OPCW

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SUMMARY OF THE FIRST MEETING OF THE SCIENTIFIC ADVISORY BOARD'S TEMPORARY WORKING GROUP ON THE ANALYSIS OF BIOTOXINS

1. AGENDA ITEM ONE – Opening of the meeting

1.1 The Scientific Advisory Board's (SAB) Temporary Working Group (TWG) on the analysis of biotoxins held its first meeting on 3 and 6 May 2021 in a virtual format using an online platform. The meeting was chaired by Dr Daan Noort on behalf of the SAB, with Dr Suzanne Kalb as Vice-Chairperson.

1.2 Dr Noort opened the meeting by welcoming TWG members and expressing his pleasure and honour to be chairing this TWG with Dr Kalb as the Vice-Chairperson. He recalled his previous experience as a member on several SAB TWGs, noting this is the first time not only chairing one, but also doing so in a virtual setting. He invited TWG members to provide any suggestions they may have that could enhance the conduct of the work of the TWG. The TWG Chairperson reiterated some of the housekeeping items for the meeting and gave an overview of the proposed programme of work during the two days of the meeting. No objections or comments were raised so the agenda was adopted.

2. AGENDA ITEM TWO – Adoption of the agenda

The TWG adopted the following agenda for its first meeting:

1. Opening of the meeting
2. Adoption of the agenda
3. Introduction of the OPCW, the Scientific Advisory Board, and the Temporary Working Group
4. Overview of the Temporary Working Group on the analysis of biotoxins
5. Introduction of Group members
6. Discussion on the Temporary Working Group's terms of reference
7. Overview of the online platform
8. Presentations of the Temporary Working Group subgroups by group leads
9. Formation of the subgroups

10. Subgroup breakout sessions

11. Final comments and next steps

12. Closure of the meeting

3. AGENDA ITEM THREE – Introduction of the OPCW, the Scientific Advisory Board, and the Temporary Working Group

3.1 The SAB Secretary provided a brief overview of the OPCW's establishment and mandate, as well as of provisions related to the establishment of the SAB and related temporary working groups as provided by the SAB terms of reference.[1] He recalled that the most recent TWG focused on investigative science and technology, which also included several of the members of the current TWG on biotoxin analysis. Furthermore, he provided background information related to the establishment of the TWG on the analysis of biotoxins.[2]

3.2 The SAB Secretary stressed the importance of understanding that both the TWG and the SAB are independent advisory mechanisms whose work focuses on science and technical aspects of the questions and topics they are mandated to consider. He recalled that the SAB has successfully maintained a very independent stance in providing advice, which has been recognised and commended by the OPCW Director-General and States Parties alike. He further explained that the TWG feeds its reports and recommendations to the SAB for consideration and discussion. The SAB then provides comments and recommendations to the Director-General, who has the latitude to comment on the recommendations, and further communicate the work of the TWG to States Parties.

3.3 The SAB Secretary recalled the relevant provisions of the SAB terms of reference and Rules of Procedure and how they translate to the current TWG in terms of its establishment and membership, the latter being comprised of some of the current members of the SAB and several external experts to provide expertise, breadth, and balance.

3.4 Turning to the logistics of TWG meetings, the SAB Secretary noted that—due to the current COVID-19 pandemic circumstances—this TWG will be more hybrid in nature, with meetings being conducted both online and in person, once the situation so allows. He noted that this should actually be seen as a positive approach which can prove to be very beneficial for the Group, with the ability to convene more frequent online meetings and the possibility of engaging external speakers more easily, amongst others.

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1 The SAB terms of reference can be found at: https://www.opcw.org/sites/default/files/documents/SAB/en/SAB_ToR_RoP.pdf.

2 See: "Report of the Scientific Advisory Board at its Twenty-Ninth Session" (SAB-29/1, dated 2 September 2020); "Report of the Scientific Advisory Board at its Thirtieth Session" (SAB-30/1, dated 12 November 2020); and "Report of the Scientific Advisory Board at its Thirty-First Session" (SAB-31/1, dated 4 March 2021).

3.5 As for the schedule of meetings, he recalled that the TWG will operate for two years from January 2021, with a possibility of extension. The idea is to have one to two virtual meetings and, hopefully, one in-person meeting in 2021, one to two virtual and two in-person meetings in 2022, and possibly another in-person meeting in 2023. He recalled that in-person meetings are generally held in The Hague unless another location can provide an interesting opportunity (e.g. one of TWG members' institutions). All meeting dates will be communicated to the members at least one month in advance to provide adequate time for scheduling considerations.

3.6 The SAB Secretary reiterated that the TWG will very much depend on the expertise of its individual members. As it can and should call upon external speakers, he encouraged TWG members to inform himself, and the Chairperson and Vice-Chairperson of any suggestions on potential speakers who could be invited to present at a TWG meeting. The TWG should also interact with the Technical Secretariat (hereinafter "the Secretariat"), mainly with the OPCW Laboratory, and the Inspectorate and Verification Divisions.

3.7 In terms of file storage and information and document sharing, the TWG will utilise Microsoft Teams for both its meetings, and hosting and sharing documents associated with the TWG.

3.8 When it comes to reporting, each TWG meeting will generate a meeting report, and each report will be presented to and considered by the SAB at their next regularly scheduled session. The final end of mandate report will contain the final recommendations for the SAB to consider and further communicate to the Director-General.

3.9 In conclusion, the SAB Secretary acknowledged the generous support of the European Union for the work of the TWG, including the funds related to travel and related costs for TWG members and external speakers, as well as any other associated costs (e.g. participation of a TWG Chairperson, Vice-Chairperson or member in an Executive Council or a Conference of the States Parties session).

4. AGENDA ITEM FOUR – Overview of the Temporary Working Group on the analysis of biotoxins

4.1 The TWG Chairperson opened his presentation with the definition of a biotoxin and the use and application of biotoxins through history, both as a weapon of war and terror, but also for legitimate reasons such as in medicine and the cosmetic industry. He further recalled the specific objectives of the TWG, and the duration of its mandate and composition (nine SAB members plus six external experts). Focusing on the TWG terms of reference, he provided a brief overview of each of the questions and subquestions to be considered by the TWG, and related deliverables and reporting. He indicated that the work of the TWG, in addressing the terms of reference, will be divided into five subgroups. He noted that several TWG members have already been contacted in preparation for the formation and management of the proposed subgroups.

4.2 An outline of the five subgroups for this TWG is as follows:

(a) Subgroup 1, led by Dr Graeme Clark, will focus on question 5(a) of the terms of reference:

(i) What are the underlying requirements for the analysis of biological toxins in order to investigate alleged use of toxic chemicals as weapons?

(b) Subgroup 2, led by Dr Anne Bossée, will focus on questions 5(b) and 5(c) of the terms of reference:

(i) What classes of biological toxins are most likely to be relevant in investigations of alleged use?

(ii) Are there other relevant compounds of biological origin that should also be considered based on their potential for misuse or technological change associated with them?

(c) Subgroup 3, led by Dr Crister Åstot and Dr Suzanne Kalb, will focus on question 5(d) (and associated subquestions) of the terms of reference:

(i) What are the technical requirements for analysis of the most relevant types of biological toxins? Please consider:

(a) analytical approaches needed for unambiguous identification of both low and high molecular weight biotoxins;

(b) instrumentation and/or procedures that should be standardised across laboratories to ensure reproducible and consensus-based results;

(c) analytical criteria that should be in place in order to match forensic requirements;

(d) the role and utility of degradation products and other markers and/or compounds; and

(e) the role of biomarkers and biomedical samples.

(d) Subgroup 4, led by Dr Brigitte Dorner, will focus on questions 5(e) and 5(f) of the terms of reference:

(i) What are the analytical standards and requirements of other international and national investigative authorities and how do these compare and/or factor into OPCW considerations and operations?

(ii) How can programmes of analytical exercises conducted by different networks of laboratories be coordinated or harmonised to minimise duplication, promote consistent practices, and develop a comprehensive picture of laboratory capabilities? Please consider:

(a) the quality system requirements for the laboratories that should be in place (e.g. consideration of ISO/IEC 17025:2005 for OPCW designated laboratories); and

(b) how the analytical exercises can be harmonised yet remain flexible to address new or emerging biotoxin threats.

(e) Subgroup 5, led by Dr Robert Mikulak, will focus on question 5(g) of the terms of reference:

(i) What institutional or legal measures need to be established to facilitate cooperation between the OPCW and other organisations working on the development of capabilities for the analysis of biological toxins?

4.3 The TWG Chairperson clarified that more detailed presentations will be given by the leads on the second day of the meeting, after which other TWG members will be asked to contribute to, ideally, two subgroups, based on their expertise, in order to fairly divide the workload. The SAB Secretary further explained that the rationale behind splitting the work into several smaller dedicated subgroups, as opposed to all members working on all questions, was to ensure efficiency. Moving forward, subgroup leads will present the work of each subgroup enabling everybody to gain insight into, and weigh in on, what each subgroup has worked on.

4.4 The TWG Chairperson added that, in case some questions require involvement of more members or advice by external experts, this can be arranged, and he stressed that the idea is not to have group leads take on all the work by themselves. He further clarified that subgroup meetings do not necessarily have to take place during a TWG meeting itself. Preferably, individual subgroups should meet during the intersessional period to discuss issues under their respective purview so that the official TWG meetings can be used to present and discuss the outcomes of such meetings. The SAB Secretary explained that the subgroups will have their first opportunity to meet on the second day of the meeting (6 May) with the help of the breakout rooms feature in the online platform.

5. AGENDA ITEM FIVE – Introduction of Group members

Each of the 15 members of the TWG gave a brief presentation about themselves, including their professional accomplishments, credentials and education, personal interests, and main expertise they can bring to the TWG. The SAB Secretary and the Senior Project Assistant also briefly introduced themselves to the Group.

6. AGENDA ITEM SIX – Discussion on the Temporary Working Group's terms of reference

6.1 The TWG Chairperson invited TWG subgroup leads and other members to reflect on a central question: "In what way does the analysis of biotoxins differ from the more regular Chemical Weapons Convention-controlled substances?", explaining that answering this question will help further discussion. The Chairperson also noted that a list of the current subgroups, their leads, and their members will be distributed prior to the second day of the meeting.

6.2 The Head of the OPCW Laboratory, Dr Hoe Chee Chua, briefly introduced herself and encouraged TWG members to reach out to her if they need any information on the current practice at the OPCW Laboratory. The SAB Secretary confirmed that the OPCW Laboratory will be participating in TWG meetings, as the advice provided by the TWG will assist the Laboratory in many aspects of their work.

7. AGENDA ITEM SEVEN – Overview of the online platform

Mr Unnikannan Ayilliath, of the OPCW Information Services Branch (ISB), introduced himself and gave a brief overview of some of the features of the online platform used by the TWG that will be of use to its members in terms of communicating and file sharing. He provided the members with a step-by-step explanation on how to access the TWG team depending on their individual circumstances (with vs without existing access to the online platform). Several TWG members reported that they had not received the original OPCW invite to access the TWG team. Mr Ayilliath confirmed that the invite will be resent to all the members concerned, including to any alternative email address they wish to provide, together with the screenshots of his PowerPoint presentation.

8. AGENDA ITEM EIGHT – Presentations of the Temporary Working Group subgroups by group leads

8.1 The TWG Vice-Chairperson began by providing an overview of the five TWG subgroups and their respective leads. She then turned the floor over to each subgroup lead in turn, to provide an overview of their subgroup and how they will look to addressing their assigned questions.

Subgroup 1

8.2 The lead for subgroup 1, Dr Clark, noted that this subgroup will consider a very broad and overarching question that includes everything, starting from investigating an alleged incident through to analysis and reporting. He noted that attribution insofar as determining who was responsible for any given incident involving a biotoxin was not within the remit of the subgroup, or the TWG in general. The subgroup will also consider initial in-field sampling and collection activities, which raises questions about what sets of tools, or possibly unique sets of tools, are required when dealing with a biotoxin incident, how much material is needed (one large vs multiple smaller subsamples), and how best to store, package, and transport such samples while maintaining the chain of custody throughout. Furthermore, in-field analysis may be required, which—if recommended—would need to be low-tech (e.g. use of lateral flow assays) and low operator burden, with defined performance criteria. Furthermore, a specific set of personal protective equipment for collectors needs to be considered, including anything unique for biotoxins, given their toxicity.

8.3 Touching briefly upon the analytical laboratory requirements, Dr Clark recalled several available techniques and technologies that could help identify biotoxin presence (e.g. immunoassays, mass spectrometry, activity assays, genome sequencing) to help answer questions related to sample provenance.

8.4 Dr Clark continued to provide a brief summary of what it might look like for an analytical laboratory to undertake biotoxin identification. It would be a staged approach involving screening, to see if there is any other hazard present in the sample, more in-depth laboratory analysis (e.g. use of ELISA, mass spectrometry techniques), followed by high-confidence procedures (e.g. 2+ orthogonal techniques) in order to underscore that one needs a laboratory regularly audited and accredited under whichever standards the group will find appropriate.

8.5 In conclusion, Dr Clark pointed out several basic but also challenging questions that will be considered by the subgroup, including which biotoxins should be considered based on which criteria (e.g. prevalence, toxicity, and history of use), and which methodologies are required for their identification; should one look for the toxin itself or for the source organism as well (e.g. genome sequencing, strain identification)? Methods of production and reliance on antibodies, regardless of approach, are other considerations.

8.6 Dr Clark was asked to comment on the appropriate approach that can be followed in cases when it is not known if biotoxins were indeed used, but there may be some indicators pointing in that direction. What kind of technology can be used in the case of biotoxins with very low concentrations, e.g. in the field (triage with lateral flow assays)?

8.7 Dr Clark commented that not many tools are available, and that lateral flows, including multiplex lateral flows, may be the first tool of choice; however, they have certain limitations when it comes to their application in cases of biotoxins use as considered by TWG. He further pointed out the challenge posed by the late onset of symptoms in case of biotoxins exposure. In conclusion, the choice of tools, in particular the ones that are fieldable, is currently very limited.

8.8 It was also suggested that additional subdivision by sample type—environmental, clinical, animal, and food samples—might be beneficial and important in terms of a laboratory's scope of analysis, but also from the aspect of concentration and shape of the analyte. Dr Clark concurred, adding that a solution could be to have laboratories that are experts in particular areas focusing only on particular matrices types (as opposed to asking a laboratory to cover many different categories or challenges).

Subgroup 2

8.9 Dr Bossée provided an overview of the proposed methodology of work on question 5(b), including comparing available open-source lists from the Centers for Disease Control and Prevention (CDC), and international and national regulation bodies to complete the biotoxins list's scope of interest. At the outset, the group will establish the criteria for selecting the biotoxins to be considered, starting initially with a very broad approach and eventually narrowing down to a selected list of biotoxins. The most important data would be compiled in a synthetic table, if possible. The initial work (i.e. the collection of available data) would be split by biotoxin (one to two members per class of biotoxins), with the initial data being further completed by other members of the group.

8.10 Turning to possible criteria which could be taken into consideration when selecting biotoxins relevant in investigations of alleged use, Dr Bossée highlighted the following:

(a) ease of production (i.e. availability from natural sources, synthetic chemistry possibility, and biotechnology available for production), including related consideration of dual purposes for several biotoxins and criteria for separating natural occurrence of toxins from alleged use as warfare agents (e.g. based on concentrations, context);

(b) historical use—incidents of weaponisation, and credible allegations of past use;

(c) toxicity and activity—possible intoxication pathways, difficulty to extrapolate from animal species lethal doses to human toxicity values, and possible definition of three ranges of toxicity instead of precise values;

(d) stability and potential ease of weaponisation—during storage, during dispersion, in the environment, and for different levels of purity (raw vs purified form);

(e) detection methods, directly linked to question 5(d)—available methods for the different types of samples, with a focus on their sensitivity vs toxicity of screened and analysed biotoxins, and speed and selectivity of methods; and

(f) medical countermeasures—available or not.

8.11 Dr Bossée proposed that question 5(c) of the terms of reference should be considered following the completion of question 5(b). This will require research into relevant open-source literature to explore different bioregulators and their historical uses, as well as external expertise (i.e. inviting experts on bioregulators to give a presentation at a TWG meeting).

8.12 It was noted that compiling the aforementioned lists with all the accompanying metadata would generate a sensitive document. Recognising that none of the members has the capacity to oversee all the intricacies and complexities of the lists, it was proposed that the group could instead concentrate on examples, such as ricin and saxitoxin, and possibly extend the list to five to ten different agents representing different groups. That list could include historically relevant toxins, as they are of particular concern. The toxins that are already covered in other national and international programmes (e.g. food and feed) could be deprioritised so as not to duplicate the work.

8.13 Dr Bossée agreed with the point regarding data sensitivity and the need to simplify some information regarding toxicity, as well as to reduce the list. However, the question is how to reduce the list—based on which criteria—at the beginning of the subgroup work. It would be sufficient to have one biotoxin leader per family. As for the biotoxins related to food concern, they do not have to necessarily be included in the list, but should be covered during the initial work, and a justification should be provided for deprioritisation in order not to lose one class of biotoxins.

Subgroup 3

8.14 Dr Åstot explained that the initial deliberations related to question 5(d) have concentrated on two toxins on Schedule 1, ricin and saxitoxin. Referring to the analytical approaches needed for unambiguous identification of both low and high molecular weight biotoxins, Dr Åstot noted that there are sensitive and selective analytical tools present for toxin analysis right now. However, given that the analysis of biotoxins differs from that of traditional Schedule 1 warfare agents, there is a need for further development in the area of functional assays for an unambiguous identification.

8.15 Turning to the subquestion of instrumentation and/or procedures that should be standardised across laboratories to ensure reproducible and harmonised results, Dr Åstot remarked that the OPCW has not standardised instrumentation and/or procedures for environmental or biomedical samples. Listing several examples of good

practices (e.g. the so-called Blue Book,[3] performance data on the methods used at PTs), he noted that a more strict standardisation may be required, given that the establishment of robust bioassays may require laboratories to use the identical cell lines and antibodies, among others

8.16 As for the subquestion on the analytical criteria that should be in place in order to match forensic requirements, Dr Åstot recalled that this is a very diverse field of analysis. The forensic analysis of toxin samples may include a more detailed analysis of the toxin and/or the analysis of non-scheduled material as toxin analogues, degradation products, and other chemicals of biological origin. That may require different analytical approaches and techniques than the ones used when first determining if a biotoxin has been used or misused in a given incident. He noted that the developed methodology is quite mature and there is good performance at laboratories, but further down the road there is a need for further development and improvements to meet OPCW requirements. It was also agreed that the quality of immunoaffinity tools is important.

8.17 Dr Kalb continued the presentation touching upon the question related to the role and utility of degradation products and other markers and/or compounds. Detection of degradation products is not desirable for unambiguous identification, especially if those degradation products are non-toxic and the biotoxin of origin is stable. Most biotoxins are associated with other, non-toxic compounds. As these compounds are non-toxic, detection of these associated compounds is also not desirable, but their presence may be used for sample matching. When considering the role of degradation products and other associated compounds, it may be helpful to ask the question: "Is it possible that the non-toxic degradation product and/or associated compound could be present in the absence of the toxin?"

8.18 Turning to the role of biomarkers and biomedical samples, Dr Kalb noted that biomarker detection might be considered as an aide to unambiguous detection; however, it is important to understand that biomarkers might have an alternate source other than the biotoxin in question. Therefore, the detection of biomarkers alone cannot yield unambiguous detection. Biomedical samples are an important matrix to consider as these matrices provide evidence for human harm from biotoxin exposure. This is a separate issue from providing evidence for the intent to harm humans, which comes from the examination of environmental samples. However, the same criteria that apply for unambiguous detection must apply to both biomedical and environmental samples, and this is often difficult in the presence of so many interferents endogenous to biomedical samples.

Subgroup 4

8.19 Dr Dorner opened her presentation by noting that the first question before the subgroup, 5(e), is which international and national investigative authorities should be considered, and how and on which (legal) basis they work. Given that the TWG members come from 14 different countries, she invited them to provide input based on their personal work experience in their respective regions of the world.

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3 For information on the Blue Book please see: https://www2.helsinki.fi/en/verifin-finnish-institute-for-verification-of-the-chemical-weapons-convention/information/blue-book.

8.20 She recalled the United Nations Secretary-General's Mechanism for Investigation of Alleged Use of Chemical and Biological Weapons (UNSGM) and the 2013–2014 OPCW-United Nations Joint Mission in the Syrian Arab Republic to implement the elimination of the Syrian chemical weapons programme.[4] She pointed out that there is no implementation body for the UNSGM for the investigation of alleged use of biological weapons as there is for the investigation of alleged use of chemical weapons.

8.21 In relation to UNSGM activities, Dr Dorner noted the United Nations General Assembly's "Guidelines and Procedures" (A/44/561, 1989) authorising the United Nations Secretary-General to launch prompt investigations in response to allegations of possible use of chemical and bacteriological (biological) and toxin weapons that may constitute a violation of the 1925 Geneva Protocol.[5] The document also contains relevant provisions related to the involvement of analytical laboratories under the UNSGM.

8.22 Turning to question 5(f), Dr Dorner indicated two points that should be taken into consideration, including the quality system requirements for the laboratories that should be in place (e.g. consideration of ISO/IEC 17025:2005 for OPCW designated laboratories),[6] and how analytical exercises can be harmonised yet remain flexible to address new or emerging biotoxin threats.

8.23 In her view, the subgroup should identify other national and international networks that are performing exercises on biotoxins, see how they approach the work on biotoxins, and what they do exactly, in order to identify overlaps, similarities, and clear differences. She once again called on all TWG members to provide input from their respective regions of the world. Dr Dorner referred to several relevant international programmes and networks which could present on analytical exercises conducted on biotoxins and other biological and chemical agents (e.g. the OPCW Laboratory, RefBio, and EuroBioTox).[7] She noted that many issues remain unresolved, including sensitivity in clinical samples. A related concern is how to ensure that methods other than mass spectrometry deliver reliable results (i.e. how we qualify the antibodies). In that respect, it is important to rely on relevant experiences from around the world.

8.24 As the final question to be considered by the subgroup, Dr Dorner pointed out the existing quality system requirements (ISO/IEC 17025:2005, ISO 15189:2012),[8] but also raised the question on the existence of other such standards and how binding they should be. What can be accepted as an alternative qualification if a laboratory is not accredited according to one of those standards, as non-accredited laboratories can also perform well?

8.25 In conclusion, based on the points raised above, Dr Dorner proposed that the TWG invite experts who can help identify other relative investigative authorities, such as representatives of UNODA, or networks (e.g. RefBio and EuroBioTox).

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4 For information on the UNSGM please see: https://www.un.org/disarmament/wmd/secretary-general-mechanism/; and for information on the OPCW-United Nations Joint Mission see: https://opcw.unmissions.org/.

5 See: https://www.un.org/disarmament/wmd/secretary-general-mechanism-old/key_documents/.

6 See: https://www.iso.org/standard/39883.html.
For more info on RefBio see: https://www.rki.de/EN/Content/Institute/International/Biological_Security/RefBio.html; and for EuroBioTox see: https://eurobiotox.eu/.

8 See: https://www.iso.org/standard/39883.html and https://www.iso.org/standard/56115.html.

Subgroup 5

8.26 Dr Mikulak provided an overview of questions to be addressed by the subgroup, while observing that they belong more to a legal and political realm rather than a technical one. These were:

(a) which other organisations are developing toxin analysis capabilities—for instance, the UNSGM, but also other organisations and networks both nationally and internationally, law enforcement in various countries, and network of laboratories working on food safety, for example, whose work can benefit that of the OPCW;

(b) how other organisations can benefit the OPCW with respect to toxin analysis—considering the importance of having representatives of both the OPCW and these other organisations discuss what they are developing and what they need for their own work;

(c) how the OPCW can assist other organisations with respect to toxin analysis—similar to (b);

(d) what institutional or legal measures might be relevant—considering a full spectrum, ranging from periodical exchanges of information on a formal and informal basis to developing joint activities (e.g. coordinating by means of signing a MoU); and

(e) what recommendations the TWG should make on measures to facilitate cooperation—the TWG report should contain recommendations covering all of the questions above.

8.27 There were some important thoughts and comments made in the subsequent discussion involving all TWG members. It was noted that some biotoxins do not have acute presentation, but chronic effect (e.g. in cases of mould exposure), and it is therefore important to differentiate biotoxins based on this distinction. Hence, the initial diagnosis by a treating clinician can be a helpful initial step in detecting the exposure to a biotoxin agent, which can then be further verified by laboratory tests.

8.28 A point was raised as to whether more biotoxins should or would be added to Schedule 1 of the Annex on Chemicals to the Convention; this is very important for the laboratories in the network, because strictly speaking, only scheduled chemicals can be reported. It was noted that it is possible, in principle, for additional toxins to be added to Schedule 1, but it is a long process, and therefore this is unlikely in the short term. It was recalled that, when speaking about the analysis of samples from an alleged use incident, and not a routine inspection, the task is to identify and report *any* toxin that may be present. It is not limited to the rules that would normally apply to the analysis of environmental samples taken during routine missions.

8.29 The TWG Chairperson noted that it is important to limit the list of biotoxins under consideration as it reflects on other subsequent questions. He further referred back to the central question from the first day on the differences between the active toxin analysis and the authentic sample analysis for chemicals. With the latter, the presence of often good indicators (e.g. hydrolysed nerve agents as indicator of the presence of a

nerve gas) can help establish that a nerve agent has been used and/or produced. How can the same conclusion be reached, for example, in case of a mass spectrometry analysis of a long sequence of protein biotoxin, when in the sample we do not see any activity? Can it be concluded that a toxin was present or is the evidence considered insufficient to reach such conclusion?

8.30 The TWG Vice-Chairperson pointed out two possible ways of looking into the question, whether the purpose of the analysis is to show intent to cause harm or to show that the harm has been caused. What is the purpose of the Group in that respect?

8.31 It was remarked that the presence of a biotoxin in an environmental or biomedical sample does not conclusively mean someone was trying to cause harm. There are more considerations involved, and the naturally occurring character of many biotoxins—as opposed to nerve agents, for example—can make identifying misuse and attributing responsibility more challenging.

8.32 A member further recalled the advisory nature of the group, and raised a more specific set of questions in terms of underlying OPCW requirements: the ability to determine whether or not a biotoxin has been used to cause harm in a particular incident; the capability to collect, process, and analyse biomedical and environmental samples for a biotoxin; and the capability to analyse environmental and biomedical samples to detect, identify, and characterise any biotoxin that might reasonably be expected to be used for weapons purposes.

9. AGENDA ITEM NINE – Formation of the subgroups

TWG members were asked to indicate during the previous day up through the second day of the meeting which subgroup(s) they were interested in participating in. This allowed the Chairperson to ensure that each subgroup had enough participants and to even out the participation as needed.

10. AGENDA ITEM TEN – Subgroup breakout sessions

10.1 Subgroup 1 discussed the broad, overarching nature of the "underlying requirements" question (i.e. as opposed to the more defined nature of the other subgroups). It was agreed that the subgroup should look at the end-to-end process of investigating an alleged release of biotoxins whilst also avoiding duplication of effort with the other subgroup topics. Subgroup 5 might therefore, for example, present an overview of the whole process, with the detailed strategic, technical, and legislative requirements being covered in the other subgroups.

10.2 One area of initial focus of discussion was around the early phase of an investigation: more specifically, the most likely indicator of biotoxin use, and therefore what the triggers would likely be in order for OPCW to investigate. Discussion was held around the clinical diagnosis of exposure being one potential first indicator (i.e. rather than a sensor and detector identifying release of a toxin). Therefore, it was felt that advice and input from clinicians and/or national poison centres, with respect to early indicators of a biotoxin event, would be of value in order to inform the group on these procedures.

10.3 Briefly, the challenge associated with in-field sampling, collection, and detection was discussed, more specifically with respect to which tools should be used and where samples could and should be taken from. This is an area of real interest for the OPCW and a requirement for the TWG to address. Therefore, it was agreed that careful

consideration would need to be made with respect to whether the "unknown (detector) tool box" would actually be required by investigators or whether there would already have been an indication and diagnosis of the presence and exposure, respectively, to a particular toxin(s) prior to arrival. This would naturally narrow down the technologies needed in the field. This topic was deemed an area of early focus for the group.

10.4 Subgroup 2 focused their discussion on the proposed initial criteria, presented on the first day, that have to be looked at for further selection and prioritisation of relevant biotoxins in investigations of alleged use. These initial criteria were accepted, with the addition of subcriteria for the toxicity criteria of distinction between acute exposure and chronic exposure. The subgroup agreed to work on these criteria, and Dr Bossée will provide a draft of a summary table with the defined criteria. The subgroup agreed to work on open literature references only and the problem of document sensitivity would be discussed after initial work on some biotoxin families.

10.5 Subgroup 3 discussion consisted of examining the differences between classic chemical warfare agents and biotoxins. In some cases, such as conotoxins and shellfish toxins, these are more similar to classic chemical warfare agents given their high polarity. For protein toxins, digestion and analysis methods for proteins in general are well characterised. In some cases, protein toxins may be difficult to digest, so this may complicate analysis. A secondary method of detection for validation might be difficult to choose. Brainstorming for potential options included gel, 2D gel, DNA sequencing, antibody binding, environmental analysis, and macroscopic analysis of how a cell dies. In addition, it was noted that biomedical data can be very powerful, and functional assays make a case stronger, but this should not be a necessity for unambiguous detection. Standardisation across laboratories may be problematic as modern methods may be difficult to include as it takes time for these to become standard. In terms of standardisation, the standardisation of ELISA could be possible with a central repository for reagents.

10.6 Subgroup 4 started its discussion with question 5(e), where it was discussed which international investigative authorities and which networks should be considered, and on which legal basis they work. For the OPCW, the International, Impartial and Independent Mechanism (IIIM) was highlighted to assist in the investigation and prosecution of persons responsible for the most serious crimes under international law committed in the Syrian Arab Republic since March 2011.

10.7 It was confirmed that the UNSGM is a central mechanism with related but also different tasks to that of the OPCW. There are basic UNSGM guidelines and procedures for laboratory analysis tasks related to the identification of biological toxins and pathogens, but the lack of an implementation body overseeing biological and chemical weapons-related activities makes it difficult to evaluate and harmonise the international process. There are currently no required criteria for UNSGM roster laboratory nominations, therefore interlaboratory exercises are critical to ensure the validity and accuracy of laboratory analysis (e.g. through activities such as under RefBio).

10.8 The International Criminal Court (ICC) in The Hague was mentioned in the context of question 5(e), which is a major instrument under international law for prosecuting genocide, crimes against humanity, and war crimes, and thus for preventing such crimes. Additionally, regional networks focusing on dedicated tasks for the surveillance of food- and health-related risks were mentioned, such as the panel of European Union

reference laboratories, targeting different, relevant pathogens and agents in the food and feed sector. European activities include proficiency tests on biological toxins conducted under the European Union projects EQuATox and EuroBioTox, joining 63 laboratories in 23 countries. In the United States of America and Canada, a dedicated Laboratory Response Network (LRN) focuses on the detection of CBRN[9] agents, including toxins. It was highlighted that there are different complementary networks working on CBRN agents driven by Asian countries, such as Singapore, Japan or China. The suggestion was made to invite representatives of those networks to future TWG meetings. Generally, it could be interesting to find out how these networks approach their analytical tasks (e.g. how they all use standardised assays, standardised tools and reagents, commercial reagents, and uniform reporting criteria files).

10.9 Dr Corbett explained that in Canada, the Human Pathogens and Toxins Act (HPTA)—with regard to who is licensed and for what organisms—has a role in biological security. There are HPTA designated analysts to conduct microbiological investigations. For criminal investigations, falling under the Canadian Criminal Code or Security Offenses Act, Canada utilises a whole government approach, wherein biological experts within the Public Health Agency of Canada would conduct the microbiological investigation for the Federal Police.

10.10 With respect to question 5(f), it was discussed that accreditation according to national and international standards is important to document analytical performance such as specificity, precision, robustness, and reliability of experimental data and thus build the basis for credibility of laboratory results in a political context. Likewise, the laboratories' participation in regular proficiency tests supports a continuous process of capability building, technical improvement, and evaluation. While for low molecular weight toxins, similar performance criteria and methodologies as for classical Chemical Weapons Convention agents can be used, for high molecular weight toxins a new approach has to be developed, where results should be accessible and acceptable by different international bodies.

10.11 In their breakout session, members of subgroup 5 highlighted the importance of identifying potential partners for the OPCW and gaining an understanding of their activities. They noted that a broad range of possibilities exist for cooperative activities and mutually beneficial relationships.

11. AGENDA ITEM ELEVEN – Final comments and next steps

11.1 The TWG Chairperson commended the members on a very productive first meeting and invited them to work on their respective questions and meet during the intersessional period, with a view to presenting preliminary results of their deliberations, including the agreed approach, during the second meeting of the TWG. After discussion, it was determined to hold a second meeting at the end of June. It was also determined to try to keep the same format with non-consecutive meeting days to allow members more time for deliberations between the two meeting days. The SAB Secretary also suggested having two meetings, one in June and another in September (possibly a one-day meeting), with an in-person meeting taking place at the end of the year. This approach will be finalised at the June meeting.

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9 Chemical, biological, radiological, and nuclear.

11.2 The SAB Secretary also invited the members to confirm by email which subgroups they would like to contribute to. The TWG Chairperson confirmed that subgroup leads can also be members of other subgroups.

12. AGENDA ITEM TWELVE – Closure of the meeting

The Chairperson ended the meeting at 17:10 on 6 May 2021.

ACKNOWLEDGEMENTS

The TWG members thank the guests and members of the Secretariat who participated in discussions. The TWG also wishes to acknowledge Ms Ernesa Ademagić of the OPCW Office of Strategy and Policy and Mr Gorjan Damjanović from the ISB for their support and contributions to the meeting and its preparations. Lastly, the TWG thanks the OPCW Director-General for his establishment and support of the TWG, and acknowledges the generous contribution of the European Union that helps to cover the costs of the Group's work.

Annex:

List of Participants at the First Meeting of the Scientific Advisory Group's Temporary Working Group on the Analysis of Biotoxins

Annex

**LIST OF PARTICIPANTS
AT THE FIRST MEETING OF THE SCIENTIFIC ADVISORY BOARD'S
TEMPORARY WORKING GROUP ON THE ANALYSIS OF BIOTOXINS**

	Participant	Institution
1	Dr Isel Pascual Alonso*	University of Havana, Cuba
2	Dr Crister Åstot	Swedish Defence Research Agency (FOI), Umeå, Sweden
3	Dr Anne Bossée*	DGA CBRN Defense, France
4	Dr Graeme Clark	Defence Science and Technology Laboratory, Porton Down, Salisbury, United Kingdom
5	Dr Cindi Corbett	National Microbiology Laboratory, Public Health Agency of Canada
6	Dr Christophe Curty*[10]	Spiez Laboratory, Switzerland
7	Dr Brigitte Dorner	Robert Koch Institute, Germany
8	Dr Mostafa Ghanei*	Baqiyatallah University of Medical Sciences, Islamic Republic of Iran
9	Dr Suzanne Kalb[11]	Centers for Disease Control and Prevention, United States of America
10	Dr Zrinka Kovarik*	Institute for Medical Research and Occupational Health, Croatia
11	Andrea Leisewitz*[12]	Universidad Santo Tomás, Chile
12	Dr Robert Mikulak*	Department of State, Washington, D.C., United States of America
13	Dr Daan Noort*[13]	TNO, Netherlands
14	Dr Yulia Polyak	Russian Academy of Sciences, Russian Federation
15	Dr Fengxia Sun*	Hebei University of Science and Technology, People's Republic of China
	Technical Secretariat Staff	**Division**
16	Mr Unnikannan Ayilliath	Information Services Branch
17	Dr Hoe Chee Chua	OPCW Laboratory
18	Dr Peter Hotchkiss[14]	Office of Strategy and Policy
19	Dr Stuart Thomson	OPCW Laboratory
20	Dr Timothy Wood	OPCW Laboratory

* Member of the SAB.

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10 Chairperson of the SAB.

11 Vice-Chairperson of the TWG.

12 Vice-Chairperson of the SAB.

13 Chairperson of the TWG.

14 Secretary to the SAB.