UNSGM Designated Laboratories Workshop Report

Spiez, Switzerland
11 – 13 September 2019

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Executive Summary

This report presents the outcomes of the fifth Swiss workshop organised by Spiez Laboratory on a network of trusted laboratories designated under the United Nations Secretary-General's Mechanism (UNSGM) to investigate allegations of the use of biological and toxin weapons. The initiative links to the Secretary-General's Disarmament Agenda, which asks for adequate preparations to respond to any credible allegation of use of biological weapons.

From its very beginning, this Swiss workshop series has focused on how to establish a functional, robust and trusted network of UNSGM designated laboratories. Initial workshops confirmed the necessity to develop such a collaborative network that would provide transparency and confidence in scientific competencies, analytical skills as well as quality assurance systems, in order to enhance the operational capacity of the UNSGM.

Of particular interest is the goal to move forward with the issue of inter-laboratory calibrations, as mentioned in the UNSGM Guidelines and Procedures[1], through active engagement of Member States and their competent laboratories. Laudably, an increasing number of relevant activities at laboratory level have recently started, including dedicated confidence building and quality assurance exercises. This shift from conceptual discussions to practical work comes with benefits for participating laboratories. These include the promotion of international collaboration between the laboratories, opportunities for laboratories to assess and improve their own capabilities and through that, provide enhanced operational capability to the UNSGM.

This fifth UNSGM Designated Laboratories Workshop reviewed past laboratory exercises, discussed the outcomes relevant to enhancing quality assurance, and looked at future exercises with a view to increase the number and geographical spread of participating laboratories. Other themes included the conceptualisation of laboratory support and assistance to a UNSGM mission team, the various laboratory interfaces, and laboratory reporting.

In August 2017, Germany started the project 'RefBio' which aimed to conduct several external quality assurance exercises in the fields of bacteriology, virology, and toxinology. It also includes dedicated evaluation workshops to specifically discuss results and make recommendations for future exercises. Most notably, the working group on bacteria was able to report a significant increase in participation over the two exercises so far. Encouragingly, almost all laboratories correctly identified or ruled out the target agent in the second exercise. However performing in-depth characterisation of target strains proved to be a challenge for a number of laboratories that do not have established high-end sequencing technologies as well as associated support with bioinformatics pipelines. The first exercise of the working group on viruses took place in 2018, but here the rate of correct identification of the target species was surprisingly low. The working group on toxins' first exercise will take place in late 2019. In light of already existing exercise formats from the OPCW, the European Framework Programme Horizon 2020 ('EuroBioTox') and the current activity of the working group on toxins highlights the need for closer collaboration.

In April 2018, Denmark and Sweden, with financial support from the United States, started a series of three dry-lab proficiency tests that focused on the genomic analysis of target species. In general, participating laboratories performed well, although some issues related to the correct identification of the target species require further attention.

[1] Guidelines and Procedures for the timely and efficient investigation of reports for the possible use of chemical and bacteriological (biological) or toxin weapons. https://www.un.org/ga/search/view_doc.asp?symbol=A/44/561

The three accomplished exercises highlighted the need of participating laboratories to obtain access to shared, curated and comprehensive reference databases.

A common element across all exercise formats conducted so far was that analyses in the context of a UNSGM investigation pose demands that go far beyond the routine work of a diagnostic laboratory. In order to extract a maximum benefit from such exercises, it is essential to design laboratory exercises to be as similar as possible to the reality of an investigation. Future laboratory exercises should take into account the numerous issues identified so far. These include the possibility of involving live agent sample analysis, the potential problems linked to import and export regulations and procedures for sample shipment, and the recognition that characterisation of genomic information has to be supplemented with the detection and characterisation of the microorganism itself. Any future efforts should, however, not discourage or prevent a broader geographic participation of interested laboratories, but rather be complemented with dedicated training of laboratory personnel and laboratory twinning initiatives. Finally, mapping out future exercises over a longer period would greatly assist with coordinated planning and fund raising.

Laboratory support and assistance is best highlighted by the central role the OPCW Laboratory plays during an investigation, which includes facilitation of sample transfers, sample splitting and preparation of control samples. In the absence of any comparable institutional resources in the biological field, any UNSGM investigation of biological weapons will have to rely on the rostered laboratories to facilitate and manage these issues. The merits of developing a concept of a designated laboratory providing support and assistance to a UNSGM mission team are obvious, in particular how such a laboratory may act as a "secure work area" for the qualified experts conducting an investigation in the field. A UNSGM designated laboratory with assisting and coordinating functions would be mandated to provide a service for the investigation team that retains full command and control. Provision of such service requires fulfilling several aspects, including a broad range of capabilities, access to a triage facility as well as high-containment facilities, accommodation of an observer, and the ability for secured long-term sample storage.

Interfaces of laboratories are multifaceted and need to be studied from the various angles of the investigation team, the expert consultants, and the laboratories themselves. The roles of expert consultants may be particularly faced with a whole range of tasks requiring expertise in a variety of areas, including assessment of laboratory competence and post-analytical reporting from scientific and legal perspectives. Another aspect is matching fieldwork with laboratory analysis by providing guidance to investigation teams for sample collection and management. One promising approach is through an amalgamation of well-established and tested protocols from different laboratories, while ensuring that such guidance would not be overly prescriptive or restrictive. Such concepts need to be tested. One opportunity will be the Capstone exercise announced for 2020 and organised by Germany and Sweden, which will cover the entire range of UNSGM actors, their tasks and interactions, with a particular focus on sampling, communications and reporting. It is also expected that the exercise will test some of the interfaces of field investigation and laboratory components.

Since laboratory reporting is a central element of an investigation, the workshop strongly benefitted from the ample expertise of the OPCW. A comprehensive presentation on the reporting for OPCW proficiency testing focused on content, structure and management of a report. For a report to be credible and demonstrate robustness, it is evident that the chain of custody, quality assurance, and technical competence are of critical importance. It remains an open question to what extent and how the OPCW experience can be transferred across to a UNSGM designated laboratories network. It was generally agreed that it is now time to develop a reporting template.

In conclusion, laboratory exercises are planned to continue with on-going efforts to further extend such activities. In addition, a number of specific issues have been identified for which volunteers are ready to develop draft guidance documents, notably in the areas of sample collection and shipment, the concept of using a designated laboratory with assisting and coordinating functions as a secure work area, and reporting templates. An overview of select activities is included at the end of this report. This significant increase of activities and engagements of Member States over the last few years requires continued intense collaboration and coordination with the UN Office for Disarmament Affairs, the custodian of the UNSGM. In order for UNODA to address these very encouraging developments it will require adequate staffing and sufficient resources, so that it may adopt a more active role.

Finally, workshop participants welcomed the Swiss initiative of providing a common platform for exchanging ideas about the setting up of the network and to further develop a roadmap of necessary steps. Switzerland will therefore continue to provide this platform dedicated to issues pertaining to UNSGM designated laboratories and announced that the sixth UNSGM Designated Laboratories Workshop will take place from 9 – 11 September 2020.

1. Introduction

This report presents the outcomes of the fifth Swiss workshop organised by Spiez Laboratory on a network of trusted laboratories designated under the United Nations Secretary-General's Mechanism (UNSGM) to investigate allegations of the use of chemical, biological and toxin (CBT) weapons. The workshop was attended by 60 participants from 16 Member States, the UN Office for Disarmament Affairs (UNODA), the Organisation for the Prohibition of Chemical Weapons (OPCW), the World Health Organisation (WHO), and the International Criminal Police Organization (INTERPOL).

This workshop series is part of a wider effort in strengthening the operational capacity available to the international community to investigate allegations of the use of CBT weapons. Cognisant of the Disarmament Agenda of the UN Secretary-General, it provides a platform for interested Member States and their laboratories to discuss and coordinate activities towards the establishment of a functional network of trusted laboratories available to the UNSGM that can support biological investigations. For biological weapons, the UNSGM remains the only international mechanism with the authority to conduct investigations into allegations of their use.

In the absence of a dedicated, adequately resourced international organisation to conduct investigations of alleged use of biological weapons, the UNSGM relies heavily on the Member States. As a consequence, the credibility and operational strength of the UNSGM crucially depends on what Member States are able and willing to make available to it, and on what partner organisations such as the WHO, the World Organisation for Animal Health (OIE), INTERPOL and the OPCW can contribute. Member States support the UNSGM in many ways, by organising exercises, providing training for qualified experts, and nominating expert consultants. In addition, conceptual discussions have led to practical steps towards setting up a trusted UNSGM designated laboratory network.

The discussion of requirements that such a network should fulfill began in 2015[2]. Key issues that needed to be addressed in setting up the network were highlighted:

- What does "identification" mean in the context of a UNSGM investigation;
- How important it is that no false positive or false negative identifications are reported;
- How can one ensure access to comprehensive and curated reference databases and reference materials;
- What needs to be done to ensure an unbroken chain of custody;
- Accreditation of methods to internationally accepted standards;
- Acceptance criteria for the identification of a target agent when the gold standard of isolation, cultivation and characterisation cannot be met;
- How important it is to ensure the highest standards of biological safety;
- How should laboratories and a field mission team interact; and
- How should analytical results be reported so that the final mission report can withstand scrutiny in a wider political and legal context.

In addition, previous discussions have identified a range of technical challenges that need to be addressed, in form of developing understandings, guidelines and practical exercises. They include:

- Sample shipment from the mission team in the field to designated laboratories;
- The concept of a hub lab to provide a quality assurance framework for an investigation and act as a service provider for the mission team;

[2] Previous workshops discussing the UNSGM designated laboratories network were held in Stockholm (June 2015), Umeå (October 2016), Geneva (April 2016), and Spiez (November 2015, June 2016, June 2017 and September 2018).

- Clarification of key terminology related to the tasking of laboratories as well as their reporting;
- Methods validation including the development of recommended or standard operating procedures (ROPs and SOPs); and
- The interpretation of laboratory data.

At the same time, it is important to increase the geographical distribution of laboratories participating in the work towards a UNSGM designated laboratories network, and to secure sustainable funding for this initiative.

As the work has moved from conceptual discussions to practical exercises, the benefits of participating in the development of the network are becoming more apparent:

- Enhancement of the operational capability of the UNSGM;
- Opportunities for enhancements and self-assessment, benchmarking, gaining confidence, and identifying gaps and areas that need improvement; and
- Promotion of international collaborations between the laboratories, including sharing of critical resources, such as databases, reference materials, methods and expertise.

The fifth UNSGM Designated Laboratories Workshop in Spiez was a further milestone on this road towards a trusted UNSGM designated laboratories network. The following report summarises the discussions, its main findings and recommendations.

2. Laboratory exercises

Background

The UNSGM Guidelines and Procedures describe in paragraphs 76-80 the capabilities expected from the laboratories nominated to the UNSGM roster. Paragraph 77 specifically mentions participation of nominated laboratories in inter-laboratory calibrations. In the chemical field, this is implemented by the OPCW in the form of dedicated proficiency testing schemes resulting in a trusted network of designated laboratories. In the absence of any comparable institutional resources in the biological field, any UNSGM investigation of biological weapons will have to rely on the rostered laboratories, currently, however, without any clarity about their quality standards and proficiency level. Certainly, these expert laboratories around the globe have the capability to identify and characterise infectious microorganisms and toxins for various types of samples. However, they maintain their own quality systems and use reporting criteria that meet their routine customers' requirements. Therefore, analysis strategies and quality assurance requirements might not fully satisfy the expectations of the international community in a particular case of an investigation of alleged use of biological weapons.

Unfortunately, only very little information can be extracted from the data submitted by Member States to the UN Secretary-General when they nominate biological laboratories for the UNSGM roster. This creates uncertainty with regard to operational planning as well as with the selection of designated laboratories in support of a particular UNSGM investigation. At the third UNSGM Designated Laboratories Workshop in Spiez in 2017, several dedicated exercises were announced that aimed at gathering practical experience and refining the understanding of the standards that UNSGM designated laboratories should meet:

- In August 2017, Germany started its project 'RefBio 2017-2020'. EUR 1.4 million were allocated to conduct eight workshops and exercises, over a period of 41 months, with gradually increasing difficulty, in the fields of bacteriology, virology, and toxinology;
- Denmark and Sweden, with financial support from the United States, organised a series of dry-lab proficiency tests, beginning in April 2018, that focused on the genomic analysis of target species including modifications of virulence factors; and
- The OPCW conducted confidence-building exercises in the field of toxin analysis. This is considered a first step towards formal proficiency testing and designation. The focus lies on the identification of ricin and saxitoxin, the two toxins listed in Schedule 1 of the Chemical Weapons Convention (CWC).

One year later, the initial results of these projects were presented and discussed at the fourth UNSGM Designated Laboratories Workshop. Germany's Robert Koch-Institute conducted a pilot External Quality Assurance Exercise (EQAE) on the detection of tularemia. Twelve laboratories from ten Member States took part. The Technical University of Denmark organised a first of three genomic dry-lab proficiency tests to identify and characterise target species. Sixty bioinformatics groups from different sectors participated in the test. The OPCW conducted confidence-building exercises in the area of toxin analysis involving ricin and abrin. Twenty-two laboratories from eighteen Member States participated.

A number of organisational issues emerged from these exercises:

- How can the geographical participation be broadened, for example by using direct approaches by UNODA and exercise providers, reaching out to Member States, and providing training to enhance laboratory capabilities;
- How can exercises be designed to accommodate both laboratories with a broad spectrum of analytical capabili-

ties, and highly specialised laboratories that cover a limited subset of biological agents and methods;
- How can recommendations be extracted for UNODA on the evaluation of the competencies and capabilities of UNSGM roster laboratories;
- Which scenarios should be covered in future exercises; and
- How can these efforts be linked up with other projects, and how can ”over-exercising” be avoided.

At the technical level, a number of additional issues were identified:

- Minimal and optimal capacities and capabilities expected from designated laboratories;
- Sample shipment, since mission success depends on timely sample transfer for off-site analysis;
- Documenting the chain of custody from sample collection to reporting of analytical results;
- How can the impact on analytical results of using different methods be evaluated;
- Managing data protection in a network of bio-analytical laboratories (secure internet platform for data exchanges, Consortium and Non-Disclosure Agreements);
- How to accurately report analytical findings without prejudging any conclusions of the mission;
- The need to ensure access to curated databases as well as to critical subject matter expertise; and
- The usefulness of standardisation of methods and benchmarking.

At this fifth UNSGM Designated Laboratories Workshop, participants reviewed the experiences gained in practical exercises conducted since the fourth workshop, and discussed key issues that need to be addressed in the process of setting up a functional UNSGM designated laboratories network.

The German initiative "to strengthen biological reference laboratories for the UNSGM"

The annual workshops organised under Germany’s project RefBio 2017-2020 have contributed to broader participation and geographical representation. The first workshop in October 2017 had 43 participants from 14 countries; in June 2018 there were 48 participants from 17 countries; and the most recent workshop in May 2019 welcomed 50 participants from 19 countries.

These workshops addressed the wide range of issues listed in the previous section of this report. The main conclusions were that designated laboratories should:

- Be able to receive and send infectious material;
- Be able to cultivate target agents which requires availability of high containment facilities;
- Have a quality system in place as well as procedures to securely store data and materials;
- Employ a variety of validated methods for analysis;
- Be able to demonstrate the absence of cross-contamination; and
- Have workflows in place that ensure the chain of custody.

With regard to in-depth analysis, screening for virulence genes was considered important. There is a need to clarify key terms (e.g. delimiting 'identical', 'similar', or 'different' strains) and to use methods that complement DNA identification. More clarity is also needed about what indications can help determine the nature of a biological event.

The second element of the project is the conduct of EQAEs in three working groups; bacteriology, virology and toxinology.

The Working Group on Bacteria has so far conducted two EQAEs, in November 2017, and November 2018. Most notably, participation has significantly increased: the number of participating laboratories rose from 12 to 23, and the number of represented Member States grew from 10 to 18. In terms of participating UNSGM roster laboratories the number expanded from 8 to 15.

In the 2018 EQAE, laboratories were asked to identify or exclude the target agent *Yersinia pestis* in 3 sets of inactivated samples, to characterise the target strains in terms of taxonomic classification, virulence genes and antibiotic resistance genes, and to respond to questions related to the possible origin of the outbreak based on the laboratory results.

The EQAE demonstrated the importance of sample shipment, because the duration for samples to arrive varied considerably, between two and eight days. In one case, the sample temperature had risen above the limit of 8° Celsius.

The results of this second bacterial EQAE can be summarised as follows:

- Almost all laboratories correctly identified / ruled out the target agent;
- Almost no false positive results were reported;
- Screening capacities for antibiotic resistances and virulence genes were available in 74-90% of laboratories;
- Exchange of best practices and methods was considered important by all, especially for next generation sequencing (NGS) and the interpretation of such data; and
- Not all laboratories were able to perform in-depth characterisation of the target strains due to limitations in agent-specific expertise and methodologies in areas like NGS or bioinformatics support.

The Working Group on Viruses conducted a first EQAE in 2018 in which 15 laboratories participated. 3 different sample sets, each with 4 inactivated samples containing species of the *Orthopoxvirus* genus were provided. Four tasks were given to the participating laboratories: identification of positive and negative samples, identification of the species, identification of the strain, and virus quantification.

97% of all samples were correctly identified as positive or negative, with 86% correct identification of the target species. This level of wrong species identification is a reason for concern. Furthermore, only 46% of the strain identifications were correct, however some samples were of low concentration or difficult to distinguish within the sample sets. In regard to quantification, 67% of the reported data were correct.

The Working Group on Toxins conducted a workshop in June 2018, which focused on sample materials and the toxins of initial interest (ricin, abrin, and botulinum neurotoxin). The workshop stressed the importance of developing collaborations. Specifically, it would be beneficial for the UNSGM to make use of the results of previous quality assurance exercises[3]. Round robin tests with ricin and abrin have been conducted under EuroBioTox and are planned under the project RefBio for November 2019. Furthermore, a certified reference standard for ricin will be available soon.

Previously, exercises involving four toxins were conducted under the EQuATox programme. The OPCW conducted ricin identification exercises in 2017 and 2018. Given this diversity of exercises, a closer collaboration should be sought. An example in this regard is the OPCW participation in the EuroBioTox advisory board.

At the same time, it was deliberated that if countries needed support with an investigation involving ricin or saxitoxin, they would be likely to turn to the OPCW. The OPCW, however, has not developed capabilities for the analysis of other toxins. Enhancing the laboratory capabilities of the UNSGM should therefore include toxins that the OPCW is unlikely to cover in the near future, in particular higher-molecular-weight agents, such as botulinum neurotoxin, for which the analytical methods typically used by OPCW designated laboratories are ill suited. For such toxins, other methods including enzymatic activity assays are essential. It was suggest-

[3] EQuATox (2012-2014) involved 35 institutions from 20 countries and created a snapshot of toxin identification capabilities and limitations. EuroBioTox (2017-2022) involves 61 institutions from 23 countries and aims at increasing detection capabilities and creating a pan-European network of competence in toxin analysis.

ed that botulinum neurotoxin could be used as a target for the RefBio exercise in 2020.

Danish - Swedish - US initiative on "dry-lab proficiency tests"

Under this project, three dry-lab exercises focusing exclusively on genomic analysis were conducted. The first exercise in April 2018 involved 60 participating laboratories. A second exercise was conducted in September 2018 in which 47 laboratories took part. Participating laboratories were tasked to identify biological threats in 15 metagenomic datasets of food and water samples that had been artificially spiked with sequence reads of highly pathogenic bacteria. The third exercise was conducted in February 2019 with 37 participating laboratories. They were tasked to identify a deliberate outbreak of brucellosis by means of a bioinformatics analysis of 260 genomes through matching the outbreak strain to a specific facility (14 metagenomic datasets).

Overall, the capability of participating laboratories was assessed as being good. Yet issues remain related to the correct identification of the target species. The evaluation of these dry-lab exercises led to a number of conclusions:

- Specific guidelines should be established for participating laboratories to clarify which findings they are expected to report;
- Data download limitations presented problems — these may be due to infrastructure limitations or IT security systems in place;
- The datasets and tools developed for the exercises can be subsequently used by laboratories for training and capacity building;
- A shared and comprehensive reference database is desirable:
    - It was recognised that there are problems with creating such a database (lack of capacity, proprietary and confidentiality issues that prevent some laboratories from sharing their reference data);
    - On the other hand, the development of the OPCW's Central Analytical Database (OCAD) has shown that despite such issues, the setting up and validation of a common database of validated analytical reference data can be accomplished; and
- Future exercises would benefit from a stronger focus on in-depth characterisation of target agents that goes well beyond identification. Additional benefits would include the combination of sequencing with other diagnostic methods, and simulations of the entire chain from sample collection to analysis and data transfer, including chain of custody issues.

Lessons learned so far

A common lesson from all exercise formats was that analyses in the context of a UNSGM investigation pose demands that go far beyond the routine work of a diagnostic laboratory. In a UNSGM investigation, a set of complementary methods are typically required and the utilisation of bioinformatics tools is essential. This needs to be bolstered with agent-specific expertise and a strong research background of the laboratory. Methods should be accredited as part of the quality assurance system. Laboratory exercises should be close to reality in order to prepare participating laboratories for what they are most likely to expect in a UNSGM investigation.

Simply cloning the OPCW's rigid system may not be practical for the UNSGM. The OPCW experience provides, however, important insights, and certain general principles developed by the OPCW are highly relevant for the UNSGM. This includes the development of scenario based exercises, a gradual build-up of competence through dedicated exercises, and the need to test all steps from sample collection and shipment to analysis and reporting. That said, it was acknowledged that an adapted "designation" model is needed for the UNSGM.

In addition, a number of specific issues emerged that will affect the design and implementation of future laboratory exercises, and these need to be discussed further:

- Should future exercises involve live agent samples? Although it remains uncertain whether UNSGM investigators would arrive on site in time to collect samples containing a live agent, isolation, cultivation and characterisation remain the gold standard for the analysis of biological agents and should whenever feasible be the goal.
- Experience shows that for the comprehensive analysis of biological agents, the characterisation of DNA is not sufficient. The detection and characterisation of the microorganism itself remains essential.
- Developing the network of UNSGM Designated Laboratories is a systematic and sustained process. At this stage, the design of exercises should therefore not discourage or prevent a broader geographic participation.
- Working with live agents does not pose any particular problems for the laboratories which work to BSL-3 or BSL-4 standards. However, the shipment of live agent samples does so, in particular with regards to import and export regulations that have to be met. Laboratories that want to support the UNSGM as designated laboratories are therefore encouraged to make advance arrangements with the relevant national authorities to facilitate any future shipments. These processes should also be tested in dedicated exercises.
- Essential is the adequate reporting of laboratory results. The standards and concepts necessary for the UNSGM need to be agreed upon as early as possible. Report templates should be created that specify the necessary content. There is no room for shortcuts or assumptions – interpretations must be solely fact-based. As a general rule, laboratory data must remain constant over time and not change in the light of other evidence. At the same time, analytical data will always require some degree of interpretation to account for context.
- Laboratory results and findings must be explained in ways that describe confidence levels as well as limitations in the data sets.
- The scoring of test results needs further refinement and discussion. For example, the scoring should reflect that in the absence of publicly available reference data, it would be sufficient for species identification to report the closest common ancestor of a target strain.
- The usefulness of developing SOPs or ROPs needs to be clarified. There are differences between national protocols. And, standard workflows for routine diagnostic analysis may not be adequate for analysis in the context of a UNSGM investigation, in particular when it comes to the characterisation of target agents. Methods standardisation in the field of microbiological analysis is low, and the bar should not be set too high, if broad participation in the evolving network is sought.
- Finally, the lack of curated reference databases and limitations in appropriate informatics tools could potentially undermine the credibility of analytical results of UNSGM designated laboratories.

The continuation of exercises in the form of EQAEs or other formats, as well as dedicated training of laboratory personnel, are all important elements for the establishment of a UNSGM designated laboratories network. The demands of what laboratories are expected to deliver in a complex investigation context are presumably very high. Mapping out future exercises over a period of several years would immensely help with coordinated planning as well as with fund raising. Such a plan should be kept flexible to adapt it as experience is gained and as new requirements emerge.

3. Laboratory support and assistance

Previous discussions have pointed to the need to have laboratory competence integrated within a UNSGM mission team. Furthermore, the UNSGM lacks an equivalent of the OPCW Laboratory that plays a central role during an investigation. It manages quality control and chain of custody compliance. It facilitates the logistics of sample transfers, splits samples, prepares control samples, and oversees the reporting of analytical results.

To facilitate and manage these issues, the concept of a designated laboratory providing support and assistance to a UNSGM mission team, also referred to as a hub lab, has been discussed at previous meetings. A number of considerations were raised that need to be clarified to operationalise this concept:

- What are the standards and capabilities that UNSGM designated laboratories should meet in order to be assigned to a mission as a hub lab?
- What administrative and legal arrangements are required for a hub lab, such as agreements on confidentiality, chain of custody, quality assurance as well as intellectual property rights?
- Would a hub lab be a separate entity assigned to a UNSGM mission, or one of the two designated laboratories selected to conduct the off-site analysis?

At this meeting the concept of a designated laboratory providing support and assistance to a UNSGM mission team was refined. An option was presented on how to provide a "secure work area" for qualified experts conducting an investigation in the field. The UNSGM Guidelines and Procedures make reference to such an area to ensure the safe work of the investigation team under appropriate conditions[4]. In an ideal situation, the host country would be able to provide a secure work area on its territory. However, the reality may likely look different and chemical fact-finding missions so far took place in high-risk countries and hostile environments. Inherent security risks were mitigated by the minimisation of on-site activities and times of exposure. Due to the existence of a technical arrangement between the OPCW and the UNSGM, the OPCW's Central Laboratory acted as the secure work area. Therefore, it is not realistic to assume that in a biological mission qualified experts from the investigation team would be in a position to carry out sample processing on-site for immediate transfer to off-site designated analytical laboratories.

A UNSGM designated laboratory with assisting and coordinating functions in a State of transit could operate as the secure work area for the investigation team. As such, it would also provide services for the investigation team that retains full command and control. Such an approach is suitable to reduce the burden for the investigation team and limit the scope for political challenge. If appropriate, the designated laboratory with assisting and coordinating functions could also be additionally tasked to analyse samples by means of a separate mandate. A designated laboratory with assisting and coordinating functions should meet the following requirements:

- Be flexible and have a broad range of capabilities to handle mixed samples and various types of biological materials;
- Have a triage facility available and expertise in risk assessment;
- Provide clean BSL-3 and BSL-4 facilities;
- Be capable of accommodating an observer (for example, to ensure the chain of custody);
- Have appropriate, quality-assured workflows with accreditation to exclude, for example, cross-contamination;
- Provide control materials;
- Have a recognised culture of biosafety, biosecurity, and (cyber)security, with appropriate measures in place;

[4] See paragraphs C.3.51; E.1.95.a.iv; E.1.97.c.i of the UNSGM Guidelines and Procedures.

- Have staff capacity for 24/7, short-notice operations;
- Possess a proven record of logistics and experience in sample distribution, in particular with regard to import and export regulations;
- Have sample splitting and screening capabilities;
- Have the ability for secured long-term sample storage; and
- Impartiality.

An alternative to such a fixed off-site designated laboratory with assisting and coordinating functions in a State of transit could be a mobile laboratory nominated to the UNSGM roster that would have to be brought into the Member State receiving the investigation and set up on-site or near-site.

Finally, issues with sample export – particularly in light of some countries' implementation of the Nagoya Protocol[5] – from the Member State receiving the investigation were discussed, since this is a mission-critical element whenever off-site analysis by designated laboratories is to be conducted. There is a need for awareness of this kind of issue whenever a UNSGM mission is set up, and it has to be addressed and arranged with the Member State receiving an investigation as part of the initial negotiations. It was proposed that issues related to sample shipment and off-site laboratory analysis should be integrated into the scenario of the upcoming Capstone exercise in 2020.

[5] Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity (29 October 2010).

4. Laboratory interfaces

The question of how qualified experts conducting a field investigation interface with designated laboratories assigned to a particular UNSGM mission has been discussed on several occasions in the past. It was acknowledged that it is important to look again at the roles of the investigation team, the designated laboratories, the potential designated laboratory with assisting and coordinating functions, and expert consultants. Their respective responsibilities have to be clarified, and requirements for command, control and communications have to be addressed. The UNSGM Guidelines and Procedures as well as their Appendices are not always getting granular on all the specifics. In turn, the terms of reference may contain detailed arrangements, such as the conditions for the presence at designated laboratories of an observer from the Member State receiving an investigation.

The role of expert consultants in the context of inter-laboratory calibration tests has already received some attention. But expert consultants could play key roles throughout the entire mission cycle of a UNSGM investigation. In the emerging picture of future UNSGM missions, involving a field investigation team of qualified experts, a designated laboratory with assisting and coordinating functions to provide a secure work area, and two designated laboratories for off-site sample analysis, expert consultants need to have expertise in a variety of areas. These include sample collection and shipment, assessment of laboratory competence, and support with post-analytical reporting and mission reporting.

Expert consultants could serve as facilitators between all the actors and render scientific and legal support during and after an investigation. To fulfil this role, they should be brought into the discussions about the various aspects of enhancing the UNSGM's operational capacity, including with regard to the role of laboratories. They need to understand the concept of a designated laboratory with assisting and coordinating functions, and the way in which designated laboratories work. Expert consultants also need to be able to communicate the underlying reasons for apparent differences in results reported by different designated laboratories. Of course, impartiality and excellent communications skills are paramount. It will be important to formalise their involvement well in advance of future UNSGM missions.

One important aspect of interfacing fieldwork and laboratory analysis is sample collection and risk assessment. It is not clear whether there are any internationally agreed standards in these work areas, but biological laboratories of course have their own standards to ensure that they remain safe. This includes pre-screening of samples in the field, acceptance criteria as well as procedures for different types of samples. The UNSGM Guidelines and Procedures mention the use of screening and preliminary analysis in the field. In practice, good indicator tests for field use have yet to be identified and validated, and existing tests on the market are prone to giving false positive or false negative readings. The test results need to be interpreted based on expert knowledge of the tools used and with an understanding of their limitations. Even emerging methods such as field deployable polymerase chain reaction (PCR) or NGS systems have limitations and their capabilities are at times overstated.

Other issues exist that require interpretation of certain provisions in the UNSGM Guidelines and Procedures; an example being the reference to "three identical sample sets". Such issues need to be understood so that field teams have appropriate guidance on how to perform sample collection, and how to manage collected samples.

To clarify these issues and provide guidance to investigation teams, technical guidelines or recommendations for sample collection and management should be developed. This could be done by an amalgamation of well-established and tested SOPs from different

laboratories. These procedures would need to be reviewed to capture generally accepted minimum requirements. Guidelines developed in this manner must not be overly prescriptive or restrictive, since the human element remains critical when it comes to appropriate collection and handling of samples. It was proposed that a small working group to work on such guidelines should be established.

Participants of the workshop also received information on the upcoming Capstone exercise 2020, organised by the Robert Koch-Institute in Berlin (Germany) in collaboration with FOI (Sweden). The exercise's objectives cover the entire range of UNSGM actors and tasks, with a particular focus on sampling, communications and reporting. In the preparation for the field exercise, a table-top exercise on pre-deployment and mission planning is scheduled for early summer 2020. It will also cover specific elements of the field investigation and laboratory components. The work of designated laboratories will be built into the exercise scenario, and communication between the mission team and the laboratories will be one of the main focusses.

5. Laboratory reporting

The reporting of the results of laboratory analyses by designated laboratories has been identified as a critical issue several times before. As an example for how such reporting can be structured and managed, the OPCW experience was presented at the workshop.

Under the CWC, it is paramount that there is a very high level of confidence in laboratory results reported by OPCW designated laboratories. This analysis is qualitative – the positive identification or confirmed absence of chemicals relevant to the CWC – quantification is not sought. The reporting structure used in official OPCW proficiency tests mirrors that of reports used in actual investigations. The documentation for a proficiency test includes detailed test instructions, copies of current quality assurance documents with rules, regulations and detailed explanations of terms, the test plan and reporting templates, an example of a laboratory report, and documents to assist with customs clearance. The participating laboratories also have the possibility of requesting clarification from the OPCW Central Laboratory during an exercise.

This detailed set of instructions is necessary because the laboratory report is the only data source submitted by the laboratories. No raw data are submitted for reasons of data protection, to avoid disclosure of proprietary information and information unrelated to the task given to the laboratory. The data contained in the report must, however, be sufficient enough to explain which relevant chemicals the laboratory has identified and how, as well as to demonstrate the absence of contamination. This includes amongst others the submission of data on blanks used, sample preparation methods employed, and instrument parameters for each analytical method used. Reporting a false positive identification or irrelevant chemicals must be avoided, and positive identifications require data from at least two different, independent analytical techniques.

For identification, the OPCW gold standard is a confirmatory test using a reference chemical (in-house preparation or commercially available). Identification can also be demonstrated by comparing data to a validated library entry (curated in-house database, the OPCW's OCAD, the National Institute of Standards and Technology (NIST) database, or a commercial database of similar standard). As a last resort, laboratories may perform spectrum interpretations.

There are a number of conditions that have been established to ensure quality, such as limits on the maximum time allowed between test runs of samples and blanks. The details provided in the report on sample coding, test runs, and other manipulations must demonstrate an unbroken chain of custody.

The report contains a chapter that identifies the submitting laboratory. Reports will, however, be anonymised before being sent for review during the evaluation of the results of a proficiency test. This is done by one of two designated laboratories to support a proficiency test – the other designated laboratory prepares spiked samples and tests sample stability. The OPCW Laboratory oversees the process and also conducts quality assurance tests as well as performs analyses.

This system is considered by CWC States Parties to be credible and robust, and to provide a high assurance of quality, chain of custody protection and technical competence. But setting up and maintaining a trusted laboratory network at such standards has its price: there is a need for heavy and sustained investment at the OPCW as well as by States Parties that wish to nominate laboratories for designation, in terms of personnel, equipment and infrastructure. There is the requirement for the regular conduct of and participation in proficiency testing. In addition, technical agreements between the OPCW and designated laboratories are necessary to cover a range of issues.

OPCW experience has shown the benefit of providing assistance to laboratories that consider joining the network. This comes in the form of training offers, twinning with experienced designated laboratories, participation in simplified competency tests, and the possibility of participation in official OPCW proficiency tests on a trial basis.

To what extent and how this OPCW experience can be transferred across to a UNSGM designated laboratory network requires further discussion. It took considerable time and effort to develop the OPCW system to its current standard. It is therefore questionable whether such a thorough system can and should be replicated under the UNSGM.

Looking at a prospective biological network of UNSGM designated laboratories, a number of specific issues need further clarification:

- Is it necessary to report quantitative data, i.e. amounts, purity and enzymatic activity levels for toxins? Such data might be important for discriminating between natural outbreaks and deliberate agent releases. At the same time, quantitation presents a big challenge, particularly with microorganisms, and should only be required if really necessary.
- A sophisticated quality assurance system with SOPs and work instructions needs to be regularly updated. The same is true for reference databases. Ways would need to be found to maintain such a system in the absence of an institutional framework like the OPCW with a central analytical laboratory and an OCAD in place.

There was broad agreement in the workshop that it is now time to begin work on a report template for designated laboratory reports to a UNSGM mission, and a working group was suggested to develop a draft template.

6. Conclusions and next steps

The fifth UNSGM Designated Laboratories Workshop organised by Spiez Laboratory marked a transition from conceptualisation to practical steps in the direction of operationalising a trusted UNSGM designated laboratory network. A number of specific issues have been recognized for which volunteers are ready to develop draft guidance documents. Exercises in the form of EQAEs and other formats are planned to continue. The annual UNSGM Designated Laboratories Workshop hosted by Spiez Laboratory has become an accepted platform for exchanging ideas about the development of the network and for planning next steps.

It is now paramount to further develop and informally agree on a clear roadmap. A key element is the continuation of quality assurance and confidence building exercises. The workshop participants welcomed Germany's efforts to continue its project RefBio beyond 2020. There was also hope that other countries might decide to offer complementing laboratory exercises that would focus on specific issues identified so far, such as genomic data analyses, testing bioinformatics pipelines, and report writing.

At the working group level, volunteers have been identified to move forward with the preparation of initial draft guidance documents on several issues: a reporting template (lead United States), guidelines for sample collection and shipment (lead Canada), and a further refined draft concept of using a designated laboratory with assisting and coordinating functions as a secure work area (lead Switzerland).

As the discussion of how to establish a trusted UNSGM designated laboratories network continues, broadening participation remains an imperative objective. On the one hand, this is a reflection of the need for inclusive geographical representation (creating ownership and political support), on the other hand it mirrors the high degree of specialisation in the field of biological laboratory analysis. It also reflects the fact that the UNSGM could be invoked in cases of alleged use of biological or toxin weapons against humans, animals or plants. This leads to a wide spectrum of possible investigation scenarios, and, as a consequence, a large variety of laboratories that may be required for the UNSGM.

Today, it is difficult to say with any degree of certainty how many laboratories are required. Experience from the OPCW suggests that the number of laboratories that are actively participating in exercises and proficiency tests may at some point reach a plateau and remain fairly constant over time. This is a reflection of the scientific and administrative challenges as well as the costs involved in obtaining and maintaining the standards required by the OPCW.

This notwithstanding, practical steps towards further developing the UNSGM designated laboratory network must continue. Necessary action items were identified during the workshop. An overview of select activities is included at the end of this report. Given the limited resources, it will be important to agree on priorities. An important milestone will be the Capstone exercise in 2020 organised by Germany and Sweden, which will include aspects of the interaction between the field investigation team and designated laboratories. The following lists key areas of action:

- Develop a clearer sense of how the designated laboratories for a particular mission would be selected – expert consultants nominated by Member States could be invited to provide ideas for the nature of exercises such as EQAEs or other suitable formats that would support future selections;
- Clarify what a model technical agreement between UNODA and a designated laboratory would look like and whether it is possible to adapt existing models such as the one of the OPCW for that purpose. A range of issues needs to be clarified in such an agreement, including tasks expected to be accomplished, financial conditions, confidentiality ar-

rangements, logistics and other practical arrangements;
- Gather more details about the actual capabilities and capacities of roster laboratories currently nominated by Member States to the UNSGM. In addition, clarify whether the results of previous participations in relevant laboratory exercises can be utilised to begin evaluating the laboratories' capabilities with the help of expert consultants;
- Making use of the Canadian offer to coordinate a working group on sampling guidance, including sampling strategies, deciding on types, amounts and numbers of samples to be collected, and views on dos and don'ts.
- Making use of the Swiss offer to draft a document for further refinement on the role and responsibilities of a designated laboratory with assisting and coordinating functions acting as a secure work area, and as such provide a service for the investigation team which retains command and control;
- Resolve the challenges that may exist with regard to sample transfer, particularly on import and export issues;
- Develop a master programme of various exercises, including table-top formats;
- Encourage additional nominations of expert consultants;
- UNODA should encourage Member States to nominate the laboratories that have taken part in the recent exercises if they are not already nominated, taking into account the specific expertise that these laboratories have; and
- Making use of the US offer to coordinate a working group on developing a draft report template for analytical laboratories, including guidance on the level of detail required, the balance between factual data reporting and scientific interpretation of results, as well as necessary terminology and definitions.

The focus of the deliberations on the establishment of a trusted UNSGM designated laboratory network has now shifted to practical work. This recognises the role that laboratories need to play as a service provider to the UNSGM. At the strategic level, the development of evaluation criteria for assessing the capabilities and performance of roster laboratories remains paramount. This is essential for providing criteria and principles that could be used when selecting roster laboratories for a particular UNSGM mission. These criteria need to be flexible and adaptable to the context and objectives of a particular mission. They should also address how to select highly specialised laboratories that focus on a single agent / disease *versus* laboratories that cover a broad range of biological threats. Additional criteria are necessary for the selection of a designated laboratory with assisting and coordinating functions.

Finally, participants welcomed the Swiss initiative of providing a platform for these discussions. Switzerland confirmed that it remains committed to continuing this workshop series, and that the sixth UNSGM Designated Laboratories Workshop will take place from 9 – 11 September 2020 in Spiez.

Roadmap of select activities of relevance to UNSGM designated laboratories

Identified need	Planned	Accomplished
Dedicated platform for designated laboratories to discuss UNSGM issues related to designated laboratories and to coordinate relevant activities	Switzerland: UNSGM Designated Laboratories Workshop 6 (Sep 2020), and on-going	Sweden: Workshop on UNSGM laboratory network 1 (Jun 2015), 2 (Oct 2016) United States: UNSGM Workshop (April 2016) Switzerland: UNSGM Designated Laboratories Workshop 1 (Nov 2015), 2 (Jun 2016), 3 (Jun 2017), 4 (Sep 2018), 5 (Sep 2019)
Periodic wet-lab exercises with a wide range of aspects covering bacteria, viruses and toxins	Germany: Project RefBio "Germany's Contribution to Strengthen the Reference Laboratories Bio in the UNSGM" Bact3 (Nov 2019), Viro2 (Nov2019), Tox1 (Nov 2019), and on-going in 2020 and maybe further OPCW: Confidence-building exercises focusing on Schedule 1 and closely related toxins, Tox4 (Dec 2019)	Germany: Project RefBio "Germany's Contribution to Strengthen the Reference Laboratories Bio in the UNSGM" Bact1 (Nov 2017), Bact2 (Nov 2018), Viro1 (Nov 2018) OPCW: Confidence-building exercises focusing on Schedule 1 and closely related toxins Tox1 (Jan 2017), Tox2 (Dec 2017), Tox3 (Dec 2018)
Periodic dry-lab exercises focused on genomic analysis		Denmark, Sweden, United States: proficiency tests and simulation exercises for confidence building in forensic genomic analysis of infectious disease pathogens 1 (Apr 2018), 2 (Sep 2018), 3 (Feb 2019)

Identified need	Planned	Accomplished
Wet-lab live agent exercises covering bacteria and viruses		
Wet-lab unknown agent exercises		
Wet-lab or dry-lab exercises focused on reporting		
Wet-lab or dry-lab exercises focused on forensic awareness and chain of custody issues		
Wet-lab or dry-lab exercises focused on agents affecting exclusively animals or plants		
Laboratory expert trainings / twinning programmes		
Working group or workshop on bioinformatics pipelines and curated reference databases		
	Germany: Project RefBio "Germany's Contribution to Strengthen the Reference Laboratories Bio in the UNSGM" Workshop 4 (Jan 2020)	Germany: Project RefBio "Germany's Contribution to Strengthen the Reference Laboratories Bio in the UNSGM" Workshop 1 (Oct 2017), 2 (Jun 2018), 3 (May 2019)
Initial draft guidance document and/or working group on the concept of a designated laboratory with assisting and coordinating functions	Switzerland: to prepare initial draft guidance document in early 2020	

Identified need	Planned	Accomplished
Initial draft guidance document and/or working group on sampling from a laboratory perspective (e.g. sample acceptance criteria)	Canada: to start working group	
Initial draft laboratory reporting template and/or working group on laboratory reporting	United States: to develop initial draft	
Table-top exercise on sample transfer (including ex-port and import) to have awareness about issues that need to be sorted out early on		
Expert consultants to map competence of designated laboratories		
Periodic outreach to Member States by UNODA to encourage additional designated laboratories nomina-tions, especially labs that performed well in past dedicated exercises	UNODA: on-going activity	UNODA: on-going activity
Formalisation through technical arrangements between UNODA and designated laboratories		
Reciprocal arrangement between UNODA and OPCW for toxin analysis		
Integration of designated laboratories in full-scale exercise	Germany, Sweden: Capstone exercise (Sep 2020)	

Group photo


UNSGM Designated Laboratories Workshop
11 – 13 September 2019, Spiez, Switzerland
Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra
Swiss Confederation