OPCW

Scientific Advisory Board

Seventeenth Session
21 – 23 November 2011

SAB-17/1
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REPORT OF THE SEVENTEENTH SESSION OF THE SCIENTIFIC ADVISORY BOARD

1. AGENDA ITEM ONE – Opening of the session

The Scientific Advisory Board (SAB) met for its Seventeenth Session from 21 to 23 November 2011 at the OPCW Headquarters in The Hague, the Netherlands. The session was opened by the Chairperson of the SAB, Philip Coleman. Mahdi Balali-Mood served as Vice-Chairperson. A list of participants appears as Annex 1 to this report. The Chairperson paid tribute to Professor Jiří Matoušek, former Chairperson of the SAB, who recently passed away, for his important contribution to the work of the Board.

2. AGENDA ITEM TWO – Adoption of the agenda

The SAB adopted the following agenda for its Seventeenth Session:

1. Opening of the session
2. Adoption of the agenda
3. *Tour de table* to introduce Scientific Advisory Board Members
4. Welcome address by the Director-General
5. Overview of developments at the OPCW since the last session of the Scientific Advisory Board
6. Establishment of a drafting committee
7. Report of the sixth meeting of the temporary working group on sampling and analysis
8. Report of the first meeting of the temporary working group on the convergence of chemistry and biology
9. Briefing on the workshop on incapacitating chemical agents

10. Production by synthesis

11. Sampling and analysis during Schedule 2 inspections: Update by the Technical Secretariat

12. Captive use of Schedule 1 chemicals

13. Scheduled chemicals, including ricin and saxitoxin

14. Future priorities of the OPCW: Scientific and technological aspects

15. IUPAC Workshop on the Impact of Advances in Science and Technology on the Chemical Weapons Convention: Status of preparations

16. Outreach to the scientific community

17. Future work of the Scientific Advisory Board

18. Any other business

19. Adoption of the report

20. Closure of the session

3. AGENDA ITEM THREE – *Tour de table* to introduce Scientific Advisory Board members

The meeting was opened with a *tour de table* in order to introduce new SAB members to existing SAB members. The new members are: Flerida Arsciwals Cariño, Volodymyr Zaitsev, and Mongia Said Zina.

4. AGENDA ITEM FOUR – Welcome address by the Director-General

4.1 The Director-General welcomed the members of the SAB, and in particular, the new members. He expressed to Herbert de Bisschop, Robert Mathews, and Jean-Claude Tabet, who were about to complete their term in office on the SAB, his appreciation for their dedicated commitment and important work done for the Board. The Director-General also conveyed his appreciation to the members of the temporary working groups for their contribution.

4.2 The Director-General recalled the report of the Advisory Panel on the Future Priorities of the OPCW (S/951/2011, dated 25 July 2011), and the informal retreat convened after its issuance with Permanent Representatives to the OPCW. Both the report of the panel and the retreat devoted attention to scientific and technological developments, and the Director-General stressed their significance, especially in the context of the preparatory phase for the Third Special Session of the Conference of the States Parties to review the Operation of the Chemical Weapons Convention (hereinafter "the Third Review Conference"), to be convened in 2013.

4.3 On sampling and analysis (S&A), the Director-General welcomed the ongoing cooperation between the OPCW Laboratory and the SAB on the topic of on-site analysis and acknowledged the work being carried out on the issue of scheduled chemicals.

4.4 He also commended the work of the temporary working group on the convergence of chemistry and biology, the first meeting of which was held in The Hague on 15 and 16 November 2011. He indicated that the SAB was the appropriate body to conduct a thorough study on this important question and invited the working group to make recommendations on this issue.

4.5 Regarding other issues on the agenda of the SAB, the Director-General appreciated the importance of the work relating to the preparation of factsheets on saxitoxin and ricin, as well as on the scope of the definition of "production by synthesis". He then pointed out the importance of ensuring effective outreach to the scientific community and referred to various proposals that he had submitted to the SAB Chairperson on ways of enhancing the involvement of the scientific community in the promotion of the goals of the Chemical Weapons Convention (hereinafter "the Convention").

4.6 He further stressed the importance for the SAB members to continue to engage in the work of the Board during the intersessional periods, not only in the context of the temporary working groups, but also on other substantive questions.

4.7 In conclusion, the Director-General recalled the preparations for the IUPAC[1] workshop to be held in February 2012, at the Spiez Laboratory in Switzerland, which will contribute to the preparation of the SAB report on developments in science and technology. The SAB report will provide information that will assist the Third Review Conference during its deliberations.

5. AGENDA ITEM FIVE – Overview of developments at the OPCW since the last session of the Scientific Advisory Board

5.1 The new Secretary of the SAB, Stian Holen, Head of the Policy and Review Branch, gave a presentation to the SAB on developments at the OPCW since the Sixteenth Session of the SAB was held. He stressed that the Convention is underpinned by science and technology, and pointed out the importance that the Director-General attaches to ensuring that science and technology continue to play a prominent role in the work of the Organisation and in the implementation of the Convention.

5.2 The Secretary informed the members of the Board on progress in the context of informal consultations on issues related to industry, destruction deadlines, the implementation of the tenure policy, Articles X and XI of the Convention, national implementation, chemical weapons production facilities, and old and abandoned chemical weapons.

5.3 The Secretary also updated the members of the SAB on the status of destruction of Category 1 chemical weapons as at 31 October 2011, as well as on the challenge inspection field exercise that the Technical Secretariat (hereinafter "the Secretariat")

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[1] IUPAC = International Union of Pure and Applied Chemistry

co-organised with Australia and Thailand from 31 October to 4 November 2011 (conducted in Thailand) in the context of its efforts towards ensuring its preparedness under Articles IX and X of the Convention. The Secretary then recalled the four priorities for the Organisation that the Director-General has identified for the future, all of which have elements related to science and technology:

(a) full and effective implementation of the Convention;

(b) prevention of the re-emergence of chemical weapons and the misuse of toxic chemicals;

(c) the retention of chemical weapons expertise and preparedness to respond to the use or threat of use of chemical weapons; and

(d) the promotion of the peaceful uses of chemistry.

6. AGENDA ITEM SIX – Establishment of a drafting committee

The SAB established a drafting committee, composed of four of its members, to prepare a draft report of its Seventeenth Session.

7. AGENDA ITEM SEVEN – Report of the sixth meeting of the temporary working group on sampling and analysis

7.1 The SAB received the report of the sixth meeting of the temporary working group on S&A, held on 17 and 18 November 2011 (see Annex 2). Robin Black, Chairperson of the temporary working group, presented the key findings, conclusions, and recommendations. The following topics were discussed:

(a) on-site analysis procedures (aqueous sample preparation and fast gas chromatography (GC));

(b) Schedule 2 inspections involving the use of S&A;

(c) applications of desorption electrospray ionisation (DESI-MS) and other direct sampling mass spectrometry (MS) techniques;

(d) toxin analysis (saxitoxin and ricin);

(e) criteria for identification using trace analysis in investigations of alleged use (IAUs) of chemical weapons;

(f) terms of reference of the temporary working group; and

(g) the conclusions and recommendations of the previous meetings.

7.2 The main conclusions and recommendations of the meeting of this temporary working group were as follows:

(a) The group commended the work being undertaken by the OPCW Laboratory on aqueous sample preparation and fast GC. It supported a proposal that the Secretariat should issue an official-series Note, requesting designated and other interested laboratories to provide assistance in assessing the new aqueous sample preparation procedure.

(b) Desorption electrospray ionisation mass spectrometry (DESI-MS) was recognised as a powerful mass-spectrometric technique for direct and rapid sample analysis, both on site and off site, and its use avoids the need for extensive sample preparation. The group recommended that a watching brief be maintained by the SAB and the Secretariat on developments in portable DESI-MS instrumentation.

(c) The group made provisional recommendations for ricin analysis. These will require further elaboration, but it was recognised that further progress could be made only by holding exercises on ricin analysis. Criteria should be evaluated in inter-laboratory collaboration exercises and modified, as appropriate.

(d) Methods and provisional criteria for the identification of saxitoxin were agreed.

(e) Criteria for trace analysis, based on guidelines published by the World Anti-Doping Agency (WADA) (for illicit drugs in urine) and the European Commission (for residues in animal products) were deemed to be generally applicable to trace analysis in IAUs. However, specific criteria to be used by the OPCW should be established after more experimental data has been collected and evaluated.

(f) The terms of reference of the group and recommendations made over the previous five meetings were reviewed. The recommendations were considered and re-endorsed by the members of the group.

(g) The group recommended that a seventh meeting of the temporary working group should be held. Topics proposed for discussion during the next meeting included:

(i) high resolution MS and its use in proficiency tests;

(ii) sample clean-up for toxin analysis;

(iii) utility of portable infrared analytical instruments during industry inspections;

(iv) analysis of mixed chemical/biological samples;

(v) use of hand-held detectors/monitors to direct sampling; and

(vi) emerging technologies and techniques;

(h) The SAB members accepted the conclusions of the meeting and the recommendation to hold a seventh meeting. In addition to infrared, the SAB

recommended that other spectroscopic techniques should be investigated to support analyses carried out during routine industry inspections.

(i) The Chairperson of the temporary working group expressed his appreciation to the Head of the OPCW Laboratory and his staff for their input.

8. AGENDA ITEM EIGHT – Report of the first meeting of the temporary working group on the convergence of chemistry and biology

8.1 The SAB received the report of the first meeting of the temporary working group on the convergence of chemistry and biology, which was held on 15 and 16 November 2011 (see Annex 3) by Robert Mathews, Chairperson of this group. The topics covered by the group were as follows:

(a) areas of overlap between the Convention and the Biological Weapons Convention (BWC);

(b) advances in the life sciences;

(c) processes included in biologically mediated synthesis;

(d) the application of chemical synthesis for the production of toxins, bioregulators and peptides;

(e) the meaning of "production by synthesis"; and

(f) other aspects of the convergence of chemistry and biology of potential relevance to the Convention, including the analysis of biologically active compounds.

8.2 The temporary working group discussed "the CBW spectrum", ranging from toxic industrial chemicals to classical biological-warfare agents in relation to areas of overlap between the Convention and the BWC (see Annex 4). It recognised the necessity to update the spectrum.

8.3 Information from the BWC process was introduced to the temporary working group under the agenda item of "advances in life sciences". It included a presentation on the outcomes of an international workshop in Beijing in 2010, and the current status of the review process for the Seventh Review Conference of the BWC.

8.4 The temporary working group discussed relevant aspects in regard to biologically mediated processes, namely, commercial scale bio-production of chemicals; production of toxic chemicals; and synthesis/production of toxins and bioregulators. It concluded that, for classical chemical-warfare agents, such as nerve agents and blister agents, there would not appear to be an advantage in trying to produce such chemicals through biologically-mediated processes. On the other hand, based on an emerging trend in production of a wide variety of chemicals through biologically mediated processes, the recommendation was made to continue monitoring these developments.

8.5 With regard to the application of chemical synthesis for the production of toxins, the temporary working group concluded that the technical capability to chemically synthesise many toxins, bioregulators, and other biologically active peptides exists today. However, there are practical limitations that need to be assessed.

8.6 The temporary working group heard a presentation on the term "production by synthesis", and was briefed on its historical background. It discussed the paper addressing the term "production by synthesis", which had been prepared by the SAB in 1999, and determined that it is not in a position to make a full assessment without further study.

8.7 The group recognised the potential benefits of the convergence of chemistry and biology (and related aspects of nanotechnology) to the Convention, including developments in detection (biosensors), medical countermeasures, decontamination, and laboratory techniques (including bioforensics). It recommended that further aspects be considered in more detail at a future meeting.

8.8 The SAB endorsed the report of the temporary working group and also approved the recommendations contained in the report. The SAB also requested that the temporary working group focus on future developments in biotechnology in regard to the synthesis of toxic chemicals, including toxins and bioregulators, beyond the laboratory scale, as well as enhanced protective measures which may flow from these advances. The SAB proposed that the chairmanship of the group be taken over by William Kane, in view of the fact that Robert Mathews' term of office on the SAB had concluded.

9. AGENDA ITEM NINE – Briefing on the workshop on incapacitating chemical agents

The SAB received a briefing by Stefan Mogl on a workshop on incapacitating chemical agents (ICAs), which was co-organised by VERIFIN and Spiez Laboratory on 7 and 8 September 2011, and which took place at the Spiez Laboratory in Switzerland. The objective of the two-day workshop was to enable participants to further their technical understanding of what ICAs are, and to enhance their knowledge as to what potential for abuse these agents could pose in the next five to 10 years. The workshop brought together policy and technical experts to discuss technical questions that may influence policy discussion on ICAs. The agenda included discussions on what characteristics were generally attributed to potential ICAs, as well as their potential effects and mode of action from a toxicological perspective; in addition, the question as to what challenges ICAs may pose in terms of detection and identification was examined. The workshop also looked at new production methods for highly active pharmaceutical ingredients and peptides. A report of the workshop will be available to all SAB members and other interested parties by early 2012.

10. AGENDA ITEM TEN – Production by synthesis

10.1 William Kane gave a presentation on "Biologically Mediated Processes – Examples of Chemical Industry Plans for Large Scale Production". Succinic acid, 1,4-butanediol, Acrylic acid, and Adipic acid are normally produced from

petroleum-based feedstock; however, biological process routes for the production of these chemicals are now being perfected. Some of these new routes will be used in commercial-scale facilities and are expected to compete economically with petroleum-based routes.

10.2 Large scale production facilities using bio-based processes (greater than 200 tonnes a year) have already been announced publically for both Succinic acid and 1,4-Butanediol. These facilities will be constructed in many regions of the world (including Asia, Europe, and North and South America) over the next five years.

10.3 Bio-based process routes for Acrylic acid and Adipic acid are being developed, but are still in the research-and-development/pilot-plant stage. However, a number of the companies involved have attracted major investors in order to further develop their plans for commercial-scale production. Industrial partnerships and joint ventures are often used to gain business and technological advantages in launching bio-based products. Commercialisation trends of biologically mediated processes should continue to be monitored.

10.4 Following the presentation, the SAB continued the discussion of the term "production by synthesis" for discrete organic chemicals (DOCs) produced in other chemical production facilities (OCPFs). The key question is whether the term "production by synthesis" should include production by a biological route. Ken Penman from the Declarations Branch of the Secretariat updated the SAB on the current practice being followed by States Parties that are declaring OCPFs. He pointed out that some States Parties declare chemicals produced by a biological process route, while others do not.

10.5 In order for there to be a consistent practice for all States Parties, the meaning of "production by synthesis" will need to be clarified. The SAB will revisit the recommendation it made in 1999, taking into consideration the increased production of chemicals using biological processes in the last 12 years. In addition, the SAB recommended that the Secretariat perform an assessment to determine whether these new commercial-scale facilities could be misused for the production of chemicals for non-peaceful purposes.

11. AGENDA ITEM ELEVEN – Sampling and analysis during Schedule 2 inspections: Update by the Technical Secretariat

11.1 An update[2] on the use of S&A during Schedule 2 inspections was given by Hugh Gregg, Head of the OPCW Laboratory. From September 2006 to June 2011, a total of 42 Schedule 2 inspections that used S&A were conducted in 22 States Parties. In general, the equipment performed well on start-up. The addition of a new item of approved equipment in 2009, the auto-sampler, has significantly improved the efficiency of on-site analysis. Knowledge and experience have been gained with regard to how sample locations are selected. Thirty-five of the inspections were undertaken with the GC-MS operating in open mode.

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2 Note by the Director-General: "Progress Report on the Use of Sampling and Analysis During Schedule 2 Inspections" (S/953/2011, dated 29 July 2011)

11.2 These inspections had identified some shortcomings in the OPCW Central Analytical Database (OCAD), which have subsequently been addressed. SAB members voiced concern that, while laboratories participating in OPCW proficiency testing have access to all data validated by the Validation Group, for verification activities, the Secretariat is restricted to data approved by the Executive Council.

11.3 The SAB recognised the progress made in S&A. It was suggested that an updated list of data that the Secretariat would like to include in the OCAD should be provided to designated laboratories. The role and future of designated laboratories were discussed.

11.4 Regarding future priorities, the Secretariat intends to study ways to improve the efficiency of the entire S&A process, with the goal of extending the technical capability to S&A at OCPFs, and possibly to Schedule 3 facilities.

12. AGENDA ITEM TWELVE – Captive use of Schedule 1 chemicals

12.1 An update was provided by Ken Penman of the Declarations Branch of the Secretariat on activities conducted by the Secretariat since the Sixteenth Session of the SAB to address the SAB recommendation that the Secretariat develop a communication plan to inform States Parties and industry associations of the implications of a case involving the production of a Schedule 1 chemical in a captive-use situation. (paragraph 12.6 of SAB-16/1, dated 6 April 2011).

12.2 The Secretariat has communicated with States Parties during regional meetings of National Authorities that were carried out in Africa, Asia, Eastern Europe, and in GRULAC States Parties[3], covering 103 States Parties and a total of 187 individual attendees.

12.3 During the aforementioned regional meetings, the Secretariat provided a briefing similar to the presentation given during the Sixteenth Session of the SAB. The obligation to fully implement the decision C-10/DEC.12 (dated 10 November 2005) on captive use was emphasised, and the attention of the attendees was drawn to the ketobemidone and pethidine synthesis cases.

12.4 The SAB recommended that the above issue should be discussed during the annual meeting of the National Authorities and that an explanatory Note on captive use could be sent to States Parties.

13. AGENDA ITEM THIRTEEN – Scheduled chemicals, including ricin and saxitoxin

13.1 Robert Mathews provided a summary on the history of the negotiations that took place in regard to including saxitoxin (and the various forms of saxitoxin) in the Annex on Chemicals of the Convention. A fact sheet was presented and adopted by the SAB (see Annex 5).

13.2 On the basis of the information contained in the fact sheet, the SAB concluded that Agent TZ, the weaponised form of saxitoxin, is covered by Schedule 1.

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3 GRULAC = Group of Latin American and Caribbean States Parties

13.3 A draft ricin fact sheet has been prepared and will be considered at a future session of the SAB.

14. AGENDA ITEM FOURTEEN – Future priorities of the OPCW: Scientific and technological aspects

14.1 The Director-General gave his views on the future priorities of the OPCW. He underlined the need to refocus the OPCW's activities through the deepening of some of its programmes and through the establishment of a new balance between activities to prevent the re-emergence and misuse of toxic chemicals on the one hand, and international cooperation and assistance on the other. It was agreed that the scientific community should remain involved in all aspects of these issues.

14.2 In the context of prevention, the Director-General referred, inter alia, to the need, through educational outreach, to raise awareness among the academic community and industry of the dual-use risks associated with toxic chemicals. To this end, he expected that the SAB would provide important inputs. With regard to chemical safety and security, both training and using the Organisation as a platform for identifying and disseminating best practices would be important elements in this process.

14.3 The Director-General highlighted a number of references to the SAB in the report of the Advisory Panel on Future OPCW Priorities. The Panel had underlined the need for more clarity about what use was made of the advice provided by the SAB and had made some proposals in this regard. It favoured a strong partnership between the SAB and the wider scientific community, including IUPAC. In keeping with such advice, the Director-General had decided to propose, in the 2012 Programme and Budget, the appointment of a science policy adviser, as well as to move responsibility for the SAB from the office of the Deputy Director-General to the Verification Division.

14.4 In conclusion, the Director-General encouraged the SAB to comment on the Panel's observations. In particular, he asked the members for their views on how to strengthen the SAB and its monitoring of developments in science and technology, for their input on whether the SAB and science and technology could play a role in encouraging cooperation among States Parties on matters related to the Convention, and for their feedback on how the SAB could contribute to the ongoing public diplomacy effort to raise the visibility and profile of the OPCW.

14.5 The ensuing discussion touched upon the following:

(a) the agenda of the SAB;

(b) CBRN[4] training;

(c) ethical rules and codes of conduct for chemists;

(d) the handling by the Secretariat of recommendations made by the SAB;

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4 CBRN = chemical, biological, radiological, nuclear

(e) the OPCW's links with the BWC process;

(f) research programmes sponsored by the OPCW;

(g) partnerships with other stakeholders in chemical safety;

(h) the use of e-learning to spread knowledge on safety and security and on emergency response; and

(i) ways to improve the public perception of chemistry through public diplomacy.

15. AGENDA ITEM FIFTEEN – IUPAC Workshop on the Impact of Advances in Science and Technology on the Chemical Weapons Convention: Status of preparations

15.1 Jan Lodding, of the Policy and Review Branch of the Secretariat, gave a presentation on an upcoming IUPAC international workshop, scheduled to take place from 20 to 23 February 2012 at the Spiez Laboratory, Switzerland, which will assess developments in science and technology relevant to the implementation of the Convention. The workshop will assist the SAB in the preparation of its report for the Third Review Conference. Jan Lodding then went through the list of topics that had been covered in the SAB's report to the Second Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention; he also provided some information on the current status of administrative preparations for the workshop, for which invitations would soon be sent out.

15.2 Robert Mathews, as a member of the Scientific Programme Committee for the IUPAC workshop, summarised the current draft agenda for the event. He explained that the IUPAC Committee was open to proposals from the SAB as far as the programme, speakers, discussion participants, and breakout group rapporteurs were concerned, and underlined the need for the SAB to participate actively in the conduct of the workshop. Several SAB members made general or specific comments on the draft agenda, and a number of them volunteered to participate in discussions or act as rapporteurs for various sessions. These proposals will be submitted by Robert Mathews to IUPAC for consideration.

15.3 The Chairperson underlined that the reports of the SAB to the Review Conferences were among the most important undertakings of the SAB. He explained that the SAB should endeavour to submit its report for the Third Review Conference to the Director-General no later than September 2012. In response to several comments from the floor, the Chairperson suggested that the second session of the SAB in 2012 should be scheduled in mid-2012. This would facilitate the early finalisation and submission of its report to the Director-General, well in advance of the Third Review Conference.

16. AGENDA ITEM SIXTEEN – Outreach to the scientific community

16.1 Mr Kumaresh Misra, Head of the International Cooperation Branch of the Secretariat, gave a presentation on outreach activities to the scientific community. The presentation covered the OPCW activities taking place under Article XI of the

Convention, and included information on the Associate Programme, the Conference-Support Programme, the Internship-Support Programme, Support for Research Projects, the Analytical-Skills-Development Course, and the Chemical-Safety Management Course.

16.2 SAB members recommended that outreach activities be directed towards supporting institutions in States Parties, rather than individuals, given that individuals can relocate and do not always have the opportunity to utilise the skills that they have acquired. On this point, SAB members suggested that attention be paid to the particular requirements of a State Party or region, and that support be provided accordingly.

16.3 The SAB also suggested that, in addition to conducting regional workshops, it was important to target academic institutions, with the aim of encouraging them to include information about the Convention in academic curricula. Several SAB members offered to share their experience in the area of education and outreach, and to circulate examples of teaching materials.

16.4 Malik Ellahi, Head of the Government Relations and Political Affairs Branch of the Secretariat, gave a presentation on the OPCW Conference on International Cooperation and Chemical Safety and Security, which took place on 12 and 13 September 2011. The conference provided support for OPCW activities in the field of chemical safety, security, and international cooperation, and provided input that would strengthen OPCW activities in the field of chemistry.

16.5 The SAB noted the role that education and outreach could play in chemical safety and security.

16.6 The SAB recommended the establishment of a temporary working group on education and outreach, which would build upon earlier work done by the SAB. The SAB proposed that the group be chaired by Djafer Benachour.

17. AGENDA ITEM SEVENTEEN – Future work of the Scientific Advisory Board

17.1 The SAB discussed its future work and, in particular, the drafting of its report to the Director-General in advance of the Third Review Conference in 2013. The SAB established a correspondence group, the task of which would be to begin drafting its report in advance of its Eighteenth Session, which it agreed would take place from 16 to 19 April 2012. Several SAB members volunteered to begin working on individual sections of the draft report and to have a draft report available before the Eighteenth Session of the SAB. The Secretary will compile an initial draft, which will be based on the SAB reports in the past five years, and will distribute a proposed workplan to the correspondence group.

17.2 The SAB also decided that, subject to funding being available, its second session in 2012 should take place before the terms of office of the current Chairperson and Vice-Chairperson expire. This session was tentatively planned for 26 to 29 June 2012. This would ensure continuity in the preparation of the report to the Director-General for the Third Review Conference.

17.3 The SAB was informed that funding had been requested under the forthcoming European Union (EU) Council Decision for two meetings of the temporary working group on the convergence of chemistry and biology in 2012 to 2013, and for two meetings of the temporary working group on education and outreach in 2012 to 2013. The SAB welcomed this funding, and recommended that, where possible, meetings of these temporary working groups be held adjacent to sessions of the SAB.

18. AGENDA ITEM EIGHTEEN – Any other business

The Chairperson of the SAB bade farewell to the three members (see paragraph 4 above) who had completed their term of office on the SAB. He thanked them for their invaluable contribution to the work.

19. AGENDA ITEM NINETEEN – Adoption of the report

The SAB considered and adopted the report of its Seventeenth Session.

20. AGENDA ITEM TWENTY – Closure of the session

The Chairperson closed the session at 18:55 on 23 November 2011.

Annexes:

Annex 1: List of Participants in the Seventeenth Session of the Scientific Advisory Board

Annex 2: (English only, unedited): Report of the Sixth Meeting of the SAB Temporary Working Group on Sampling and Analysis, The Hague, the Netherlands, 17 – 18 November 2011

Annex 3: (English only, unedited): Report of the First Meeting of the SAB Temporary Working Group on the Convergence of Biology and Chemistry, The Hague, the Netherlands, 15 – 16 November 2011

Annex 4: (English only, unedited): The Relationship of the CWC & BTWC CBW Spectrum

Annex 5: (English only, unedited): Saxitoxin Fact Sheet

Annex 1

LIST OF PARTICIPANTS IN THE SEVENTEENTH SESSION OF THE SCIENTIFIC ADVISORY BOARD[5]

	Participant	State Party
1.	Djafer Benachour	Algeria
2.	Alejandra Graciela Suárez	Argentina
3.	Robert Mathews	Australia
4.	Herbert De Bisschop	Belgium
5.	Nan Zhang	China
6.	Neivy Fernández Manresa	Cuba
7.	Paula Vanninen	Finland
8.	Jean-Claude Tabet	France
9.	Michael Geist	Germany
10.	Devendra Kumar Dubey	India
11.	Mahdi Balali-Mood	Iran (Islamic Republic of)
12.	Shuzo Fujiwara	Japan
13.	José González Chávez	Mexico
14.	Muhammad Zafar-Uz-Zaman	Pakistan
15.	Flerida Arsciwals Cariño	Philippines
16.	Slawomir Neffe	Poland
17.	Igor V. Rybalchenko	Russian Federation
18.	Abdullah Saeed Al-Amri	Saudi Arabia
19.	Philip Coleman	South Africa
20.	Stefan Mogl	Switzerland
21.	Mongia Said Zina	Tunisia
22.	Volodymyr Zaitsev	Ukraine
23.	Robin Black	United Kingdom of Great Britain and Northern Ireland
24.	William Kane	United States of America

[5] Slavica Vučinić of Serbia did not participate in the Seventeenth Session of the SAB.

Annex 2

REPORT OF THE SIXTH MEETING OF THE SAB TEMPORARY WORKING GROUP ON SAMPLING AND ANALYSIS THE HAGUE, THE NETHERLANDS 17 – 18 NOVEMBER 2011

1. Introduction

1.1 The Temporary Working Group (TWG) on Sampling and Analysis (S&A) of the Scientific Advisory Board (SAB) held its sixth meeting on 17 and 18 November 2011 at the OPCW Headquarters in The Hague.

1.2 The meeting was chaired by Robin Black on behalf of the SAB.

1.3 The list of participants in the meeting is given in Appendix 1.

1.4 The following agenda was adopted:

(a) Opening of the meeting by the Chairperson

(b) Adoption of the agenda

(c) Sample preparation for aqueous solutions of degradation products – update by the OPCW Laboratory

(d) Update on work of fast GC by the OPCW Laboratory

(e) Update on Schedule 2 inspections

(f) Applications of desorption electrospray ionisation (DESI) and other direct sampling mass spectrometry techniques

(g) Toxin analysis (ricin and saxitoxin), off-site and on-site

i) Ricin: review of draft criteria and way forward for the Technical Secretariat

ii) Saxitoxin: review of draft criteria and way forward for the Technical Secretariat

(h) Criteria for trace analysis in investigations of alleged use of chemical weapons

(i) Update on the Second OPCW Confidence Building Exercise on Biomedical Sample Analysis

(j) Review of Terms of Reference and recommendations of the Temporary Working Group

(k) Update on the new VERIFIN 'Blue Book'

(l) Notes on the performance of mobile laboratories during exercise ASSISTEX 3

(m) Any other business

(n) Elaboration and adoption of the TWG report

(o) Summary of conclusions and recommendations

(p) Closure of the meeting.

2. Opening of the meeting by the chairperson

2.1 The Chairperson welcomed the members of the TWG. He paid tribute to Professor Jiří Matoušek, who was a standing member of the TWG when he died in April 2011. He served on the TWG from 2007 and was chairperson of the SAB from 2004 to 2007. Jiří possessed a very broad and deep knowledge of chemical defence plus an enviable command of languages.

3. Sample preparation for aqueous solutions of degradation products – update by the OPCW Laboratory

3.1 Hugh Gregg, Head of the OPCW Laboratory, presented the current status of efforts to reduce sample preparation and analysis time for on-site analysis.

3.2 A major limitation of on-site gas chromatography-mass spectrometry (GC-MS) analysis, as currently performed by inspectors, is the time and equipment required for the identification of polar degradation products and precursors of chemical warfare (CW) agents in aqueous samples. The current operating procedure for aqueous samples requires concentration to dryness prior to derivatisation, a procedure which is lengthy and requires additional equipment. A new procedure ('Sample Preparation for Thermal Desorption'), developed by Oliver Terzic of the OPCW Laboratory, was presented at the fifth meeting of the TWG on S&A. Small aliquots of aqueous or mixed solvent samples are absorbed onto Tenax tubes, the water is removed by a short period of heating under a stream of helium, and polar compounds are converted on-tube to their trimethylsilyl derivatives. Analysis is performed using thermal desorption GC-MS. Compared to the current on-site sample preparation and analysis procedure, the time required for removal of water is reduced from 2 hours to 5 minutes, and overall sample preparation time from 3 hours to 25 minutes. The procedure utilises equipment already used for on-site analysis, and reduces the logistic burden of equipment compared to the current procedure.

3.3 A draft work instruction (QDOC/LAB/WI/SP3) has been prepared for this procedure, which continues to look very promising. The laboratory is exploring the use of a thermal desorption auto-sampler in order to allow samples to be analysed unattended, e.g. overnight. Before it could be accepted for on-site analysis, it is essential that the method is assessed for ruggedness and applicability. Quite large variability in yields had been observed for some analytes (e.g. methylphosphonic acid, thiodiglycol, chlorovinylarsonous acid), possibly due to variability in the tubes.

3.4 In its report of the fifth meeting (held November 2010), the TWG encouraged other laboratories to assist in assessing the procedure. To date, no other laboratories had offered to undertake this. One of the reasons may be that the method as configured requires a particular GC injector, which may not be available in other laboratories.

The TWG agreed with the Head of the OPCW Laboratory that a formal note should be sent to designated and other interested laboratories requesting their assistance.

4. Update on work on fast GC by the OPCW Laboratory

4.1 An additional approach being explored by the OPCW laboratory is 'fast GC', to reduce the time required for instrumental analysis. The method as developed by the OPCW Laboratory does not meet current quality control standards, specifically with regard to the retention indices of some of the chemicals in the quality control test mixture. The laboratory has recently reviewed other work on fast GC undertaken in the OPCW laboratory by an intern from the Finnish Institute for Verification of the Chemical Weapons Convention (VERIFIN). The VERIFIN method uses a shorter, smaller bore GC column, and has a run time shorter than the method developed by the OPCW laboratory. A small project has commenced to assess this promising fast GC procedure with regard to retention indices of the quality control test mixture.

4.2 The Technical Secretariat (TS) has also started a review of the entire sampling and analysis process for on-site analysis. Sample preparation and analysis are only components of the overall process, and some time may be saved by modifying other aspects of the overall process.

5. Progress report on the use of sampling and analysis in Schedule 2 inspections

5.1 An update[6] on the use of sampling and analysis during Schedule 2 inspections was given by Hugh Gregg. From September 2006 to June 2011 a total of 42 Schedule 2 inspections with sampling and analysis were conducted in 22 States Parties. The purpose of such analysis is to provide factual evidence for the presence of declared scheduled chemicals and/or to support a conclusion of absence of undeclared scheduled chemicals (above the declaration threshold). The majority of the inspectable Schedule 2 plant sites are in seven States Parties; ten States Parties have only one inspectable site. In general, the equipment performed well on start up. Introduction of the auto-sampler in 2009 has significantly improved on-site analysis. Knowledge and experience have been gained with regard to how sample locations are selected. Thirty-five of the inspections were undertaken with the GC-MS operated in open mode, the remainder with the GC-MS in restricted mode, including two in the flexible restricted mode that was introduced in 2009.

5.2 A number of matches against the OPCW Central Analytical Database (OCAD) in respect of chemicals other than the declared chemical(s) were reported. These resulted from process-related impurities (some scheduled) or 'false positives'. False positives were resolved through a detailed analysis of the mass spectrum, or by comparison with the National Institute of Standards and Technology (NIST) database (if agreed by the Inspected State Party). Additionally, it was noted in early inspections that the spectra of some scheduled chemicals being manufactured (fire retardants containing a P-C bond) were not in the OCAD; this has now been resolved by additions to the OCAD. An enhanced version of the Automated Mass Spectral Deconvolution and

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6 Note by the Director-General: Progress Report on the Use of Sampling and Analysis During Schedule 2 Inspections (S/953/2011 dated 29 July 2011)

Identification System (AMDIS) software allows access to the NIST database with Inspected State Party (ISP) consent – even in restricted mode.

5.3 It is proposed to enhance the 'DBsetup' module to be able to select the data needed for specific types of missions. For example, for a Schedule 2 S&A mission, the inspection team (in conjunction with the ISP) would select data for the following: all scheduled chemicals; all derivatives of scheduled chemicals that could be prepared by the inspection team on-site using approved equipment, reagents and procedures; possibly data for non-scheduled chemicals useful in reducing the possibility of false positives.

6. Applications of desorption electrospray ionisation (DESI) and other direct sampling mass spectrometry techniques

6.1 Paul D'Agostino of Defence Research and Development Canada (DRDC) provided an overview of work on desorption electrospray ionisation (DESI) mass spectrometry undertaken at DRDC Suffield. DESI and related techniques offer a convenient method of direct sample analysis with little or no sample preparation. The technique has been used for a variety of compounds including chemical warfare agents, explosives and illicit pharmaceuticals, on numerous media including glass, metal, fabrics, skin, polymers and solid phase microextraction (SPME) fibres. The presentation focused on SPME applications related to field sampling and analysis of CW agents, their hydrolysis products and related compounds. Analysis was rapid (seconds to minutes) with identification based on the acquisition of high resolution tandem mass spectrometric (MS^n) and/or ion mobility spectrometric data. The DESI-MS/MS data obtained are similar to ESI-MS/MS data acquired using liquid chromatography (LC)-ESI-MS/MS.

6.2 Armando Alcaraz of the Lawrence Livermore National Laboratory, USA provided a video demonstrating a portable DESI-MS instrument, with size approximately 45 cm^3. The video also showed the principle and mechanism of the technique. The wider use of DESI for on-site analysis will be dependent on the commercial development of portable and robust instrumentation. The TWG members recommended that a watching brief be maintained by the SAB and TS on developments of portable DESI.

7. Toxin analysis (ricin and saxitoxin)

Ricin

7.1 Sten-Åke Fredriksson, of FOI, Sweden, gave a very detailed presentation of proposed criteria for the identification of the proteinaceous toxin ricin. There was considerable discussion on the relative merits of lateral flow assays (LFA) (which are well-suited for on-site screening) *versus* enzyme linked immunosorbent assays (ELISA), which are generally regarded as more reliable. Also different views were expressed on the requirement for a functional assay that demonstrates biochemical or biological activity. These aspects will require further consideration. Recommendations were made for the selection of peptide fragments specific to ricin that should be identified by mass spectrometry after enzymatic digestion. Identification of three or four selected peptides, accounting for 10% of the amino acid structure of ricin, should provide confirmation of identification. It was proposed that, for all methods, data should be compared to an authentic reference sample analysed under the same

conditions. These will require further elaboration but it was recognised by the TWG members that further progress could be made only by holding exercises on ricin analysis. Criteria should be evaluated in inter-laboratory collaboration exercises and modified as appropriate. An exercise involving ricin analysis will be held under the auspices of the European Union (EU) project 'Establishment of Quality Assurances for the Detection of Biological Toxins of Potential Bioterrorism Risk' (EQuaTox). This inter-laboratory exercise is scheduled to be held in 2012 or 2013.

Saxitoxin

7.2 A summary of identification criteria for saxitoxin, provisionally agreed at the fifth meeting of the TWG, was provided by Martin Schaer of the Spiez Laboratory, Switzerland. These criteria propose a screening procedure based on lateral flow assay, enzyme linked immunosorbent assay or LC-fluorescence, combined with a confirmatory procedure using LC-tandem mass spectrometry with full product ion spectrum, or using selected reaction monitoring. The view of the TWG was that, as the screening assays have long been accepted by the food industry, they should be acceptable for screening purposes by the TS. The use of high resolution LC-MS or LC-MS/MS was recognised as an alternative to low resolution LC-MS/MS as a confirmatory analytical method, but drafting of criteria would require input from laboratories with greater experience of this technique. It was recommended that LC of saxitoxin should be performed only on columns with suitable retention characteristics, e.g. using hydrophilic interaction chromatography (HILIC) or ion exchange columns. On C18 columns, which are widely used for the analysis of polar degradation products and precursors of scheduled chemicals, saxitoxin is essentially not retained and elutes in the dead volume.

8. Criteria for trace analysis in investigations of alleged use of chemical weapons

8.1 Paula Vanninen, of VERIFIN, Finland, provided a summary of the World Anti-Doping Agency (WADA) and EU guidelines on trace analysis that may be applicable to trace analysis in investigations of alleged use. After discussion, it was recommended that criteria specifically for the purposes of the TS should be established after more experimental data is collected and evaluated.

8.2 An intern[7] is currently working at VERIFIN on the project 'Evaluation of Criteria for Trace Analysis of Scheduled Chemicals Using ROP Methods'. The three-month project is funded by the International Collaboration Branch (ICB) of the OPCW and the Ministry for Foreign Affairs of Finland. Mass spectral information relevant to trace analysis is being collected using GC- and LC-based mass spectrometric techniques for sarin, soman, tabun, sulfur mustard, pinacolyl methylphosphonic acid, ethylphosphonic acid and thiodiglycol. The report will be available by the end of 2011. The Second OPCW Confidence Building Exercise on Biomedical Sample Analysis (see section 9) should also provide useful data for the establishment of criteria that can be applied to trace analysis in biomedical and environmental samples.

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7 Che Nin binti Man from the Toxicology Laboratory, National Poison Centre, University Sains, Malaysia.

8.3 Specific points that were made on trace analysis criteria were:

- It was recommended that maximum tolerance windows should be stipulated for relative ion abundances (as in the WADA and EU guidelines) to ensure appropriate confidence in identification. It was agreed that the EU guidelines, which are simpler and based only on relative ion abundances, should be applied.

- A mass spectrum should be acquired at the retention time of the peak(s) of interest to ensure that a co-eluting substance could not give rise to the observed diagnostic ions.

- Identification should be confirmed by comparison with a reference chemical spiked into a matrix similar to that of the sample. The reference matrix should be reported and the reference chemical spiked at a concentration similar to that of the unknown chemical.

- Chemicals of interest should be sufficiently retained by the GC or LC column used. They should have retention factors (k') in the range 3-10 to optimise the separation factor, detectability, and to avoid ion suppression effects.

8.4 Currently the TS rules for identification require that a chemical must be identified by two analytical methods, preferably two spectrometric methods. Different views were expressed by members of the TWG on whether this should also apply to trace environmental and biomedical sample analysis. A particular point of discussion was that high resolution mass spectral data, which contain more information and provide a greater degree of specificity compared to low resolution data, could be deemed sufficient for identification as a single technique. It was agreed that additional experimental data should be acquired by the OPCW laboratory before criteria for identification using trace analytical techniques is finalised.

8.5 The SAB was requested to consider under what circumstances trace analysis criteria should be applied to verification analysis.

9. Update on the Second OPCW Confidence Building Exercise on Biomedical Sample Analysis

9.1 The Chairperson and the Head of the OPCW Laboratory summarised plans to hold the Second Confidence Building Exercise on Biomedical Sample Analysis. The exercise will be held in February 2012. It will be along similar lines to the first exercise, using urinary metabolites as spiking chemicals. The matrix will be commercial human urine, rather than the synthetic urine which caused some unexpected problems in the first exercise. Spiking levels will be lower than in the first exercise, in the range 5-25 ng/ml. These lower levels are considered to be more realistic with regard to samples associated with allegations of CW use. Reports will be requested in a more structured format than in the first exercise, and laboratories will be asked to provide peak height or area ratios for techniques such as selected ion and selected reaction monitoring. This will enable all results to be evaluated against the WADA and EU criteria for identification using trace analysis. Samples will be prepared by the TNO Laboratory, Rijswijk, and evaluation of the reports will undertaken by Dstl, Porton Down and the OPCW Laboratory.

10. The performance of mobile laboratories during exercise ASSISTEX 3

10.1 Francesco Pilo, of the Firefighters Department, Italy, gave an overview of the operation of a mobile laboratory during the ASSISTEX 3 exercise held in 2010. Problems encountered in the mobile laboratory during the exercise included: the time to report the first qualitative report (approximately 5 hours); the time for sample collection; a long sample preparation time; the number of unusable samples resulting sampling errors and problems during decontamination. A maximum of 15 samples could be analysed per day.

10.2 Suggested ways of improving the performance of the laboratory were: training of personnel to collect more appropriate samples with the aid of hand-held detectors; better training of laboratory personnel; modified methods to reduce sample preparation time; carefully consider which levels of analysis are required, i.e. screening with appropriate equipment; selection of samples for GC-MS analysis; selection of samples for 'critical analysis'. One suggestion by the TWG was to include an analytical chemist in the sampling team to guide the selection of samples.

11. Review of the terms of reference and recommendations of the TWG

11.1 The Chairperson reviewed the terms of reference of the TWG, and summarised the recommendations made over the previous five meetings. These were considered and re-endorsed by the TWG.

12. Progress on the 2011 edition of the VERIFIN 'Blue Book' on 'Recommended Operating Procedures for CWC-Related Analysis'

12.1 Paula Vanninen outlined progress being made in compiling the new edition of the VERIFIN 'Blue Book'. The previous edition was issued in 1994 and formed the basis of the recommended operating procedures now used in OPCW proficiency tests and inspections. The new edition will be Web-based and significantly more extensive in its coverage than the 1994 edition. A workshop will be held in Helsinki, 8-9 December 2011, and a review meeting will be held at the OPCW Headquarters in February 2012 following a proficiency test meeting.

13. Any other business

13.1 The members considered that a seventh meeting of the TWG, proposed for 2012, would continue to be productive and provide the SAB and TS with appropriate advice. Topics proposed for a seventh meeting included:

- High resolution mass spectrometry, and its use in proficiency tests
- Sample clean up for ricin and saxitoxin analysis
- Utility of portable infra-red analytical instruments to support S&A in routine industry inspections
- Analysis of mixed CB samples

- Use of hand-held detectors/monitors to direct sampling

- Emerging technologies and techniques

13.2 The chairperson expressed his appreciation to the Head of the OPCW Laboratory and his staff for their input into the meeting.

14. Conclusions and recommendations

14.1 The TWG commended the work being undertaken by the OPCW Laboratory on aqueous sample preparation and fast GC. The TWG supported a proposal that the Head of the Laboratory should issue a formal note, addressed to designated and other interested laboratories, requesting their assistance in assessing the new aqueous sample preparation procedure for ruggedness and applicability.

14.2 DESI-MS was recognised as a powerful mass spectrometric technique for direct and rapid sample analysis, avoiding the need for extensive sample preparation. The TWG members recommended that a watching brief be maintained by the SAB and the Secretariat on developments of portable DESI-MS instrumentation.

14.3 The TWG have made provisional recommendations for ricin analysis. These will require further elaboration but it was recognised that further progress could be made only by holding exercises on ricin analysis. Criteria should be evaluated in inter-laboratory collaboration exercises and modified as appropriate.

14.4 Methods and provisional criteria for the identification of saxitoxin were agreed. It was recommended that LC of saxitoxin should be performed only on columns with suitable retention characteristics.

14.5 Criteria for trace analysis based on WADA and EU guidelines were deemed to be generally applicable to trace analysis in investigations of alleged use. However, specific criteria for the purposes of the OPCW should be established after more experimental data is collected and evaluated.

14.6 The terms of reference of the TWG, and recommendations made over the previous five meetings, were reviewed. These were considered and re-endorsed by the members.

14.7 The TWG recommended that a seventh meeting of the TWG should be held; topics were proposed.

15. Closure of the meeting

The Chairperson closed the session at 17.00 h on 18 November 2011.

Appendices:

Appendix 1: List of Participants in the Sixth Meeting of the Temporary Working Group on Sampling and Analysis

Appendix 1

LIST OF PARTICIPANTS IN THE SIXTH MEETING OF THE TEMPORARY WORKING GROUP ON SAMPLING AND ANALYSIS

1.	Robert Mathews (Australia)
2.	Paul D'Agostino (Canada)
3.	Paula Vaninnen (Finland)
4.	Jean-Claude Tabet (France)
5.	Anne Bossée (France)
6.	Francesco Pilo (Italy)
7.	Jose Luz Gonzalez-Chavez (Mexico)
8.	Mui Tiang Sng (Singapore)
9.	Philip Charles Coleman (South Africa)
10.	Professor Roberto Martinez-Alvarez (Spain)
11.	Sten Åke Fredriksson (Sweden)
12.	Robin Black[8] (United Kingdom of Great Britain and Northern Ireland)
13.	Armando Alcaraz (United States of America)

8 Chairman of the TWG

Annex 3

REPORT OF THE FIRST MEETING OF THE SAB TEMPORARY WORKING GROUP ON THE CONVERGENCE OF BIOLOGY AND CHEMISTRY THE HAGUE, THE NETHERLANDS 15 – 16 NOVEMBER 2011

1. Opening of the meeting and adoption of the agenda

1.1 The Temporary Working Group (TWG) on the Convergence of Biology and Chemistry of the Scientific Advisory Board (SAB) held its first meeting on 15 and 16 November 2011 at OPCW Headquarters in The Hague.

1.2 The meeting was chaired by Robert Mathews on behalf of the SAB.

1.3 The meeting was opened by the Chair. In introducing the agenda, the Chair referred to the introductory letter that he had provided to the TWG members prior to the meeting. In particular, he highlighted that in recent years, there has been increasing interest in the potential implications of the rapid advances in the life sciences, including the convergence of chemistry and biology, for the CWC. There was recognition that these developments could potentially be misused, for example, leading to the production of toxic chemicals, including toxins and bio-regulators, through "biologically mediated processes". It was noted that many of the articles published about the implications of the rapid advances in life sciences for the CWC have tended to discuss the potential future implications from a theoretical perspective, and there appears to be limited information available as to what is realistically possible to achieve with the current state of development of science and technology. This led to the view expressed by the Director-General that the convergence of chemistry and biology warrants further study at the practical level, and that additional advice might be sought from the SAB, from States Parties that have assessed these developments, and from stakeholders in industry and academia.

1.4 The list of participants in the meeting is given in Appendix 1.

1.5 The following agenda was adopted:

(a) Opening of the meeting and adoption of the agenda

(b) Areas of overlap between the CWC and BWC

(c) Advances in life sciences

i A brief review
ii Advances in life sciences relevant to the production of chemicals.

(d) What processes are included in the biologically mediated synthesis for the:

i Commercial scale production of chemicals
ii Production of toxic chemicals

iii Synthesis/production of toxins and bioregulators.

(e) The application of chemical synthesis methods for the production of toxins, bioregulators and peptides.

(f) Biotechnological processes, other than biologically mediated synthesis, of relevance to the OPCW.

(g) What is meant by 'production by synthesis'?

(h) Other aspects of convergence of chemistry and biology of potential relevance to the CWC, including the analysis of biologically active compounds.

(i) Any other business.

(j) Elaboration and adoption of the TWG report.

(k) Summary of conclusions and recommendations; review of minutes.

(l) Closure of the meeting.

2. Areas of overlap between the CWC and BWC

The Chair gave an overview of the history of the Biological Weapons Convention (BWC) and CWC and highlighted the potential areas of overlap between the two regimes. Robin Black gave an in-depth explanation of one of the slides presented which depicts a spectrum of chemical and biological agents ranging from toxic industrial chemicals to classic biological warfare agents. He emphasised that the origin of this spectrum dates back to the mid-1980s and it should be updated to reflect today's situation. Piers Millett then stressed three areas of overlap including packaging, scale and distribution of relevant facilities, and relevant quantity of mid-spectrum agents.

3. Advances in life sciences

3.1 Roderick Flower gave a presentation on the international workshop, *Trends in Science and Technology Relevant to the BWC* held in Beijing in November 2010.[9] He stated that there were three main themes, namely, the pace of change, diffusion of knowledge, and integration and convergence. He outlined nine findings, which were: fundamental changes, access and availability, integration and convergence, bioreactors and transgenics, microbial forensics biosensors, disease surveillance, role of States Parties in the BWC, and progress and roadblocks. Finally, he noted four conclusions of the workshop regarding treaty obligations, treaty implications, surprise discoveries, and the role of the scientific community.

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9 A report based on the outcome of the workshop has been published by the National Research Council of the US National Academies, *Life Sciences and Related Fields: Trends Relevant to the Biological Weapons Convention*, National Academies Press, 2011.

3.2 Piers Millett informed the TWG of the review process of the relevant scientific advances prior to the 7th Review Conference of the BWC. In addition to the report of the Beijing workshop, BWC States Parties have submitted national papers on developments. The BWC Implementation Support Unit (BWC ISU) has summarised these advances in an official background document.[10] He also referred to a forthcoming US National Academy of Sciences report on high containment facilities and said this will be useful because little is presently known about such facilities. He emphasised that it is difficult to assess the current state of development of the life sciences because the time lag between discovery and publication of research results is many months. Therefore engagement with the scientific community is essential. He furthermore pointed out that the life sciences today are increasingly information-based and he emphasised the necessity to be able to handle large amounts of data. There have been significant advances in both sequencing and synthesising DNA. He referred to changes in the publication and dissemination of scientific research results and data.

4. Biologically mediated synthesis:

Commercial scale production of chemicals

4.1 William Provine discussed with the TWG a variety of current industrial practices in support of chemical production via biological routes, most notably the large scale production (greater than 60 million tonnes per year) of Bioethanol from corn grain and sugar cane globally. Also, bio-production of organic acids (e.g. Lactic acid), Acetone-Butanol-Ethanol synthesis, and 1,3 Propanediol are manufactured at large scale (greater than 45,000 tonnes per year) today. In addition, there is pilot scale production of isoButanol, Farnesene, Squalene, PHA, and Artemisinic acid.

4.2 William Kane gave a presentation on "Biologically Mediated Processes - Examples of Chemical Industry Plans for Large Scale Production". Succinic acid, 1, 4-Butanediol, Acrylic acid, and Adipic acid are normally produced from petroleum-based feedstock, however, biological process routes are being perfected. Some of these new routes are very efficient due to advances in biotechnology. The bio-based routes are expected to compete economically with petroleum-based routes. Over the last 20 years, crude oil prices have increased fourfold and have resulted in higher costs for petroleum-based products. This is now a major driver for the chemical industry to explore alternative process feedstocks that become available with bio-based process routes.

4.3 Large-scale production facilities using bio-based processes (greater than 200 tonnes/year) have already been announced publically for both Succinic acid and 1, 4-Butanediol. These facilities will be constructed in many regions of the world (including Europe, North and South America, and Asia) over the next five years.

4.4 Bio-based process routes for Acrylic acid and Adipic acid are being developed but are still in the R&D/pilot plant stage. However, a number of companies have attracted

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10 BWC ISU, *New Scientific and Technological Developments Relevant to the Convention: Background Information Document Submitted by the Implementation Support Unit*, available at www.unog.ch/bwc/science.

major investors to plan for future commercialisation. Industrial partnerships and joint ventures are often used to gain business and technological advantages in launching bio-based products. Commercialisation trends of biologically-mediated processes should continue to be monitored.

Production of toxic chemicals

4.5 The group discussed the possibility of toxic chemicals being produced by biologically-mediated processes and concluded that for classical chemical warfare agents such as nerve agents and blister agents there would not appear to be an advantage in trying to produce such chemicals through biological means. More information would be required about the feasibility and practicability of synthesising precursor-type chemicals by biological means. The group recommends the conduct of a survey involving relevant biotechnology industry representatives on the range of chemicals being produced today using biologically-mediated processes.

Synthesis/production of toxins and bioregulators

4.6 The TWG was informed that capacity in this area was evolving rapidly and being driven by advances in systems and synthetic biology. Examples of current capacity included:

- Biocatalysis – the use of enzymes to catalyse chemical reactions has become increasingly practical and affordable in recent years, and great use is expected in coming years, both for high-volume manufacturing of commodity chemicals (including biofuels), and also for the low-volume production of specialty chemicals and pharmaceutical ingredients.
- Metabolic pathway engineering – research groups have demonstrated an ability to engineer the pathways for biologically active metabolites, such as psychoactive narcotics and their precursors into yeast and bacteria.
- Biopharming – this involved the production of protein-based pharmaceuticals in transgenic plants and animals, for the cost-effective production of vaccines, microbiocides and therapeutic antibodies.
- Chemical DNA synthesis of biological molecules – it is now possible to using DNA synthesizers to construct genes and entire microbial genomes by joining the four chemical units of DNA in any desired sequence. This has enables the synthesis of a number of pathogenic viruses, and the synthesis of a bacterial genome consisting of more than 1 million base pairs. This enables the development of ‘designer bacteria’ that can mass-produce a range of chemicals, ranging from bio-fuels to biological molecules including therapeutic peptides, including possibly bioregulators.

4.7 These advances take advantage of developments in relevant enabling technologies, including in genetic sequencing, genetic synthesis, as well as in the manipulation and design of sequences.

4.8 The group considered the chemical synthesis of biological systems to produce toxins, bioregulators and other biologically active peptides under this agenda item. The group recommends conducting a detailed technical feasibility analysis of production of Saxitoxin and/or Ricin via synthetic biology and/or biopharming.

5. The application of chemical synthesis methods for the production of toxins, bioregulators and peptides

The group concluded that the technical capability to chemically synthesise many toxins, bioregulators and peptides exists today, however practical limitations exist and need to be assessed at a future meeting.

6. Biotechnological processes, other than biologically mediated synthesis, of relevance to the OPCW

This issue has been covered under Paragraph 4 (above).

7. 'Production by synthesis'

7.1 Robert Mathews provided the TWG with a briefing on the origins of the term "production by synthesis" which is used in Part IX of the Verification Annex of the Convention. There was no agreement during the CWC 'end-game' negotiations whether the OCPF regime should cover production of chemicals using biologically-mediated processes, and the term "production by synthesis" was used as a 'creative ambiguity'. A key issue in the implementation of Part IX is whether biologically-mediated processes are also considered chemical synthesis and thus are covered by the term "production by synthesis". This subject was subsequently discussed in the Preparatory Commission, without agreement, at least in part because OCPF inspections were not scheduled to start until 2000. The TWG was briefed by the Secretariat on the different practices adopted by States Parties when declaring OCPFs employing biologically-mediated processes.

7.2 A report was prepared by the SAB in 1999 addressing the term "production by synthesis"[11]. At that time, the SAB concluded that there were few discrete organic chemicals that were manufactured in declarable quantities using biological processes. Based on the report discussed under item 4 and other information presented at this meeting, the TWG noted that this situation had changed significantly in the past 12 years. There is now an increasing trend towards the commercial production of chemicals using biological processes.

7.3 The TWG determined that it is not in a position to make a full assessment without further study (including the surveys referred to in Paragraph 4).

8. Other aspects of convergence of chemistry and biology of potential relevance to the CWC, including the analysis of biologically active compounds.

8.1 The TWG recognised the potential benefits of the convergence of chemistry and biology (and related aspects of nanotechnology) to the CWC, including developments in detection (biosensors), medical countermeasures, decontamination, and laboratory identification techniques including bioforensics.

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11 SAB-II/1, dated 23 April 1999.

8.2 Aspects discussed included advances in developing faster assays for toxins, such as for the Clostridium Botulinum Neurotoxin Type A. There have also been relevant advances in developing therapies to deal with toxins, including: the identification of genetic sequences in hosts required for intoxication by Ricin and Pseudomonas exotoxin (offering treatment opportunities by blocking the functionality of these genes); nanocarriers designed to allow toxins to be flushed from the system; nanoparticles designed to trap toxins and carry them to the liver for destruction; compounds designed to prevent the uptake of toxins into certain cell types, such as Botulinum toxin into nerve cells; as well as small binding agents designed to latch on to toxins enabling them to be identified by antibodies, also allowing it to be flushed from the system.

8.3 These aspects were discussed briefly at the TWG, and the TWG recommends the other aspects be considered in more detail at a future meeting.

9. Any other business

10. Recommendations for future work:

10.1 With the rapid advances in science and technology, there will be increasing convergence of biology and chemistry, so regular evaluation of the implications for CWC implementation will be required.

10.2 A structured process to continue monitoring the convergence of chemistry and biology should be established, including for example, by convening meetings of experts in chemistry and biology (including through the CWC and BWC meeting processes).

10.3 Commercialisation trends of biologically-mediated processes should continue to be monitored.

10.4 A survey involving relevant biotechnology industry representatives on the range of chemicals being produced today using biologically-mediated processes should be conducted.

10.5 While the technical capability to chemically synthesise many toxins, bioregulators and peptides exists today, practical limitations exist, and these areas need further to be assessed.

10.6 A detailed technical feasibility analysis of production of bioregulators, peptides and toxins (including Saxitoxin and Ricin) via synthetic biology and/or biopharming should be conducted.

10.7 Other aspects of the convergence of chemistry and biology of potential relevance to the CWC should be studied, including the development of improved protective measures, and analysis of biologically active compounds.

11. Closure of the meeting

The Chairperson closed the meeting at 17:40 on 16 November 2011.

Appendices:

Appendix 1: List of Participants in the First Meeting of the Temporary Working Group on the Convergence of Biology and Chemistry

Appendix 1

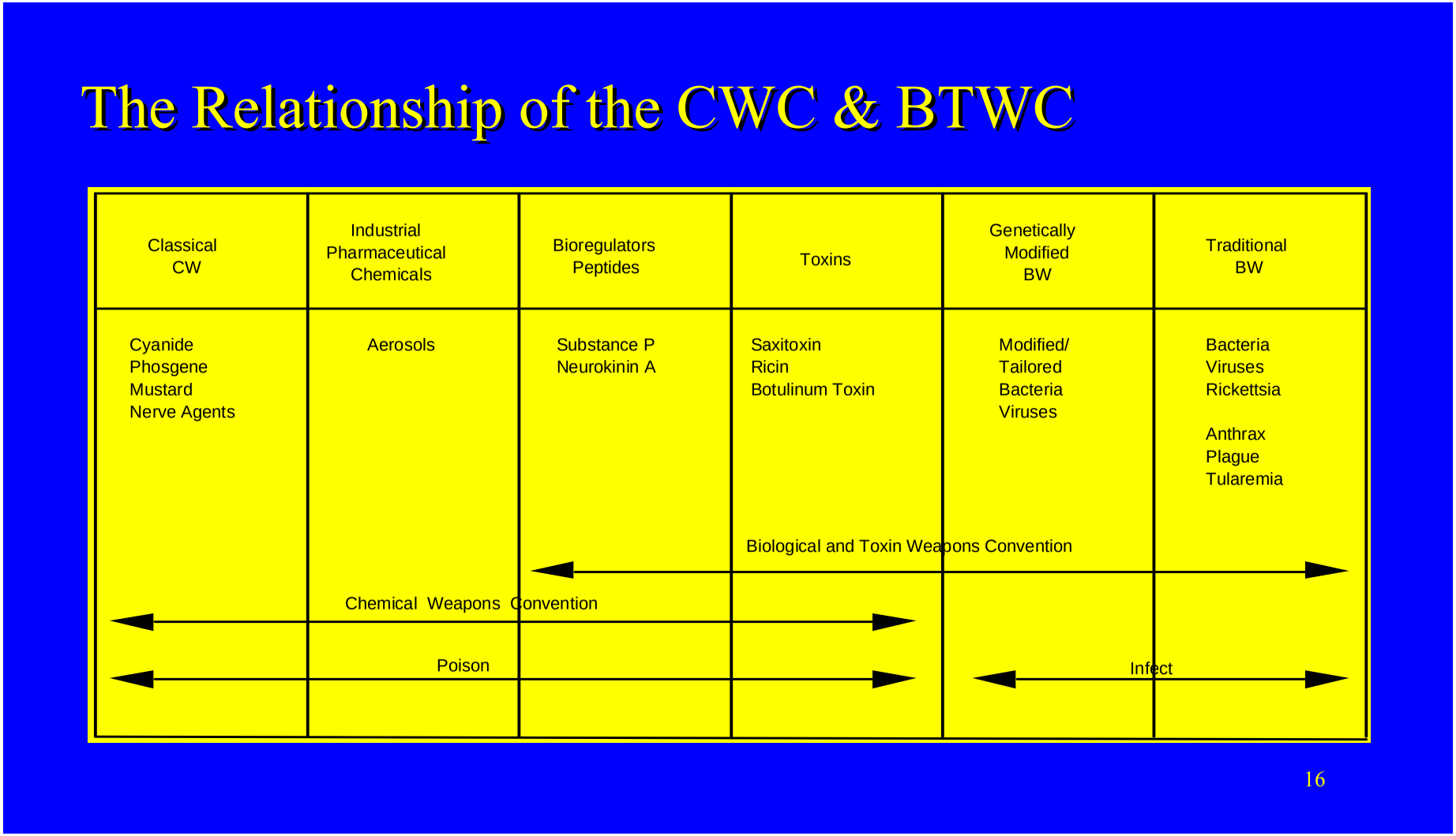
LIST OF PARTICIPANTS IN THE FIRST MEETING OF THE TEMPORARY WORKING GROUP ON THE CONVERGENCE OF BIOLOGY AND CHEMISTRY

1.	Djafer Benachour (Algeria)
2.	Robert Mathews[12] (Australia)
3.	Hua Li (China)
4.	Mahdi Balali Mood (Islamic Republic of Iran)
5.	Muhammad Zafar-Uz-Zaman (Pakistan)
6.	Igor Vladimirovich Rybalchenko (Russian Federation)
7.	Philip Charles Coleman (South Africa)
8.	Stefan Mogl (Switzerland)
9.	Robin Black (United Kingdom of Great Britain and Northern Ireland
10.	Roderick Flower (United Kingdom of Great Britain and Northern Ireland)
11.	Piers D. Millett (BWC Implementation Support Unit, Geneva, Switzerland)
12.	William Kane (United States of America)
13.	William D. Provine (United States of America)

12 Chairman of the TWG

Annex 4

THE RELATIONSHIP OF THE CWC & BTWC CBW SPECTRUM



Annex 5

SAXITOXIN FACT SHEET

Introduction

Saxitoxin (STX) is a neurotoxin which is naturally produced by certain species of marine dinoflagellates (including *Alexandrium sp.*, *Gymnodinium sp.*, *Pyrodinium sp.*) and cyanobacteria (including *Anabaena sp.*, some *Aphanizomenon spp.*, *Cylindrospermopsis sp.*, *Lyngbya sp.*, *Planktothrix sp.*). Ingestion of Saxitoxin (usually through shellfish contaminated by toxic algal blooms) is responsible for the human illness known as paralytic shellfish poisoning (PSP).

The term Saxitoxin has also been used to refer to the entire suite of related neurotoxins produced by these microorganisms, which in addition to Saxitoxin, includes a number of analogs, *inter alia*, neosaxitoxin (neoSTX), the gonyautoxins (GTX) and decarbamoylsaxitoxin (dcSTX). These molecules range in MW from 250 to 500Da, depending on the substituent side groups.

Nomenclature

The term Saxitoxin originates from the species name of the butter clam (*Saxidona giganteus*) from which the toxin was first isolated.

A survey of the literature demonstrates how the nomenclature of Saxitoxin has changed since the toxin was first isolated in 1957.[13] In particular, the term 'Saxitoxin' was originally used in reference to the dihydrochloride salt of the molecule.[14] In the early 1980s, one chemistry manual referred to the free base as Saxitoxin.[15] However, since the late 1980s, the doubly charged cation has been referred to as Saxitoxin.[16] More recently (and since the negotiations on the Chemical Weapons Convention were concluded in 1992), the nomenclature of Saxitoxin compounds has become more specific—distinctions are now made between Saxitoxin dihydrochloride and Saxitoxin dihydrate.[17]

The systematic IUPAC name for Saxitoxin dihydrate is:
(3aS-(3a-α,4-α,10aR*))2,6-diamino-4-(((amino-carbonyl)oxy)methyl)-3a,4,8,9-tetrahydro-1H,10H-pyrrolo(1,2-c)purine-10,10-diol.

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13 R. J. Mathews, 'Saxitoxin and the CWC: Personal Recollections and Reflections', Presentation to the Thirteenth Session of the Scientific Advisory Board, Annex 4 in Report of the Thirteenth Session of the Scientific Advisory Board, SAB-13/1 (1 April 2009).

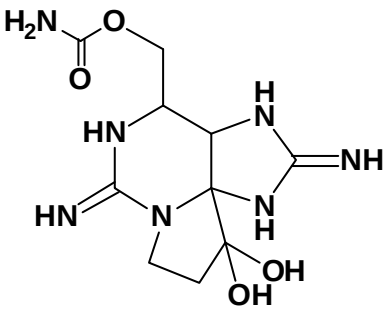
14 See, for example, Dictionary of Organic Compounds, 4th Edition (1965); SIPRI, The Problem of Chemical and Biological Warfare Vol. I, pp. 67-68, (1971), P.J. Scheuer, Chemistry of Marine Natural Products, (1973).

15 Dictionary of Organic Compounds, 5th Edition (1982).

16 See for example, The Concise Encyclopedia Biochemistry, 2nd Edition (1988), The Merck Index 11th Edition (1989); The Merck Index 14th Edition (2006).

17 Richard J. Sax Sr, Sax's Dangerous Properties of Industrial Materials, 9th Edition (1995).

Structure of Saxitoxin dihydrate



Sources of Saxitoxin

Saxitoxin can be isolated from bivalve molluscs (such as the butterclam *Saxidona giganteus*) that have accumulated PSP-producing dinoflagellates (such as *Gonyaulax catanella*) during feeding. In one reported experiment, about 8 tonnes of clams were processed to produce a single gram of Saxitoxin.[18]

Saxitoxin has been synthesised in very small quantities and with considerable difficulty. Saxitoxin was first synthesised in 1977 in a 17-step synthesis with an overall yield of 0.2%.[19] More recently, Saxitoxin has been synthesised in a 19-step synthesis with an overall yield of 1.6%.[20]

Saxitoxin can also be produced by culture of the dinoflagellate species *Gonyaulax catanella.*

Main clinical features[21]

Saxitoxin is a powerful neurotoxin that binds with high affinity to sodium channels on cell membranes, inhibiting the influx of sodium ions into cells, with resulting suppression of cell action potentials, which results in paralysis.[22] Following ingestion of Saxitoxin, the onset of symptoms is typically within 10-60 minutes. Numbness or tingling of the lips and tongue (attributable to local absorption) spreads to the face and neck, followed by a prickling feeling in fingers and toes. With moderate to severe exposure, the paralysis spreads to the arms and legs. Motor activity is reduced, speech becomes incoherent and respiration laboured and subjects die from respiratory arrest. The terminal stages may occur within 2 – 12 hours. Fatalities in adults have been reported following ingestion of 0.5 – 12.4 mg. With exposure through inhalation, most of the symptoms would occur much faster.

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18 WHO, Public health response to biological and chemical weapons, (World Health Organization, Geneva, 2004).

19 H. Tanino, T. Nakata, T Kanedo and Y. Kishi, A Stereospecific Total Synthesis of d,l-Saxitoxin, *J. Amer. Chem. Soc*., 1977, 2818.

20 J. Fleming and J. Du Bois, Total Synthesis of (+) Saxitoxin, *J. Amer. Chem. Soc*., 2006, 3926.

21 WHO, Public health response to biological and chemical weapons, (World Health Organization, Geneva, 2004).

22 It has been shown that the doubly-charged cation is the form of Saxitoxin that binds to the sodium channels on cell membranes.

Protective Measures[23]

Diagnosis of Saxitoxin poisoning is confirmed by detection of the toxin, using ELISA or mouse bioassay, in samples of, for example, stomach contents, water or food.

No specific antidotes to Saxitoxin poisoning exist, and treatment is symptomatic. The toxin is normally cleared rapidly from the body via the urine, so that victims who survive for 12 – 24 hours usually recover. Diuretics may help. Specific antitoxin therapy has been successful in animals. No vaccine against Saxitoxin exposure has been developed for human use.

Saxitoxin: Peaceful applications

Saxitoxin is a component in diagnostic testing kits for PSP. It is also used in neurochemical research, including electrophysiological studies.

Saxitoxin as a CB weapon

Saxitoxin dihydrochloride was first isolated at the US Army Fort Detrick laboratory in the 1950s, designated as Agent TZ, and was investigated as a potential weapon.[24] Agent TZ was apparently weaponised in the M1 Biodart (E1) flechette system in the 1950s and 1960s.[25]

Saxitoxin is soluble in water and stable, and dispersal as an aerosol is feasible. No cases of inhalation exposure have been reported in the medical literature, but animal experiments suggest that the entire syndrome is compressed, and that death may occur within minutes.[26]

Saxitoxin and the CWC

Saxitoxin was proposed for inclusion in the CWC Schedules of Chemicals by the USA in 1984,[27] and was subsequently included in the CWC Rolling Texts within Schedule 1, with a footnote reflecting the view of some negotiators that Saxitoxin would be more appropriate in Schedule 2. From the record of negotiations it appears that what negotiators wanted to include in the Schedules was the form of Saxitoxin that had been weaponised in the past (that is, Agent TZ, the dihydrochloride salt), and other forms of weaponisable Saxitoxin.[28] When CAS Numbers were assigned to the chemicals in the CWC Rolling Text in the late 1980s, Saxitoxin was assigned that the CAS Number of Saxitoxin dihydrate on the understanding that the CAS Numbers were intended to be essentially 'identification aids' rather than

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23 WHO, Public health response to biological and chemical weapons, (World Health Organization, Geneva, 2004).

24 The military symbol TZ was derived after the name of its principal investigator, Dr Edward Shantz, who spent three decades working on toxins at the US Army Fort Detrick laboratory before joining the University of Wisconsin in 1972.

25 The M1 Biodart (E1) was a 7.62mm rifle cartridge flechette system filled with either Botulinum toxin A (XR), Saxitoxin (TZ), or possibly a combination of the two. There were reportedly 4,450 filled and 5,315 unfilled M1s in the US arsenal just prior to their destruction in the early 1970s. (Information from wikipedia).

26 WHO, Public health response to biological and chemical weapons, (World Health Organization, Geneva, 2004).

27 USA, CD/500, (1984)

28 R.J. Mathews, 'Saxitoxin and the CWC: Personal Recollections and Reflections', Annex 4 in Report of the Thirteenth Session of the Scientific Advisory Board, SAB-13/1 (1 April 2009).

'unique identifiers' for the various Scheduled chemicals.[29] In the CWC 'end-game' in 1992, it was agreed that Saxitoxin would be placed in Schedule 1.

Saxitoxin was the subject of the first simplified amendment procedure (technical change) to the CWC, based on concerns that delays in the transfers of diagnostic testing kits for PSP in shellfish (with each kit containing 5 micrograms of Saxitoxin) by the 30 day advance notification requirement for Schedule 1 chemicals[30] could cause humanitarian problems. The technical change resulted in the 30 day advance notification requirement being waived for inter-states parties transfers of less than 5 milligrams of Saxitoxin for medical/diagnostic purposes.[31]

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29 The issue of what constitutes Saxitoxin shows again that the CAS registry numbers given in the Convention cannot be considered to have regulatory power. They are essentially identification aids. See Paragraph 4.4 in Report of the Eighth Session of the Scientific Advisory Board, SAB-8/1 (19 February 2006).

30 CWC Verification Annex, Part VI, Paragraph 5.

31 CWC Verification Annex, Part VI, Paragraph 5bis, entered into force on 12 October 1999.