Application for a Joint Action
19. March 2010
QUANDHIP – "Quality Assurance Exercises and Networking on the Detection of Highly Infectious Pathogens"

Executive summary

General objectives: The envisaged Joint Action (JA) aims to link and consolidate the objectives of two existing networks dealing with highly infectious bacteria and viruses that emerged from the EU funded project EQADeBa, coordinated by the Robert Koch-Institut (RKI), Germany (EAHC n° 2007 204) and the ENP4-Lab project, coordinated by L.Spallanzani National Institute for Infectious Diseases (INMI), Italy (EAHC n° 2006 208). A major objective of the current application is to stabilise these network activities sustainably, comprising 33 partners from 21 European countries. This will ensure an exchange of best diagnostic strategies for the detection, identification and characterisation of highly pathogenic infectious agents and also the generation of appropriate reference materials. In addition, the JA will provide a supportive infrastructure that includes an agreed strategy for antibiotic susceptibility testing of bacteria, training, and external quality assurance exercises (EQAE). The JA will consider, evaluate and recommend appropriate biosafety and biosecurity practices.
Strategic relevance and contribution to the programme: The project is directed at ensuring and improving citizens´ health security and bridging Security and Health by improving the laboratory diagnostic capabilities of appointed European laboratories to detect high consequence pathogens in situations arising from natural outbreaks and deliberate or accidental release. These would not respect national borders. A closely aligned European network of specialised laboratories will have the ability for rapid diagnostics of highly pathogenic bacteria or viruses. Moreover, the network could become actively committed to support other agencies dealing with suspected or confirmed bioterrorist incidents. Participants of the JA will evaluate rapid diagnostic tools that will provide the necessary infrastructure to support the effectiveness of mobile "field" diagnostics. This would also contribute to enhance the global health security capacity.
Methods and means: Repositories of reference material for BSL 3 and BSL 4 pathogens will be extended and distributed to network participants for evaluation of implemented as well as innovative diagnostic tools. The focus will be laid on high threat bacteria of a potential bioterrorism risk, causing anthrax, tularemia, plague, glanders, melioidosis, brucellosis, and Q-fever as well as on RG 4 agents such as VHF (Filovirus, Arenavirus, CCHFV), OPV, Nipah and Hendra viruses. The Repository of reference material will be used for several EQAEs. Such exercises offer the opportunity to evaluate the accuracy of rapid assays, the processing of complex sample matrices; evaluate antibiotic susceptibility for bacteria, sampling strategies, and data interpretation. Need for training will be identified and courses will be provided by more experienced partners, making use of the experience gained in previous projects such as EURONHID (European Network of Highly Infectious Diseases) and ETIDE (European Training in Infectious Disease Emergencies) and outbreak experience. The project will be managed by the Main Partner and two Technical Coordinators supported by two project managers explicitly employed for this purpose. An advisory board will be established to support the evaluation of the activities.
Expected outcome: Both, the EQADeBa and ENP4-Lab project revealed a need for further European capacity and capability building for the detection and identification of highly infectious bacteria and viruses that is based on national and international cooperation. The consolidation of the existing networks on high threat bacteria and viruses ensures European laboratory preparedness to manage natural and deliberate outbreaks of high consequence pathogens. This structure supports and informs public health control measures, clinical patient management, epidemiological and forensic investigations.

Horizontal Work Packages

Work package Number: 1

Work package title: Coordination of the joint action

Work package Leader: RKI

Starting Date: 1

Ending date: 36

Total budget of this WP: 398 069

Number of person / days of this WP: 1183

List of the acronyms of associated partners involved (please list collaborating partners separately) (max 700 characters):

RKI; AGES; VAR; SMI-NIB; HPA-NIB; NCE; FLI; NIPH; INMI; PUM; SMI-NIV; BNI-TM; CEPR-HPA-NIV; INSERM

Description of the work (max 2000 characters):

The Main Partner of the Joint Action will be the RKI, Germany. The JA will carry out common and separate actions for both the bacterial and viral networks based on previously EU funded projects EQADeBa on high threat bacteria (EAHC n° 2007 204) and the ENP4-Lab on risk group 4 viral pathogens (EAHC n° 2006 208). These activities will be coordinated by the two Technical Coordinators and Project Managers administered by the RKI for the Network on Highly Infectious Bacteria (NIB) and IMNI for the Network on Highly Infectious Viruses/P4-Laboratories (NIV). The JA consists of 5 Core Work Packages led by designated Associated Partners or Main Partner. Two Technical Coordinators will organise the exchange of information on all activities between partners. Each network plans 6 meetings within the framework of the JA. Three meetings will bring together all participants of both the NIB and NIV. The final meeting will review the JA outcomes and present laboratory strategies and capabilities to respond to biological threats within the European Community. The JA will develop a communication and laboratory diagnostic management infrastructure. A list of European laboratories with diagnostic capabilities and expertise will be posted on the restricted area of the web site. This list will be made available to European and national health authorities and law enforcement. In addition, information relating to the NIV will be available to the health authorities of Member States that do not have a BSL4 laboratory or RG4 agent diagnostic capabilities.
All major decisions to be monitored will be agreed with board members. The network websites and electronic mail transfer will ensure regular communication between participants. All finances will be overviewed by the main partner using the experienced financial management at the Robert Koch-Institut. A Consortium Agreement will regulate all interactions inside and outside the networks.

Work package Number: 2

Work package title: Dissemination of the joint action

Work package Leader: INMI

Starting Date: 3

Ending date: 36

Total budget of this WP: 121 911

Number of person / days of this WP: 455

List of the acronyms of associated partners involved (please list collaborating partners separately) (max 700 characters):

RKI; AGES; VAR; SMI-NIB; HPA-NIB; NCE; FLI; NIPH; INMI; PUM; SMI-NIV; BNI-TM; CEPR-HPA-NIV; INSERM

Description of the work (max 2000 characters):

A dissemination plan will be agreed with Associated Partners and Collaboratoring Partners. It will include the interim and final report on the JA. It will be recommended that Associated Partners and Collaborating Partners report to their national stakeholders to aid future planning on laboratory response requirements. Stakeholders at national and EU levels should gain access to the network website to monitor project achievements and access the list of designated diagnostic laboratories. This access will improve national and international incident response time by contracting the appropriate laboratory directly for support in case of biological emergencies. In agreement with EAHC, outcomes of the project will be published in scientific literature and presented on scientific conferences. ECDC, WHO, GHSI and other networks (see Specific Objective 7) are further target structures for dissemination. The Technical Coordinators of both networks are responsible for the dissemination. Regular meetings and JA websites will be used for the dissemination of project information. The final meeting will be used to disseminate the achievements of the JA on laboratory approaches to fight biological threats in Europe.
The project will provide an overview to stakeholders on the level of preparedness, improvements required, and further identify the need for optimization of highly infectious pathogens detection strategies. In addition, experiences gained from the EQAEs will prove beneficial to additional Member States´ laboratories who are also interested in improving capabilities by means of EQAEs. The developed appropriate BSL 3 and BSL 4 biosafety and biosecurity checklist covering infrastructure requirements, containment, training requirements and practices will be offered as a guidance system to evaluate and monitor new and established laboratories.

Work package Number: 3

Work package title: Evaluation of the joint action

Work package Leader: PUM

Starting Date: 4

Ending date: 36

Total budget of this WP: 198 811

Number of person / days of this WP: 696

List of the acronyms of associated partners involved (please list collaborating partners separately) (max 700 characters):

RKI; AGES; VAR; SMI-NIB; HPA-NIB; NCE; FLI; NIPH; INMI; PUM; SMI-NIV; BNI-TM; CEPR-HPA-NIV; INSERM

Description of the work (max 2000 characters):

An Advisory Board will be set up consisting of the Technical Coordinators and most experienced Aassociated Partners. In addition, external experts in the field of biosafety, biosecurity and high consequence pathogen laboratory practitioners will be invited in agreement with the EAHC for a peer review and external evaluation at various stages of the programme. Any arising issue will be reviewed and remedial action undertaken in a timely manner. In addition, we will discuss with experts from the WHO and other European organizations (ECDC) on the principle objectives and outcomes of the JA. A continuous evaluation process will be established to ensure that the project meets its defined targets, milestones and outputs being used as indicators.
The evaluation strategy for coordination, dissemination and performance of core work packages will be agreed at the first network meeting. The intermediary meetings will be used to monitor and discuss with all participants the progress of the programme and to evaluate the results of the EQAEs. Although major problems are not expected, any issues occurring in performing the Horizontal or Core Work Packages will be communicated and disussed with Advisory Board and solved in a timely manner together with the EAHC.
The comments by external reviewers for publishing data will also be implemented for evaluation of the actions and approaches.
The quality of meetings will be controlled by questionnaires. The training approaches will also be routinely monitored and evaluated at each stage by protocol and questionnaire.

Core Work Packages

Work package Number: 4

Work package title: External Quality Assurance Exercises

Work package Leader: RKI

Starting Date: 6

Ending date: 32

Total budget of this WP: 1 667 876

Number of person / days of this WP: 4262

List of the acronyms of associated partners involved (please list collaborating partners separately) (max 700 characters):

PUM; RKI;
AGES; FLI; SMI-NIB; THL; NKUA; NCE; NVSPL; NIZP-PZH; RIVM; NIPH; BIOEF; VAR; IMBBw; SUJCHBO; CEVDI/INSA; ISS; NCIPD; IZSLER; ISCIII; IZSPB; CEPR-HPA-NIB; DGA; NVRI; MDH; LCD; DTU-VET; INMI; SMI-NIV; BNI-TM; CEPR-HPA-NIV; INSERM

Description of the work (max 2000 characters):

The aim is to ensure that the quality of laboratory methods at the participants' laboratories is adequate for a sensitive and specific detection and identification of highly infectious pathogens within appropriate biosafe and biosecure facilities and acceptable operational practices. It is based on three rounds of an external quality assurance exercise (EQAE) separately for bacteria and viruses. The EQAEs on bacteria are focused on B. anthracis, Y. pestis, F. tularensis, C. burnetii, B. pseudomallei, B. mallei, B. melitensis, and B. abortus. 20-30 samples containing inactivated bacteria in complex matrices and living bacteria, partially mixed with typical “contaminating” bacteria will be provided by RKI. Data on antibiotic susceptibility of high threat bacteria will be developed. Laboratory response time will be measured with some of the samples. Previously, EQAEs were performed for the diagnosis of Arenaviruses, Orthopoxviruses, Filoviruses, and CCHF viruses by the European BSL-4 laboratories. In the course of the JA, under the lead of PUM, 3 exercises will include additional BSL-4 agents, such as the newly discovered Arena and Filoviruses, and Henipaviruses. A syndromic approach will underpin the design of future exercises, to further test the capacity of the network to identify infectious, thus help to perform a differential diagnosis in a timely way. The results will be reported to corresponding coordinators for analysing and providing an individual protocol including recommendations for further improvements. The face-to-face meetings will be used to exchange experiences regarding methodology. The final report on EQA activities will identify and recommend improvements (if required) and will aim at standardising European laboratory diagnostic strategies in order to develop a “Gold Standard”. This would contribute to improve clinical management of patients, case tracing, inform public health authorities and increase the protection of European citizens.

Work package Number: 5

Work package title: Setting up of a repository for reference materials

Work package Leader: RKI

Starting Date: 4

Ending date: 35

Total budget of this WP: 977 231

Number of person / days of this WP: 2658

List of the acronyms of associated partners involved (please list collaborating partners separately) (max 700 characters):

RKI; INMI; PUM
AGES; FLI; SMI-NIB; THL; NKUA; NCE; NVSPL; NIZP-PZH; RIVM; NIPH; BIOEF; VAR; IMBBw; SUJCHBO; CEVDI/INSA; ISS; NCIPD; IZSLER; ISCIII; IZSPB; CEPR-HPA-NIB; DGA; NVRI; MDH; LCD; DTU-VET; SMI-NIV; BNI-TM; CEPR-HPA-NIV; INSERM

Description of the work (max 2000 characters):

For highly infectious bacteria, the setting up of a repository for reference materials has been started during the previous project EQADeBa. All associated and other network partners are asked to provide relevant and characterised bacterial isolates, clinical, and environmental samples. The Main Partner will carry out an additional quality control such as growth control or molecular and immunological typing, if applicable. The samples and preparations containing living bacteria, inactivated bacteria or DNA will be appropriately stored at the Main Partner's laboratory. Best practices for sample inactivation will be evaluated. All project participants and, in agreement with the providers, third parties can have access to the material for quality control and for validation of relevant diagnostic approaches. An appropriate 'material transfer agreement' will be arranged between the Main Partner and Associated Partners. The appropriate meeting will be used to develop an approach for usage of this repository for third parties. Data on antibiotic susceptibility of high threat bacteria will be generated in order to propose standards for these bacteria.
All BSL-4 laboratories of the network have their own repository of viral agents. In order to facilitate the circulation of reference biological materials and procedures within the network we plan (1) to create a list of key reference strains of all BSL4 viruses within the participating members´ laboratories; (2) to promote the exchange of all reference strains of all BSL4 viruses with accompanying memorandum of understanding on use and dissemination where appropriate; (3) to exchange SOPs and supporting cells/reagents to facilitate the growth of all reference strains in each members laboratories, and (4) to exchange SOPs for the molecular detection and specific identification of all key reference strains in all members´ laboratories.

Work package Number: 6

Work package title: Training on best diagnostic practices and biosafety / biosecurity

Work package Leader: NIPH

Starting Date: 5

Ending date: 30

Total budget of this WP: 883 229

Number of person / days of this WP: 2530

List of the acronyms of associated partners involved (please list collaborating partners separately) (max 700 characters):

RKI; AGES; FLI; SMI-NIB; THL; NKUA; NCE; NVSPL; NIZP-PZH; RIVM; NIPH; BIOEF; VAR; IMBBw; SUJCHBO; CEVDI/INSA; NCIPD; IZSLER; ISCIII; IZSPB; CEPR-HPA-NIB; DGA; NVRI; MDH; LCD; DTU-VET
INMI; PUM; SMI-NIV; BNI-TM; CEPR-HPA-NIV; INSERM

Description of the work (max 2000 characters):

Partners of the network will offer practical laboratory based training for other participants in terms of preparation and analysis of samples performed in BSL-3, and/or BSL-4 facilities according to best practices. The training programmes will also be available for Collaborating Partners on their own account. The training courses will be organised with respect to identified agents or sample specific themes. The duration of the training is estimated to last one week and includes the required biosafety and biosecurity instruction for work in the partners BSL3 and BSL4 facilities. All Associated Partners will agree on rhe content of the courses, learning objectives and techniques. Although there is no standard training, courses will facilitate the exchange of bacteriological and virological expertise. At the end of the project, the accumulated knowledge and experience would identify the most effective training approaches which could facilitate future activities and underpin future training approaches and personnel skill requirements. To avoid conflicts with national requirements, all countries reserve the right to final selection of participants based on security requirements and professional experience. Training quality will be monitored by participant questionnaires, which will also be part of the project outcome. Questionnaires returned to the training institution will also form the basis of the network-internal evaluation. Finally, best practices of training will be identified, reported and a future curriculum recommended. Whenever possible, the experience of other networks ETIDE (European Training in Infectious Disease Emergencies) and EURONHID (European Network of Highly Infectious Diseases), that have worked in similar areas, will ensure that training will cover all issues of best laboratory practices related to infectious diseases (clinical management, appropriate diagnostic algorithm, syndromic approach, differential diagnosis, biosafety and biosecurity).

Work package Number: 7

Work package title: Biosafety and Biosecurity: implementation of results of audits / reviews

Work package Leader: RKI

Starting Date: 9

Ending date: 33

Total budget of this WP: 356 134

Number of person / days of this WP: 1086

List of the acronyms of associated partners involved (please list collaborating partners separately) (max 700 characters):

RKI; AGES; FLI; SMI-NIB; THL; NKUA; NCE; NVSPL; NIZP-PZH; RIVM; NIPH; BIOEF; VAR; IMBBw; SUJCHBO; CEVDI/INSA; ISS; NCIPD; IZSLER; ISCIII; IZSPB; CEPR-HPA-NIB; DGA; NVRI; MDH; LCD; DTU-VET
INMI; PUM; SMI-NIV; BNI-TM; CEPR-HPA-NIV; INSERM

Description of the work (max 2000 characters):

The work is meant to approve and disseminate a checklist on construction and handling of primary and secondary containments, building design and infrastructure, integrated special equipment, disinfection, and biosecurity issues etc. In the later phase, it will incorporate current expert opinions and form the basis for any assistance required by new projects considering the construction of new European class 3 and 4 laboratories.
During the previous project EQADeBa, a checklist for Biosafety and Biosecurity was developed based on existing recommendations from EC, WHO, CDC, and national authorities. In this JA, the checklist will be further improved and validated. It will be used by the partners of the JA for setting up or evaluating their biocontainment facilities, operational management and for training courses.
The format and content of the P4 laboratory checklist will be finalised and approved including input from existing and experienced members of the P4 Network and other biosafety networks/organizations (Biosafety Europe, WHO, ECDC) who can provide cross-disciplinary input concerning Containment Level 4 facility design, building and containment strategies as well as safe and secure working practices. It will take into account the most updated guidelines/procedures and technological advances available.

Work package Number: 8

Work package title: Support to the creation of a mobile laboratory

Work package Leader: BNI

Starting Date: 6

Ending date: 29

Total budget of this WP: 134 354

Number of person / days of this WP: 488

List of the acronyms of associated partners involved (please list collaborating partners separately) (max 700 characters):

INMI; PUM; SMI-NIV; BNI-TM; CEPR-HPA-NIV; INSERM

Description of the work (max 2000 characters):

It is recognised that other EU projects are evaluating the possibility of building mobile laboratories to be deployed mainly outside Europe. The findings of a mobile laboratory feasibility study, carried out under the previous ENP4-Lab project, will be used to develop a model cooperation agreement. This will identify an agreed strategy for design, implementation, staffing, testing, and maintenance of the mobile laboratory. It will also agree on standard operating procedures, identify and deal with legal issues, care of biosafety and biosecurity, responsibilities of staff and deployment agency in relation to national demands, andacquisition of long-term funding. Additional issues such as guidelines for staff deployment, sharing of information and specimens, research and publication policies will be addressed. There will be a sustainable and proven set of standard operating procedures that ensure safe and secure working practices for operating a ‘mobile laboratory’ facility. Specific training modules will be identified to address needs and tasks of personnel dedicated to the mobile laboratory, including scientists from the country of deployment (in or outside Europe). In this content it should be taken into account that microbiological class 3 cabinets as part of the the primary containment strategy are usually not considered in Europe and would require staff to be trained and retrained.

Statistics

Total budget:	**4 737 615 EURO**
EU Co-funding:	**3 316 326 EURO (70%)**
Main Partner:	**1**
Associated Partners:	**32**
Collaborating Partners:	**2**
EU Member States:	**21**
EFTA/EEA Countries:	**2**