the isolate formed pink colonies, which grew well at 42°C but not at 45°C. The isolate did not grow on BBL Mycosel Agar containing 0.4 g/L cycloheximide. The isolate assimilated N-acetyl glucosamine. The isolate was further characterized by sequencing of internal transcribed spacer and D1/D2 domains of ribosomal DNA. Genomic sequences for the internal transcribed spacer and D1/D2 regions (EMBL accession numbers LN624638 and LN626311) shared 99%-100% identity with sequences for corresponding regions of several C. auris strains (CBS 12874, CBS 12875, CBS 12876, CBS 12880, CBS 12882, CBS 12886, and CBS 12887).

Annex 8 Sample pdf report

Emerging AMR event

First case of Candida auris candidemia in Malta

Reporting details

Reporting Institution:
Country: Malta
Reporting person:
    First Name: Elizabeth
    Surname: Scicluna
    Telephone:
    E-mail: elizabeth.a.scicluna@gov.mt

Status of the event: Accepted

Date of reporting to GLASS:

- First reporting: 22 Nov 2017 10:31:45
- Date of last edit: 22 Nov 2017 13:45:01
- Date of last comment: 22 Nov 2017 13:45:01

Reason for reporting: Other, First occurrence in the country

Level of confidentiality: Not-confidential

The event

Involved microorganism(s): Fungi

Name(s) of the involved microorganism(s): Candida auris

Phenotypic R details (including original MICs or zone diameters): The isolate was resistant to fluconazole (MIC >256 µg/mL) and susceptible to amphotericin B (MIC 0.064 µg/mL), voriconazole (MIC of 0.38 µg/mL), and caspofungin (MIC of 0.064 µg/mL) by using gradient strips

Genotypic R details (molecular mechanism(s)): Genomic sequences for the internal transcribed spacer and D1/D2 regions (EMBL accession numbers LN624638 and LN626311) shared 99%-100% identity with sequences for corresponding regions of several C. auris strains (CBS 12874, CBS 12875, CBS 12876, CBS 1288

Source(s) of the microorganism(s) and date of sampling:

Human

      ○ Human: October 2017
      ○ Animal:
      ○ Food:
      ○ Environment:
      ○ Other:

Event detection:
Date of first identification of the event: 21 Oct 2017

Event Confirmation: Has this event/finding been confirmed by a (national/regional) reference laboratory? Yes

- Name of reference laboratory: national reference laboratory

ECDC risk assessment:
https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/Candida-in-healthcare-settings_19-Dec-2016.pdf

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Comments

Jens Thomsen, United Arab Emirates, 26/11/2017
In Dubai and Abu Dhabi, United Arab Emirates we recently had a few cases of C. haemulonii, that turned out to be C. auris. Furthermore, first cases of C. auris candidemia in the EMRO region have been reported from Kuwait in 2014 (Emara et al., EID 2014), and Oman in 2016/2017 (Mohsin J et al, Mycoses 2017; Al-Siyabi et al, J Infect 2017) .
Would be good to know if there is a travel history or epidemiological link of this patient to one of these or other countries where C. auris has been reported?

Jens Thomsen, United Arab Emirates, 26/11/2017
Regarding C. auris diagnostics:
Obviously most commercial yeast identification systems have a problem to correctly identify C. auris. For labs that are using VITEK-2 there is a now software update available (version 8.01) which obviously enables VITEK-2 users to detect C. auris correctly. Otherwise confirmation of C. auris would usually require sequencing, or MALDI-TOF, which may not widely available or easily accessible

Annex 9 List of participants

Czech Republic
Vladislav Jakubu

Gambia
Bakary Sanneh

Georgia
Lile Malania
David Tsereteli

Germany
Muna Abu Sin

India
Sunil Gupta

Malta
Elizabeth Scicluna

Mozambique
Charlotte Come

Sweden
Barbro Mäkitalo

Switzerland
Andreas Kronenberg

Thailand
Thitipong Yingyong
Wantana Paveenkittiporn

Tunisia
Ilhem Boutiba

United Arab Emirates
Jens Thomsen

USA
Jean Patel

Zambia
Chileshe Lukwesa-Musyani

European Centre for Disease Prevention and Control (ECDC)
Diamantis Plachouras

WHO Collaborating Centre for Reference & Research on Antimicrobial Resistance and Healthcare Associated Infections (UNK-105)
Neil Woodford

WHO Participants

Ana Paula Coutinho Rehse (EURO)

Shoaib Hassan (WHO HQ)

Mona Elshokry (EMRO)

Sergey Eremin (WHO HQ)

Martina Escher (WHO HQ)

Pilar Ramon-Pardo (PAHO)

Simulation Exercise Consultant

Tamara Curtin Niemi