



# Newsletter

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## Editorial

Dear Reader,

This issue of the Newsletter will report on recent activities and achievements made in the framework of our Joint Action (JA) EMERGE. The conducted External Quality Assurance Exercises for highly pathogenic bacteria and viruses again required a very challenging preparation phase including all aspects of quality assurance of samples, shipment and data analysis. The results revealed a high standard of preparedness within the participating laboratories, but also room for further improvement.

The broad participation of partners in two additional technical meetings on diagnostic approaches in Berlin and Rome showed the great interest to discuss possibilities for improvement of diagnostic approaches and their implementation.

In addition, reports from the different work packages underline the work intensive activities of the project partners. The work package leaders and the Steering Committee ensure the

correct implementation of the JA according to the planned activities. We hope to further raise your interest in our activities.

*The Editors*

## Recent meetings

“ECDC Expert consultation on ranking and prioritizing EIDT for preparedness”; Stockholm, 14-16 February 2017

Final meeting of PANDEM project; Brussels, 15 March 2017

ERINHA workshop for the scientific community and potential users; Brussels, 10 May 2017

Preparedness, Alert and Response conference; Madrid, 15 June 2017

## Recent developments

### External Quality Assurance Exercises – EQAE

In the framework of the JA EMERGE, the second round of EQAEs was performed in May, 2017 – one bacterial and one viral EQAE. The principle aim of the EQAEs is to assess, to maintain and to improve European laboratory diagnostic activities for real outbreak situations.

#### Bacterial EQAE

For the bacterial EQAE, the focus was on the identification of Risk Group (RG) 3 bacteria in clinical samples, with special attention to *Brucella* species and *Francisella tularensis* subspecies

diagnostics. Three sample types were offered to the participants: living, and inactivated test items spiked with target/non-target bacteria and, serological test items, seropositive or negative for *Brucella* or *Francisella*. The analysis of serological samples was optional. As an extra task, Antimicrobial Susceptibility Testing (AST) was performed on target bacteria of the living test items during the exercises, to evaluate newly developed Standard Operational Procedures (SOPs).

To summarize the bacterial EQAE, a total of 30 partners of the JA participated in the exercises, among them one new Romanian partner laboratory. 26 partners analysed both sample types (living and inactivated material); 4 partners analysed inactivated material only and 14 partners examined additional serological test items. All participants submitted their results successfully using a web interface developed with QuoData. The reports of the exercises and the individual certificates will be available end of August and the results are going to be discussed at the face-to-face meeting in Lisbon (October 2017).

#### Viral EQAE

The second virological EQAE focused on the detection of different Crimean-Congo haemorrhagic fever (CCHF) strains, Marburg virus strains and Ebola virus strains. Travel history and description of symptoms were added as

information to the 12 inactivated samples to allow a decision which assay might be valuable for the detection of these viruses by nucleic acid detection technologies. 21 partners from 15 EU member countries took part in the viral EQAE. Optional 4 samples for the detection of Ebola virus specific antibodies were included in the second EQAE. 10 partner laboratories participated in the exercise. All participants submitted their results successfully using a web interface developed with QuoData. The reports of the exercises and the individual certificates will be made available and the results are going to be discussed at the face-to-face meeting in Lisbon (October 2017).

### **Technical meeting in Berlin**

For the participants of the bacterial EQAE, an additional meeting was organized in Berlin in February, 2017. The meeting was meant to address diagnostic gaps identified during the first EQAE of the JA performed in 2016 as well as to prepare for the EQAE in May 2017. During the meeting, best laboratory working practices were exchanged and diagnostic issues (especially *Brucella* spp. identification) discussed, as well as suggestions for improvements made. Plus, laboratories that scored best during the first bacterial EQAE, shared their laboratory workflows that are applied to identify and/or to rule out target bacteria of the JA inside of samples, with the aim to

improve laboratory capacities within the network for the second EQAE (please see above).

### **Technical meeting in Rome**

The WG2 workshop titled “Controversial aspects of RG4 diagnostics: neutralisation assays and Lassa molecular detection” was held on the 14th of June 2017 in Rome

Representatives of all partner institutes with a BSL4 laboratory were present as well as representatives from other partner institutes for a total of 25 participants were present.

This meeting was a good opportunity to compare the serum neutralization procedures for RG4 agents, in particular for Filoviruses (EBOV Gueckedou, EBOV Mayinga, EBOV Makona) and Arenaviruses (Machupo and Guanarito).

It was also an occasion to face up the problems in molecular diagnosis of Lassa fever infection. A new diagnostic kit, that will be commercially available in September 2017, was presented by Altona. A wet lab exercise was carried out during the workshop to evaluate the performance of the kit.

An inter-institutional comparative study for Ebola neutralisation test was proposed by BABS and Marburg, the applicability will be discussed at the SC.

## **Work Package & Working Group activities**

### **Coordination of the Joint Action (Work Package 1 (WP1))**

WP leader: Robert Koch-Institute (RKI) Germany.

The interim report on activities and achievements performed during the second project year was prepared and submitted in time. It contains a technical and a financial part and is composed in a way to allow an insight in the use of the allocated EC funding. For the second reporting period, it was foreseen to provide eight deliverables and ten milestones. Both of the aims were achieved.

The 3rd project meeting, which will take place in Lisbon from 18 to 20 October 2017, is currently being prepared. The organization of the meeting is shared between the Instituto Nacional de Saúde Dr. Ricardo Jorge (INSA), the Portuguese EMERGE partner and the coordinator.

As EMERGE is funded in the framework of the 3rd Health Programme 2014-2020, it has been involved in the mid-term evaluation of the Health Programme. Moreover, EMERGE has been selected as case study for the mid-term evaluation, and the coordinator has been interviewed by the evaluators.

A further activity at EU level, was the “Public Health Conference: Preparedness, Alert and Response:

Lessons Learned in Europe from Last Cross-Border Health Infectious Threats” in Madrid in June 2017, organized by the Consumers, Health, Agriculture and Food Executive Agency (Chafea) and EMERGE partner Instituto de Salud Carlos III (ISCIII), Spain, where EMERGE coordinator and co-coordinator participated as presenters.

In order to gain an overview on the partners’ attitude towards the usefulness of EMERGE, a survey on the benefits of the project has been launched. The results clearly show that the vast majority of partners considerably profits from participating at various activity levels.

### **Dissemination of the Joint Action activities (Work Package 2 (WP2))**

WP leader : Institut National de la Santé et de la Recherche Médicale (Inserm), France.

This work package (WP) focuses on two types of dissemination activities of EMERGE Joint Action:

- 1/ The communication activities that tend to support the EMERGE consortium using different communication tools (internal communication);
- 2/ The dissemination activities toward the external stakeholders in relation with the EMERGE activities and results (external communication).

EMERGE Partners are frequently asked about the external events related to EMERGE in which they are involved to

promote the events through the website or through the Newsletter.

In the same way, all new publications related to the EMERGE JA scope can be highlighted in the EMERGE website or in the Newsletter.

Inserm is developing in partnership with all the consortium members an up to date contact database of key organizations and contact persons to be informed regularly by JA EMERGE on its activities, its results and the added value created.

This database included so far all EMERGE partners, EC, ECDC, the National Focal Points (NFP) and the Health Security Committee (HSC) and has been extended with the list of relevant networks shared by WP4 leaders.

The contribution of all EMERGE partners for fulfilling this database is essential to have an updated document and to communicate to the relevant stakeholders about EMERGE.

### **Evaluation of the Joint Action (Work Package 3 (WP3))**

WP leader: Department of Health - Public Health England (PHE).

This work package (WP) provides the Joint Action with a clear overview of progress against measured Deliverables and Milestones. It also evaluates the quality of the meetings and reports and improvements or issues to the Steering Committee to allow for continuous

improvement during the Joint Action.

To date four evaluation exercises have been performed with the latest in March 2017 which demonstrated the Joint Action was broadly on track with no major delays or issues reported.



Questionnaires have also been produced and evaluated for the meetings. For the last meeting in Thessaloniki 96% of responses to all questions being 'good' or 'very good' which demonstrated excellent satisfaction and quality of the meetings being held.

### **Networking of networks for laboratory response (Work Package 4 (WP4))**

WP leader: Erasmus Medical Center (EMC) and co-leader: Istituto per le malattie infettive "Lazzaro Spallanzani" (INMI).

On 30 November 2016, an Outbreak, Preparedness and Response Coordinators meeting was organized in Amsterdam. Invited were representatives from projects and networks operating in the field of (emerging) disease preparedness and response (identified in the above mentioned report), ranging from networks with diagnostic mandate, to research networks. In addition, representatives from funding organizations as well as international

organizations were invited. The objective of this first meeting was to gather initial ideas about the process and content of the European Interoperability Protocol as well as the identification of relevant organizations/networks/projects to be involved in the development of the Interoperability Plan. To gain insight in the extent to which information is exchanged among these networks and organizations, a mock disease outbreak scenario was used. Participants were asked to map where they would get information from, who they would inform and who they would consult.

From this meeting was concluded that the variety in information sources (who informs whom at what stage) may lead to differences in the level of preparedness and responsiveness between the networks. Even the laboratory networks with diagnostic capacity indicated that they are not certain if they would receive information on alerts directly. These incomplete and informal sources of initial information provision may hamper the initiation and execution of interoperable actions.

In the coming period the conclusions from this meeting will be addressed in the Interoperability Protocol that is being developed within EMERGE WP4.

#### **Rapid capabilities for diagnoses (Work Package 5 (WP5))**

WP leader: Istituto per le malattie infettive “Lazzaro Spallanzani” (INMI)

and co-leader: Public Health Agency of Sweden (FoHM).

Following the decisions taken during the 2nd General Meeting, we have disseminated among all partners three questionnaires:

1/ Set up the lists of agents on which EMERGE will perform the activities for the second year of the project.

The aim of this questionnaire was to identify the pathogens on which focus the activity for the second year of the project.

In particular for the 2nd EQA, the majority of partners have asked to focus the exercise on:

- CCHF and Filoviruses for the viral part
- Brucella, F. tularensis, B. anthracis, Coxiella burnetii, B. mallei and B. pseudomallei for the bacterial part

2/ Verify the availability of human samples to perform Ab detection in order to implement serology of agents relevant for our project

Concerning the diagnostic capacity among EMERGE partners, during the first year of the project, many gaps have been identified in serology. With the aim to implement serological methods, we have made a census to define the human samples available. Some samples for the use in anti – Ebolavirus antibody specific ELISA, NT, WB, IFT or other serological methods have been used

during the second EQA (voluntary participation).

3/ Sharing the survey on "criteria selection" with all partners to assign a score to each agents and eventually redefine the pathogens with highest score.

The results are reported in the Table: no substantial differences have been highlighted with respect the list of the first year of the project.

Viruses			Bacteria		
Agent	Weighted Average*		Agent	Weighted Average*	
1. HPI	11.7		1. Coxiella burnetii	10.3	
2. CCHF	10.1		2. B. anthracis	10.1	
	8.8		3. F. tularensis	9.6	
3. Cowpox			4. Brucella spp.	9.5	
4. Ebola Zaire	8.6		5. Vibrio cholerae	9.2	
	8.6		6. Yersinia pestis	8.5	
4. MERS	8.5		7. Burkholderia spp.	7.6	
5. Marburg	8.3				
6. Lassa					
6. Junin	8.3				
7. Ebola Sudan	8.2				
7. Ebola Bundib	8.2				
8. Machupo	8.0				
9. Guanarito	7.9				
10. Ebola C. d'Ivoire	7.7				
10. Monkey pox	7.7				
11. Sabia	7.5				
12. Nipah	7.3				
13. Lujo	7.2				
14. Hendra	6.7				

\*To calculate the weighted average, the sum of individual scores was divided by the number of respondents, as not all pathogens were scored by all laboratories.

## Working Groups activities:

### WG1

The Bundeswehr Institute of Microbiology, leader of this WG, has provided different plates to perform AST (2nd EQA), two AST-trainings were organized (January and April 2017), a pre-testing for improvement of Brucella SOP was done, a questionnaire regarding strain collections for AST testing was distributed.

### WG2

All Metagenomics Working Group members have been asked to fulfil the state of the art on the deep sequencing technics. The last information from members has been gathered in January 2017.

The Metagenomics Working Group is now working on gathering specific protocols for each technics used for deep sequencing among the partners, classifying the protocols used for each technics and analyzing the differences among each group.

Finally an exercise of deep sequencing (EQAE) and comparison of the results should be organized at the beginning of 2018.

### WG3

Neutralization and sample inactivation are the main topics. To compare these methods a workshop was hosted by

INMI in June 2017. All partners with a BSL4 lab have presented their serum neutralization procedures for RG4 agents and the problems in molecular diagnosis of Lassa fever infection were dealt with also Altona support (new diagnostic kit were illustrated).

### **Quality assurance of laboratory diagnostics (Work Package 6 (WP6))**

WP leader: Robert Koch-Institute (RKI) and co-leader: Philipps University of Marburg (UMR).

A total of four EQAEs were performed by the WP so far – two bacterial and two viral EQAEs. The first performed EQAE had a direct impact on WP7 for the identification of training needs as on focus points of former EQAEs (as outlined above). Additional technical meetings took also place – for the bacterial part in Berlin in February (outlined above) and for the viral part in Rome in June. For the upcoming project period a third round of EQAEs is planned (spring 2018). The exercises will be a joint EQAE increasing the level of difficulty as offered coded test items are spiked either with bacteria or viruses. The EQAE will foster the collaboration inside the network comprising of about 40 laboratories specialized in the diagnosis of highly pathogenic agents (RG 3 bacteria and RG 4 viruses).

### **Training on diagnostics and biorisk management (Work Package 7 (WP7))**

WP leader: Public Health Agency of Sweden (FoHM) and co-leader: Public Health England (PHE).

This work package (WP) supports practical and theoretical training for partners of the JA. The training is an important part of capacity building and provides opportunities for each partner to gain new knowledge and subsequently implement new, or change existing, routines or methods in their respective laboratory.



Participants at the DH-PHE MinION sequencing of viral pathogens 9th-12th May 2017

Up until year two of the JA, 13 trainings have been carried out; these have been hosted by six partners. Out of the 13 training courses, eight focus on laboratory methods, four on biorisk management and one on field diagnostics with mobile laboratory infrastructure. In total 46 trainees, from 16 partners, have participated and in addition, trainees from two collaborating partners have participated in one training session.

Out of the 46 trainees that have so far participated in any of the available courses, 45 have responded to the evaluation survey distributed to them shortly following the completion of the course. Overall the trainees have been satisfied with the courses and also given useful feedback to course organizers. In summary 49% responded “excellent”, 42% “very good”, 9% “good”, 0% “fair” and 0% “poor” when asked to overall rate the course that they participated in (figure 1).

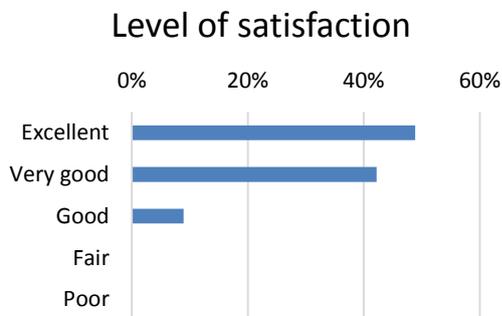


Fig. 1. Trainees satisfaction with the training courses.

During June to August 2017, an electronic survey has been distributed to all partners assessing their current need for trainings and a new version of the training program is planned to be finalized after the general meeting in Lisbon in October.

## Recent publications

- “Prioritization of High Consequence Viruses to Improve European Laboratory Preparedness for cross-border health threats” has been published : Nisii C et al Emerging and Re-emerging Viral Infections, 2016 Vol 972 of the series Advances in Experimental Medicine and Biology pp 123-129

## Other news and interesting information

- EU Laboratory Capability Monitoring System (EULabCap): Report on 2015 survey of EU/EEA country capabilities and capacities:  
<https://ecdc.europa.eu/en/publications-data/eu-laboratory-capability-monitoring-system-eulabcap-report-2015-survey-eueea>

## Coming soon

- The next consortium meeting will take place in Lisbon, Portugal, 18-20 October 2017.