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**Name of the University, Hospital, Research Institute, Academy or Ministry**

Robert Koch Institute

**Name of the Division, Department, Unit, Section or Area**

Zentrum für Biologische Gefahren und Spezielle Pathogene/Centre for Biological Threats and Special Pathogens (ZBS)

**City** Berlin **Reference Number** DEU-135

**Title** WHO Collaborating Center for Emerging Infections and Biological Threats

**Report Year** 04-2017 to 04-2018

**1. Annual report on the agreed workplan**

**Describe progress made on the agreed workplan. For each activity, detail (1) the actions taken, (2) the outputs delivered, as well as (3) any difficulties that may have been encountered. Three responses are expected. [maximum 200 words per activity]. Indicate, if an activity has been completed previously, has not yet started or has been placed on hold.**

**Activity 1**

Title: Support diagnostics for known emerging infections and biological threats

Description: RKI holds specialized units on highly pathogenic bacteria, viruses and toxins. For some pathogens (anthrax, tularemia, smallpox) and toxins (Clostridium botulinum) it also holds the consultant laboratories for Germany. The units have in place evaluated diagnostics including isolation and cultivation of causative pathogens under BSL3 conditions, molecular identification and characterization, whole genome sequencing, PCR, and serology with best practice approaches. The units are experienced in analysing clinical and environmental samples. These diagnostics will be offered on WHO request for the laboratory confirmation of clinical diagnosis of emerging infections and biological threats under BSL 3 and in the future BSL4 requirements. Further, advice on patient care as well as outbreak management could be given.

Status: ongoing

The Robert Koch Institute (RKI) as the Collaborating Centre of the World Health Organization (WHO CC) for Emerging Infections and Biological Threats has supported laboratories in numerous countries in Europe, Africa, and South America in enhancing their diagnostic capabilities.

In accordance with the work plan agreed between WHO and RKI, in the framework of the Joint Action “Efficient response to highly dangerous and emerging pathogens at EU level” (EMERGE; <http://www.emerge.rki.eu>; see Activity 23423), RKI supports the networking of laboratory networks to provide surge diagnostic capacities and laboratory diagnostics in outbreaks caused by highly pathogenic bacteria and viruses throughout Europe and to support outbreak management outside Europe. Laboratory and networking capacities are available for requests of WHO (see also Activity 23423). In October/November 2017, EMERGE was involved in the development of recommendations for laboratory diagnoses in the framework of the plague outbreak in Madagascar. These recommendations were published on the EMERGE website and were well accepted by stakeholders and decision makers.

Upon request, RKI provided the Pan American Health Organization (PAHO) and WHO with reference materials (quantified molecular standards and positive controls) for the diagnosis of Zika virus disease, Yellow fever and Chikungunya fever.

Further, PAHO/WHO made a request to RKI for the preparation of a quality assurance Yellow fever molecular panel to be distributed to laboratories that received specific training and capacitation from PAHO to perform Yellow fever diagnostics, or those that requested to participate in the diagnosis of cases. This Yellow fever quality assurance panel was validated by the Centers for Disease Control and Prevention of the United States of America (US-CDC; WHO CC for Arthropod-Borne Viruses) and released to PAHO in June 2017. The panel was already widely distributed and was used for training purposes in an international workshop on “Molecular Detection and Surveillance of Arboviruses” organized by PAHO in the Dominican Republic in October 2017, with the participation of representatives of 10 American countries.

RKI contributed to the collaborative study led by the Paul Ehrlich Institute (PEI; WHO CC for Quality Assurance of Blood Products and in vitro Diagnostic Devices) for the development of the “WHO 1st International Standard for Chikungunya” for the use with molecular assays, calibration of secondary reference materials and standardization of Chikungunya viral load measurements. This standard was presented and approved by the WHO Expert Committee on Biological Standardization (ECBS) in October 2017.

Staff of RKI was appointed by WHO as observer to the First Consultation on the Expert Laboratory Technical Working Group for “Eliminating Yellow Fever” (EYE) Strategy that was held in WHO Headquarters in Geneva on 18-19 December 2017. The main goal of this consultation was to review and update laboratory methodology, to enhance operational readiness and to launch a Technical Working Group. RKI led the preparation of a review on Yellow fever diagnostics, in cooperation with Erasmus University Hospital Rotterdam (EMC; WHO CC for Arbovirus and Haemorrhagic Fever Reference and Research), Aix-Marseille University, Marseille (AMU), Bernhard Nocht Institute for Tropical Medicine (BNITM; WHO CC for Arbovirus and Haemorrhagic Fever Reference and Research) and the European Centre for Disease Prevention and Control (ECDC) on arbovirus diagnostics from the EVD-Labnet Network (emerging viral diseases).

Further in accordance with the work plan agreed between WHO and RKI, RKI organized and conducted the Glienicke workshop on “Electron microscopy in infectious diseases” in September 2017 in order to conserve and to improve the diagnostic standards in this particular field of pathogen detection (see also Activity 23422). Further in accordance with the work plan agreed between WHO and RKI, the External Quality Assurance program for Electron Microscopy of Virus Diagnostics (EQA-EMV) was completed in March 2018 (see also Activity 23422).

Since June 2017, RKI contributed as expert to the WHO Laboratory Biosafety Manual Revision for the Monograph “Laboratory Biosafety for Outbreak Response”. This contribution included the attendance and oral contribution at the WHO BSL-4/high containment network meeting at 13-15 December 2017 in Lyon. As part of the WHO team of international experts, the RKI carried out a biosafety inspection at one of the two WHO-authorized Maximum Containment Laboratories for Variola virus (causative agent of smallpox) repositories at the US-CDC (WHO CC for Smallpox and Other Poxvirus Infections) in May 2017 in accordance with World Health Assembly resolution WHA60.1 (2007).

## **Activity 2**

Title: Support identifying unknown pathogens and developing specific diagnostic tools

Description: Identification of infectious agents with a focus on viruses in clinical specimens from WHO Member States and facilitated by WHO. Applied techniques would include Electron Microscopy, PCR, Multiplex PCR, Next Generation Sequencing to identify the pathogen(s).

Status: ongoing

RKI developed, evaluated and already published a novel method for targeted amplification and Next Generation Sequencing (NGS) based identification of viral hemorrhagic fever agents and assessed the feasibility of this approach in diagnostics.

RKI organizes and conducts the Glienicke workshops on "Electron microscopy in infectious diseases" which assemble specialists from all over the world at the RKI to conserve and to improve the diagnostic standards in this particular field of pathogen detection. The last workshop in September 2017 was attended by 50 participants from 12 countries (e.g. Canada, Japan, United Kingdom, France) with a focus on case studies (e.g. on Zika virus) and methods. The diagnostic aspects were flanked by presentations on virus cell biology of selected groups, like Flaviviruses, Poxviruses and the newly identified giant viruses. Presentations on particular bacterial life forms, such as biofilm and spores, and on the ultrathin pathology of prion diseases opened the mind for rather uncommon infectious pathogens and strengthened the preparedness for the detection of unexpected pathogens.

The External Quality Assurance program for Electron Microscopy of Virus Diagnostics (EQA-EMV) completed the 30th run end of March 2018. Six samples were sent out to 87 participants in 30 countries, including South Africa, Brazil, Singapore and Japan. RKI received about 83% correct diagnosis. However, only 38% of the participants reported correct results for all samples of the panel. The final report about the results and the sample panel will focus on the faults and difficulties of the diagnosis and will finally help to improve the diagnostic performance of the participants.

Both activities, the Glienicke workshops on "Electron microscopy in infectious diseases" and the EQA-EMV program, represent worldwide unique activities supporting the identification of unknown pathogens and development of specific diagnostic tools, which are organized and conducted by RKI.

### **Activity 3**

Title: Support establishing and managing of laboratory networks to develop guidance, tools and specific diagnostic capacities

Description: Supporting and consolidating of laboratory networks including institutions and organizations, e.g. the European Centre for Disease Prevention and Control (ECDC) and WHO to initiate worldwide quality assurance measures, harmonization of detection methods, production of reference materials, identification of best practices, and capacity building in an international context. Besides laboratory based outbreak management, training on specific diagnostic approaches and laboratory risk management could be provided.

Status: ongoing

In accordance with the work plan agreed between WHO and RKI, the EMERGE network (<http://www.emerge.rki.eu>; CHAFEA n° 677 066), funded by the European Union (EU) with the duration 1 June 2015 – 31 May 2018, has been further consolidated including 40 European diagnostic laboratories specialized on highly pathogenic infectious agents, consolidating a European network on outbreak response against these biological agents. The main tasks of EMERGE include:

- to ensure an efficient response to serious emergent and re-emergent cross-border events;
- to support a coordinated and effective response to such outbreaks by linking up laboratory networks and institutions;
- and to perform external quality assurance exercises and give appropriate trainings and to ensure laboratory responsiveness, diagnostics and bio-risk management during outbreaks.

Furthermore, a project entitled “German Contribution to Strengthen the Reference Laboratories Bio in the UNSGM (RefBio)” was started aiming to set up a global laboratory network serving for the United Nation Secretary-General Mechanism (UNSGM) in case of an alleged use of bioweapons.

Staff of RKI is member of the roster of WHO experts for Orthopoxviruses. RKI participated in the Advisory Committee for Variola virus Research (ACVVR) and the following Monkeypoxvirus meeting in November 2017. In both meetings, RKI re-initiated the establishment of a smallpox/orthopoxvirus laboratory network. The details of the network are subject of further meetings.

In accordance with the work plan agreed between WHO and RKI, with respect to biological toxins, RKI coordinates since June 2017 the new initiative EuroBioTox (“European programme for the establishment of validated procedures for the detection and identification of biological toxins”; <https://www.eurobiotox.eu>). This project brings together 60 expert institutions – laboratories, industrial partners and end users – from 23 countries from the health, food and security sectors to improve detection and identification methods for biological toxins which could be misused as potential biothreat agents. The project addresses the need for standard analytical tools and procedures, reference materials, state-of-the-art training and will establish a European proficiency testing scheme. Thereby, RKI provides laboratory capacities for the detection of prioritized biological toxins which are available for WHO requests.

#### **Activity 4**

Title: Support the identification of antimicrobial resistance (AMR) mechanisms

Description: Support the implementation of national AMR surveillance by building on experience from a project with 4 sub-Saharan African countries including strengthening national laboratory capacities in identifying pathogens and antimicrobial susceptibility testing according to international recognized standards and identification of resistance mechanisms; and through the Global Antimicrobial Resistance Surveillance System (GLASS) implementation and regional collaboration by sharing best practice experiences.

Status: ongoing

In the framework of antimicrobial resistance (AMR), RKI participated at the 2nd High Level Technical Meeting of WHO AMR Surveillance and Quality Assessment Collaborating Centres Network on 26-28 April 2017 in Sweden, including the back-to-back meeting of the WHO CC Network meeting. RKI is contributing to the work plan and several target products, such as the network of supranational laboratories to provide reference testing of unusual AMR, the emerging AMR reporting and risk assessment framework and the guidance on detection and reporting of colistin resistance. Based on the description of a plasmid-encoded colistin resistance in Enterobacteriaceae isolates from food animals in Asia, RKI initiated a country-wide request to send in human clinical Enterobacteriaceae strains with colistin resistance (together with the German National Reference Centre for Gram-negative bacteria) to search for *mcr 1* and *mcr 2* plasmid-mediated resistance by PCR (sequencing for confirmation) and to elucidate alternative resistance mechanisms by sequence comparisons (e.g. mutations in *mgrB*; the vast majority of human, clinical colistin-resistant Enterobacteriaceae lacks *mcr*-mediated resistance).

RKI has participated in the WHO survey "Assessment of laboratories conducting AMR testing" aimed towards national reference laboratories (NRL) providing a landscape analysis of AMR testing activities and capacities of NRLs which are associated with Global Antimicrobial Resistance Surveillance System (GLASS).

RKI distributed samples for the annual European Antimicrobial Resistance Surveillance Network (EARS-Net) Quality Control proficiency test for all laboratories reporting AMR data to EARS-Net and therefore GLASS.

RKI has participated at the 2nd WHO AMR Surveillance and Quality Assessment Collaborating Centre Network meeting on 12-14 March 2018, where 24 representative of 21 WHO CCs from 14 different countries and 24 representatives of WHO Regional Offices and WHO Headquarters participated.

RKI has participated in the Emerging Antimicrobial Resistance Reporting (EAR) simulation exercise in November 2017, an online simulation on data reporting and sharing component of the workflow of the EAR component of GLASS.

#### **Activity 5**

Title: Support provided to the WHO clinical network EDCARN through the inclusion of the German Permanent Working Group of Competence and Treatment Centres for patients with highly infectious life-threatening diseases (STAKOB) and RKI into the EDCARN

Description: The responsible unit within RKI will contact the treatment centres of the German Permanent Working Group of Competence and Treatment Centres for patients with highly infectious life-threatening diseases (STAKOB). The unit will highlight the advantage for treatment centres to join the Emerging Disease Clinical Assessment and Response Network (EDCARN). On behalf of RKI, the responsible unit will join EDCARN. In case EDCARN needs in depth support, e.g. detailed information, collection of expert opinions, technical meetings, the responsible unit within RKI will coordinate the process, e.g. contact experts, collect information/opinions, organize and host technical meetings to support STAKOB in fulfilling WHO request.



Status: ongoing

RKI coordinates the permanent working group of competence and treatment centres in Germany (STAKOB). In November 2017, the permanent working group was renamed to better reflect the characteristics of diseases caused by highly pathogenic agents. It is called now "Permanent Working Group of Competence and Treatment Centres for High Consequence Infectious Diseases (STAKOB)". In response to the plague outbreak in Madagascar, RKI and STAKOB clinical experts offered their support to WHO and to the Global Outbreak Alert and Response Network (GOARN) to strengthen clinical management.

- STAKOB expert (treatment centre Berlin) was sent to Madagascar to assess and support outbreak response, clinical management and infection prevention and control (IPC).
- STAKOB experts (treatment centres Berlin, Leipzig) participated at improving national guidelines on therapy of patients with pneumonic plague in Madagascar.
- RKI launched an international project together with experts from France and Madagascar in order to analyze possible causes of infections amongst health care workers with plague.

RKI and STAKOB conducted an international meeting on pneumonic plague on 21 November 2017 at the RKI, facilitating a knowledge exchange between renowned plague experts from affected countries (e.g. Madagascar, USA), STAKOB clinicians and public health authorities. A WHO Emerging Diseases Clinical Assessment and Response Network (EDCARN) representative who was previously deployed to Madagascar participated and highlighted the need for WHO guidelines on clinical management of plague.

A STAKOB expert (treatment centre Berlin) participated in telephone conferences to develop interim guidelines for clinical management of Lassa fever. A STAKOB expert (treatment centre Hamburg) was sent to Nigeria for Lassa fever outbreak response. The expertise of further STAKOB experts (treatment centres Berlin and Frankfurt) was offered to WHO/GOARN to support the response to the Lassa fever outbreak in Nigeria, but was not selected.

STAKOB experts (treatment centres Berlin, Hamburg and Frankfurt) participated at the WHO Clinical Alert, Reporting and Diagnosis, Integrated Management of Adolescents and Adult Illnesses (CARD-IMAI) Quick Check Plus Course in Mbarara, Uganda, 19-23 February 2018, to better support WHO in outbreak response in the future.

The European Epidemic and Biological Risk Clinical Coordination (EBRC) network consists of High Consequence Infectious Diseases clinical management experts – mostly infectious diseases physicians working at High Level Isolation Units (HLIU) in Europe who are WHO/EDCARN members at the same time. Under lead of the French HLIU Network COREB, EBRC launched a survey evaluating preparedness towards high consequence infectious diseases (HCID) in emergency departments of HLIU. Results of the survey are going to be presented at the European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) in Madrid/Spain in April 2018.

### **Activity 6**

Title: Support for WHO's normative functions in development of guidelines and tools. RKI will host and facilitate, in collaboration with WHO, an international workshop to draft a global guideline (interim guideline) for Crimean-Congo haemorrhagic fever

Description: The responsible unit within RKI will organize an international workshop for Crimean Congo Hemorrhagic Fever (CCHF) together with WHO. Relevant treatment centers, public health authorities, research laboratories and experts from affected countries will be identified and invited. The workshop will allow experts to exchange information, e.g. on treatment, clinical management, hospital preparedness, and to identify research and knowledge gaps. The meeting report will be provided by the unit. A WHO guideline will be drafted afterwards and consolidated by participants (working group) following WHO recommendations. WHO will be the main partner/co-leader in the whole process to assure that documents fulfill WHO requirements.

Status: ongoing

RKI and STAKOB conducted an international meeting on pneumonic plague (see Activity 23425). A WHO/EDCARN member participated and highlighted the need for WHO guidelines on clinical management of plague. RKI offered subject matter experts to WHO for the development of guidelines. RKI also offered co-hosting a WHO Guideline Development Group Meeting in Berlin in 2018.

A Crimean Congo Haemorrhagic Fever – WHO Guideline Development Group Meeting was co-hosted by WHO/EDCARN, STAKOB and RKI on 4-5 April 2017 (see Activity 23426 report in 2017). Further support in finalizing the guideline for clinical management of CCHF patients was offered, but not needed.

STAKOB treatment centre (Berlin) continued support to WHO in drafting the emergency guidance document on clinical management of patients with Yellow fever.

### **Activity 7**

Title: 2.3. Provide expertise in outbreak response to the field

Description: On request of WHO, GOARN or related WHO networks, RKI will provide technical support and expertise in outbreak and/or emergency response including support and assessment missions for WHO Member States.

Status: ongoing

Following the request for assistance of GOARN two RKI staff provided technical support in the response of the plague outbreak in Madagascar between October and November 2017. The colleagues were based in the regions Haute Matsiara and Vakinankaratra. In collaboration with Malagasy colleagues, training was carried out for doctors and nurses on the clinical picture of (pneumonic) plague, furthermore the colleagues participated in active case finding and contact tracing.

GOARN Operational Support Team (OST) approached the RKI directly asking for technical and scientific support for the investigations of the Hepatitis E (HEV) outbreak in Nigeria. The Global Health Protection Programme of the Federal Ministry of Health provided funding for test kits for HEV diagnosis to the Nigeria Center for Disease Control (NCDC). Molecular analysis performed by the RKI indicated the presence of two separate HEV outbreaks in Borno State and areas neighboring Niger.

Three RKI staff members were deployed under WHO/GOARN to provide technical assistance in the response of the diphtheria outbreak in Bangladesh among the “Forcibly displaced Myanmar Nationals” since March 2018. The RKI colleagues supported the epidemiology and information management unit and preparedness activities for the coming rainy season.

For the Lassa fever outbreak in Nigeria the Epidemiology Unit of the Emergency Operation Center of the NCDC was supported by two RKI staff members (epidemiologists) in March 2018. One RKI colleague (anthropologist) collaborated with designated WHO research focal point and NCDC risk communication unit. The GOARN Outbreak Response Training Courses in 2017 were attended by four RKI colleagues in Australia, Mexico, Portugal and the Philippines. Three of the trained colleagues were deployed for the diphtheria outbreak response in Bangladesh.

To address the need for stronger alert and rapid response capacity, the First Partners Coordination Meeting on Health Emergencies in the African Region was jointly organized by the WHO Regional Office for Africa (AFRO), GOARN and Africa Centres for Disease Control and Prevention (Africa CDC), and was held in Dakar, Senegal on 18-20 July 2017. The meeting was attended by 72 participants representing 40 global, regional and national organizations, agencies and networks. RKI was represented at the meeting by an expert. RKI staff participated as WHO/PAHO consultant in different meetings and expert panels as part of the outbreak response activities of PAHO related with the on-going Yellow fever outbreak in the Americas:

- On 12-13 April 2017 RKI participated in an External Consultation at WHO/PAHO Headquarters (Washington D.C.) for the revision of the epidemic situation and adjustment of the laboratory diagnosis and detection guidelines for Yellow fever due to the Yellow fever emergency in Brazil and in preparation of cases being detected in other countries in the region of the Americas. A complete update of the testing algorithm was proposed and agreed by the participants from the engaged institutions. The resulting recommendations were published on the PAHO website. A follow-up consultation is planned for summer 2018.
- RKI staff participated as PAHO consultant in the joint meeting held in Brasilia, 10-12 July 2017, between the Coordination of General Laboratories (CGLAB), the Health Surveillance Secretariat and the Health Ministry of Brazil for the revision of the primary and confirmation procedures for Yellow fever diagnosis in the context of the American strategy for arboviruses surveillance. This meeting was focused on the establishment of adequate collaboration mechanisms within the country to strength the Public Health Laboratory Network of Brazil.
- RKI staff attended to the Workshop for Scientific and Technical Actualization on Yellow Fever and other Emerging and Re-emerging Arbovirose held in Rio de Janeiro (2-6 October 2017) as WHO/PAHO consultant. This workshop was organized by Fundação Oswaldo Cruz and UNASUR (American Nations Association). The goal of this meeting was to strengthen the capacities of the national Institutes of Health within UNASUR for knowledge generation, improvement of services to the authorities, and training of human resources with special focus on prevention and control of sanitary emergencies, specifically on emerging and re-emerging arboviruses. RKI staff delivered a session on challenges and limitations on Yellow fever and other arboviruses diagnostic laboratories during outbreaks.

### **Activity 8**



Title: Develop training modules on epidemic intelligence exchange and outbreak response

Description: The responsible unit within RKI will develop training modules that will guide participants in implementing systems on how to gather and exchange epidemic intelligence for early warning. Units with experience both from implementing this work in Germany and from supporting partner countries will guide the development of the training materials. The training could involve study visits, workshops and follow up direct support to WHO Member States.

The training modules for outbreak response will focus on developing national guidance documents on structured outbreak responses. This work will be conducted through workshops by using scenarios and follow up support.

Status: ongoing

Under the aegis of the WHO's Pandemic Influenza Preparedness (PIP) framework, RKI collaborates with the WHO Regional Office for Europe (EURO) to improve the capacities of countries of Central Asia and the Caucasus to rapidly detect and investigate outbreaks of influenza viruses with pandemic potential and other emerging respiratory pathogens. A generic outbreak response training package, based on previously developed national outbreak response plans, was developed by the RKI in collaboration with partner countries (Armenia, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan). It consists of a 4-day Outbreak Investigation and Response (OIR) training module and a 1-day Training-of-Trainers module. Prior to the implementation of the training, modifications were made to tailor the training package to each country's specific needs. RKI epidemiologists trained national health experts in the package via Training-of-Trainers methodology in Armenia (November 2016), Tajikistan (April 2017) and Kyrgyzstan (July 2017). As a next step, RKI epidemiologists also acted as observers/supervisors for the first in-country cascade training by national trainers in Armenia (October 2017) and Tajikistan (November 2017).

In 2016, the Early Alerting and Reporting (EAR) project held a Rapid Risk Assessment Consultation Meeting at the RKI in Berlin. One of the key results of this meeting was the expressed need for a more standardized approach to the assessment of events which incorporates evidence based management options to inform decision making by Senior Officials. Since then, WHO, ECDC and Global Health Security Initiative (GHSI) countries have developed individual risk assessment approaches. In March 2018, the RKI organized a follow-up meeting to further develop and standardize the current EAR risk assessment approach in close collaboration with WHO Epidemic Intelligence Open Source (EIOS) initiative and GSHI/EAR. It enabled a productive face-to-face inter-group exchange between experts from different GHSI groups like EAR and the Risk Management and Communications Working Group as well as from WHO's EIOS initiative.

Further, the RKI collaborates with a number of African (Sudan, Tunisia) and Southeastern European partner countries (Albania, Kosovo, Macedonia, Montenegro) in the areas of epidemiology and surveillance in consultation with WHO EURO and/or WHO Country Offices. The objectives of these partnerships are to rapidly detect unexpected events linked to infectious diseases, to prepare for infectious disease outbreaks by improved preparedness planning and to enable the implementation of targeted control measures in order to stop further spread through fast and efficient response to the outbreak. This is achieved through the development and implementation of training courses and tools to strengthen national detection and response capacities. A weekly national epidemiological telephone conference to allow both horizontal and vertical exchange on infectious disease events among all states and RKI was established in Germany in 2009. This procedure has been adapted and successfully implemented in Albania and Tunisia with RKI support. The epidemiological teleconference is being prepared for launch in other countries (such as Macedonia and Montenegro). RKI epidemiologists developed and delivered training modules comprising data management during outbreaks, outbreak investigation and response including laboratory involvement, applying a One Health approach and event-based surveillance in several partner countries. In collaboration with partners, such as the respective WHO Country Offices, the German Corporation for International Cooperation (GIZ; WHO CC for Health System Strengthening) and national ministries, RKI has started preparing context-adjusted simulation exercises of different formats to test current national health emergency response plans (Sudan, Tunisia).

### **Activity 9**

**Title:** Support national antimicrobial resistance (AMR) surveillance systems including AMR and healthcare associated infection (HAI) outbreak detection and response

**Description:** Support the implementation of national AMR surveillance by building on experience from RKI's work in sub-Saharan African countries. Support and strengthen epidemiological capacity in data collection and analysis; national-level GLASS implementation; and regional collaboration by sharing best practice experiences. Support national activities to detect and respond to AMR and HAI outbreaks and provide technical support to AMR/HAI outbreak investigations in Member States upon request by WHO.

**Status:** ongoing

RKI is project partner and is working closely together with the Public Health Agency of Sweden (WHO CC for Antimicrobial Resistance Containment) within the Northern Dimension Partnership in Public Health and Social Wellbeing initiative (NDPHS) in a project to promote GLASS early implementation in participating countries. The objectives of the project are to identify logistic obstacles in implementation of GLASS in countries, to assess the supporting material developed by WHO and to identify needs for clarification or additional material and share the experiences with WHO and other countries. The final project meeting was held in December 2017 and the project report was prepared and circulated by colleagues from the Public Health Agency of Sweden; RKI submitted the study protocol for Germany, participated at the meeting and commented the report before finalization.

In 2017, RKI submitted AMR data for 2016 to GLASS and contributed to the first GLASS report, including review of the entire document before publication (see also Activity 23424).

RKI supported Ivory Coast and Burkina Faso in building bacteriological laboratory capacity. Together, a Minimal Standard Laboratory for bacteriological species identification and antimicrobial sensitivity testing was developed.

RKI conducted a one-week IPC training course for facilitators in Nigeria co-organized with the NCDC in February 2018 and a one-week pilot training course in a university teaching hospital in Abuja, Nigeria.

WHO has released "Antimicrobial Stewardship: A competency-based approach" on OpenWHO, a course that will equip clinicians who frequently prescribe antimicrobials with knowledge and tools to improve their use of these essential medications in daily clinical practice. RKI was involved in the review process of this online course.

Between 12-14 March 2018 RKI staff participated at the 2nd Meeting of the WHO AMR Surveillance and Quality Assessment Collaborating Centres Network.

### **Activity 10**

**Title:** Support IHR implementation activities of WHO and its Member States

**Description:** Self-assessment of the implementation of IHR core capacities is required annually by WHO. As necessary RKI can serve as an external, independent partner to participate in Member States assessment bringing specific expertise in order to provide relevant recommendations to the requesting countries.

RKI has a long standing experience in the area of infectious diseases and aviation. The importance of Points of Entry (PoE) core capacities for IHR is increasing with increasing air travel worldwide and RKI can assist countries seeking advice and support in implementing the relevant measures at the points of entry in close collaboration with WHO and ICAO.

All rights to the data and information provided by a Member State hereunder will exclusively be and remain vested in that Member State. RKI will treat such data and information as strictly confidential, and use them only for the purpose of performing the work hereunder. In this regard, RKI shall provide the data and information only to those persons in RKI who have a need to know for the aforesaid purpose, and are bound by appropriate obligations of confidentiality and restrictions on use. It is explicitly understood and agreed that any other use by RKI of the samples and information, as well as any disclosure other than to the aforesaid persons, shall be subject to the express advance approval in writing of WHO and the Member State concerned.

With the exception of any pre-existing intellectual property rights of RKI, all rights to the results of the work performed by RKI hereunder shall also exclusively be owned by the Member State concerned.

Status: ongoing

RKI has supported the implementation of the International Health Regulations (IHR) 2005 at national and subnational level in numerous countries in Europe, Asia and Africa.

The IHR Review Committee on Second Extensions for Establishing National Public Health Capacities and on IHR Implementation (WHA 68/22 Add.1) recommended "...to move from exclusive self-evaluation to approaches that combine self-evaluation, peer review and voluntary external evaluations involving a combination of domestic and independent experts." In light of this, WHO, in collaboration with partners and initiatives, such as the Global Health Security Agenda (GHS), developed the Joint External Evaluation (JEE) process as part of the IHR 2005 Monitoring and Evaluation Framework (IHRMEF). The JEE tool is intended to assess country capacity to prevent, detect and respond to public health threats independently of whether they are occurring naturally, deliberately or accidentally.

Countries can request a JEE mission to help them identify the most urgent needs within their health system. The JEE will facilitate engagement with stakeholders and partner initiatives to support the country's national outbreak and health emergency preparedness.

RKI has provided experts for several JEEs to evaluate core capacity implementation, including the Technical Area "Points of Entry":

- Latvia: 7-12 May 2017
- Slovenia: 4-9 June 2017
- Belgium: 18-23 June 2017
- Switzerland: 30 October – 3 November 2017

Within the same IHRMEF, RKI experts have participated in two regional workshops organized by WHO Regional Office for the Eastern Mediterranean (EMRO). One was the 6th Stakeholder Meeting to review the implementation of the IHR, held in December 2017 in Amman, Jordan. The goal was to share experiences between countries on approaches to IHR implementation reflecting on lessons learned and best practices over the past 10 years, to promote components of the IHRMEF, and to identify solutions for improved global health security and the way forward. The second workshop was a Regional Simulation Exercise Training in January 2018 in Marrakesh, Morocco, where the methodology outlined in the WHO Exercise Manual was introduced and immediately applied by the participants. This included the preparation of planning, development and implementation of table top exercises, and helped enhance an exercise experts' network.

### **Activity 11**

Title: Organise an IHR summer school with a focus on emerging infectious diseases

Description: The aim of the summer school is to strengthen surveillance, alert and response systems for public health events by introduction of IHR concepts to epidemiologists in relevant positions in the public health system of various countries for strengthening IHR core capacity implementation.

The methodology of the summer school will consist of a broad range of interactive teaching methods, such as didactic lectures, e.g. on legal aspects, structural requirements and basic principles of radiological, chemical and biological hazards, input presentations from the participants, e.g. concerning their experiences and specific obstacles in IHR implementation, group discussions, and table top exercises, e.g. scenario simulation of an unexpected event with application of IHR, exercise of inter-sectorial and international cooperation. A field trip to a point of entry (PoE), e.g. the Hamburg harbour and airport will provide insights to the working of different points of entry at the local level in Germany.

The Summer school will be open to representatives from all Member States, focusing primarily on the WHO European Region to allow some exchange of similar experiences. Ideally information about the summer school should be sent through the WHO European Regional Office to the respective NFPs with the offer to identify people with experience in the IHR relevant topics like Surveillance, Coordination, Point of Entries or Chemical/Radiological threats.

Status: ongoing

From 2017 onward, the RKI organizes an annual 5-day IHR Summer School. The aim of the IHR Summer School is to strengthen the IHR core capacities of interested partner countries especially regarding infectious disease surveillance, early warning and response systems.

Although the focus is on the identification and management of biological hazards, inter-sectoral collaboration and communication remains a core element of the course. In addition, the training course intends to foster national and regional networks and exchange of experiences and knowledge. During the IHR Summer School, the main topics are taught via reciprocal presentations, case studies and group discussions (peer-peer learning). Despite the name "Summer School", the course offers a platform for horizontal, collegial exchange. Concrete examples are invited from participating countries to help explain and compare different methods and procedures. Relevant key experts from RKI, WHO Regional Offices and other relevant partners are invited to facilitate, chair sessions and share experiences about implementation of the IHR in Germany and abroad as well as the challenges to be overcome.

The first summer school was held between 4-7 July 2017 with 23 participants from South East Europe (Albania, Bosnia & Herzegovina, Kosovo, Montenegro, Macedonia, Serbia). The course evaluation was extremely positive from both participants and facilitators. The objectives and participants' expectations were met and the interactive teaching methods utilised were very well received. Based on the feedback received, a similar format will be used for future IHR Summer Schools. The 2018 IHR Summer School is aimed at 25-30 public health experts from selected partner countries in Africa and will be held between 25-29 June 2018 in Berlin.

## 2. Annual report on other activities requested

**Should WHO have requested activities in addition to the agreed workplan, please describe related actions taken by your institution [maximum 200 words]. Please do not include in this report any activity done by your institution that was not requested by and agreed with WHO.**

Within the reporting period, RKI deployed 5 highly experienced staff members (Muna Abu Sin, Justus Benzler, Matthias Niedrig, Ole Wichmann and Sandra Beermann) as secondments to WHO. Amongst others, they contributed to the response to the Yellow fever outbreak in Angola and the Democratic Republic of the Congo, the Yellow fever strategy, GLASS, immunization policies and strategies as well as GOARN.

## 3. Resources

**Indicate staff time spent on the implementation of activities agreed with WHO (i.e. those mentioned in questions no. 1 and no. 2 above). Do not include any data related to other activities done by your institution without the agreement of WHO. Please indicate staff time using the number of "full-day equivalents" – a day of work comprising 8 hours (e.g. 4 hours work per day for 7 days should be recorded as 3.5 full-day equivalents).**

**Number of staff involved (either partially or fully)**

Senior staff	Mid-career staff	Junior staff, PhD students
19	8	3

**Number of full-day equivalents, total for all staff involved**

Senior staff	Mid-career staff	Junior staff, PhD students
986	761	450

**Implementation of the agreed workplan activities (i.e. those mentioned in questions no. 1 and no. 2 above) normally require resources beyond staff-time, such as the use of laboratory facilities, purchasing of materials, travel, etc. Please estimate the costs of these other resources as a percentage of the total costs incurred (e.g. if you incurred costs of USD 100 and the value of your staff time was USD 50 which makes the total of USD 150, please report 33.3% and 66.7%).**

Percentage of costs associated with staff time	Percentage of costs associated with other resources	Total
77.00	23.00	100.00

#### 4. Networking

**Describe any interactions or collaboration with other WHO Collaborating Centres in the context of the implementation of the agreed activities If you are part of a network of WHO Collaborating Centres, please also mention the name of the network and describe your involvement in that network [maximum 200 words].**

The following collaborations with other WHO CCs took place; please refer to the indicated activities for further details:

- In June 2017 RKI supported the US-CDC (WHO CC for Arthropod-Borne Viruses) in the validation activities of the Yellow fever quality assurance panel (see also Activity 23421).
- RKI contributed to the collaborative study led by PEI (WHO CC for Quality Assurance of Blood Products and in vitro Diagnostic Devices) for the development of the “WHO 1st International Standard for Chikungunya” for the use with molecular assays, calibration of secondary reference materials and standardization of Chikungunya viral load measurements.
- In December 2017 RKI led the preparation of a review on Yellow fever diagnostics, amongst others in cooperation with EMC (WHO CC for Arbovirus and Haemorrhagic Fever Reference and Research) and BNITM (WHO CC for Arbovirus and Haemorrhagic Fever Reference and Research; see also Activity 23421).
- In May 2017, RKI carried out a biosafety inspection at one of the two WHO-authorized Maximum Containment Laboratories for Variola virus repositories at the US-CDC (WHO CC for Smallpox and Other Poxvirus Infections) as part of the WHO team of international experts (see also Activity 23421).
- In February 2018 in cooperation with the BNITM (WHO CC for Arbovirus and Haemorrhagic Fever Reference and Research) and GIZ (WHO CC for Health System Strengthening), RKI staff was deployed to support the establishment of laboratory capacities for the diagnosis of Lassa fever in the National Laboratory for Haemorrhagic Fever in Cotounou, Benin. The mission team provided laboratory support for the diagnosis of Lassa cases.
- In the framework of AMR, RKI participated at the high level meeting of the WHO AMR Surveillance and Quality Assessment Collaborating Centres Network on 26-28 April 2017 in Sweden, including the back-to-back meeting of the WHO CC Network meeting (see also Activity 23424).
- RKI is working closely together with the Public Health Agency of Sweden (WHO CC for Antimicrobial Resistance Containment) in a project to promote GLASS early implementation in participating countries (see also Activity 23429).
- In February 2018 in cooperation with GIZ (WHO CC for Health System Strengthening) RKI staff gave technical support for the diagnosis of Dengue fever in Colombo, Sri Lanka.