



# Newsletter

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## Editorial

Dear Reader,

The final phase of the Joint Action EMERGE is about to be entered. As there are quite some tasks to be tackled more profoundly than originally foreseen, a cost-neutral extension will be requested. Among other activities, a simulation exercise is planned to mimic a cross-border outbreak of highly pathogenic agents at European level. Fortunately, such an event has not occurred in reality during the project duration so far.

In the present issue of the Newsletter, you will find information on cooperation between EMERGE and other relevant networks, the involvement of EMERGE in the latest Plague outbreak in Madagascar, and of course, on the various Work Package and Working Group activities that were carried out.

Now, we hope to have raised your interest in the recent project developments.

The Editors

## Recent developments

### Cooperation between EMERGE and EVD-LabNet

To increase the effectiveness and efficiency of European laboratory preparedness and response to infectious disease outbreaks, an Interoperability Protocol between the JA EMERGE and the network EVD-LabNet has been e-signed the 31<sup>st</sup> of January 2018

This cooperation aims to formalise and solidify the collaboration already existing between these two networks that have specific complementary roles and mandates in laboratory preparedness and response.

In support of the implementation of the Interoperability Protocol, a permanent Liaison Team, responsible for implementing the Interoperability Protocol, is established. The Liaison Team consists of two representatives of the coordination teams of the two networks and two replacements.

In case of outbreaks, laboratories in EMERGE and EVD-LabNet can go into "Outbreak Response Mode", following established procedures and processes, and will enter into heightened alert and engage into laboratory response activities specific to the (potential) outbreak. In case of outbreaks caused by suspected risk group 4 viruses, EMERGE will take the lead; in case of outbreaks caused by suspected risk group 3 viruses, EVD-LabNet will take the lead, when not otherwise agreed between Both Parties.

Laboratory preparedness and response activities related to bacterial infections/bacteria fall outside the scope of this protocol.

### Cooperation between EMERGE and COMPARE

Collaboration during the next EMERGE EQAE in spring 2018 is under evaluation. The idea is to compare the results that each laboratory of the Metagenomics Working Group will obtain during next metagenomics EQAE with the automated analysis of the data hubs developed in the framework of the COMPARE project.

### Latest plague outbreak

During the latest outbreak of plague in Madagascar, the peculiarity and particular threat laid in the high rate of pneumonic plague infections. The regularly occurring cases of plague in the endemic areas of the island are usually infections of bubonic plague. Another very threatening fact was the spreading into the capital Antananarivo.

Very shortly after the first cases of pneumonic plague infections were reported, the EMERGE coordinator, the Robert Koch Institute, lead a working group with the contribution from the Istituto Nazionale per le Malattie Infettive "L. Spallanzani, and the Bundeswehr Institute of Microbiology as consultant laboratory for plague in Germany, developed diagnostic recommendations, which have instantly

been made available on the EMERGE website

[https://www.emerge.rki.eu/Emerge/SharedDocs/Downloads/EMERGE-Plague-recommendations.pdf? blob=publicationFile](https://www.emerge.rki.eu/Emerge/SharedDocs/Downloads/EMERGE-Plague-recommendations.pdf?blob=publicationFile)

Such recommendations have not been available at EU level beforehand.

These recommendations describe:

- the different clinical manifestations of plague
- the taking of clinical specimens
- shipment of clinical specimens and submission to the responsible diagnostic laboratory
- diagnostic procedures, such as:
  - ✓ Microscopy
  - ✓ Culturing
  - ✓ Molecular methods
  - ✓ Antimicrobial Susceptibility Testing
  - ✓ Antigen and antibody detection (serology)
  - ✓ Differential diagnosis
  - ✓ Biosafety and biosecurity
- Additional links to the websites of WHO, ECDC, CDC etc. for further information.

EMERGE has received positive feedback from various sides and hope that it will also be a useful document in the future.

### **Update on the diagnostic procedures for RG4 pathogens**

The development and evaluation of Lassa virus real-time PCR assays is a demanding task due to the high variability of the virus (which explains

why these tests are not yet available). A large number of virus strains and specimens covering the whole sequence space of the virus are required for evaluation to ensure the test is reliable.

BNITM, that lead RG4 pathogens detection and characterization methods working group, through its long term relationship with endemic countries such as Nigeria, Guinea, Togo, Benin, Sierra Leone, can provide the necessary number of isolates of all lineages for evaluation (about 100 different isolates).

The evaluation of prototype Altona Lassa RT-PCR Kit is ongoing as well as the evaluation of an optimized Lassa RT-PCR assay (based on Nikisins S et al. PLoS Negl Trop Dis. 2015).

### **Information on Altona kit and Life River**

In parallel to the Altona Lassa RT-PCR Kit Version 2 (GPC gene) and the optimized Lassa Nikisins RT-PCR (L gene), the Lassa Virus kit from Life River has been tested

<http://www.liferiverbiotech.com/Pages/Product/ProductDetail.aspx?productId=431>

While there is a good concordance between Altona and the optimized version of Nikisins assays, the Life River kit cannot detect some of the Lassa strains.

### **Training sessions to come**

Following the survey of partners training needs that was conducted in summer 2017, the training program has been

updated. The table shows upcoming training courses exclusively reserved for EMERGE consortium members. Outside training remain possible for collaborating partners own costs.

Who	Title	Suggested dates	Duration	Trainees
PHAS	Next generation sequencing- Microbiological NGS workflow and data processing	February 12-13, 2018	2 days	5 to 6
PHE	MinION sequencing of high containment viral pathogens	September 25-27, 2018 (tentative)	3 days	6
PHE	Processing possible high consequence infections in a clinical laboratory for rare and imported pathogens (RIPL)	March 2018	1 day	TBD
RKI	BSL3 Biorisk management (BMR) training	11-13 April or 16-18 April 2018	3 days	6 to 8
SPIEZ	Neutralization test for RG3/4 viruses	24 April midday 27 April 17:00	3.5 days	4
UL-IMI	Laboratory methods for detection of arboviruses	Organized upon request and availability Tentatively December 2017 or January 2018	3 days	TBD
FLI (JENA)	Molecular identification of risk group 3 bacteria	March 2018	3.5 days	2

Table 1. Upcoming training courses.

The topics of the upcoming trainings cover diagnostic algorithms, biorisk management and laboratory methods, the latter including both methods for specific pathogens as well as training in Next Generation Sequencing methodology and bioinformatics.



## Work Package & Working Group progress

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

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

After an intensive and fruitful process, a Memorandum of Understanding has been established between the EMERGE network and the European Centre for Disease Prevention and Control

- to increase the capacity within the EU for detection and characterisation of risk group 3 bacteria and risk group 4 viruses,
- to strengthen microbiology laboratory capacity with respect to risk assessment and containment of highly dangerous and emerging pathogens,
- to build synergies, defining respective roles and responsibilities, and to avoid duplication of activities in response to infectious disease threats,
- to facilitate regular mutual exchange of information, expertise and support, and
- to define relevant aspects of collaboration regarding threats caused by highly dangerous and emerging pathogens, which might constitute a serious cross border threat to the EU.

All participating parties considered this MoU as an important step forward to strengthen European laboratory preparedness and responsiveness

against cross-border threats caused by serious infectious agents.

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

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

In the framework a Joint Action (JA) the communication within stakeholders and between partners is important.

This newsletter contributes to achieve the dissemination strategy of the JA and aims at giving efficient and effective visibility of the EMERGE project to external stakeholders and to the broader general public.

The newsletter allows highlighting relevant activities of the network and supporting EMERGE partners in communicating and disseminating their work.

It is sent to the EMERGE database of key organizations and contact persons to be informed regularly by JA EMERGE on its activities, its results and the added value.

It is also published on the EMERGE website [www.emerge.rki.eu](http://www.emerge.rki.eu)

Emerge consortium members participated to recent meetings of interest:

“WHO Consultative Meeting on High Containment (Biosafety level 4) Laboratories Networking - Lyon, France, 13-15 December 2017“. Antonino Di

Caro and Giuseppe Ippolito presented the EMERGE Joint Action;

Goarn Global Meeting of Partners (GMP), Centre International de Conférences (CICG) and WHO Headquarters, Geneva, Switzerland, 6-7 December 2017. Antonino Di Caro and Giuseppe Ippolito attended.

GHSAG-LN meeting in Mexico City 29 and 30 November 2017 and Andreas Nitsche presented EMERGE activities. Antonino Di Caro supported the discussion;

“High threat pathogens preparedness and response workshop for south-eastern European countries“, Sofia, 23-24 November 2017. Barbara Bartolini presented the EMERGE JA;

Bacteriology and parasitology unit of the Center for Infectious Disease Research, Diagnostics and Perinatal Screening (IDS) of the RIVM, 26 September 2017. Maaïke de Vries presented "De zware jongens onder de bacteriën: the bad boys within the bacteria".

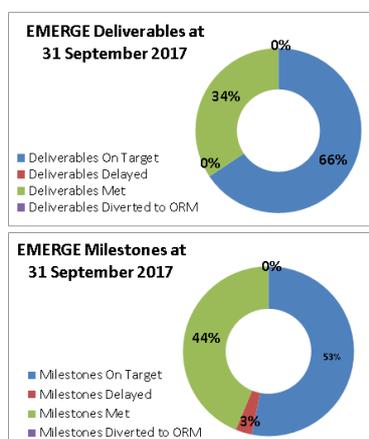
Ebola MoDRAD 3rd Outbreak Management Workshop at PHE Porton Down 5-7 April 2017. Robert Watson presented the EMERGE JA.

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

WP leader: Department of Health - Public Health England (PHE). In June 2017 a survey was performed of EMERGE partners by RKI to evaluate the benefits for partner laboratories participating in the Joint Action

EMERGE. Nearly all survey participants agreed that EMERGE helped to improve the overall situation in the laboratories fostering international alliances and increasing preparedness for possible cross-border outbreaks involving highly pathogenic agents.

We have recently evaluated the Joint Action General Assembly meeting that was held in Lisbon 18-20 October 2017. The evaluation revealed that the majority of participants were very pleased with the Joint Action and 94% of responses were 'very good' or 'good' to all questions posed. The evaluation highlighted areas such as information exchange between participants as excellent. Partners also found the real world cases and examples to be very informative and useful.



This WP also evaluates the progress of the entire Joint Action and to date five evaluation exercises have been performed with the latest in September 2017 which demonstrated the Joint Action was broadly on track with no major delays or issues reported.

## 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).

In WP4 the interoperability protocol of EMERGE JA and EVD-LabNet was established. Furthermore both networks joined forces to look at the status, quality and specific needs of Ebola virus (EBOV) diagnostic capacity and capability in laboratories in both networks through an online questionnaire that was conducted in 2016. Laboratories associated with these two European preparedness expert laboratory networks were invited to participate in an assessment of the response of European laboratories to the EBOV outbreak, to identify learning points and training needs to strengthen future outbreak responses. Response aspects assessed included diagnostics, bio-risk management and quality assurance. The overall coverage of EBOV diagnostics in EU/EEA was found to be adequate although some points for quality improvement were identified. These included the need for relevant ISO accreditation, the provision of "inter-epidemic" EBOV External Quality Assessments, facilitating access to controls and knowledge, bio-risk management without compromising biosafety and a rapid Public Health response, and the need for both sustained and contingency funding for preparedness and response activities. The report has been accepted for

publication in Eurosurveillance and will be soon available (within 1 month).

### **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).

#### **EMERGE Inter-Institutional Comparative Study for Ebola Neutralization Tests:**

In the sequel of the Ebola outbreak in West Africa from 2014-2016 and the attempts to investigate the immune correlates of protection and to characterize a vaccine response, determination of the neutralising capacity of anti-Ebola antibodies has become an important scientific question to understand vaccine-induced immunogenicity and protection against Ebola virus. Due to the urgent requirements for this kind of analysis, laboratories worldwide had to develop and to establish neutralisation assays against Ebola virus under heavy time constraints. A first comparative study performed by NIBSC in collaboration with WHO showed that the results of the different assay formats vary strongly, and only very few of the assay results correlate on a reasonable level. This report highlighted the need to further optimize and evaluate individual neutralisation test protocols. Since studies analysing convalescent sera and immune responses of vaccines are ongoing, we have proposed an additional comparative study would be valuable to get further information on

how the different test formats correlate to each other and to determine the most sensitive and accurate methods.

Assessing the neutralising capacity of sera against wild type Ebola is a typical activity of a BSL-4 lab, and therefore supporting a comparative study for BSL4 labs is a very reasonable activity within the frame of the EMERGE program. This study would help participating BSL4 labs and other partners to further improve their neutralisations assays against Ebola virus. Thus, the results from this comparative study will allow better interpretation of test results obtained by using different assay platforms. Furthermore, the exchange of scientific knowledge as well as materials and methodologies further strengthen the collaborative relationship among BSL4 labs.

#### **Working Groups activities:**

##### **WG1**

The Metagenomics Working Group has gathered from its members specific protocols for each technique used for deep sequencing among the partners, and is classifying the protocols used for each technique and analyzing the differences among each group.

An exercise of deep sequencing (EQAE) and comparison of the results should be organized in the beginning of spring 2018.

##### **WG2**

See "Update on the diagnostic procedures for RG4 pathogens" and "Information on Altona kit and Life River" sections.

The evaluation of Altona Lassa RT-PCR Kit Version 2 and the optimized Lassa RT-PCR (based on Nikisins S et al.), is going to be extended to the other EMERGE partners involved in laboratory diagnosis of viral infections

### **WG3**

The members of the AST working group finalized the inter-laboratory validation of the microdilution method for three agents (*B. anthracis*, *B. pseudomallei* and *F. tularensis*) and results were presented. The leader of AST working group invited two representatives from the European Commission for antimicrobial susceptibility testing (EUCAST) to join the meeting in Lisbon. At this meeting the results and problems of the working group were discussed and the EUCAST representatives introduced the working group members to the regulations for testing of strain collections. In December 2017 the 3rd AST training was held focused on the reading of AST plates. And the working group started to prepare a reading guide for AST plates.

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

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

The next exercise planned by the Work Package will be a joint EQAE. Offered test items are spiked either with inactivated bacteria or viruses - blank samples are also included. The EQAE will be challenging, fostering the active collaboration inside the network between laboratories specialized in the diagnostic of highly pathogenic agents

of Risk Group (RG) 3 bacteria and/or RG 4 viruses. The EQAE is foreseen to take place in the first quarter of 2018. Preparation of test items is ongoing.

### **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).

Up until December 2017, 17 training courses have been carried out including a total of 54 trainees. During the fall of 2017, focus has been on updating the training program to meet partners training needs, for this purpose all partners were asked to respond to a survey in which they described what kind of training they would like to participate in. The need for training in bioinformatics and NGS work-flow was expressed by several partners together with needs for training in biorisk management as well as methodology for specific pathogens. The results from the survey was discussed during the meeting in Lisbon (October 18 to 20, 2017) and shortly thereafter a requests to organize new courses, to meet the needs reported, was sent to all partners. The training program was thereafter updated and published on the EMERGE intranet as well as sent out to all partners of the JA.