The project
“German Contribution to Strengthen the Reference Laboratories Bio in the UNSGM (RefBio)”

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RKI/ZBS2

2018 BWC Meeting of States Parties
4-7 December 2018, Geneva, Switzerland
Secretary-General Mechanism - Activities in regard of Analytical Laboratories (General Assembly Oct. 1989 A/44/561)

- To carry out with the assistance of the consultant experts inter-laboratory calibration in order to evaluate the validity and accuracy of the analytical methods employed by the laboratories;

- The inter-laboratory calibration study (or External Quality Assurance Exercise – EQAE) should be carried out with a view to,
  - first, demonstrating competence on the part of the individual designated laboratories for the detection and identification of known CBT agents;
  - second, evaluating the capability of the individual laboratories to detect the presence of other toxic (biological) substances unknown to the laboratory in biomedical and environmental samples;
  - and third, demonstrating the level of competence represented by the laboratories collectively for the analysis of all types of samples that may require analysis in the course of the investigation
The project

“German Contribution to Strengthen the Reference Laboratories Bio in the UNSGM (RefBio)”

- **Project duration:** August 2017 – December 2020 (41 months)
- **Funding:** German Federal Foreign Office
- **Execution:** Robert Koch Institute (RKI), Berlin, Germany; the main federal public health institute in Germany belonging to the German Ministry of Health

**RKI/Centre for Biological Threats and Special Pathogens (ZBS)**

**ZBS 2** Roland Grunow (project coordinator; and bacteriology)
Accreditation as EQAE (Proficiency Test) Provider according EN DIN ISO 17043
- 3 employees (scientist, technician, project manager)

**ZBS1** Andreas Nitsche (co-coordinator virology)
- 2 employees (scientist, technician)

**ZBS3** Brigitte Dorner (co-coordinator bio-toxins)
- 2 employees (scientist, technician)
Planned activities and general objectives 2017-2020

- **Annual workshops** of participating laboratories to share experiences and best practices in order to draw relevant recommendations to the SG, planning and evaluation laboratory EQAE (Proficiency Tests).

- **Annual External Quality Assurance Exercises (EQAE)**
  
  **Focus:** close to reality samples and scenarios for diagnostic purposes and molecular forensic analyses in framework of UNSGM investigation.

- **Coordination with other activities in strengthening the UNSGM**

- **First steps for establishment of a trusting network of designated microbiological analytical laboratories**
Performed activities 2017-2018

2017

- Meeting
  - 25-27 October 2017
  - 43 participants from 14 countries

- EQAE UN1
  - Start: 20 Nov 2017
  - Target bacteria: Francisella tularensis
  - Participants: initially 14 (12 countries), finally 12 laboratories from 10 countries

2018

- Meeting
  - 20-21 June 2018
  - 48 participants from 17 countries

- EQAE UN2
  - Start: 5 Nov 2018
  - Target bacteria: Yersinia pestis
  - Target virus: Different species of the Orthopoxviridae family
  - Participants: 23 laboratories from 16 countries
UN1 EQAE – samples in concordance with the UN-regulations

❖ Scenario simulating an UNSGM investigations in response to an alleged use of *F. tularensis* as a bioweapon

❖ Preparatory phase:
  - Quality assured samples, *Francisella tularensis holarctica* Wt FDC408 heat-inactivated, non-infectious
  - Agreements, documents, shipment

Two coded sample sets according to UNSGM requirements

3 ‘clinical’ samples
- 10⁵ GE per mL
  - UN-RKI-17_C1
  - UN-RKI-17_C2
  - UN-RKI-17_NC-C1-2

3 ‘environmental’ samples
- 10⁷ GE per mL
  - UN-RKI-17_E1
  - UN-RKI-17_E2
  - UN-RKI-17_NC-E1-2

Sample matrix: human AB serum

Sample matrix: environmental water,

‘Possibly contaminated’
‘Uncontaminated’
(control sample, matrix only)
UN1 EQAE

- Two parts with increasing levels of difficulties

(1) - To identify or to rule out the target in samples

(2) - To characterize the target:
- molecular forensic: taxonomic classification, virulence genes, antibiotic resistance genes
- To answering to a couple of relevant questions:
  → Could the laboratory identify peculiarities of the biological agent(s) that are ‘unusual’ indicating deliberate genetic manipulations?
  → Are there hinds for a natural or intentional outbreak considering laboratory findings and epidemiological data?
  → Were targets in positive samples identical or different?

Evaluation by the EQAE provider:
(1) 100% correct; (2) Diverse response

Key issue for diversity:
- Various methodological approaches
- No standardized interpretation of results
Possible target bacteria: *Bacillus anthracis*, *Francisella tularensis*, *Yersinia pestis*, *Brucella melitensis*, *Brucella abortus*, *Burkholderia pseudomallei*, *Burkholderia mallei*, *Coxiella burnetii* (so far planned as INACTIVATED material; identification and deep characterization)

Possible target viruses: Different species within different virus families; detection of unknown virus from non-inactivated samples with PCR-based methods

Possible target toxins: Ricin due to current events in EU; lower priority: Abrin; BoNT; Open to different methods (immunological, functional, spectrometric; [DNA-based methods])
RefBio: Some of open questions at this point

• How to improve geographical coverage of bio-analytical laboratories?
• What are the minimal and optimal capabilities required for bio-analytical laboratories?
• How to draw recommendations on laboratory proficiency for UNODA/UNSGM?
• How to involve highly specialized laboratories not covering the entire BT panel of agents?

• Which scenarios should be covered (type, origin, number of samples)?
• What are the logistics for sample shipment and dissemination in real scenarios?
• How to document the chain of custody (template)? (OPCW Blue Book: Chapter II chain of custody)
• Assessment of impact of different methods on analytical outcomes?
• How to write the report?

• How to handle data protection within the network of bio-analytical laboratories (Consortium Agreements, secure internet platform)?
• How to link up with other relevant projects and draw common conclusions?
RefBio: Expected outcomes

**Short-term:**

- To get a better understanding of reference laboratories and their role in the UNSGM
- **Self-evaluation** of participants for own laboratory capabilities and capacities using the EQAE
- Possibilities for improvement
- Definition of laboratory analytical requirements in the framework of the UNSGM
RefBio: Expected outcomes

**Long-term:**

- Development and **recommendations for minimal and optimal laboratory requirements** as tool for nomination used by MS
- **Setting up a network of UNSGM bio-analytical laboratories** with information on their specific capabilities and specializations
- **Trusted exchange** of results and best practice between members of the laboratory network
- **Recommendations to the UNSGM** for involvement of laboratories dependent on specific scenarios
Thank you for your attention.
Questions?

Many Thanks to:
- German Federal Foreign Office for funding the initiative
- All participants
- Team at RKI

Sources of pictures: Internet or RKI