UNSGM Designated Laboratories Workshop Report

Spiez, Switzerland
12 – 14 September 2023

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Contents

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The eighth UNSGM Designated Laboratories Workshop took place from 12 – 14 September 2023 in Spiez, Switzerland.

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Executive summary

This report presents the outcomes of the eighth Swiss UNSGM Designated Laboratories Workshop organised by Spiez Laboratory on a network of trusted laboratories designated under the United Nations Secretary-General's Mechanism (UNSGM)[1] to investigate allegations of the use of chemical, biological and toxin weapons. The workshop series is a Swiss contribution to strengthen the operational readiness of the UNSGM. This activity is part of Switzerland's Arms Control and Disarmament Strategy 2022-2025[2] and links to the Secretary-General's Disarmament Agenda[3], which calls for adequate preparations to respond to any credible allegation of use of biological weapons.

Today, the UNSGM is the only instrument available to the international community to investigate an alleged use of biological weapons. The UNSGM strongly depends on what Member States make available to the Mechanism and invest into its key components. Due to the central role played by analytical laboratories nominated by Member States, Switzerland actively supports and promotes through its workshop series a capable, robust and trusted network of UNSGM designated laboratories that is fit for purpose.

The success of such a collaborative network greatly depends on the sustained engagement and active contributions of participating laboratories. To this end, the Swiss workshop series serves as an authoritative platform to further strengthen the UNSGM by providing transparency and confidence in scientific competencies, analytical skills as well as quality assurance systems. The conduct of regular laboratory exercises organised by a number of countries has become a true asset in that regard.

Since 2015, the workshops in Spiez have witnessed the evolution of a multidisciplinary and geographically diverse community of dedicated laboratories willing to share their knowledge and ideas, and most importantly to plan and orchestrate the many activities – in line with the UNSGM Guidelines and Procedures[4] – together with the UN Office for Disarmament Affairs (UNODA), the custodian of the Mechanism.

This eighth UNSGM Designated Laboratories Workshop covered an impressive set of recent activities of relevance for the laboratory community. It included the many laboratory exercises, the specific aspects of laboratory reporting and technical arrangements, lessons learned from the Capstone exercise, technological advancements of value for purposes of attribution, issues of importance at the interface with the mission team, and the future approach to toxin analysis.

The workshop took stock of the many external quality assurance exercises (EQAEs) organised by a number of countries. The wet- and dry-lab exercises greatly helped to address the different needs of the laboratory community. Workshop participants recognised that such a diverse set of exercises not only gives participating laboratories the opportunity to improve their skills, but offers other benefits as well, such as benchmarking, external evaluation and interlaboratory comparison, which can prove very useful for purposes of accreditation. Future efforts are required to encourage the participation of laboratories, particularly from under-represented regions. However, it must be said that the diverse set of exercise formats has demonstrably helped to improve this situation in recent years.

Previous workshops already recognised the particular challenges associated with the analysis of toxins in a UNSGM investigation, notably the significant differences between high molecular weight (HMW) and low molecular weight (LMW) toxins, which require

[1] https://www.un.org/disarmament/wmd/secretary-general-mechanism

[2] https://www.eda.admin.ch/content/dam/eda/en/documents/aussenpolitik/strategien/strategie-ruestungskontrolle-und-abruestung-2022-2025-EN.pdf

[3] https://www.un.org/disarmament/sg-agenda/en

[4] Guidelines and Procedures for the timely and efficient investigation of reports for the possible use of chemical and bacteriological (biological) or toxin weapons. https://undocs.org/a/44/561

different analytical methods to be used. On the recommendation of the OPCW Director-General's Scientific Advisory Board (SAB) Temporary Working Group (TWG) on the Analysis of Biotoxins that the OPCW should work more closely with the United Nations, an informal network for toxin analysis is now being formed to facilitate building international capabilities for forensic analysis of toxins. This will help to avoid unnecessary duplications and allow for a simple and flexible approach.

In recent years, the Swiss workshop series has evolved from focusing on laboratory aspects in isolation towards broadening the scope to the multiple interfaces between laboratory analysis and the wider investigative process of a UNSGM mission. Practically speaking, guidance documents and templates as well as an equipment list are now being refined, based on experience gained from trainings and exercises.

A draft template for UNSGM analytical laboratory reports, prepared by a working group under the project RefBio, met the expectations of workshop participants and will soon be submitted to UNODA as a useful tool that could be used in both exercises and real missions.

A model template for a Technical Arrangement (TA) was deemed useful by workshop participants, because it would convey realistic expectations to laboratories on important aspects like sample transport and handling, chain of custody, results reporting, and costs. A future deliverable of the workshop series should therefore be a draft model TA. To that end, a working group was tasked with the drafting of a TA outline and will report back at the next workshop in Spiez.

The workshop was also a good opportunity to take stock of new and emerging technologies and innovations that may support and facilitate sampling, chain of custody management, and forensic analysis of samples. For instance, workshop participants learned about recent advances and performance levels of targeted sequencing using hybridisation-based enrichment, the development of digital chain of custody approaches for seamless documentation, and intricacies to be aware of when using 2-colour chemistry versus 4-colour chemistry in some of today's sequencing technologies. Furthermore, the project RefBio, with the assistance of a newly formed working group, is now gradually setting up a curated reference genome database of high-quality that can support microbial forensic investigations and outbreak analysis in the future.

The lessons learned from the Capstone exercise are manifold. A future Capstone exercise would benefit from an even stronger involvement of rostered laboratories at multiple points of the interface with the mission team, particularly the mandate for analysis, laboratory reporting, and results interpretation. A next Capstone exercise is expected to be conducted in 2027 or 2028, and is proposed to be a 4- or 5-week exercise bringing in participation from different UN entities as well as rostered laboratories and experts. In the meantime, there would be value in smaller exercise formats involving laboratories that could focus on the aforementioned specific elements and may include testing of the new reporting template.

Past workshops have underscored the importance of linking up with other laboratory and expert networks. Workshop participants were briefed on a new opportunity for future sharing of guidelines and experience with the network of ASEAN CBR defence experts that engages regionally in enhancing cooperation and building capacities.

Finally, several cross-cutting issues like the emerging topic of concurrent investigations in a given scenario and their impact on a UNSGM investigation and the analysis of samples will be addressed in the near future through an appropriate exercise format.

In conclusion, the current knowledge base is broader than ever before, which greatly increases confidence in selecting appropriate laboratories, should this become necessary in the context of a specific UNSGM investigation. There is also more clarity about the roles and division of labour between UNODA

and partners such as the OPCW, WHO and WOAH.

Continuity and sustainability of the many efforts highlighted at this workshop will be critical to ensure that the UNSGM is and will remain fit for purpose. More remains to be done, particularly with regard to the further enlargement of the geographical participation in activities and the strengthening of partnerships with other international, regional and national organisations and networks. In terms of practical activities, continuing the now initiated collaboration between the UNODA and the OPCW in the field of toxin analysis, testing and refining guidance documentation and templates, revisiting issues like the secure work area concept, and the accessibility of specialised equipment will all be important steps to improve capabilities and through that ensure the readiness of the UNSGM.

In more general terms, this eighth UNSGM Designated Laboratories Workshop brought together a growing community of dedicated and motivated participating laboratories that are willing to engage and tackle the many issues at hand. UNODA's support and coordination remains key, also in terms of promoting the activities through outreach to garner more interest and secure funding.

The Swiss workshop series will continue to serve its role as an effective platform for all partners geared at bolstering the network of trusted and capable laboratories for UNSGM investigations. To that end, the ninth UNSGM Designated Laboratories Workshop will take place from 11 to 13 September 2024.

1. Introduction

The eighth workshop organised by Spiez Laboratory on a network of Designated Laboratories of the United Nations Secretary-General's Mechanism (UNSGM) was held from 12 to 14 September 2023, as a Swiss contribution to strengthen the operational capacity and readiness of the UNSGM. This effort is part of Switzerland's arms control, disarmament and non-proliferation strategy[5]. The workshop convened 71 participants from 18 Member States as well as the UN Office for Disarmament Affairs (UNODA), the Organisation for the Prohibition of Chemical Weapons (OPCW), the Biological Weapons Convention Implementation Support Unit (BWC ISU), the World Health Organization (WHO), the World Organisation for Animal Health (WOAH, prev. OIE) and the International Criminal Police Organization (INTERPOL). This report summarises the discussions and outcomes of the workshop.

The COVID-19 pandemic, the recent controversies and accusations about the nature of certain biological research activities as well as mounting fears of biological weapons use underscore the need to ensure that the UNSGM – an impartial, science-based international investigative mechanism for alleged use of chemical and biological weapons and the only instrument available to the international community today to investigate an alleged use of biological weapons – is fit for purpose. To this end, Switzerland supports the establishment of a sustainable, effective and impartial network of laboratories designated to the UNSGM.

Such a trusted laboratory network complements the other UNSGM assets. It ties in with the training of qualified experts to conduct field investigations, the work of expert consultants, and the conduct of field exercises that test procedures and capacities under realistic conditions. New challenges emanate from the expectation to support the attribution of responsibility for the use of chemical or biological weapons.

The efforts to strengthen the UNSGM also contribute to developing institutional, scientific and investigative capabilities of the BWC. The recently established Working Group to Strengthen the BWC – which amongst other things considers measures on compliance and verification – is expected to benefit from the availability of a trusted network of UNSGM designated laboratories.

Within the United Nations, UNODA acts as the custodian of the UNSGM and coordinates an Internal Task Force (ITF) that brings together UN departments and agencies that support UNSGM missions. Supported by resources made available by Member States, UNODA implements a strategic concept to maintain operational readiness of the mechanism. It manages the rosters of qualified experts (currently 562), expert consultants (currently 60) and laboratories nominated by Member States to the UNSGM (currently 88), coordinates basic as well as skill development training and exercises, and conducts outreach. These activities are being coordinated with international partners including the OPCW, the WHO and the WOAH. Other international partners support workshops and training activities, including INTERPOL and the Food and Agricultural Organization (FAO). Outreach to Member States benefits from the partnership with the BWC ISU as well as the Organization of American States - Inter-American Committee against Terrorism (OAS-CICTE).

The UNSGM training programme recognises that a mission would likely be time-sensitive, interdisciplinary in nature, politically complex, potentially hazardous, and involving team members that may not be familiar with each other. Training is important to ensure a

[5] https://www.eda.admin.ch/content/dam/eda/en/documents/aussenpolitik/strategien/strategie-ruestungskontrolle-und-abruestung-2022-2025-EN.pdf

timely, efficient, secure, and procedurally accurate conduct of UNSGM missions. The 3-phased training programme conveys aspects such as interviewing, evidence management including chain of custody, report writing, team building, and security awareness including incident prevention and response. Between 2009 and 2019, UNODA coordinated the implementation of five basic training courses, seven leadership and two skill development courses, three workshops and tabletop exercises and one field exercise. In 2022, the Capstone Exercise – funded by the German Federal Foreign Office – was conducted by the Robert Koch-Institute (RKI) in partnership with the Swedish Defence Research Agency (FOI).

Work toward a network of designated laboratories began in 2015[6], and since 2017, several countries and organisations[7] have organised exercises to gain experience and share best practices. UNODA coordinates interlaboratory calibration studies (external quality assurance exercises or EQAEs), the results of which are being assessed by expert consultants. A first workshop involving expert consultants and focal points of UNSGM roster laboratories was held in May 2023. It discussed criteria for the assessment of results of EQAEs and made recommendations for EQAE providers. Furthermore, criteria for assessing UNSGM roster laboratories that did not participate in EQAEs were discussed as well as the reassessment of laboratories before assignment to a mission.

Key findings from past UNSGM Designated Laboratories workshops can be summarised as follows:

- There are three stages of a microbial forensic investigation: unambiguous agent identification, comprehensive agent characterisation (unexpected or unusual features of the agent, epidemiological anomalies), and attribution (examination of evidence to help identifying possible sources and perpetrators of an agent release).

- Whilst many laboratories are able to conduct the types of analysis required in a UNSGM investigation, a designated laboratory must also have in place a strong quality management and assurance system, meet the highest biosafety standards, and meet forensic and procedural requirements including an unbroken chain of custody.

  Unambiguous agent identification typically requires the use of multiple orthogonal analytical techniques. There is a need for validated methods, recommended operating procedures, agreed acceptance criteria, reference standards and curated databases, as well as open-source software. Accreditation is desirable.

- The analysis aims at differentiating natural outbreaks from manmade events. Analytical targets and sample types may differ from the agents that public or animal health laboratories routinely investigate.

- Guidance is needed regarding sample collection, packaging and shipment to laboratories, and close interaction is desirable between field teams and the laboratories performing the analysis.

- Laboratory expertise should be embedded in field teams, and possible support structures (such as designated laboratories performing an assistance / coordination role for sample processing) have been proposed.

- Reporting of analytical results must withstand both scientific and political / legal scrutiny, demonstrate an unbroken chain of

[6] Previous workshops that discussed the setting-up of a UNSGM Designated Laboratory network were held in Stockholm (June 2015), Umeå (October 2016), Geneva (April 2016) and Spiez (November 2015, June 2016, June 2017, September 2018, September 2019, September 2021 and September 2022). Complementing these discussions was a workshop on toxin analysis (Berlin 2020). In 2021, the OPCW established an SAB Temporary Working Group on biotoxins analysis; its report was published in April 2023.

[7] Dry-lab exercises in genomic sequence analysis from bacteria were organised by Denmark and Sweden with US funding, between 2016 and 2018. Germany is implementing the RefBio project of wet-lab exercises including training and workshops, related to the analysis of viruses, bacteria and toxins. The project started in 2017 and has now been extended until 2027. Germany, Denmark and Sweden, with financial support from the US, have been conducting dry-lab exercises for virus identification and characterisation between 2021 and 2023. China conducted a wet-lab exercise on the identification of a disease X in 2022; a further wet-lab exercise is under way and will be completed in 2024. The OPCW has conducted seven toxin analysis exercises (2016-2023). Biotoxin EQAEs were also conducted under the EU projects EQuATox (2012-2014) and EuroBioTox (2017-2023).

custody, show the quality assurance and validation processes applied, and describe the findings as specific as capabilities allow.

The development of such a trusted laboratory network is a step-by-step process involving discussions and learning through practical exercises. Whilst coordinated by UNODA and linked to other initiatives to enhance the operational capacity and readiness of the UNSGM, it must be driven by the participating laboratories themselves, who should come from the widest geographical background as possible.

The network activities also help UNODA and rostered expert consultants assess the capabilities of laboratories nominated to the UNSGM. Analysing the results of EQAEs helps UNODA to better understand the actual capabilities of laboratories nominated to the UNSGM, and supports future mission leaders in selecting appropriate off-site analytical laboratories for their mission.

At the same time, more and more laboratories appreciate the benefits of participating in the development of this network. It provides opportunities for self-assessment and benchmarking through learning from others, sharing expertise, testing new solutions and gaining access to new analytical methods and standards.

The Spiez UNSGM Designated Laboratories workshop series has evolved into a widely recognised and effective platform for discussions and planning towards such a trusted laboratory network. It has also helped to clarify the roles different partners would play, such as UNODA and the OPCW with regard to toxin analysis. The 8th UNSGM Designated Laboratories Workshop organised by Spiez Laboratory was another important milestone in the development of a trusted UNSGM Designated Laboratory network.

2. Capstone Exercise

The workshop received a briefing on the Capstone Exercise organised in Berlin, which kicked off in 2020 with a virtual tabletop exercise, and culminated in a 10-day field exercise in 2022. It involved 19 UNSGM qualified experts, coming from 16 countries, and simulated an entire UNSGM mission involving a wide range of stakeholders: UNODA and the ITF, expert consultants, the mission team, designated laboratories, the Foreign Ministry and National Public Health Institute of the host country, relevant International Organisations, as well as witnesses and victims.

The exercise started with a team briefing by the Head of Mission on the mission planning and the selection of team equipment at a simulated UN headquarters. The Robert Koch-Institute (RKI), Spiez Laboratory and the Swedish Defence Research Agency (FOI) participated as designated laboratories during the pre-mission consultations.

The field exercise followed with activities related to team deployment, border control, host country negotiations, on-site investigation including securing of evidence material, post-deployment activities, and report writing. Sampling was a key element to be exercised in the field. Environmental samples were collected and the acquisition of biomedical samples (corpse and animal carcass) simulated.

The exercise was evaluated by a team from FOI together with a multidisciplinary group of evaluators/observers. They found the exercise valuable in demonstrating that the UNSGM is operational, and identified areas of improvement. The evaluation also highlighted a number of challenges: the complexity of the exercise, a lack of guidance documents for UNSGM investigations, the deployment of a large and diverse mission team, severe time constraints for certain activities, limited knowledge within the mission team of the way the UN works, and the need to use preselected equipment, which mission team members may not necessarily be familiar with. The evaluation called for building stronger interfaces between the different stakeholders through networking, and identified respective training needs: UN structures and mechanisms, team building, Safe and Secure Approaches in Field Environments (SSAFE), external communications including the handling of social media, standardised personal protective equipment (PPE) and decontamination equipment, sampling, interviewing, and evaluation of laboratory reports.

At the same time, the exercise allowed participants to connect with other experts from the UNSGM roster, to experience working in a UN Mission, to gain an overview of the roles of different UN stakeholders, to learn how to manage challenging situations, and to experience an entire UNSGM Mission from beginning to end.

With regard to sample analysis, there were three opportunities for the mission team to contact the selected laboratories by means of virtual platform exchanges. Different sampling scenarios and possibilities were tested in the exercise, bringing together various perspectives and limitations of the field team and the laboratories. Critical steps such as safety, evidence management including chain of custody, as well as gaps and training needs were identified. Evaluators assessed the entire process, from the development of sampling strategies to the use of sampling techniques, sample processing and packaging, sample receipt by the laboratory and the provision of the preliminary laboratory report. It became evident how important it is to ensure an effective interface between the field investigation team and the laboratories. This included exchanges about the capabilities and capacity of the laboratories; import restrictions and laboratory acceptance criteria; methodologies, accreditation and expertise needed to implement the mission's mandate; precise sample recording; the definition of a secure work area within the host country; and a clear mandate for laboratory

analysis of samples, including sample prioritisation. The discussions also highlighted the need for collaboration between field team and laboratories in the development of the analytical plan.

Recommendations addressed guidance for the interaction between a mission team and laboratories and related training needs. Furthermore, agreed forms / templates to facilitate communication of analytical requirements for the analysis of samples, as well as agreement on the reporting of laboratory results would greatly reduce the room for interpretation.

Subsequent discussion of these findings and recommendations at the workshop highlighted the need to further fine-tune training to enable some qualified experts to command a wider set of skills, to continue work on an equipment checklist, and to provide simplified guidelines for the use of the equipment. Procurement of PPE and other equipment, using a retainer system, is about to begin. There were also suggestions to standardise the content of the basic training course offered by Member States and apply the concept of UN certification to such courses. An eLearning platform is being developed and will soon be audited in accordance with UN practices.

UNODA has requested that expert consultants assess all previous EQAE results to have a better sense of current capabilities of roster laboratories (anonymised, no performance ranking, confidential, intended to support mission planning). An updated designated laboratories database is expected to be implemented in 2024.

UN Headquarters activities and the involvement of expert consultants will require more attention in future exercises. Current concepts for the next Capstone exercise planned to be held after 2026 envisage an overall extended timeframe, possibly with rotations of actors from UNHQ and the mission team. Training in the use of exercise guidance documents and templates should be carried out and also tested in focused, smaller scale exercises before the next Capstone exercise.

3. Laboratory Reporting

Previous UNSGM Designated Laboratories workshops have highlighted the critical role of laboratory reporting to a UNSGM mission, and a working group had been formed under the German RefBio project to develop a reporting template and test it. The template drew on experience of the OPCW and other international verification systems, while appreciating at the same time the distinct nature of the UNSGM.

The current draft report template is structured into several sections, and contains options to customise and through that maintain flexibility:

- Analytical plan
- Summary of analyses
- Detailed report on analyses

  Option A: Guidelines to report results on agent identification and characterisation using own laboratory format

  Option B: Proposed template for voluntary usage (mandatory for EQAE)
- Appendices

Both options A and B ensure that all necessary administrative data in the report are captured, including refence to how the chain of custody was ensured and which samples had been received by the laboratory, and that the results of each set of analyses are supported by information on the quality assurance system in place, together with information on accreditations and references to validation data. Non-accredited methods would be clearly marked and results would include any particular observations. Results and conclusions of the laboratory analyses would be limited to interpretations corroborated by the analyses actually conducted, supported by data contained in the Appendices.

The Appendices to the proposed report template included:

- Information on Chain of Custody
- Information on sample processing for different methods, including biosafety level; and description of each applied method and their validation

In addition, and on request (considering personnel and laboratory data protection):

- Accreditation certificates associated with the laboratory methods that have been applied
- Laboratory SOPs applicable to the conducted analyses
- Validation data, required to define assay performance and support accreditation. If a method is not accredited, the documentation provided must contain the data necessary to demonstrate the validity of the assay
- Raw data from analyses captured in the report must be available on request
- Others

This draft template was reviewed in detail in a breakout group to solicit feedback from the laboratories present. The discussions confirmed that:

- The reporting template allows the documentation of samples received, results obtained and methods applied for each sample; and it documents the involved disciplines / units of a laboratory;
- The Appendices allow the inclusion of all necessary documentation to support the conclusions set out in the main body of the report.

The breakout group also discussed whether there was a need for separate report templates for bacteria, viruses and toxins. The consensus was that at this stage, a single template is sufficient. In any event, the template would remain a “living document” that would be revised based on practical experience and feedback from use in EQAEs and table-top exercises.

The participants concurred that with regard to toxin analyses, it was important to coordinate the work on the report template with the OPCW. Other issues that the participants identified as deserving further discussion included:

- Performance criteria necessary for each standard method;
- Storage of raw data (at UNODA or at the laboratories, duration of storage);
- Inclusion of raw data and analysis results in the appendices.

A revised draft will be submitted to UNODA as the repository of UNSGM documentation. The template should be further tested in future EQAEs and subsequently refined. Whilst not being a binding format, it may be offered to the Head of Mission as a helpful template in the event of a UNSGM investigation being launched.

4. Technical Arrangements with Laboratories

Previous UNSGM workshops noted the need to address the content and scope of technical arrangements (TA) that UNODA and laboratories selected to support an UNSGM mission would have to agree on. To facilitate the swift conclusion of such arrangements, and to clarify what laboratories should expect, a model would be useful.

The OPCW presented its approach to the content and structure of a TA. Based on the provisions of the CWC, the OPCW has established a stringent regime governing all activities related to samples. The Director-General certifies laboratories designated to perform different types of analysis, oversees standardisation and monitors quality control and overall standards with regard to designated laboratories as well as mobile equipment and procedures used by inspection teams. The Director-General then selects from among the designated laboratories those that support a specific investigation.

Detailed criteria for designation and performance assessment have been adopted by the Conference of the States Parties. Based on these criteria and the performance in OPCW Proficiency Testing, 26 laboratories in 21 countries have currently been designated to analyse environmental samples, 17 of which (65 %) have a TA in place. 19 laboratories are designated for the analysis of biomedical samples. 13 of them (68 %) have signed a TA. 16 of the designated laboratories are designated to analyse both environmental and biomedical samples.

A TA provides a vehicle for engagement of services required by the OPCW whilst maintaining the rights and privileges of all parties. The Articles of the TA focus on the:

- purpose (defining the scope of the engagement)
- service request (general timelines and communication medium)
- sample transport (responsibilities and mechanisms for sample transport)
- sample handling and analysis (chain of custody and confidentiality in data handling)
- monitoring (capacity for OPCW staff to escort samples)
- reporting results (minimum criteria for reporting of results and limits on data use for specific purposes)
- costs (basic framework for remuneration terms and invoicing procedures)
- confidentiality (minimum requirements for confidentiality and commitments by all parties)
- references (authoritative sources per CWC and specified Annexes as part of more detailed elements of the TA)

The Annexes of the TA contain the detail of the agreement, as follows:

TA Annex 1 (General Provisions):

- Entry into Force, Duration, and Termination
- Liability and Force Majeure
- Privileges and Immunities
- Tax Exemptions
- Subcontracting
- Dispute Settlements
- Amendments and Notices

TA Annex 2 (Guidelines for off-site analysis of authentic samples):

- Confidentiality considerations
- Notifications and sample arrival
- Sample reception, unpacking and verification
- Handling and analysis of samples
- Reporting results and data requirements
- Waste management and sample storage
- Handling of confidential sample records

TA Annex 3 (Laboratory Details)

- Specific contact details
- Point of entry and authorised persons to facilitate sample transport and receipt at the laboratory
- Costing options selected by the laboratory

TA Annex 4 (Secrecy agreement)

- Restrictions on use, disclosure or dissemination of confidential information or any other information to which the laboratory had access in performing its tasks

The OPCW's TA is a key element of the off-site analysis of authentic verification samples and ensures that this task is performed under predefined terms and conditions. It provides a standardised approach to the engagement between the OPCW and designated laboratory conducting off-site analysis whilst retaining an element of flexibility, and works similar to quality assurance measures. In the experience of the OPCW, agreement on the technical parameters is usually not overly challenging whilst the legal parameters (such as privileges and immunities as well as third party liability) tend to be more complex and nuanced.

The subsequent discussions in a breakout group underlined that the OPCW TA model contains important elements for the UNSGM but may be too exhaustive and detailed. The UNSGM does not strive for a very detailed TA template that could easily lend itself to protracted negotiations.

A UNSGM model TA should inform UNSGM roster laboratories about the requirements they would have to address should they be selected for a mission. It was suggested to separate the legal from the more technical issues and aim for an agreement with the laboratory on the technical parameters whilst negotiating arrangements on legal matters with the host country. This would mirror the negotiation of other host-country arrangements, and to further develop the approach for a TA under the UNSGM the experience of the UN Office of Legal Affairs (UNOLA) should be sought.

A number of participants volunteered to be part of an informal working group after the workshop to develop an initial draft UNSGM TA outline for subsequent discussions.

5. Attitudes and Expectations of Investigations and Evidence for Biological Attribution and Promising Technologies

Attribution has been addressed at previous UNSGM Designated Laboratories workshops with a focus on technical requirements, ranging from identification of the causative agent to its characterisation and source attribution.

At this workshop, the results of an expert survey[8] were presented. It involved 41 experts with diverse backgrounds (science, forensics, public health, medicine, safety and security, international relations, non-proliferation, law). The survey was based on the understanding that attribution typically relied on multiple types of evidence, that it had a deterrent effect, could help in developing interventions to prevent a similar incident from reoccuring, and that it was important to hold those responsible to account.

There is at present only a very limited record of attributions of biological attacks. The US investigation of the Anthrax attacks in 2001 was conducted before certain modern techniques such as high-throughput sequencing became available. The controversy about the origins of SARS-CoV-2, whilst not covered in the survey, has affected attitudes and expectations regarding attribution investigations. Politisation, mis- and disinformation are likely components of future disease emergencies.

The survey looked at a range of factors at different stages of an investigation. These included accessibility (to evidence, sites, individuals), timeliness, trust (in actors, methods, validation etc.), coordination within a mission, cooperation between the different actors (mission, governments, laboratories), neutrality, perceptions (rigour of the processes and the underlying science, validation, chain of custody etc.), flexibility, procedures, and politics.

With regard to the characteristics of an investigation team, the survey stressed the need for diversity in expertise, neutrality, and wide international respect for the Head of Mission, whether a scientist or political expert. Good communications are critical, and the investigation should be designed to minimise the risk of attacks on the team. All potential sources of evidence ought to be considered.

With regard to laboratories, the majority of experts surveyed thought that the laboratories selected for an investigation ought to be pre-screened in some way. Views differed regarding the degree of flexibility that laboratories should have, whether there should be communications between laboratories during the investigation, and what the right balance was between gold standard methods and innovation. Most interviewees considered reporting of the validation of methods and respective controls as helpful. The confidence in national-level evidence collectors was higher than in local actors.

The survey considered a wide range of relevant evidence, including epidemiological / medical / clinical / autopsy data and observations; statements by witnesses, victims and others; medical and other records; intelligence signals; results of laboratory analyses (transcriptomics, genetics, isotopic analyses, genetic analysis of the agent, environmental sample analysis); forensic data; and financial data.

A majority of survey participants felt that technology was not the limiting factor in attribution analysis, and that legal, political and social factors constituted the greater barriers. High throughput omics and computa-

[8] K. L. Warmbrod and G. K. Gronvall: Attitudes and Expectations of Investigations and Evidence for Biological Attribution, https://www.preprints.org/manuscript/202210.0365/v1

tional advances were seen as the technologies that would make the most significant contributions to attribution.

Developing a capability for attribution will require UNSGM laboratories to expand from detection / identification to full characterisation. EQAEs have shown that several laboratories can already support investigation missions. It needs to be clarified, however, what can reasonably be expected from such analyses and what the related technology thresholds are: what are the roles of whole genome sequencing, activity assays, or proteomics, and will genomics capabilities become sufficiently widely available to support attribution investigations?

Complementing the update on the survey results, the workshop was briefed on a promising new technology that could help with the aspect of attribution: Targeted sequencing using hybridisation-based enrichment. It focuses the sequencing effort on areas of interest only, thus allowing greater multiplexing, increasing the reads from targets of interest and reducing host or environmental nucleic acid background, and reducing cost. Regions of interest can be captured using complementary RNA or DNA probes of typically 80-120 nucleotides. Probes can be custom designed to target small regions of interest or entire genomes, and probe sets can consist of several hundred to more than one million unique probes.

The technology has a wide range of possible applications, including infectious disease diagnostics and characterisation, exome sequencing, genetic mutation screening, and sequencing of ancient human remains.

Hybridisation-based enrichment involves six discrete steps:

- Collection of the sample containing the nucleic acid of interest at low concentration
- Extraction of nucleic acid and preparation of the sequencing library
- Hybridisation of the sequencing library using biotinylated probes
- Enrichment of the library fragments of interest using Streptavidin beads
- Recovery and amplification of the enriched library
- Sequencing and analysis

Experimental data presented showed that this approach substantially increases viral reads of interest (more than a thousand-fold enrichment of reads was achieved with orthopoxvirus DNA spiked into Vero cell DNA). It also allows for full genomic coverage with increased sequencing depth, while non-targeted sequences only gain in depth but not in breadth.

The technology was recently deployed to characterise a virus causing a cluster of paediatric hepatitis cases of unknown etiology. Enrichment yielded a superior genome coverage compared to unenriched sequencing data. This example underlined that hybridisation-based enrichment increases the number of target reads obtained from low concentration and / or complex samples, increases depth and breadth for genomes directly targeted by a probe panel, and increases depth but decreases breadth for novel / divergent genomes not directly targeted by a panel.

Certain panels are commercially available off the shelf; panels can also be custom-made.

Targeted sequencing using hybridisation-based enrichment has been shown to work well in complex samples, including when little DNA is present. However, targeting inevitably means that some information will be lost. At the same time, attribution cannot solely be based on genomic sequencing data, but other approaches, including non-biological investigative methods are equally important. For a UNSGM mission, there is a need for a flexible approach with regard to selecting team members with specialised expertise, including competencies other than biology such as information management / processing, data fusion, forensics / crime scene management and prosecution. Given the broad range of potentially important skill sets, and the unpredictability of the circumstances of a future investigation, a strong core team with a broad knowledge base complemented by experts with special skills will be required.

6. External Quality Assurance Exercises

6.1 RefBio Exercises (Germany)

6.1.1 Overview

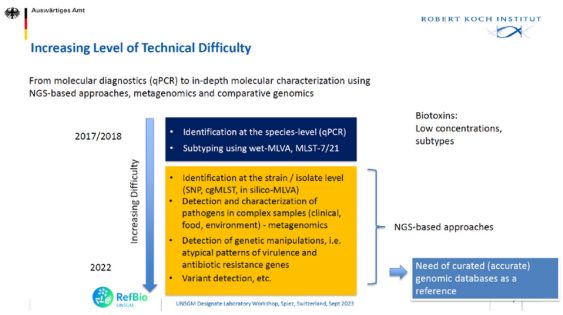
The RefBio project to strengthen the diagnostic capabilities of UNSGM roster laboratories began in 2017. Funded by the German Federal Foreign Office, it is currently in its second phase and a further extension from 2024 to 2027 has been approved. The project organises annual EQAEs in three diagnostic areas (viruses, bacteria, toxins), combined with annual workshops and laboratory training for participating laboratories to exchange methods and enhance capabilities.

The project has attracted an increasing number of participating laboratories from a growing number of countries, as shown below:

Year	Number of participating laboratories	Number of participating countries
2017	12	12
2018	20	16
2019	28	18
2020	30	20
2021	37	22
2022	38	21

Despite this encouraging progress, South America, the Middle East and parts of Asia remain under-represented. Other concerns include the rapidly increasing cost of sample transport (+30 % in 2022), and the impact of import regulations in certain countries (restrictions regarding the import of living strains and certain matrices).

The design of the project builds on a gradual increase of difficulty over time, moving the bar from molecular diagnostics (qPCR) to in-depth molecular characterisation using Next Generation Sequencing (NGS), metagenomics and comparative genomics. This is shown in the following graph:



This project design mirrors the three stages of microbial forensics investigations from agent identification to characterisation and finally towards attribution.

In 2022, the RefBio project began setting up a curated reference genome database (validated sequence data as well as metadata) for bacterial genome sequences. The need for such databases has been highlighted in several previous UNSGM workshops. They are important for strain identification and comparison (analysing genetic relatedness), molecular-epidemiological outbreak analysis, source tracking and phylogeographical analysis in microbial forensics, and as a basis for further comparative genomics.

Setting up this genome database has raised a number of questions:

- Which strains (sequences and metadata) should be included, taking into account such factors as spatial distribution, genetic diversity, selection from own strain collection and / or selected reference strains, and criteria for deciding whether or not to include publicly available sequences?

- Which are the best sequencing techniques to consider (short / long reads, 2- versus 4-colour chemistry, minimum coverage)?

- What are the best procedures for raw-reads (FastQC, trimming, etc.)?

- What are the best assembly pipelines (which assemblers with which parameters)?

- Which are the best typing methods / pipelines (Single Nucleotide Polymorphisms (SNP), Multi Locus Sequence Typing

(cgMLST), in-silico Multi Locus Variable Number of Tandem Repeats (MLVA), etc.)?

- Which are the best pipelines to determine peculiarities relevant to distinguish deliberate from natural events (unusual antimicrobial resistance profiles, virulence factors, genetic manipulation)?

- What are the best approaches for the analysis of complex samples – metagenomics (clinical and environmental) – and how best to interpret the data?

Validation is critical and each mutation counts, as most security relevant bacteria are genetically highly clonal and the difference between strains may be minimal. Whole Genome Sequencing (WGS) data therefore must be as accurate as possible, and typing assays to assess genetic relatedness must be robust.

Today's standard for the generation of accurate sequencing reads is Illumina sequencing. To speed up sequencing and data processing, Illumina has recently switched from 4-colour chemistry (MiSeq, HiSeq) to 2-colour chemistry (NextSeq, NovaSeq, MiniSeq). 4-colour chemistry uses four fluorescent dyes for base identification – one for each base – whilst 2-colour chemistry only uses two fluorescent dyes. Illumina claims that quality and accuracy of WGS data are not affected by this switch.

Experiments using two *Burkholderia* reference strains used in a RefBio EQAE showed, however, that the 2-colour method as compared to the 4-colour method can lead to errors that need to be corrected. Using identical sample preparations, libraries, and assembly pipelines, the genetic relatedness assessment showed that the 2-colour method did not match the reference sequenced using 4-colour chemistry (cgMLST). The discrepancy between 2- and 4-colour chemistry was confirmed by analysing the results and methods used by the laboratories that participated in the EQAE, and validated using an independent laboratory.

In short, 2-colour raw data are more error-prone than 4-colour raw data. Results with 2-colour raw data strongly depend on the QC-procedures, genome-coverage and assembly pipeline used. This is not to suggest that 2-colour chemistry should not be used, but correction of assemblies (e.g., with pilon) is a mandatory step and laboratories must be aware of the issue.

More than 1000 strains of security relevant bacterial species from the RKI-ZBS2 strain collection of the Robert Koch-Institute in Berlin have been sequenced using 2-colour chemistry. There was thus a need to re-assemble the sequences from raw data using an optimised pipeline – this is currently under way. Raw data and optimised assemblies will be available in 2024. The inclusion of selected viruses into the curated database is also being considered.

Attention was drawn to the way in which the OPCW has developed its Central Analytical Database (OCAD): a Validation Group evaluates spectra submitted by States Parties' laboratories for inclusion into the OCAD. The UNSGM could foster a similar approach to develop acceptance criteria and the methodology for a validated analytical UNSGM database, as a shared resource. This would also support future trainings, exercises, and it may encourage other laboratories to join the UNSGM designated laboratories network. International cooperation will be critical to elaborate methods and databases for use in attribution investigations.

6.1.2 RefBio bacterial EQAEs and training

Between October 2022 and June 2023, RefBio conducted an EQAE using *Burkholderia pseudomallei* and *B. mallei* strains. 26 laboratories from 21 countries participated in the exercise, 18 of which were laboratories nominated to the UNSGM roster. With the consent of the laboratories, their individual results were shared with UNODA.

The exercise simulated an agent release from drones over an area where *B. pseudomallei* was endemic. Sample shipment to the laboratories was done in accordance with the relevant regulations and under temperature-logged non-stop cooling at 2-8 °C. Samples reached their destination after 4 days on average, without any border / customs issues reported. Sample matrices included mud,

urine, house dust, and lake water. With increasing levels of difficulty, the laboratories were asked to:

- Identify / exclude the targets in the samples
- Characterise the target (e.g., microbial profiling)
- Identify the bacterial strain
- Identify any virulence genes
- Identify any antibiotic resistance
- Identify genetic fingerprints (cgMLST, MLVA)
- Identify signs of genetic manipulations

The results (data) were to be reported via a data entry form.

Almost all participating laboratories were able to correctly exclude the bacterial target in the samples. Most laboratories also correctly identified *Burkholderia* in target-positive samples, as well as the correct *Burkholderia* species.

For the more difficult tasks of target characterisation and screening for peculiarities, results varied. It was noted that not all laboratories work at the same level. There are technical differences between them, such as non-implemented methods or a lack of certain types of equipment (NGS). Good judgement is required particularly when dealing with low target concentrations and / or interfering backgrounds. The decision which agents are part of the natural background, is something that not all laboratories are proficient in. Consequently, laboratories interpret their results differently. An on-line training event on the identification and characterisation of *Burkholderia* species is scheduled for November 2023, with 27 laboratories having registered.

The next bacterial EQAE is scheduled to start on 10 October 2023, using *Bacillus anthracis* (anthrax) as the target. 30 laboratories from 20 countries have signed up for the exercise, 22 of which are UNSGM roster laboratories.

6.1.3 RefBio Virus EQAEs

RefBio has organised five virus EQAEs between 2018 and 2022. A next EQAE and associated training are scheduled to start in October 2023, simulating an Mpox outbreak with possible re-emergence. Laboratories will be tasked to detect and identify the virus, perform clade and lineage characterisation, and screen for mutations.

Over the years, the participation in the virus EQAEs has gradually increased, with a peak in 2020 reflecting the exceptional demand triggered by the COVID-19 pandemic. The participation in previous EQAEs is shown in the following table:

Year	Viruses	Number of laboratories participating	Number of countries participating
2018	Orthopoxviruses	15	12
2019	Orthopoxviruses	18	12
2020	SARS-CoV-2 and other human coronaviruses	32	20
2021	Haemorrhagic fever viruses	24	17
2022	Encephalitis viruses	22	18

In the latest EQAE (2022), participants were requested to identify and characterise encephalitis viruses, including the identification of viral strains and the detection of peculiarities. Genome comparison of the strains and *de novo* genome assembly were among the challenges that laboratories faced. 97 % of all species were identified correctly, however the proficiency for strain identification was assessed as low. Participating laboratories noted peculiarities such as insertions / SNPs, contaminations with other viruses, and the presence of synthetic constructs. It should be noted that this was a wet lab exercise, and integrating “real” peculiarities are difficult to achieve in such exercise scenarios.

Across all viral EQAE conducted so far, a high proficiency in species identification has been demonstrated whilst the proficiency in fur-

ther characterisation (strains, variants, mutations) was low. The performance in genome characterisation, which is important for forensic analyses, attribution, and the detection of markers for genetic engineering, needs to be increased. As a step towards such improvements, a training on MinION sequencing and data analysis was provided in 2022.

6.1.4 RefBio Toxin EQAEs

RefBio has conducted three toxin EQAEs since 2019; a next exercise is currently being prepared for 2023. Between 13 and 16 laboratories participated in previous exercises, which involved potentially active toxins of security relevance at concentrations between 10 and 3000 ng/ml in clinical (e.g., human plasma), environmental (swab) and food (e.g., milk) matrices. Participating laboratories were tasked to identify the samples positive or negative for the toxin, and perform characterisations including activity determination, quantification, identification of subtypes / isoforms, and to answer specific questions related to possible source attribution, matrix composition and purity. The following table provides an overview of the exercise designs:

Year	Matrices	Target toxin(s) and concentration(s)
2019	Cat faeces Milk Swab	Ricin D/E (100 ng/ml) Ricin D/E (500 ng/ml) Ricin D (3000 ng/ml)
2021	Buffer Plasma Milk Sand	BoNT/A1 (40 ng/ml); BoNT/A1+B1 (10+30 ng/ml) BoNT/A1 (10 ng/ml) BoNT/A1 (80 ng/ml); BoNT/A3 (90 ng/ml) BoNT/B1 300 (ng/ml)
2022	Plasma Buffer Swab Beans	BoNT/E1 (10 ng/ml) BoNT/E3 (10 ng/ml); TeNT (60 mg/ml; BoNT/A1+B1 20+60 mg/ml; BoNT/A2+F4 150+40 ng/ml) BoNT/A1(B) (150 ng/ml) (extract) BoNT/A2 (150 ng/ml)

The 2022 exercise involved 13 laboratories from 12 countries. The EQAE provider performed qualitative and quantitative analysis as well as statistical analysis to assign values and homogeneity, and confirm stability (5 weeks). Endopep suspension immunoassay was used to perform functional detection and confirm that the toxins retained their activity throughout the exercise.

All laboratories participated in the qualitative tests, using immunological, mass spectrometric and functional assays to analyse the samples. The main challenges were low concentrations and multiple and / or rare serotypes. Only a few methods for the identification of tetanus toxin (TeNT) were available.

The results of the exercise are summarised below:

Task	Participants	Success rate for positive samples	Conclusion
Toxin presence	13	78%	Most labs able to identify toxin pos./neg. samples; Main challenges: - Low toxin concentration - Presence of 2 serotypes - Rare sero-/subtypes
Toxin activity	6	94%	Only half the labs screen for toxin activity
Sub-typing	6	>95%	Only a few labs can identify at subtype level
Quantification	9	71%	Challenges: - Precise quantification - Standardised reference materials

The toxin EQAEs have shown that at the moment, only advanced laboratories can undertake the types of analysis that are required for source attribution / batch matching, such as differentiating toxin variants, undertaking precise quantification, detecting substances related to possible deliberate production or purification, or characterise the matrices.

A next EQAE is planned for September to October 2023, involving ricin and abrin in diverse matrices (buffer, swabs, milk, baby

food). Future options for toxin EQAEs may include mixed panels (ricin, abrin, botulinum neurotoxin (BoNT), epsilon toxin and Staphylococcus enterotoxin).

A training course on sandwich ELISA for ricin detection was conducted in 2022, which involved 26 participants from 10 counties. For November 2023, an online workshop has been scheduled on the detection and quantification of BoNT by sandwich ELISA. Future training offers may include multiplex ELISA (suspension immunoassay) and functional methods.

6.2 Dry-Lab Exercises (Germany, Denmark, Sweden, United States)

The US Department of State has been funding three dry-lab EQAEs over a 2-year period that involved poxviruses, highly pathogenic Influenza viruses, and Mpox virus. Virtual workshops were conducted before and again after each EQAE. The objectives of these exercises included skills development in:

- Target identification (bioinformatic pipelines and tools, databases)
- Results interpretation (clinical versus virological data, sensitivity and specificity, the role of contamination)
- Target characterisation (technical forensics – characterisation of agents as "novel", emerging or natural; signs of genetic engineering or synthesis; genetic attribution – retracing to a suspected origin or source)

The following table provides an overview of the exercises conducted:

Exercise	Virus(es)	Number of participants	Main results
EQAE 1 2021	Genetically engineered poxviruses (Variola, Cowpox)	42	50 % of the participants reached at least 75 % of the total score
EQAE 2 2022	Highly pathogenic Influenza virus	67	65 % of the participants reached at least 75 % of the total score
EQAE 3 2023	Mpox virus	111	87 % of the participants reached at least 75 % of the total score

EQAE 1 (2021) was a species identification exercise with difficulties relating to genetically engineered and hybrid viruses. EQAE 2 (2022) was scenario-based and simulated a deliberate agent release (person X using a dispersing device) and samples collected from a variety of locations and sources (air filter, dead bird, patients, vial from a production site), and involved data analysis aimed at attribution. EQAE 3 (2023), too, was scenario-based, involving three neighbouring countries entangled in a regional conflict and outbreaks of Mpox in two of them. It involved an assessment of whether a suspicious new outbreak had been a re-emergence of the previous Mpox virus, whether the virus genomes sampled at different locations differed from those collected elsewhere, whether any peculiarities, mutations or signs of genetic engineering could be detected in the genomes, and how the genomes were placed phylogenetically and whether they aligned with travel between the three countries. The participating laboratories were tasked to identify Mpox virus and perform a metagenomic analysis (detection of additional viruses) and genome characterisation (viral genome assembly, viral clade and strain identification). They were requested to look for mutations and signs of genetic engineering, and compare phylogenetic placement of identified strains with strains from a database provided. They were also asked to provide answers to certain specific questions raised by the Head of Mission to help solve the investigation.

Across all laboratories, target identification was correctly done in 98 % of the cases. The results show that laboratories scored high in metagenomic analyses, clade identification, strain identification and phylogenetic placement (>90 % correct). Lineage identification was correct in 83 % of the reports, whilst the

identification of peculiarities posed more problems (49 % correct). Characterisation proved to be even more challenging (12.5 % correct).

It is noteworthy that the 111 participating laboratories came from 59 different countries, with a wide geographical spread (10 from Africa, 21 from Asia, 50 from Europe, 6 from North America, 10 from Oceania and 14 from Latin America). This shows that there is a growing global capacity in bioinformatics that the UNSGM could tap into. It could also connect with other laboratory networks such as those of the Pan American Health Organization (PAHO) and WHO, as well as the WOAH's laboratory twinning programme.

7. Toxin Analysis

Previous UNSGM Designated Laboratories workshops have already looked at the particular challenges that toxin analysis poses for a UNSGM investigation. Relevant concentrations of toxins are much lower than in the analysis of other chemical agents, and there are differences between high molecular weight (HMW) and low molecular weight (LMW) toxins which affect the analytical methods to be used. There also is a broad range of international, regional and national actors and networks that deal with toxin analysis.

7.1. Recommendations of the OPCW SAB on Biotoxin Analysis

The seventh UNSGM Designated Laboratories workshop in Spiez in 2022 had been briefed on the work of the OPCW Scientific Advisory Board (SAB) Temporary Working Group (TWG) on toxin analysis. This group has now completed its work and published its results and recommendations.[9]

The TWG report responded to seven specific questions posed by the OPCW Director-General, which the group had worked on in five subgroups. It contained 23 recommendations, 9 of which categorised as "strong".

The TWG identified significant differences to the analysis of traditional chemical agents in two stages of an investigation: the sample collection including in-field detection and analysis (including clinical diagnostics), and the comprehensive molecular profiling of a sample. It recommended that the OPCW:

- Compile and disseminate information on the diagnosis and treatment of biotoxin exposure and perform a technical workshop on this topic;

- Investigate available methods for in-field detection of biotoxins and evaluate whether in-field detection devices for biotoxins should be included on the OPCW's list of approved equipment;

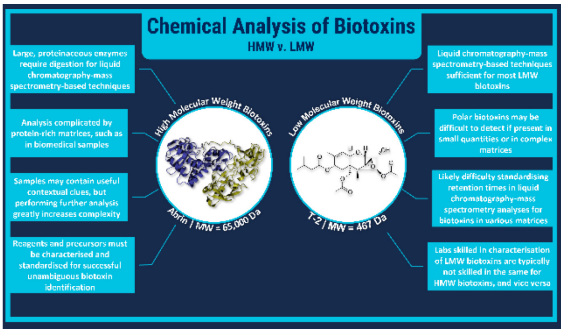
- Adopt a comprehensive forensic approach to every investigation of alleged biotoxin use.

With regard to the most relevant classes of biotoxins, the TWG developed criteria (historical use, availability, toxicity / activity, stability), screened open literature data for biotoxins and biotoxin families, and recommended that the OPCW should:

- Focus on nine "most relevant" biotoxins,[10] drawing on sophisticated analysis capabilities that may exist in other fields;

- Survey existing literature and recognised experts in biotoxin analysis to identify laboratories with specialised capabilities for the analysis of each of the "most relevant" biotoxins.

The analytical requirements for these most relevant biotoxins differ depending on their molecular weight, as shown in the following graph:



The TWG recommended that the OPCW should:

- Take full account of these differences: LMW biotoxin analysis would generally rely on traditional mass spectrometry-based techniques, whilst HMW biotoxin analysis requires a combination of MS-based techniques and orthogonal methods, such as

[9] For the report see https://www.opcw.org/sites/default/files/documents/2023/04/Analysis%20of%20Biotoxins%20Final%20Report.pdf
[10] These are: Abrin, aflatoxin, botulinum neurotoxin (BoNT), epsilon toxin, ricin, saxitoxin, tetrodotoxin, and T-2 toxin.

immunological or functional assays. At very low concentrations, such as in biomedical samples, a combination of immunoaffinity enrichment and a functional method may be the only option with sufficient sensitivity;

- Document and disseminate best practices for the unambiguous identification of specific biotoxins;

- Develop minimum specification requirements for performance criteria of immunological and functional assays for the analysis of HMW biotoxins, including specifications for immunological components (antibodies) as well as overall immunoassay and activity assay performance criteria (in partnership with the UNSGM laboratory network);

- Consider a proficiency test regime for biotoxin analysis to enable laboratories to seek separate designation for ricin and saxitoxin analysis.

With regard to the analytical standards and requirements of other investigative authorities and the coordination of programmes and exercises conducted by different laboratory networks, the SAB undertook a comparison between the approaches and activities of the OPCW, the RefBio project, and the EuroBioTox[11] project. It strongly recommended that the OPCW work closely with the United Nations, drawing on the relationship agreement for cooperation between the two organisations, in order to establish an informal network for biotoxin analysis to facilitate building international capabilities for forensic analysis of biotoxins. The SAB also identified areas where such coordination and collaboration would be most fruitful, such as common guidelines and best practices, requirements for quality assurance management systems, reporting formats, and efforts to minimise gaps and unproductive duplications, including exercises and proficiency testing.

A final recommendation related to institutional and legal measures to facilitate cooperation between the OPCW and other relevant organisations, urging for sustainability and the utilisation of existing structures such as the UN-OPCW relationship agreement. Arrangements should be kept simple and flexible and the SAB did not see a need for new formal legal agreements.

To implement these recommendations, the OPCW has received financial support under the Global Partnership Against the Spread of Weapons and Materials of Mass Destruction (see below), and is enhancing its partnership with UNODA.

7.2 Seventh OPCW Exercise on Biotoxin Analysis and Follow-up on Biotoxin Analysis

The OPCW conducted its seventh biotoxin exercise in July 2023. 23 Laboratories from CWC States Parties participated, of which 21 submitted a report. 85 % of these laboratories identified Saxitoxin whilst the identification of another PSP toxin was a major challenge. Furthermore, the OPCW conducted a workshop on confirmation criteria, reporting of analytical results and a new scoring system for future proficiency tests for LMW toxins. No further OPCW biotoxin exercise will be conducted in 2023 but instead, a mock Proficiency Test (PT) will be held in 2024, using a LMW biotoxin as target.

The financial support received through the Global Partnership from the UK Ministry of Defence allows the OPCW to:

- Enhance its ability to respond to the threat of use of biotoxins;

- Develop analytical capabilities (qualitative and quantitative) to more effectively detect biotoxins in environmental and biomedical samples, as well as to characterise in detail biotoxins and their crude extracts;

- Develop and recommend a viable ricin detection test kit;

- Strengthen the relationship with the UNSGM and work towards harmonisation.

In pursuit of these objectives, the OPCW has launched a formal biotoxin PT scheme to-

[11] https://www.eurobiotox.eu/#

wards designation of laboratories for biotoxin analysis. It is developing tools for biotoxin forensics and a validated ricin detection kit, and is collaborating with the laboratories on the UNSGM roster in the selection of security relevant biotoxins, the development of a generic sample work-up approach for biotoxins, and in the development of methods to enable batch-matching and unravelling production methods.

An initial scoring scheme for the evaluation of results of LMW biotoxin analysis has been proposed and tested against the reported data of the 7th biotoxin exercise. The scoring scheme seems to work well, but there remain a number of issues to consider further with regard to the point scoring system.

With regard to HMW biotoxins, the development of an accepted scoring scheme is still some distance away. The experience from seven OPCW biotoxin exercises with regard to ricin identification and characterisation should be taken into account when working towards such a reporting and scoring system. Developing a point scoring system for HMW biotoxins will be challenging, as sensitivity of the methods will be an issue given the very low concentrations of these toxins in clinical samples. There also is a need to make high-quality monoclonal antibodies available.

8. ASEAN CBR Laboratory Network

Past UNSGM Designated Laboratories workshops have underscored the importance of linking up with other laboratory and expert networks. In this context, the workshop was briefed on the achievements and future activities of the network of ASEAN CBR defence experts. It was established to:

- Provide timely, adequate and effective assistance as part of an integrated response in the event of a regional CBR incident;

- Serve as a regional confidence building mechanism, and promote multilateral cooperation and coordination for the benefit of the region's collective peace and security;

- Function as a single node for regional CBR defence experts to make contact, and share information, best practices, expertise and experiences on common CBR threats and hazards;

- Encourage regional CBR defence experts to deepen professional links with peers from other ASEAN Member States, and to advance their knowledge and techniques for responding to CBR attacks;

- Enhance regional safety, security, and safeguards through close cooperation with existing mechanisms at the regional framework, and in line with the implementation of relevant international instruments, standards and guidelines.

The network employs a secure web portal to exchange information and provide access to technical guidelines and advice. It brings together CBR experts as they prepare for and respond to regional CBR incidents, and it helps in organising activities to enhance cooperation and build capacity.

The web portal is a members-only platform with a directory of CBR experts of the region, information resources and links to open-source guidelines, technical documents, protocols and tools, and updates on network activities and events such as workshops, training and visits. It allows members to contact each other and provide mutual assistance in the preparation for and response to regional CBR incidents. The network cooperates with a number of international organisations (including the OPCW and the IAEA) and other (including national) institutions.

Between 2019 and 2022, the network conducted 12 events, including annual meetings, tabletop exercises and training workshops, and an ASEAN Defence Ministers-Plus CBR conference with 101 in-person and 16 virtual delegates attending.

In 2023, a number of network events have been or will be hosted by Singapore, including a network technical meeting for harmonisation of sampling protocols, three training workshops (C, B, and R, respectively), and the 5th annual meeting of the network in conjunction with CBR technical seminars.

Work on harmonising best sampling protocols and methods is progressing in four areas (sample collection, sample documentation and chain of custody, international transportation of samples, reporting analytical findings), with the aim of developing harmonised guidelines by June 2024. The guidelines may be shared beyond ASEAN countries at a later stage.

9. Sampling

9.1. Sampling and Equipment

Previous activities to strengthening the operational capacity of the UNSGM have highlighted how important it is that samples gathered by a UNSGM investigation are acquired, handled, stored, transported and transferred to the analytical laboratories in ways that protect and preserve their integrity, conform to the UNSGM Guidelines and Procedures, and meet the requirements of the recipient analytical laboratories. To this end, Canada has submitted to UNODA a package of sampling guidance documentation including training options and a proposed equipment list. Experts from Australia, France, Germany, Switzerland, the United Kingdom and the United States have provided peer review and feedback to the package. As a result, a number of technical notes in the form of guidance documents have been developed as part of the quality management structure (QMS) of the UNSGM.

These guidance documents are meant to facilitate a more structured framework for enhancing and sustaining the UNSGM capabilities for investigating biological incidents. These include:

- A technical guidance document including procedures, aide memoire and field guide for sample packaging and transport
- A technical guidance document including procedures, aide memoire and field guide for environmental biological sampling
- An example sample data sheet
- An example chain of custody form

The documents allow flexible adaptation to the context of a specific investigation. The sample data sheet and chain of custody form were made available for the Capstone exercise. The executive report of the exercise identified a number of lessons with regard to sampling, including the value of periodic training of sample processing in specific terms of the UNSGM Guidelines and Procedures, as well as on chain of custody aspects. The exercise report and the observations of the exercise evaluators also suggested to provide:

- A UNSGM mission equipment list with a variety of equipment to be adaptable to different situations (e.g., regarding Personal Protective Equipment);
- More guiding documents for UNSGM procedures (e.g., for evidence collection);
- collective forms for the mission team and the laboratories to facilitate the analysis of laboratory results.

The sample guidance documents will need updating once lessons learned can be applied or opportunities for improvement are met. Feedback from the Capstone exercise already resulted in the refinement of the Aide Memoire, and sample receipt and collection documentation will be used in training to further customise the documents for the needs of the UNSGM.

In March 2023, several UNSGM experts participated in INTERPOL's "Biological Crime Scene Management Course", which provides guidance on the investigation of a biological crime scene. This included the development of a sampling strategy, the use of training stands, the documentation of samples, location / forensic imagery recording, sample packaging, and chain of custody procedures to ensure traceability from the time of sample collection to the moment when it is introduced as evidence into legal proceedings.

Samples must withstand legal and political scrutiny, which requires correct labelling to ensure that sample identity cannot be challenged, cross-refencing of sample identity to each sample data sheet, and use of sample data sheets during submission of the samples to the analytical laboratories. The laboratory sample receipt documents and the sample data sheet were utilised in the course. Based on participants feedback and cross-refencing with other international experts and organi-

sations, a sample data sheet and chain of custody document fit for purpose for a UNSGM investigation has been developed.

These tools have been used in a UNSGM skill training course on "Sampling and transport of infectious substances" conducted in 2023 in Germany. Constant improvement based on feedback from use in training and exercises and cross-referencing with the experience of other relevant organisations (including prosecution services and the International Criminal Court) should be ensured for these and other protocols. QMS framework documents, to foster synergy in training of qualified experts provided by Member States, ensure continuity and aid product development. The same strategy might be applied to equipment and material supplies. Also, utilising the same material for training and small emergency stocks to support future operations may be considered.

9.2. Sampling and Chain of Custody

The workshop received a briefing on the Horizon 2020 project STRATEGY, funded by the European Union, which aims at building a pan-European pre-standardisation framework for interoperability for crime scene management, and specifically on its thematic stream 6 which deals with CBRN threats. CBRN investigations are complex and multidisciplinary in nature, and chain of custody procedures often turn into a bottleneck. A digital Chain of Custody (dCoC) process can facilitate the auditing of data related to the transfer of custody of evidence items. The project is developing guidelines for characterising the resources allocated to each Custody Transfer Point (CTP) in a mission CTP dendrogram.

The system provides clarity in the roles of different actors involved in the evidence chain. It works online as well as off-line. Digital logs for each custody transfer ensure data availability, integrity, authenticity, confidentiality and non-repudiation of transfer actions.

The project has been defining the concepts underlying the dCoC process, has developed guidelines for data governance within the custody transfer lifecycle, and developed metadata policies to facilitate compliance with good practices for non-repudiation of reported data. A second part of the project focuses on data management and audit, including guidelines for the management and audit of digital custody metadata (DCM), a metadata structure that helps to manage mission resources at each CTP and creates a chain of custodianship, and outlined the core activities within each DCM data governance workflow.

This approach is highly innovative, robust with regard to documenting a chain of custody in a complex scenario, and transparent with regard to the roles of the various actors in a mission. It uses a metadata-centric approach to record ownership, action, location, reason and method of each custody transfer, ensures non-repudiation, enables the auditing of inconsistencies in the CTP process, and supports operational decision making for each transfer of custodianship along the entire lifecycle.

Issues that need to be considered further include vulnerability to cybersecurity threats and the practicalities of electronic data entry under field conditions whilst wearing PPE.

10. Concurrent Investigations

The workshop received an overview on recent and planned projects to strengthen the UNSGM that have been or are being supported or implemented by the United States. These include:

- The identification of legal restrictions on international transfers of samples for analysis (a database has been developed to this end)
- EQAE in genome sequence analysis (bioinformatics) to connect more laboratories that could support a UNSGM mission and widen geographical participation
- An overview of resources of other international organisations that might be called upon to support a UNSGM investigation
- Interview skills training
- Capacity building through laboratory twinning, for example in the area of biotoxin analysis
- Practical challenges in international transfers of samples for analyses
- Concurrent national and international public health and forensic investigations

The latter topic on potential challenges encountered in settings of concurrent investigations will be addressed in the format of a tabletop exercise in order to identify problems and possible solutions.

Reports on the results of these activities will be shared. The activities are aimed both at finding solutions and identifying competent laboratories, with a view to create tangible benefits for them. It was recognised that the process of developing capabilities for the UNSGM has entered a more practical phase, which creates challenges with regard to maintaining momentum, whilst ensuring that the different activities and projects tie neatly together.

11. Conclusions and next steps

This eighth UNSGM Designated Laboratories workshop confirmed that many of the designated laboratories of the UNSGM – the only international mechanism to investigate allegations of biological weapons use – are ready for the task. Over the past years, substantial progress has been made thanks to efforts by UNODA and Member States. The participation in this effort has grown, with many more countries and laboratories involved, including some that are not yet nominated to the UNSGM roster but may form a reserve that, if necessary, could be called upon.

The workshop series has evolved into an authoritative platform to discuss and plan activities related to the setting up of a network of trusted and capable laboratories for UNSGM investigations. These workshops provide an opportunity for laboratory representatives to think about what information they would need to look for in samples, how to communicate their findings, and what the broader implications might be. The workshop series has moved away from focusing on the laboratory in isolation and toward viewing laboratory analysis as one element of a broader investigative process.

On the practical side, proposed guidelines, templates, a list of equipment, and other tools are being developed and refined based on feedback from training and exercises as well as cross-referencing with the experience of other organisations. A working group under the auspices of the RefBio project has created a draft template for UNSGM analytical laboratory reports. The template includes two options for reporting analytical results: one that draws on the laboratory's own format (with certain mandatory criteria for the UNSGM) and a second one that provides a more structured approach drawing on the findings of EQAEs. The new template met expectations and after further refinement will be submitted to UNODA as a useful tool that could be used in training and real missions.

Taking note of the OPCW's experience with contractual arrangements for the analysis of authentic samples and related laboratory services, the workshop participants concluded that a simplified template for a Technical Arrangement (TA) would be helpful in conveying realistic expectations to laboratories on issues like sample transport and handling, chain of custody, results reporting, and costs. Such arrangements predefine the terms under which the laboratory would operate when requested to perform specific services for a mission. A TA model would also ensure that UNODA has the appropriate legal and technical elements in hand prior to the commencement of an investigation. A future outcome of the workshop series should be a draft template TA, focusing initially on the technical elements pending advice from UNOLA and other stakeholders on the broader legal issues. Some of the participants volunteered to prepare such a draft.

The workshop was another opportunity to take stock of new technologies and innovations that support sampling, forensic analysis, chain of custody management and other aspects of a UNSGM investigation. Examples included targeted sequencing using hybridisation-based enrichment, the use of digital metadata for chain-of-custody documentation, and the setting up of a curated reference genome database of high-quality that can support microbial forensic investigations and outbreak analysis. The workshop also took stock of the different activities that are being implemented by a number of countries, including wet and dry lab EQAEs. Such exercises not only give participants the opportunity to improve their skills, but also offer other benefits such as the demonstration of external evaluation which can be helpful for accreditation.

The workshop also addressed more general issues related to the UNSGM, and provided a space for discussing national contributions to enhance its capacity, as well as UNODA's ef-

forts as the mechanism's custodian and repository of tools and documentation to support UNSGM missions. This includes the conduct of skill training and tabletop exercises as well as occasional field exercises. The next Capstone exercise is expected to be conducted in 2027 or 2028, and is proposed to be a 4- or 5-week exercise bringing in participation from different UN entities as well as rostered laboratories and qualified experts. In the meantime, there would be value in smaller exercises involving laboratories and focusing on elements such as interaction with the mission team or testing the new reporting template.

All in all, there is today a broader knowledge base and more confidence regarding the selection of laboratories for a specific UNSGM investigation, and more clarity about the division of labour between UNODA and partners such as the OPCW, WHO and WOAH. Opportunities are being created to test competencies and procedures, and to develop guidance documents to support (and be refined through) training and exercises and to facilitate the conduct of a real mission.

Continuity and sustainability of these efforts will be critical to ensure that the UNSGM is fit for purpose and can take full advantage of new technologies, innovations and practical tools. Equally important remains the further enlargement of the geographical participation in these efforts and the strengthening of partnerships with other international, regional and national organisations that can support the UNSGM and help it further enhance its capabilities.

The workshop series organised by Spiez Laboratory remains an effective platform to discuss these issues and help all partners coordinate their activities and share the results. The ninth UNSGM Designated Laboratories workshop will be held in Spiez from 11 to 13 September 2024.

Group photo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