OPCW

Scientific Advisory Board

Eighteenth Session
16 – 19 April 2012

SAB-18/1
19 April 2012
Original: ENGLISH

REPORT OF THE EIGHTEENTH SESSION OF THE SCIENTIFIC ADVISORY BOARD

1. AGENDA ITEM ONE – Election of the Chairperson and of the Vice-Chairperson of the Scientific Advisory Board

In an informal meeting chaired by Robin Black prior to the commencement of its formal session, the Scientific Advisory Board (SAB), by a consensus of its members, elected Stefan Mogl as the new Chairperson of the SAB for a term of one year. Mahdi Balali-Mood was re-elected as Vice-Chairperson for the Board's Eighteenth Session.

2. AGENDA ITEM TWO – Opening of the session

The SAB met for its Eighteenth Session from 16 to 19 April 2012 at the OPCW Headquarters in The Hague, the Netherlands. The session was opened by the newly elected Chairperson, Stefan Mogl. A list of participants appears as Annex 1 to this report.

3. AGENDA ITEM THREE – Adoption of the agenda

The SAB adopted the following agenda for its Eighteenth Session:

1. Election of the Chairperson and of the Vice-Chairperson of the Scientific Advisory Board
2. Opening of the session
3. Adoption of the agenda
4. *Tour de table* to introduce Scientific Advisory Board Members
5. Welcome address by the Director-General
6. Overview of developments at the OPCW since the last session of the Scientific Advisory Board
7. Establishment of a drafting committee
8. Developments in science and technology:

(a) IUPAC[1] International Science and Technology Workshop: Insights gained into developments in science and technology

(b) The SAB's report on developments in science and technology: Discussion of the initial draft

(c) The convergence of chemistry and biology: Intersessional work since the first meeting of the temporary working group

(d) Incapacitating chemical agents and novel toxic compounds: Further consideration by the SAB of this topic

9. Education and outreach in science and technology:

(a) Report of the first meeting of the temporary working group on education and outreach in science and technology

(b) Outreach activities of the Secretariat

(c) Outreach activities by members of the SAB

10. Scientific and technological elements of verification methodologies, emerging technologies, and new equipment:

(a) Sampling and analysis:

(i) Intersessional work since the sixth meeting of the temporary working group

(ii) Update on Secretariat action in regard to sampling and analysis

(b) Developments in chemical agent-detection and identification

11. Scheduled chemicals and advice on the Annex on Chemicals

12. Further scientific and technological advice relevant to the Convention

13. Future work of the Scientific Advisory Board

14. Any other business

15. Adoption of the report

16. Closure of the session

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

4. AGENDA ITEM FOUR – *Tour de table* to introduce Scientific Advisory Board members

The session was opened with a *tour de table* in order to introduce new SAB members to existing members. The new members are: Roberto Martínez Álvarez, Augustin Baulig, and Ferruccio Trifirò.

5. AGENDA ITEM FIVE – Welcome address by the Director-General

5.1 The Director-General welcomed the members of the SAB, and congratulated Stefan Mogl on his election as Chairperson of the SAB. The Director-General expressed his appreciation to the outgoing Chairperson, Philip Coleman, for his contribution to the SAB, both as a member, and as its Chairperson for the past six years. The Director-General welcomed the new members of the SAB, and expressed to Mahdi Balali-Mood and José Luz González Chávez, who were about to complete their final term in office on the SAB, his appreciation for their dedicated commitment and important work done for the Board. Mahdi Balali-Mood has made an additional contribution as Vice-Chairperson. The Director-General also conveyed his appreciation to the members of the temporary working groups (TWGs) for their contributions.

5.2 The Director-General emphasised that 2012 and 2013 will be important years in the evolution of the OPCW, with the beginning of preparations 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"), which will be held in April 2013. He said that the two previous review conferences, in 2003 and 2008, met at a time when attention was focussed on the destruction of chemical weapons declared by possessor States Parties. While this function of the OPCW will continue for some years to come, a long-term vision of the work of the Organisation needs to also take into account existing and emerging demands and trends.

5.3 The Director-General referred to the report on developments in science and technology, which the SAB is preparing for the Third Review Conference. He emphasised that the report will be an important document, in that its assessment of the impact of these developments on the Chemical Weapons Convention (hereinafter "the Convention") will be widely read by States Parties and other stakeholders. The Director-General stated that he expects that the SAB will produce a high-quality document providing a comprehensive overview of the likely impact of developments in science and technology on the implementation of the Convention, thus stimulating consideration and discussion of these issues amongst States Parties.

5.4 Referring to a workshop organised by IUPAC at Spiez in Switzerland in February 2012, the Director-General highlighted the fact that the Convention is a multilateral security instrument that is rooted in science. Every new development that potentially impacts the implementation of the Convention needs to be understood in the context of its possible implications for the Convention's prohibitions. The Director-General noted that such watchful attention requires channels of communication and discourse with the larger scientific community—a task in which the SAB has a key role to play.

5.5 The Director-General welcomed the work of the three currently operating TWGs, and thanked their Chairpersons for their dedicated work. In this respect, he shared his

view that there is further scope to take forward work between the formal SAB sessions, not only in the context of the TWGs, but also on the other substantive questions, some of which can be handled by correspondence groups by means of electronic communications. The Director-General stressed that it is important that all members of the SAB contribute their expertise.

5.6 In conclusion, the Director-General reminded members of the SAB trust fund, which was created in 2006 to support the activities of the SAB. A call for voluntary contributions had recently been issued, and the Director-General thanked the Governments of Turkey and the United Kingdom of Great Britain and Northern Ireland for their contributions. He also thanked the European Union (EU) for its recent Council Decision in support of the OPCW; this funding is used for meetings of the TWGs.

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

6.1 The 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 Seventeenth Session of the SAB was held. His presentation emphasised that science and technology underpin many Articles of the Convention, and thus are central to the OPCW's future work.

6.2 The Secretary informed the members of the Board on the progress being made in the context of informal consultations on issues related to industry, destruction deadlines, the implementation of the tenure policy, Article XI of the Convention, and verification of converted former chemical weapons production facilities (CWPFs). He described a number of decisions on these issues that had been taken by the Conference of the States Parties (hereinafter "the Conference") during its Sixteenth Session (from 28 November to 2 December 2011). The Secretary also informed the SAB about several other issues, including preparedness under Articles IX and X, universality, and chemical safety and security.

6.3 In terms of the management of the finances of the SAB, the Secretary recalled that there are three funding sources: the Programme and Budget of the OPCW, voluntary contributions to the SAB trust fund, and funds provided by the EU Council Decision (2009/569/CFSP of 27 July 2009). Due to the need to prepare for the Third Review Conference, there will be two SAB meetings in 2012. Four current members of the SAB will be leaving this year, and a call for nominations for new members was issued in February 2012.

6.4 Regarding the future work of the SAB, the Secretary highlighted five key topics: the SAB report on developments in science and technology for the Third Review Conference; engagement with the policy-making organs and policy-makers; follow-up to the IUPAC workshop in February 2012; SAB involvement in the preparatory process for the Third Review Conference; and better engagement between scientists and the wider world.

7. AGENDA ITEM SEVEN – Establishment of a drafting committee

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

8. AGENDA ITEM EIGHT – Developments in science and technology

Subitem 8(a): IUPAC International Science and Technology Workshop: Insights gained into developments in science and technology

8.1 Several members of the SAB attended the IUPAC/OPCW workshop on the impact of advances in science and technology on the Convention, held from 20 to 23 February 2012 at the Spiez Laboratory, Switzerland. The workshop was structured into plenary sessions, and discussions in breakout groups addressed the following topics: the convergence of chemistry and biology; new synthesis and toxicological analysis methods; the development of new materials and delivery mechanisms; advances in industrial production methods; chemical safety and security: possession, transfer, and acquisition; defence against chemical weapons agents; and engagement with the chemical sciences community. The SAB commended the organisers for how well the event had been organised and conducted, and also thanked IUPAC for making available a draft version of the workshop report. The outcomes of the workshop will make an important contribution to the Board's preparations for its own report to the Director-General on developments in science and technology. The SAB discussed a number of key points that will be considered for inclusion in this report.

Subitem 8(b): The SAB's report on developments in science and technology: Discussion of the initial draft

8.2 The SAB considered a first draft of its report on developments in science and technology. The Board recognised the contributions received from SAB members to date. Chapters of the first draft were discussed in breakout groups, and key substantive points were debated. Each chapter will be further discussed and modified by correspondence during the intersessional period before the next SAB meeting. The preliminary chapter headings include the following topics: developments in science and technology; schedules of chemicals and advice on the Annex on Chemicals; verification methodologies; further scientific advice; and education and outreach. The report will be finalised when the SAB meets for its Nineteenth Session.

Subitem 8(c): The convergence of chemistry and biology: Intersessional work since the first meeting of the temporary working group

8.3 The Chairperson of the TWG on the convergence of chemistry and biology, William Kane, gave an overview of the first meeting of the TWG, which was held on 15 and 16 November 2011. The meeting focused on the production aspects of the convergence of chemistry and biology. The Director-General requested that at subsequent meetings, this TWG also address related issues, including the potential benefits of convergence. William Kane proposed that the terms of reference of the TWG should be updated to reflect this request. The appointment of additional members was proposed, possibly including experts in medical countermeasures, protective countermeasures, and diagnostics. The Chairperson of the TWG and the Secretary to the SAB will address the terms of reference and the need for additional members. The second meeting was scheduled for 6 and 7 September 2012.

8.4 On the topic of production by synthesis, William Kane referred to his presentation to the SAB at its Seventeenth Session, which included examples of chemicals being

made using biologically mediated processes. By 2020, it is estimated that 10% of the volume of all chemical products will be made by these green processes. An important issue that requires further discussion is the fact that there are differing views on the meaning of the term "production by synthesis". It remains an open issue for the policy-making organs to address the definition, and specifically, whether it should include biological processes that take place on an industrial scale.

8.5 Manuel Rivero of the Inspectorate (INS) presented the results of a study undertaken by the Technical Secretariat (hereinafter "the Secretariat") to assess the potential for misuse of these bio-production facilities for the production of toxic chemicals for prohibited purposes. The assessment compared the equipment suitable for the production of toxic chemicals with the equipment that is used in commercial-scale facilities for the production of chemicals by means of biologically mediated processes. The similarity of the equipment was noted: The study concluded that such commercial-scale facilities could also be used for the production of other discrete organic chemicals (DOCs) and scheduled chemicals. It was recommended that awareness on this matter should be increased, for example, among National Authorities.

8.6 The SAB suggested undertaking a further short study to determine the products or product classes that are being produced by biologically-mediated processes. National Authorities might assist in providing additional information to the Secretariat.

Subitem 8(d): Incapacitating chemical agents and novel toxic compounds: Further consideration by the SAB of this topic

8.7 The report of the workshop on incapacitating chemical agents, organised by VERIFIN and the Spiez Laboratory, which was held on 7 and 8 September 2011, has been distributed to all members of the SAB. Stefan Mogl informed the SAB that all States Parties should have received a copy of the report through the Swiss delegation to the OPCW. Further copies can be obtained via the website of the Spiez Laboratory.[2] Some members of the SAB and the OPCW have been invited to an International Committee of the Red Cross (ICRC) expert meeting titled: "Incapacitating Chemical Agents: Law Enforcement, Human Rights Law and Policy Perspectives". Attending SAB members will report on the outcome of this meeting when the SAB meets for its Nineteenth Session.

8.8 No recent scientific advances in regard to incapacitating chemical agents have been reported. There are no indications that problems of safety have been solved.

8.9 A brief discussion was held on recently publicised non-scheduled toxic chemicals, and whether they should be included in the schedules. It was noted that information that is currently available is largely anecdotal. The technical information available to the SAB is insufficient to make a recommendation.

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2 See http://www.labor-spiez.ch/de/dok/hi/pdf/web_e_ICA_Konferenzbericht.pdf.

9. AGENDA ITEM NINE – Education and outreach in science and technology

Subitem 9(a): Report of the first meeting of the temporary working group on education and outreach in science and technology

9.1 The SAB received a comprehensive report from Djafer Benachour, Chairperson of the TWG on education and outreach, of the first meeting of this group, which was held on 12 and 13 April 2012. The main recommendations of the TWG were that educational and outreach materials should be prepared, not only in the form of books and printed documents, but also in the form of electronic platforms, documentaries, and short video films; in addition, the suggestion was made to take advantage of other education and outreach activities made by similar organisations, international scientific bodies, professional associations, and non-governmental organisations (NGOs). The TWG, which enjoys the strong support of the Director-General, has a three-year mandate and funding for two further meetings.

9.2 The SAB had the opportunity to review OPCW outreach material and viewed a short film made by the Media and Public Affairs Branch of the Secretariat in cooperation with Chrétien Schouteten, a former chemistry teacher in the Netherlands. The SAB encourages its wide distribution.

9.3 The SAB emphasised the importance of raising awareness in academic and scientific communities, as well as civil society, about the Convention and the work of the OPCW. New approaches should be considered. The SAB endorsed the report of the TWG (see Annex 2) and also approved the recommendations contained therein.

Subitem 9(b): Outreach activities of the Secretariat

9.4 Daniel Feakes of the Secretariat gave a general overview of the outreach activities of the Secretariat. The audiences at which the Secretariat's activities are directed include the following: National Authorities; legislators; the chemical industry; the scientific community; and civil society. Since entry into force of the Convention, the Secretariat has primarily used traditional means of outreach, such as formal diplomatic communications; global, regional and subregional meetings; official visits by the Director-General; and the OPCW website. However, many of these methods are limited in terms of their reach and their interactivity. In addition, it can be difficult to evaluate their effectiveness and to ensure the sustainability of the Secretariat's activities.

9.5 In response, the Secretariat has recently launched a number of new initiatives, including: a series of *e*-learning modules which will be placed on the OPCW website; an OPCW presence on social media platforms (such as Facebook, Twitter, and YouTube); and discussions with civil society actors to improve collaboration. In addition, as recommended by the Advisory Panel on Future OPCW Priorities, the OPCW is discussing with the International Council of Chemical Associations the modalities for working together more closely.

9.6 In the subsequent discussion, SAB members recommended that National Authority meetings should be organised in a manner that would make them more interactive.

Subitem 9(c): Outreach activities by members of the SAB

9.7 A number of SAB members described related activities in which they are involved.

10. AGENDA ITEM TEN – Scientific and technological elements of verification methodologies, emerging technologies, and new equipment

Subitem 10(a): Sampling and analysis

Intersessional work since the sixth meeting of the temporary working group

10.1 Robin Black, Chairperson of the TWG on sampling and analysis (S&A), summarised the current status of the work. Over the period of its existence since 2007, the TWG had moved the Secretariat forward into addressing important areas that had previously been neglected, and which had attracted comment from some observers, particularly from NGOs. The TWG had made recommendations on verification procedures and equipment, reducing sample analysis time, the application of trace analysis in investigations of alleged use, biomedical samples, and toxin analysis (saxitoxin and ricin). The TWG held its own informal exercise on saxitoxin analysis.

10.2 The TWG, in cooperation with the OPCW Laboratory, had discussed fast gas chromatography (GC) as one approach to shortening sample analysis time. In response to this, the Director-General requested a briefing note on fast GC. This had now been prepared by Robin Black and was presented to the SAB meeting. The briefing note was approved by the SAB with minor modifications (see Annex 3).

10.3 A second OPCW confidence-building exercise on biomedical sample analysis, as recommended by the TWG and its predecessor on biomedical samples, was currently in progress. The samples consisted of commercial human urine spiked with sulfur mustard and nerve agent metabolites at low parts per billion. Criteria for identification using trace analytical techniques were being trialled as part of this exercise.

10.4 A proposal to hold a final meeting of this TWG in September 2012 was endorsed by the SAB at its Seventeenth Session. It was proposed that this meeting would address outstanding issues on ricin and trace analysis, and important areas such as applications of the new generation of high resolution mass spectrometers in proficiency tests and trace analysis, protocols for the analysis of mixed chemical and biological samples, and emerging techniques and instrumentation that have possible applications in verification analysis. The TWG Chairperson expressed his disappointment that the SAB trust fund currently cannot financially support the final meeting of this TWG.

<u>The Blue Book, 2011 Edition</u>

10.5 Paula Vanninen of VERIFIN introduced the publication, "Recommended Operating Procedures for Analysis in the Verification of Chemical Disarmament, 2011 Edition", the so-called "Blue Book", to the SAB. The Blue Book was last published in 1994. Starting in 2009, the recommended operating procedures (ROPs) for analysis in the verification of chemical disarmament have been updated through international collaboration with expert laboratories working in the field of Convention-related analysis. These methods form the basis for accreditation, and provide guidelines for

designated laboratories of the OPCW or laboratories applying for designation. The ROPs are also used to train personnel working in the field of defence against chemical-warfare agents. The contents of the Blue Book were presented at the "Third International Workshop on Analysis of Chemical Warfare Agents to Mark the International Year of Chemistry 2011", held on 8 and 9 December 2011 in Helsinki, Finland.

10.6 Scientists from 14 laboratories, including the OPCW Laboratory, collaborated in updating the ROPs. More than 40 authors and reviewers took part in the project. The Blue Book, 2011 Edition was edited by VERIFIN. All authors and reviewers of this edition of the Blue Book, their corresponding organisations, and the financial contributions from the Ministry for Foreign Affairs of Finland were highly acknowledged. The Blue Book, 2011 Edition is available in hardcopy from VERIFIN or as a free-of-charge electronic copy from the VERIFIN website.[3]

10.7 The Chairperson of the SAB and other members expressed their appreciation for this valuable publication, which provides a practical guideline for designated laboratories and for teams working in the field. Members of the SAB complimented the efficient organisation of the workshop held in December 2011.

Update on Secretariat action in regard to sampling and analysis

10.8 Kieran Carey of the INS gave a presentation to the SAB on two topics related to S&A.

10.9 The first was a summary of the recent quality review of the S&A process—undertaken by an observer from the OPCW Laboratory—which examined the entire process of the use of S&A during an inspection. This culminated in a report that recorded the precise time of all stages of the process from unpacking the truck to reaching operational status of the mobile on-site laboratory, sampling, analysis, report writing, and completion of supporting documentation. This highlighted some key areas of the process, particularly related to bureaucratic aspects, which offered potential for significant time savings.

10.10 The second part of the Secretariat's presentation reported on the status of a number of recently completed and ongoing projects in the Laboratory. These included the use of Siltek-coated GC inlets and/or liners to eliminate carry-over during analysis of alkylphosphonic acids and the status of projects to shorten analysis time (fast GC, thermal desorption, and combining multiple samples on large sites). Good progress was being made in these projects. The Secretariat plans to evaluate the Agilent 5975T portable gas chromatography-mass spectrometry (GC-MS) system in the summer of 2012.

Subitem 10(b): Developments in chemical-agent detection and identification

10.11 Sorinel Manta of the INS presented an overview of current detection technologies and equipment. While he deemed the detection equipment used by the Secretariat as adequate, he emphasised that new developments should be monitored to address present shortcomings. The SAB offered its assistance in this regard. Chemical detectors are an essential component of safety for Secretariat operations in a potentially contaminated environment. While current detectors are regarded as fit for

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3 See http://www.helsinki.fi/verifin/VERIFIN/english/

purpose, there is still considerable scope for improvement in terms of sensitivity, the number of chemicals detected, and the elimination of false positives.

10.12 The SAB expressed its appreciation for the contributions from the Secretariat.

11. AGENDA ITEM ELEVEN – Scheduled chemicals and advice on the Annex on Chemicals

11.1 Robin Black proposed some corrections and additions to the fact sheet on saxitoxin that had been adopted by the SAB at its Seventeenth Session. In particular, the name "saxitoxin dihydrate", which had been used for the free-base form of saxitoxin in the fact sheet, was incorrect and should be corrected to "saxitoxin hydrate". An error in the IUPAC name was corrected by Paula Vanninen. A short section on verification was added to the fact sheet. These modifications were adopted by the SAB (see Annex 4).

11.2 Robin Black also summarised a draft fact sheet on ricin that he and Philip Coleman had written. The fact sheet included sections on structure; source; toxicity; mechanism of action; the clinical features of poisoning and the relevant medical treatment for it; the possible therapeutic applications of ricin-derived drugs; the military, criminal and terrorist interest in the use of ricin; detection and verification; and decontamination. The fact sheet was adopted by members of the SAB (see Annex 5).

12. AGENDA ITEM TWELVE – Further scientific and technological advice relevant to the Convention

12.1 Stian Holen (as co-Chairperson of the Secretariat's cross-divisional task-force on chemical safety and chemical security) presented the Secretariat's emerging thinking on this topic. Chemical safety and chemical security are relevant to several Articles under the Convention and to the key priorities of the OPCW (for example, preventing the misuse of toxic chemicals). Furthermore, the Conference at its Sixteenth Session in decision C-16/DEC.10, dated 1 December 2011, suggested that, among other issues, action should be taken in regard to chemical safety and chemical security.

12.2 At the IUPAC workshop (in February 2012) on the impact of advances in science and technology on the Convention, it was clear that science is relevant to chemical safety and chemical security—for example, in relation to scientific research activities. In the Secretariat, a cross-divisional task force has been charged with sharpening and clarifying the role for the OPCW in chemical safety and chemical security, with liaising with potential partners, and with ensuring that duplication with existing mechanisms and the work of other entities is avoided.

12.3 SAB members made some suggestions, especially in regard to the following topics:

(a) the importance of creating sustainable networks;

(b) the necessity of including the International Programme on Chemical Safety (IPCS);

(c) including a component on safety and security in international-cooperation courses;

(d) the relevance to chemical safety and security of the SAB's discussion on education and outreach in science and technology;

(e) the need for the proactive involvement of the OPCW in chemical security; and

(f) that the added value of chemical security was in ensuring that chemical weapons do not re-emerge.

12.4 The SAB looked forward to hearing from the Secretariat as to what contributions the Board could make in the area of chemical safety and chemical security.

13. AGENDA ITEM THIRTEEN – Future work of the Scientific Advisory Board

The SAB discussed its future work, including preparations for its Nineteenth Session and the next meetings of its TWGs; the drafting of its report on developments in science and technology during the intersessional period; and other intersessional work.

14. AGENDA ITEM FOURTEEN – Any other business

14.1 The Chairperson of the SAB bade farewell to Philip Coleman, Mahdi Balali-Mood, and José Luz González Chávez, who would be completing their terms of office on the SAB during 2012. He thanked them for their invaluable contribution to the work of the Board.

14.2 The Director-General requested that the SAB provide advice on situations where a Schedule 1 chemical is an unavoidable by-product in a reaction mixture (see Annex 6). SAB members were asked to consider this request during the intersessional period. A discussion on this topic will be scheduled for the Nineteenth Session.

15. AGENDA ITEM FIFTEEN – Adoption of the report

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

16. AGENDA ITEM SIXTEEN – Closure of the session

The Chairperson closed the session at 17:30 on 19 April 2012.

Annexes:

Annex 1: List of Participants in the Eighteenth Session of the Scientific Advisory Board
Annex 2: (English only, unedited): Report of the First Meeting of the SAB Temporary Working Group on Education and Outreach in Science and Technology Relevant to the CWC, The Hague, the Netherlands, 12 – 13 April 2012
Annex 3: (English only, unedited): Fast Gas Chromatography-Mass Spectrometry in On-Site Analysis, Briefing Note to the Director-General Prepared by the Scientific Advisory Board, April 2012
Annex 4: (English only, unedited): Revised Saxitoxin Fact Sheet
Annex 5: (English only, unedited): Ricin Fact Sheet, Prepared by the OPCW Scientific Advisory Board, April 2012
Annex 6: (English only, unedited): Director-General's Request to Provide Advice on Situations Where a Schedule 1 Chemical Is an Unavoidable By-Product

Annex 1

LIST OF PARTICIPANTS IN THE EIGHTEENTH SESSION OF THE SCIENTIFIC ADVISORY BOARD[4]

	Participant	Institution
1.	Al-Amri, Abdullah Saeed	Saudi Basic Industries Corporation, Riyadh, Saudi Arabia
2.	Álvarez, Roberto Martínez	Complutense University, Madrid, Spain
3.	Balali-Mood, Mahdi	Medical Toxicology Centre, Imam Reza Hospital, University of Medical Sciences, Mashhad, Islamic Republic of Iran
4.	Baulig, Augustin	Secrétariat général de la défense et de la sécurité nationale, France
5.	Benachour, Djafer	Ferhat Abbas University, Ministry of Higher Education and Scientific Research, Setif, Algeria
6.	Black, Robin	Defence Science and Technology Laboratory (Dstl), Porton Down, United Kingdom of Great Britain and Northern Ireland
7.	Cariño, Flerida Arsciwals	Institute of Chemistry, University of the Philippines, Diliman, Quezon City, Philippines
8.	Chávez, José González	Universidad Nacional Autónoma de México, Mexico City, Mexico
9.	Coleman, Philip	Protechnik Laboratories, Lynnwood Glen, South Africa
10.	Dubey, Devendra Kumar	Vertox Laboratory, Gwalior, India
11.	Geist, Michael	BASF SE, Ludwigshafen, Germany
12.	Kane, William	Monsanto Company, United States of America
13.	Mogl, Stefan[5]	Spiez Laboratory, Spiez, Switzerland
14.	Muhammad Zafar-Uz-Zaman	National Engineering and Scientific Commission (NESCOM), Islamabad, Pakistan
15.	Neffe, Slawomir	Military University of Technology, Warsaw, Poland
16.	Rybalchenko, Igor V.	Military Science Centre of the Ministry of Defence, Moscow, Russian Federation
17.	Suárez, Alejandra Graciela	Universidad Nacional de Rosario, Argentina
18.	Trifirò, Ferruccio	Faculty of Industrial Chemistry, University of Bologna, Italy
19.	Vanninen, Paula	VERIFIN, Department of Chemistry, Faculty of Science, University of Helsinki, Finland
20.	Vučinić, Slavica	National Poison Control Centre, Military Medical Academy, Belgrade, Serbia
21.	Zaitsev, Volodymyr	Taras Shevchenko National University of Kyiv, Ukraine
22.	Zhang, Nan	Ministry of National Defence, Beijing, China
23.	Zina, Mongia Said	Faculty of Sciences of Tunis, Tunisia

4 Neivy Fernández Manresa and Shuzo Fujiwara did not attend the Eighteenth Session of the SAB.

5 Chairman of the SAB.

Annex 2

**REPORT OF THE FIRST MEETING OF THE SAB TEMPORARY WORKING GROUP ON EDUCATION AND OUTREACH IN SCIENCE AND TECHNOLOGY RELEVANT TO THE CWC
THE HAGUE, THE NETHERLANDS
12 – 13 April 2012**

1. Opening of the meeting and adoption of the agenda

1.1 The Temporary Working Group (TWG) on Education and Outreach of the Scientific Advisory Board (SAB) held its first meeting on 12 and 13 April 2012 at OPCW Headquarters in The Hague.

1.2 The meeting was chaired by Professor Djafer Benachour on behalf of the SAB.

1.3 The meeting began with a tour de table to introduce the members of the TWG. The list of participants in the meeting is given in Appendix 1.

1.4 The following agenda was adopted:

(a) Introduction by TWG chair and adoption of the agenda

(b) Aims and objectives of the TWG

(c) What has been done so far, by OPCW, IUPAC, and other bodies, and lessons learnt:

i. OPCW
ii. IUPAC
iii. Work in the BWC context
iv. National academies
v. Contributions by individual TWG members. What role/s can and should individual SAB members play?

(d) Briefings by OPCW and other international organisations on education initiatives in science and technology and disarmament/arms control, and lessons learnt:

i. OPCW
ii. IAEA
iii. CTBTO

(e) Ways in which to raise awareness of the Convention in the education sector

(f) How can the OPCW further develop its relationships with the scientific community and the chemical industry with a view to raising awareness of the requirements of the Convention and promoting universal adherence to it

(g) How can the OPCW contribute towards expanding and promoting a culture of responsibility in the scientific community and the chemical industry

(h) Sustainable ways in which the OPCW can take forward its education and outreach activities:

i. What tools can the Secretariat use now?
ii. Which other tools are necessary?
iii. How can electronic platforms best be used?

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(i) Existing initiatives in this area with a view to avoiding duplication and allowing the OPCW to build relationships with other international organisations, professional associations, networks etc:

i. Which organisations can the Secretariat usefully work with now?
ii. Interaction with the chemical industry (chemical safety and security?)
iii. Should other partnerships be developed?
iv. How can/should the media be used?

(j) Topics for intersessional work and next meeting

(k) Any other business

(l) Elaboration and adoption of the TWG report

(m) Summary of conclusions and recommendations; review of minutes

(n) Closure of the meeting.

2. Aims and objectives of the TWG

2.1 Daniel Feakes of the Technical Secretariat gave an overview of the aims and objectives of the TWG as set out in its terms of reference. The objectives of the TWG are to build on earlier work in this area by the SAB and its members, to utilise the experience of other initiatives in this field and related areas, and to make recommendations to the SAB for sustainable activities which could be pursued by the OPCW and its Member States. Referring to its terms of reference, Mr Feakes said that the TWG is requested to give advice to the SAB on the audiences and methods on which education and outreach activities should focus, and possible synergies with other actors. The TWG should also focus on sustainability and "practical procedures", "bottom-up" as well as "top-down" approaches, learning from other processes/initiatives, and the importance of education and outreach for national implementation and safety and security.

3. What has been done so far, and what lessons have been learnt?

3.1 Boitumelo Kgarebe of the Technical Secretariat briefed the TWG on the activities of the International Cooperation Branch, which include integrated chemicals management, chemical knowledge promotion and exchange, enhancing laboratory

capabilities, and industry outreach. Ms Kgarebe provided statistics of participation in these activities which showed that over 3,500 participants had benefitted from these programmes and over 430 research projects had been sponsored.

3.2 Alastair Hay provided an overview of the IUPAC "multiple uses of chemicals" project. Educational material on multiple uses of chemicals and chemical warfare is available as the output of a working group established by OPCW and IUPAC in 2005. Produced with educators in mind, the material is available as a resource for teachers to use to plan their own teaching. Professor Hay said that by using case studies, the material promotes chemistry as an essential science for human welfare but also discusses how and where chemical warfare was used. It discusses the importance of chemists in the process to make chemical weapons and aims to encourage debate about responsible conduct. Additional resource material in the form of supporting background material on the CWC, OPCW, and codes of conduct is also available in the working languages of the OPCW. Professor Hay informed the TWG that using this IUPAC material as background, new interactive teaching material has now been developed to encourage debate in either the classroom or seminar. This IUPAC/OPCW output is available on a website under "Multiple uses of chemicals".[1]

3.3 Robert Mathews provided the TWG with an overview of relevant activities under the Biological Weapons Convention (BWC). Education and awareness-raising have been explored in the BWC Intersessional Process, especially in 2005 and 2008, resulting in recognition of the important role of codes of conduct in facilitating the development of a responsible culture and behaviour in individual scientists in workplaces, and that the development of appropriate workplace regulations and oversight processes would minimise the risk of misuse of biological sciences for hostile purposes. Dr Mathews suggested that it may be useful to think of codes of conduct as occurring in a number of layers, including: (i) a universal code; (ii) codes developed by scientific societies; and (iii) codes developed by workplaces (or institutional codes); and that the various layers of codes (universal, scientific society and workplace) were recognised as complementary and mutually reinforcing, and would be most effective as a package. It also became apparent, based on discussions with representatives from a number of scientific societies and workplaces, that in many situations, there was a preference to add BWC-related elements to an existing Code, rather than developing a new Code specific to BWC issues.

3.4 Dr Mathews said that awareness-raising about the BWC in the broad scientific community, including developing the necessary culture of responsibility in the workplace, has presented many challenges. It is important to have high levels of cooperation: between relevant government agencies; and between government and relevant educational, scientific and industrial communities. To be effective, this cooperation will need to extend to government agencies, scientific societies, educators, scientific researchers and industry representatives who have not traditionally been involved with BWC-related activities. BWC-related awareness-raising clearly needs to be both a 'top-down' and 'bottom-up' process, and 'top-end' champions are needed, both within Government (ideally high level decision-makers in key agencies) and in the academic, research and industrial

[1] See http://multiple.kcvs.ca/

communities (including scientific societies, academies of science, and senior executives). Finally, Dr Mathews said that the education, awareness-raising, and codes of conduct activities will need to be a continuing process because of the changing players and changing technologies in the various biological sectors. Clearly, a State Party cannot simply 'do it once' and then put a 'tick in the box'.

3.5 Jo Husbands summarised work carried out in the life sciences by international scientific unions and by the National Academy of Sciences in the USA. She said that the OPCW has an important opportunity to promote awareness of the CWC, and more broadly chemical security, by developing partnerships with scientific organisations to develop and carry out educational activities, and by seeking potential partners at national, regional, and international level. The OPCW already has a good experience of working with IUPAC on education and outreach, as well as on assessments of science and technology trends. Dr Husbands said that the OPCW could also take advantage of broader international initiatives related to the responsible conduct of science as the opening for introducing more focused discussion of the CWC and chemical security. Furthermore, there may be ideas and examples from current activities to promote bio-safety and bio-security on which the OPCW can draw. In some cases, there may be opportunities for collaboration.

4. Contributions by individual TWG members

4.1 Djafer Benachour gave a presentation on "Education and Outreach: Towards whom and at what levels". He said that there had been many education and outreach programmes organised by different institutions towards different audiences and engaged at different levels. The main objective of these programmes was to increase awareness of the good uses of chemicals, in academic institutions as well as in chemical industries. Professor Benachour said that despite all these efforts, the impact had not been what was expected. New questions now arise concerning the tools and means to be used: should the mass media (TV, internet etc.) be used? Should the OPCW work closely with related international organizations (BWC, IAEA, CTBTO, WHO etc.)? What role would international scientific bodies play (IUPAC etc.)?

4.2 Temechegn Engida said that the Federation of African Societies of Chemists (FASC) is a federation of national chemical societies in Africa. It has conducted workshops on chemical safety and security in collaboration with Sandia National Laboratories in the USA. It also has an electronic journal entitled *African Journal of Chemical Education* (*AJCE*). Professor Engida said that *AJCE* is ready to publish a special issue on the CWC as it relates to education and outreach provided that the TWG members, or others, contribute articles. FASC will hold its 4th Congress on Green Chemistry for Sustainable Development in Africa from 7-9 May 2013 in Morocco.

4.3 Ting-Kueh Soon introduced the Federation of Asian Chemical Societies (FACS), a federation of 30 national chemical societies from the Asian Pacific region. Its main objective is to promote the advancement of chemistry and the interests of chemistry professionals in Asia. FACS is fairly active with a number of core activities including the flagship biennial Asian Chemical Congress. In recent years, members of FACS are actively involved in chemical safety and security issues and activities. Dr Soon said that together with Sandia National Laboratories, FACS has organized a number

of workshops on chemical safety and security, waste and pollution management, etc. in countries such as Malaysia, Thailand, Indonesia and the Philippines. Participants come from all over Asia including from Pakistan, Bangladesh, India and Afghanistan. FACS is interested in collaborating with the OPCW in promoting education and outreach on the OPCW, CWC, chemical safety and security, dual or multiple uses of chemicals etc. The target audience is academia, practicing chemists, secondary school students and the general public.

5. Briefings by OPCW and other international organizations on education initiatives in science and technology and disarmament and arms control, and lessons learnt

5.1 Michael Luhan of the Technical Secretariat presented the public diplomacy activities of the OPCW. The presentation covered several topics, including the OPCW website, social media, audiovisual productions, NGOs/civil society initiatives, and special projects (including a WMD Summer Programme, the Week of Disarmament and Non-proliferation, and the Open Day/Teachers' Day). The TWG then viewed a film, produced by the Technical Secretariat, focusing on the work of Chrétien Schouteten as a chemistry teacher and a writer of a theatre play about Fritz Haber. For many years, Mr Schouteten has developed educational materials for secondary schools in the Netherlands on the subject of chemical warfare and the social responsibility of chemists. The TWG members made many positive comments about the film, and emphasised the value in an educational setting of material which can inspire young students and which addresses ethical and moral questions. Many TWG members expressed an interest in using the film in their own teaching activities.

5.2 Jean du Preez and Ryan Gonzalez from the Preparatory Commission for the Comprehensive Nuclear Test-Ban Treaty Organisation (CTBTO) presented the capacity development initiative of the CTBTO and demonstrated its e-learning tools. Launched in 2010, the Capacity Development Initiative (CDI) is a key element of the CTBTO Preparatory Commission's training and education activities. The Initiative is focused on building and maintaining the necessary capacity in the technical, scientific, legal and political aspects of the Treaty and its verification regime. Through live lecture courses by Commission staff and top experts, and a robust e-learning platform, CDI promotes the active engagement with the current and next generation of CTBT experts. In addition, Mr du Preez said that a network of global partnerships with academic and research institutions is being established which represents mass educational outreach and collaboration. This provides the opportunity for integration of CDI modules into university curricula further expanding and sustaining the pool of CTBT expertise. By leveraging cutting edge technologies such as an open-source learning management system, social media, collaboration technologies and iTunes U, Mr du Preez said that the CDI has the potential to reach beyond the traditional pool of stakeholders. Further collaboration with international organizations, especially the OPCW, could result in a "one stop shop" culminating in a comprehensive disarmament curriculum. Lessons learned to date from utilizing e-learning platforms and education activities between the various organizations are very useful and should be further explored.

5.3 Andrea Braunegger-Guelich from the International Atomic Energy Agency (IAEA) briefed the TWG on the nuclear security education programmes of the IAEA. The presentation covered several topics including: What nuclear security is and why the international community is concerned about it; International instruments for nuclear security; Objectives of the IAEA Human Resource Development Programme; Nuclear Security Training Programme; IAEA Efforts supporting Nuclear Security Education; and how the IAEA collaborates with the academic and scientific community through the International Nuclear Security Network (INSEN). Ms Braunegger-Guelich highlighted several areas of potential commonality between the initiatives of the IAEA, the OPCW, and other international organisations including: teaching approaches; development of faculty members; development of stimulating teaching materials; faculty exchange; evaluation methods; and ways in which to bring educators together with subject matter experts.

6. Ways in which to raise awareness of the Chemical Weapons Convention in the education sector

6.1 The TWG discussed a range of options for raising awareness in the education sector, and members suggested the following activities or initiatives:

- Make contact with the steering committee of the International Chemistry Olympiad (IChO) to see whether information on the OPCW and CWC can be included in future events.

- Update the IUPAC/OPCW "Multiple Uses of Chemicals" material to include new video content and other technology. This material is intended specifically for use within universities. The TWG recommended that the material should be accessible through both the OPCW and IUPAC websites. It is not on the OPCW website at present.

- Prepare targeted teaching and other resource materials for high school teachers and involve the teachers who will be using the material in its development. One TWG member offered to follow-up this recommendation with teacher development groups in his own country, and to involve other TWG members.

- Encourage national chemical societies and national associations of science education to promote awareness of the CWC in educational institutions and with science educators.

- Suggest that, during his regular visits to States Parties, the Director-General should request to visit Ministries of Education/Science and talk to Ministers, senior civil servants, and industry.

7. How can the OPCW further develop its relationships with the scientific community and the chemical industry?

7.1 Following a discussion, the TWG suggested that the OPCW should consider, *inter alia*, the following:

- Further development of the OPCW's contacts with IUPAC's Committee on Chemistry Education;

- Identification and promotion of "top-end champions" (i.e. presidents of national chemical societies) at a high-level within States Parties, and identification of key organisations, with which the OPCW can cooperate;

- Seek opportunities to arrange side events at selected scientific conferences which attract large numbers of chemical professionals;

- Encouraging the teaching of ethics as part of the training for scientists by incorporating the CWC into existing ethics courses within the context of the responsible conduct of science; and

- Engage the scientific and academic communities and the chemical industry in awareness-raising and professional conduct on the CWC and OPCW, through the amendment of existing codes of conduct or the development of new ones, and through training.

7.2 With respect to the chemical industry, the TWG suggested that the OPCW could focus activities on chemical traders and brokers, and also on industry associations. The TWG also referred to the recommendations contained in the Report of the Advisory Panel on Future OPCW Priorities (see paragraphs 45 and 119 of S/951/2011, dated 25 July 2011), particularly the recommendation to establish a group of experts from industry.

7.3 TWG members also felt that the National Authorities should be informed of all activities, in order that they might offer their support. National Authorities will be an important partner in future education and outreach activities.

8. How can the OPCW contribute towards expanding and promoting a culture of responsibility in the scientific community and the chemical industry?

8.1 With respect to fostering a culture of responsibility within the scientific community and the chemical industry, the TWG made a number of suggestions, *inter alia*:

- Seek connections with those implementing Responsible Care, to encourage that adequate attention is given to the CWC;

- Review existing codes of conduct in industry associations and explore whether they need to be expanded or amended. All TWG members were encouraged to undertake comparable activities in their own home countries; and

- TWG members to review existing national codes of conduct, in particular any elements related to the CWC and to explore processes for inclusion of elements into existing codes if not already there. Based on these results to consult with the IUPAC leadership about possible additional initiatives.

9. Sustainable ways in which the OPCW can take forward its education and outreach activities

9.1 Mark Albon of the Technical Secretariat, provided a presentation on the OPCW's recent e-learning initiative.

9.2 TWG members made several proposals for sustainable ways in which the OPCW can take forward education and outreach:

- Development of a museum exhibition, perhaps in collaboration with other international organisations, and perhaps as a travelling exhibition. Members noted that the OPCW has a science museum within its immediate vicinity;

- Engage "top-end champions" in strategic planning discussions about what it will take to make the proposals emanating from the TWG sustainable;

- In the medium to long-term, funding for education and outreach activities should be included in the regular OPCW budget. In the short term, States Parties should be encouraged to provide voluntary contributions for education and outreach activities;

- Identify sources of funding at the national level, and encourage government funding to support national education and outreach activities;

- Have a separate topic item on education and outreach at the annual meetings of National Authorities;

- Engage States Parties on education and outreach during the annual sessions of the Conference of the States Parties and during the Review Conferences; and

- Encourage NGOs to become more engaged with OPCW education and outreach activities, and assist the OPCW to examine how to engage more effectively with NGO community.

10. Existing initiatives in this area with a view to avoiding duplication and allowing the OPCW to build relationships with other international organisations, professional associations, networks etc

10.1 The TWG recommended that the OPCW strengthen its links with other selected relevant international organisations, such as the CTBTO, the Implementation Support Unit of the Biological Weapons Convention, the IAEA, the World Health Organization, the Intergovernmental Forum on Chemical Safety, the International Programme on Chemical Safety, the World Anti-Doping Agency, the United Nations Office of Disarmament Affairs, United Nations Educational, Scientific and Cultural Organization etc. In addition, the OPCW should also strengthen, and initiate where necessary, relations with IUPAC, the International Union of Toxicology, the International Union of Biochemistry and Molecular Biology, the InterAcademy Council, the InterAcademy Panel, the International Council for Science, and other

umbrella scientific organizations. It would be worthwhile for the OPCW to look for fora that bring together several international organisations, and to make links with relevant regional security organizations.

10.2 TWG members suggested that attendance at high-level international conferences such as the Science and Technology in Society Forum and the World Science Forum would allow the Director-General or other senior Technical Secretariat staff to raise awareness of the CWC to large numbers of chemistry professionals.

11. Topics for intersessional work and next meeting

11.1 TWG members agreed to several topics for intersessional work and for discussion at the Group's next meeting. TWG members will:

- Look at commonalities, lessons learned and successful practices of other international organisations, professional associations, NGOs etc;
- Review the conclusions and findings of an IUPAC/OPCW conference in 2005 at Oxford University on education and outreach and on codes of conduct;[2]
- Compile a list of codes of conduct and post them on the TWG portal;
- Explore the development of high school and university teaching materials, including the conduct of a pilot project to develop materials for high school students within the Netherlands;
- Explore the development of materials for awareness-raising within the chemical industry;
- Approach their own domestic partners and identify any relevant domestic resources;
- Put together a calendar of related conferences at which side events might be arranged; and
- Undertake a stakeholder analysis and explore the most effective ways to identify and engage the most relevant partners.

11.2 The TWG felt that it would be useful to hold the next meeting of the TWG no later than early 2013, and that it would be good to take advantage of the presence of TWG members at other events during the intersessional period. The TWG will also utilize electronic communication tools to conduct its work intersessionally.

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2 Graham Pearson and Peter Mahaffy, "Education, outreach, and codes of conduct to further the norms and obligations of the Chemical Weapons Convention (IUPAC Technical Report)", *Pure and Applied Chemistry*, (2006), Vol. 78, No. 11, pp. 2169-2192. Available on the internet at http://stage.iupac.org/publications/pac/78/11/2169/

12. Any other business

None.

13. Summary of conclusions and recommendations

In conclusion, adequate funding is essential for sustainable education and outreach activities, the Technical Secretariat should identify a focal point specifically for issues relating to education and outreach, and the Director-General can play an effective role as an "ambassador" for education and outreach. The TWG will take forward the intersessional work identified above.

14. Closure of the meeting

The Chairperson closed the meeting at 18:25 on 13 April 2012.

Appendices:

Appendix 1: List of participants in the First Meeting of the Temporary Working Group on Education and Outreach in Science and Technology Relevant to the CWC

Appendix 2: Terms of Reference of the Temporary Working Group on Education and Outreach in Science and Technology Relevant to the CWC

Appendix 1

LIST OF PARTICIPANTS IN THE FIRST MEETING OF THE TEMPORARY WORKING GROUP ON EDUCATION AND OUTREACH IN SCIENCE AND TECHNOLOGY RELEVANT TO THE CWC
THE HAGUE, THE NETHERLANDS[1]
12 – 13 April 2012

	Participant	Institution
1.	Apotheker, Jan	University of Groningen, the Netherlands
2.	Benachour, Djafer[2]	Ferhat Abbas University, Ministry of Higher Education and Scientific Research, Setif, Algeria
3.	Coleman, Philip	Protechnik Laboratories, Lynnwood Glen, South Africa
4.	Engida, Temechgn	Addis Ababa University, Ethiopia
5.	Hay, Alastair	University of Leeds, United Kingdom
6.	Husbands, Jo	National Academy of Sciences, Washington, D.C., United States of America
7.	Maennig, Detlef	Evonik Industries AG, Hanau-Wolfgang, Germany
8.	Mahdi Balali-Mood	Medical Toxicology Centre, Imam Reza Hospital, University of Medical Sciences, Mashhad, Islamic Republic of Iran
9.	Mathews, Robert	Defence Science and Technology Organisation, Melbourne, Australia
10.	Soon, Ting-Kueh	Malaysian Institute of Chemistry, Kuala Lumpur, Malaysia
11.	Suárez, Alejandra Graciela	Universidad Nacional de Rosario, Argentina

[1] Peter Mahaffy (King's University College, Edmonton, Canada) could not attend the first meeting of the TWG.

[2] Chairman of the TWG.

Appendix 2

TERMS OF REFERENCE OF THE TEMPORARY WORKING GROUP ON EDUCATION AND OUTREACH IN SCIENCE AND TECHNOLOGY RELEVANT TO THE CWC

1. Education and outreach in science and technology relevant to the Chemical Weapons Convention (hereinafter "the Convention") is important to the Convention's future implementation. Education and outreach serves a number of purposes including, *inter alia*:

    a. raising awareness of the Convention among the broad community of relevant professionals who should be aware of the Convention, including: students, educators, the global scientific community and the chemical industry;

    b. stressing the potential risks posed by the multiple uses of chemicals;

    c. contributing to national implementation of the Convention;

    d. contributing to the prevention of the misuse of toxic chemicals;

    e. facilitating chemical safety and chemical security; and

    f. building skills and capabilities in areas relating to the peaceful uses of chemistry.

2. More broadly, the United Nations undertakes work on disarmament and non-proliferation education and training, following the report of the Secretary-General (A/57/124).

3. At its Seventeenth Session, the Scientific Advisory Board (SAB) recommended that a temporary working group on Education and Outreach on Science and Technology Relevant to the Convention be established (paragraph 16.6 of SAB-17/1, dated 23 November 2011). The Director-General endorsed this recommendation and, in accordance with paragraph 9 of the terms of reference of the SAB, established the working group and appointed Professor Djafer Benachour as the Chair of the group.

4. The objective of the temporary working group is to build on earlier work in this area by the SAB and its members, to utilise the experience of other initiatives in this field and related areas, and to make recommendations to the SAB for sustainable activities which could be pursued by the OPCW and its Member States.

5. The temporary working group on education and outreach will consist of individuals with expertise in: the state of play of education and outreach in science and technology relevant to the Convention; potential developments in science and technology relevant to the Convention; state-of-the-art tools and techniques for education and outreach; public and media affairs; science and technology research

and education policy; and perspectives from the chemical industry. Qualified experts of the SAB may also wish to join the group. Members of relevant international organisations, professional associations and scientific unions may also be invited to join the group. The temporary working group will also, when necessary, draw upon the expertise of the Technical Secretariat.

6. The temporary working group is requested to report to the SAB on the following:

    a. Ways in which to raise awareness of the Convention in the education sector, in particular through:

        i. the development of teaching materials;

        ii. promoting faculty development and student exchange;

        iii. promoting the inclusion of the Convention in educational curricula.

    b. Proposals for how the OPCW could further develop its relationships with the scientific community and the chemical industry with a view to raising awareness of the requirements of the Convention and promoting universal adherence to it;

    c. Proposals for how the OPCW could contribute towards expanding and promoting a culture of responsibility in the scientific community and the chemical industry;

    d. Existing initiatives in this area with a view to avoiding duplication and allowing the OPCW to build relationships with other international organisations, professional associations, networks etc;

    e. Sustainable ways in which the OPCW can take forward its education and outreach activities once the TWG completes its work.

7. This temporary working group will exist for three years from the date of its first meeting, at which time its work will be reviewed by the SAB and the Director-General and a decision will be made as to whether it should continue its work and whether the Terms of Reference should be revised.

Annex 3

FAST GAS CHROMATOGRAPHY-MASS SPECTROMETRY IN ON-SITE ANALYSIS

BRIEFING NOTE TO THE DIRECTOR-GENERAL PREPARED BY THE SCIENTIFIC ADVISORY BOARD, APRIL 2012

1. INTRODUCTION

On-site inspections involving sampling and analysis must be completed within a time frame of 24-72 hours, depending on the nature of the inspection. This makes it essential that procedures for setting up equipment, analysis and reporting are as efficient as is reasonably possible. In recent Schedule 2 inspections, only 2 or 3 samples were analysed during each inspection.

The primary technique used for on-site analysis is gas chromatography combined with mass spectrometry (GC-MS). The individual stages of the analytical procedure are:

- sample preparation (to a form suitable for analysis)
- separation of the individual chemicals on a gas chromatograph
- detection and identification of these chemicals using on-line mass spectrometry
- data analysis and reporting.

The time limiting elements of this procedure are usually sample preparation and gas chromatographic separation. Fast GC is a modification that allows shortening of the time for gas chromatographic separation.

2. GC-MS AS USED FOR ON-SITE ANALYSIS

Gas chromatography separates volatile chemicals in a mixture in the gas phase on the basis of boiling point and/or differential interactions with the internal coating (stationary phase) of a long (typically 25-30 m) coiled capillary column. The sample is introduced into the column through a heated injector, into a stream of carrier gas (usually helium). The column is enclosed in a programmable oven and the temperature is progressively raised, typically from ~40°C to 280°C. As the components elute from the column they are introduced directly into the ion source of the mass spectrometer. The time taken for a chemical to pass through the column is characteristic of that chemical and is known as the absolute retention time.

In the ion source of the mass spectrometer the molecules are ionised by an energetic stream of electrons (electron ionisation, EI). This produces a positively charged molecular ion, which breaks into structurally characteristic fragment ions. Measurement of the mass and relative abundance of these ions provides a mass spectrum, which is a near-unique fingerprint of the chemical. The mass spectrometer is equipped with a data system which automatically compares the mass spectrum with those in its database.

In addition to its mass spectrum, each chemical is identified on the basis of its 'retention index (RI)'. This is a numerical measure of the time taken to elute from the GC column, i.e. the retention time, relative to a series of hydrocarbon standards. Retention indices minimise

the effects of small differences in GC conditions between runs, between laboratories and different instruments, and are much more reproducible than absolute retention times.

For OPCW inspections approved by the Executive Council, the primary database used is the OPCW Central Analytical Database (OCAD), which contains mass spectra and retention indices of more than 4000 scheduled chemicals and their derivatives. This data has been assessed and accepted by the validation groups consisting of experts from the Technical Secretariat and Designated Laboratories. Inspectors may also use other more comprehensive databases if approved by the inspected party. The software used to process and interrogate the data is called AMDIS.[1] In setting up the GC-MS system for on-site analysis, a quality control mixture of seven carefully chosen chemicals is used to test a range of instrumental parameters. The OPCW Standard Operating Procedure requires the RIs for these chemicals to be within ±5 RI units of the OCAD specified values.[2] For OPCW Proficiency Tests and authentic sample analysis, RI values, if used for identification, must be within ± 20 units of the OCAD values.

3. FAST GC

As its name suggests, fast-GC allows mixtures of chemicals to be separated in a much shorter time than conventional GC whilst maintaining adequate chromatographic resolution. There is no strict definition of fast GC but typically it refers to total GC separation times of 5-10 minutes, compared to 25-40 minutes for a conventional GC run. This can be achieved by one or more of the following modifications:

- increasing the heating rate of the oven
- reducing column length
- reducing column inner diameter
- reducing the thickness of the inner coating of the column (the stationary phase)
- increasing the carrier gas flow-rate
- using hydrogen instead of helium as carrier gas

Each of these modifications has limitations, e.g. resolution of components may be compromised, the capacity of the column with regard to sample loading may be reduced, very fast separation may put additional demands on the acquisition rate required of the mass spectrometer. For OPCW on-site identification, an important limitation is that retention indices for chemicals in the quality control mixture, and those for scheduled chemicals, must remain within specified criteria, otherwise false negative or false positive identifications may occur.

GC separation times may be reduced up to 5-6 fold using conventional GC-MS instrumentation by simple modification of the temperature programme, column dimensions, and carrier gas. It should be noted that the time taken for the GC oven to cool to its starting temperature between runs adds significantly to analysis time (approximately 10 minutes). With instrumentation designed or modified specifically for the purpose of fast GC (e.g. with specially heated and cooled ovens) reduction in separation time can be much greater and may be referred to as 'very fast' or 'ultra fast' GC. In these cases, a different type of mass

1 Automated Mass Spectral Deconvolution and Identification System
2 QDOC/LAB/W1/GCMS10

spectrometer (time of flight) is more appropriate than the quadrupole instruments used in on-site inspections.

The suitability of fast GC is application dependent, according to the complexity of the samples, the range of analytes to be identified, and the demand for high throughput. For on-site inspections, sufficient resolution must be maintained by the GC to reliably identify the very wide range of scheduled chemicals, and the error margin allowed for retention indices must be maintained. The incorporation of fast GC into on-site procedures would be counterproductive unless it is robust with regard to the reproducibility of RIs and mass spectra.

4. INVESTIGATIONS BY DESIGNATED LABORATORIES AND THE OPCW LABORATORY

Fast GC in the context of on-site inspections and other applications has been discussed by the SAB Temporary Working Group on Sampling and Analysis. Members from three Designated Laboratories, VERIFIN (Finland), Defence Science and Technology Laboratory, Dstl, (United Kingdom) and Protechnik (Republic of South Africa), reported results of preliminary or on-going fast GC studies. The procedures used faster GC oven programmes, shorter, narrower columns with thinner stationary phases, and faster carrier gas rate. All three laboratories achieved significantly reduced GC run times (up to five-fold reduction) whilst maintaining good resolution of a wide range of scheduled chemicals plus quality control mixtures. However, with a 5-fold reduction in run time, some variance in RIs was observed beyond acceptance criteria for some components of the OPCW test mixture. Acceptable results were reported for a range of scheduled chemicals. Dstl found that changing the carrier gas to hydrogen reduced retention times compared to helium, but was not acceptable because of distortion of some of the mass spectra.

Work undertaken in the OPCW Laboratory has indicated that a modest 50% reduction in separation time (17 min *vs* 32 min) provides a more robust procedure with regard to RIs and peak identification using AMDIS software, although minor variance in RIs remains a problem. Two shorter procedures (separation times 8.4 and 13.6 minutes respectively) have been investigated by a VERIFIN intern.[3] VERIFIN recommended that for on-site analysis the OPCW laboratory assess the second of these, which significantly reduces run times whilst maintaining good resolution.

A 50-70% reduction in GC separation time represents a relatively small reduction in the overall time for setting up, sample preparation, analysis and reporting. Sample preparation can be time consuming, particularly in the case of aqueous samples, and is another aspect of the analytical procedure that is being investigated. The Technical Secretariat has also commenced a review of the entire on-site process to determine if time may be saved in other aspects.

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[3] Tran Duc Hung, The applicability of fast GC-MS for the analysis of CWC – related chemicals. Finnish Institute for Verification of Chemical Weapons Convention (VERIFIN), 19th January – 18th May 2009.

5. CONCLUSIONS

Fast GC has the potential to shorten one component of sampling and analysis time in on-site inspections. By changing the temperature programme, column dimensions and carrier gas flow rate, GC run times can be shortened up to approximately five fold using conventional equipment without significant loss in resolution of a wide range of scheduled chemicals. A limitation of fast GC is that some variation in retention indices, compared to those in the OCAD, has been observed. This limitation has to be weighed against a relatively modest reduction in overall setting up and analysis time. Further development of a fast GC procedure is in progress in the OPCW Laboratory in collaboration with VERIFIN, to assess the most suitable method for on-site analysis.

Fast GC also has applications in off-site laboratories where high throughput is required, and in mobile laboratories where rapid identification is required to ensure public safety. In these cases GC-MS instrumentation designed specifically for fast GC may be used, and small variations in retention indices may be less of an issue. Because of the problem with retention indices, this type of fast GC is probably not appropriate for the requirements of OPCW on-site analysis.

Annex 4

REVISED 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 generically to refer to structurally related neurotoxins (analogues of saxitoxin) produced by the same microorganisms. These include neosaxitoxin (neoSTX), the gonyautoxins (GTX) and decarbamoylsaxitoxin (dcSTX). These molecules range in molecular mass from 250 to 500 Da, depending on the substituent groups.

Nomenclature

The term saxitoxin originates from the species name of the butter clam (*Saxidomus 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.[1] The term 'saxitoxin' was originally used in reference to the dihydrochloride salt.[2] In the early 1980s, one chemistry manual referred to the free base as saxitoxin.[3] Since the late 1980s, the di-cation, in which the two basic nitrogens are protonated, has frequently been referred to as saxitoxin, without specifying the associated anions (i.e. which salt).[4] More recently (and since the negotiations on the Chemical Weapons Convention were concluded in 1992), the nomenclature of saxitoxin has become more specific, distinctions are now made between saxitoxin hydrate[5] (free base) and the dihydrochloride salt, which have different CAS numbers.[6] To avoid confusion, the former is hereinafter referred to as saxitoxin hydrate (free base). For consistency, the dihydrochloride salt should strictly be referred to as saxitoxin hydrate dihydrochloride salt.

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1 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).

2 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).

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

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

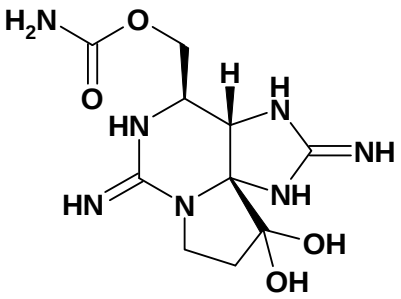
5 The inclusion of 'hydrate' in the name arose from initial uncertainty on whether the 10 position on the molecule was a ketone [C=O] or its hydrate [$C(OH)_2$].

6 Richard J. Sax Sr, Sax's Dangerous Properties of Industrial Materials, 9th Edition (1995); saxitoxin hydrate CAS No 35523-89-8; saxitoxin dihydrochloride CAS No 35554-08-06.

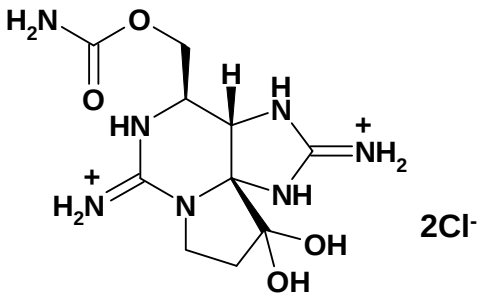
The systematic IUPAC name for naturally occurring (+)-saxitoxin hydrate (free base) is: (3aS, 4R, 10aS) 2,6-diamino-4-[[(aminocarbonyl)oxy]methyl]-3a,4,8,9-tetrahydro-1H,10H-pyrrolo[1,2-c]purine-10,10-diol.

Saxitoxin is traded, e.g. in diagnostic kits, mainly as the dihydrochloride salt or as the diacetate salt. Saxitoxin hydrate (free base) has poor stability and is rarely traded.

Structure of saxitoxin



saxitoxin hydrate (free base)



saxitoxin dihydrochloride salt

Sources of saxitoxin

Saxitoxin can be isolated (usually as a salt) from bivalve molluscs (e.g. the butter clam *Saxidomas giganteus*) that have accumulated PSP-producing dinoflagellates (e.g. *Gonyaulax catanella*) during feeding. In one reported experiment about 8 tonnes of clams were processed to produce a single gram of saxitoxin.[7]

Saxitoxin can also be produced by liquid culture of the dinoflagellate species *Gonyaulax catanella*, although yields have been well below those that would be required to use saxitoxin as a chemical warfare agent.

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%.[8] More recently, saxitoxin has been synthesised in a 19-step synthesis with an overall yield of 1.6%.[9]

Main clinical features[10]

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

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

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

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

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

action potentials, leading to muscle paralysis.[11] 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, with death 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. Following exposure through inhalation, most of the symptoms would occur much faster.

Protective Measures[12]

Diagnosis of saxitoxin poisoning is confirmed by detection of the toxin, most commonly using enzyme linked immunosorbent assay (ELISA), other immunoassay, LC-fluoresence or LC-MS/MS in samples of, for example, stomach contents, water or food. A mouse bioassay, commonly used in the past, is declining in use.

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 casualties 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 as a tool in neurochemical research, including electrophysiological studies.

Saxitoxin as a CB Weapon

Saxitoxin hydrate dihydrochloride salt was first isolated in small quantity at the US Army Fort Detrick laboratory in the 1950s, designated as Agent TZ, and was investigated as a potential weapon.[13] Agent TZ was weaponised in the M1 Biodart (E1) flechette system in the 1950s and 1960s.[14]

Saxitoxin hydrate (free base) and its salts are soluble in water. The free base dissolves in water to produce an alkaline solution but is unstable at this pH. Saxitoxin has good stability in water at neutral and weak to moderately acidic pH. It is supplied in acidic solution in diagnostic kits. Dispersal of saxitoxin hydrate dihydrochloride as an aerosol is feasible. No cases of human inhalation exposure have been reported in the medical literature, but animal

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11 The dication is the form of saxitoxin that binds to the sodium channels on cell membranes. At physiological pH saxitoxin exists predominantly as the di-cation, partly as a mono-cation.

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

13 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.

14 *The Problem of Chemical and Biological Warfare*, Vol II, CB Weapons Today. SIPRI, Stockholm, 1973, p. 62.

experiments suggest that the entire syndrome is compressed, and that death may occur within minutes.[15]

Saxitoxin and the CWC

Saxitoxin was proposed for inclusion in the CWC Schedules of Chemicals by the USA in 1984,[16] 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 (i.e. Agent TZ, the dihydrochloride salt), and other forms of weaponisable saxitoxin.[17] When CAS Numbers were assigned to the chemicals in the CWC Rolling Text in the late 1980s, saxitoxin was assigned the CAS Number of saxitoxin hydrate (free base) on the understanding that the CAS Numbers were intended to be 'identification aids' rather than 'unique identifiers' for the various scheduled chemicals.[18] In the CWC 'end-game' in 1992, it was agreed that 'saxitoxin' would be placed in Schedule 1.

Verification

The identification of saxitoxin in environmental and man-made samples has been addressed by the SAB Temporary Working Group (TWG) on Sampling and Analysis.[19] The TWG recommended two methods of identification should be used, one essentially for screening, and the second for confirmation. Lateral flow immunoassays (LFA), qualitative ELISA and LC with fluorescence detection were recommended as screening assays, as widely used in the food and fishing industries, ^{1}H-NMR is also appropriate if obtainable. For confirmation the TWG recommended liquid chromatography combined with tandem mass spectrometry (LC-MS/MS) or with high resolution mass spectrometry (LC-HRMS).

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

16 USA, CD/500, (1984)

17 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).

18 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).

19 SAB-16/1 Annex 2.

Annex 5

RICIN FACT SHEET

PREPARED BY THE OPCW SCIENTIFIC ADVISORY BOARD, APRIL 2012

1. INTRODUCTION

Ricin[1] is a potent proteinaceous toxin found in the seeds of the castor bean plant (*Ricinus communis*) (Figure 1). It is a controlled chemical under Schedule 1A of the Chemical Weapons Convention (CWC), and is a Category B substance under the Biological and Toxins Weapons Convention (BTWC). Ricin has attracted interest as a military chemical/biological warfare agent and as a poison for criminal and terrorist use.[2]

Figure 1: The castor bean plant *Ricinus communis* and its seeds (castor beans).
[Seed figure from Wikipedia]

2. STRUCTURE

Ricin is a glycosylated protein consisting of two globular polypeptide chains, an A-chain and a B-chain containing 267 and 262 amino acid residues respectively, linked by a disulfide bond, and to which various glycoside (sugar) chains are attached.[3] Both chains are required for high toxicity (see below). Ricin has an approximate molecular mass of 65 kDa but is not a homogeneous chemical entity. Variations occur in the attached glycoside chains, and a small number of variants (isoforms) have been identified in the amino acid sequence of the polypeptide chains.[4] Genetically modified forms of ricin are possible. In response to a request from the Director General, the Scientific Advisory Board (SAB) proposed the following definition of ricin for verification purposes:[5]

"*All forms of ricin originating from Ricinus communis, including any variations in the structure of the molecule arising from natural processes, or man-made modification*

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1 CAS registry number as listed in Schedule 1, 9009-86-3

2 Ricin. Threat, effects and production. FOI User Report FOI-R-1261-SE (2004).

3 Lord J M, Roberts L M and Robertus J D. Ricin: structure, mode of action, and some current applications. *FASEB J*, 8, 201-208 (1994).

4 Despeyroux D, Walker N, Pearce M et al. Characterization of ricin heterogeneity by electrospray mass spectrometry, capillary electrophoresis, and resonant mirror. *Analytical Biochemistry*, 279, 23-36 (2000).

5 OPCW Scientific Advisory Board, SAB-14/1, 11 Nov 2009.

designed to maintain or enhance toxicity, are to be considered ricin as long as they conform to the basic 'native' bipartite molecular structure of ricin that is required for mammalian toxicity, i.e. A and B chains linked only by a disulfide bond (A-S-S-B). Once the inter-chain S-S bond is broken or the protein denatured it is no longer ricin."

3. SOURCES OF RICIN

The castor bean plant is widespread in hot climatic regions and is grown in temperate regions as an ornamental plant. It is cultivated industrially for the production of castor oil (used in a wide range of products including lubricants, hydraulic fluids, paints, textiles, polymers, and medically as a purgative). More than one million tonnes of seeds are processed annually. India, China and Brazil are the major producers of castor oil. The seeds typically contain 30-60% by weight of castor oil (predominantly ricinolate, a triglyceride of 12-hydroxyoleic acid); the ricin content is typically 1-5% by weight of the residual solid after removal of the oil. The oil is extracted by cold or more commonly hot hydraulic pressing, plus solvent extraction (hexane or heptane) of oil remaining in the mash. The residue from these processes is used as livestock feed or as fertiliser after the ricin has been deactivated by heating. Castor oil production plants are not subject to Schedule 1 inspections under Article VI of the CWC, but the SAB recommended that the Director-General encourage National Authorities in producing countries to promote hot pressing and other techniques that ensure inactivation of residual ricin in the waste mash.[6]

Several recipes for the isolation of ricin from castor seeds are available in the scientific literature and on the Internet. Crude ricin is easily prepared from ground seed by extractive removal of the oil with acetone, ether or hexane, and extraction of the water-soluble protein fraction into mildly acidified water (e.g. with acetic acid). If not detoxified, ricin and other proteins can be extracted into dilute acid from the waste mash from castor oil production, and precipitated with ammonium sulfate. The ricin can be purified by chromatography. The isolated ricin is a water-soluble white powder that is stable under normal ambient conditions.

4. TOXICITY

The lethal doses of ricin in experimental animals by inhalation and by parental routes of administration are mostly in the low microgram per kilogram range, typically 1-10 μg/kg.[7] For comparison, the most toxic nerve agents would fall within the upper part of this range. A lethal dose of botulinum toxin A, the most potent bacterial toxin, would be in the range 1-10 ng/kg. Inhalation toxicity is also likely to be in the range 1-10 μg/kg, depending on aerosol particle size, particles that are able to penetrate deep into the lungs (1-5 μm diameter) being considerably more toxic than larger

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6 OPCW Scientific Advisory Board, SAB-II/1, Section 2 and Annex 1

7 Millard B and LeClaire R D. Ricin and related toxins: review and perspective. In: Romano J, Lukey B, Salem H (eds), *Chemical Warfare Agents 2nd Edition*, CRC Press, New York, 2008, pp. 423-467.

particles.[8] Ricin is approximately 3 orders of magnitude less toxic by ingestion due to poor absorption from the gastro-intestinal tract, lethal doses being in the low mg/kg range. There are significant species differences in toxicity, up to 100 fold, rabbits being one of the more susceptible species. The human lethal dose by ingestion has been estimated as 1-20 mg/kg, and by injection 1-10 μg/kg, but no reliable data exists. There is no documented information on confirmed human exposure to ricin by inhalation. Ricin is unlikely to be effective by contact with intact skin due to poor absorption. No toxicity was observed in mice dermally exposed to ricin at 50 μg per spot.[9]

5. MECHANISM OF ACTION

The toxicity of ricin results from its ability to inhibit protein synthesis in eukaryotic cells.[10] It is part of a larger group of proteins known as type 2 ribosome-inactivating proteins (RIPs). This group includes other toxins from higher plants, e.g. abrin, pulchellin, modeccin, volkensin and viscumin, and some bacterial Shiga and Shiga-like toxins. RIPs have enzymatic *N*-glycosidase activity. They catalyse the hydrolytic cleavage of a specific *N*-glycoside bond between an adenine base and ribose residue of ribonucleic acid (RNA) in the 28S subunit of eukaryotic ribosomes. The catalytic glycosidase activity of ricin and similar toxins resides in the A-chain. The B-chain is a lectin (a sugar binding protein), which binds to terminal galactoside residues in sugar chains on cell surfaces. The attached A-chain is subsequently delivered to its ribosomal target inside the cell through a process of endocytosis, and after cleavage of the disulfide bond inside the cell. Both A and B chains are required for high toxicity. Following termination of protein synthesis a process of programmed cell death occurs (apoptosis).

6. CLINICAL FEATURES OF RICIN INTOXICATION

Cell death following ricin intoxication may lead to tissue damage, organ failure and eventual death.[11] This progression generally occurs over 1-5 days in experimental animals and man, depending on the dose and route of intoxication. Clinical signs of poisoning and pathology reflect the organs most effected, which vary with the route of exposure. Many features can be explained by damage to endothelial cells resulting in fluid/protein leakage and tissue oedema (vascular leakage syndrome). Loss of appetite, lethargy and flu-like symptoms are common early signs.

Poisoning by ingestion is characterized by lesions of the gastro-intestinal tract, manifested by slow onset (hours) of vomiting, diarrhoea, gastric haemorrhaging,

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8 Data submitted to the SAB Temporary Working Group seminar by Gareth Griffiths, CBD Porton Down, United Kingdom, in his presentation 'Toxicity of ricin (parenteral and inhalation routes)', 22–23 March 1999.

9 Franz D R and Jaax N K. Ricin toxin. In: Sidell F R, Takafuji E T, Franz D R (eds), *Medical Aspects of Chemical and Biological Warfare*, Office of the Surgeon General, Dept. of the Army, United States of America, 1997, pp. 631-642.

10 Audi J, Bebon M, Patel M *et al*, Ricin poisoning a comprehensive review, *JAMA*, 294, 2342-2351 (2005).

11 Bradberry S M, Lord J M, Rice P and Vale J A. Ricin and abrin poisoning. In: Marrs T C, Maynard R L, Sidell F R (eds), *Chemical Warfare Agents Toxicology and Treatment*, Second Edition, John Wiley & Sons Ltd, Chichester, UK, 2007, pp 613-632.

hypovolemic shock (from loss of blood volume) and organ failure, particularly of the spleen, liver and kidney. Depending on the dose, death may occur within 2-5 days. Injection of ricin produces swollen and haemorrhagic lymph nodes, severe internal bleeding and tissue damage, with the collapse of major organ systems. Inhalation of ricin causes slow onset (several hours) of respiratory distress (difficulty breathing), coughing, fever, pulmonary lesions and oedema. Depending on the severity of the exposure, respiratory failure and death may occur in 1.5-3 days. Exposure of the eyes causes severe irritation and conjunctivitis.

7. MEDICAL TREATMENT

No approved antidote to ricin is currently available although vaccines are in development.[7] Animal studies have shown that both passive administration of anti-ricin antibodies and active immunization with a formalin-inactivated toxoid have the potential to protect against ricin challenge. At least one vaccine for active immunization (for use in situations where a threat of exposure exists) has progressed to clinical trials, based on a recombinant A chain of ricin, modified to prevent vascular leakage through damage to blood vessel walls.

The progressive nature of ricin intoxication requires hospitalization and continual supportive care. Medical treatment is focused on eliminating the toxin from the body as quickly as possible, and symptomatic and supportive treatment to minimize the effects of poisoning. Examples are flushing of the stomach with active charcoal in the case of ingestion, administration of intravenous fluids and electrolyte replacement in cases of severe dehydration and hypovolemic shock, and ventilatory support following inhalation. Following ingestion of castor beans, patients who receive prompt treatment are likely to survive (and even without treatment survival rates are generally high).

8. POTENTIAL MEDICAL APPLICATIONS OF RICIN

Ricin was first shown to inhibit tumour growth in 1951. In more recent years it has been explored, as yet unsuccessfully, as the cytotoxic component of potential anti-tumour agents called immunotoxins. Ricin, or the catalytic A-chain (or genetic modifications thereof), is targeted at cancer cells by conjugation to a tumour cell-specific monoclonal antibody.[12] Ricin-based immunotoxins have also been studied for use in bone marrow transplants to destroy unwanted cells.

9. PRIOR MILITARY INTEREST AND WEAPONIZATION

Military interest in ricin arose from its relatively high toxicity (though significantly less than some bacterial toxins) combined with its widespread occurrence. For military use, other than for small scale poisoning, ricin would have to be disseminated as an inhalable aerosol, or possibly impregnated onto flechettes. It was investigated by the USA as a chemical agent towards the end of WW I but problems were encountered with thermal instability and aerosolization using explosive dissemination.

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12 Griffiths G, Leith A and Green M. Proteins that play Jeckyll and Hyde, *New Scientist*, 16 July 1987, 59-61.

Further development and field trials during WW II, under the code name 'W', resulted in limited weaponization in bombs.[2] Iraq reportedly attempted to weaponize ricin in the 1980s. Ricin is not known to have been used as a military weapon so its effectiveness as a chemical/biological warfare agent is unproven. Some observers have questioned its utility as a military warfare agent.[10]

10. CRIMINAL AND TERRORIST INTEREST

The availability of castor beans, plus the relatively simple procedure for the isolation of crude ricin, has attracted criminal and terrorist interest for small scale poisoning, or for causing disruption (e.g. letters containing traces of ricin in a white powder). There have been many reported incidents of individuals possessing or attempting to isolate small amounts of ricin at home or in makeshift laboratories. In many cases the motive was murder of an individual.[2] Publicity given to instances of illegal possession or use, often with exaggerated claims of the hazard ricin presents, has added to public awareness.[13] Trace amounts of ricin, and documents describing its isolation, have been found in laboratories in Afghanistan.

The most widely publicized criminal use of ricin was the politically motivated assassination of the dissident Bulgarian journalist Gorgi Markov in London in 1978, following an attempted assassination two months earlier of a second Bulgarian exile in Paris by similar means. Ricin was administered by injection of a tiny engineered metal pellet from a compressed gas device hidden in an umbrella. Markov felt immediate pain at the site of injection in the thigh, with slowly developing fatigue, nausea, vomiting and fever. These signs progressed to necrotic swollen lymph nodes, gastro-intestinal haemorrhage, hypovolemic shock and renal failure after 36 h, with death on the third day. It was estimated that he had received a dose of ~500 μg although ricin was never isolated or confirmed analytically.[14]

11. DETECTION AND VERIFICATION

Field detection

Many developmental field detectors for biological agents and toxins have been reported to have the capability to detect ricin.[15] Most rely on molecular recognition by antibodies. Enzyme linked immunosorbent assay (ELISA) in various formats has been the most widely used, e.g. using colorimetric, electrochemiluminescent, or colloidal gold reporter systems. Other types of immunoassay include immunochromatographic hand-held devices, and more recently fluorescence based immunoassays using fibre optics or quantum dots. As an alternative to antibodies, molecular recognition based on aptamers (nucleic acid or peptide sequences with selective recognition properties) has been described for multiple agent detection including ricin, e.g. in a microarray format, or coupled with surface enhanced Raman spectroscopy.

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13 Schep L J, Temple W A, Butt G A and Beasley M D. Ricin as weapon of mass terror – separating fact from fiction. *Environment International*, 35, 1267-1271 (2009).

14 Crompton R and Gall D. Georgi Markov – death in a pellet. *Medico-Legal Society Journal*, 48, 51-62 (1980).

15 Ler S G, Lee F K and Gopalakrishnakone P. Trends in detection of warfare agents. Detection methods for ricin, *Staphylococcal enterotoxin* B and T-2 toxin. *Journal of Chromatography A*, 1133, 1-12 (2006).

Laboratory detection and identification

As a large biologically active molecule, laboratory screening for ricin as a powder or in aqueous solution can be performed using immunoassays and functional bioassays.[16,17] Molecular recognition using different types of immunoassay, particularly ELISA, is widely used. ELISA is generally very sensitive (e.g. pg-ng/ml in aqueous solution) although cross reactivity with structurally related proteins can be a shortcoming. Functional bioassays have the advantage that they detect the biologically active molecule although specificity may be low. Examples of bioassays are toxicity in a small animal model or cell culture, and enzymatic activity (cleavage of an adenine residue) on an RNA preparation. The latter may be detected using fluorescence, electrochemiluminscence or mass spectrometric based assays. Specificity can be increased by using immunocapture to isolate the protein. Polymerase chain reaction (PCR) technology may identify the plant source of an environmental sample from residual traces of DNA from *Ricinus communis*, unless the ricin has been rigorously purified.

As a protein of known structure, ricin can be identified using mass spectrometry, usually in combination with liquid chromatography (LC-MS). Molecular masses are determined for the intact molecule, plus the mixture of smaller peptides ('peptide map') formed on selective digestion with enzymes such as pepsin or trypsin. The amino acid sequences of a selection of these peptides (minimum of three) are determined by liquid chromatography-tandem mass spectrometry (LC-MS/MS). Identification is confirmed by searching against protein databases or by comparison with an authentic sample. The SAB Temporary Working Group (TWG) on Sampling and Analysis has recently addressed identification criteria for the verification of ricin.[18] For OPCW purposes, the TWG recommended that ricin should be identified by at least two different techniques, a screening technique, for example from the immunoassays and bioassays described above, and confirmatory identification using LC-MS and LC-MS/MS.

Biomedical samples

Ricin is rapidly excreted from the body, predominantly as smaller peptide metabolites; typically up to 90% is excreted within 24 h in experimental animals. ELISA has been used for the detection of intact ricin in blood and other tissues up to at least 48 h after exposure, and in swab samples from nasal mucosa following inhalation in experimental animals. Circulating antibodies may be detectable after approximately two weeks in subjects who survive ricin intoxication. Some forensic laboratories analyse for the alkaloid ricinine in gastric contents and urine as a biomarker of ricin intoxication.[19] Ricinine is a low molecular mass (164 Da) component of castor seeds (typically 0.05-0.3% by weight) and is usually present in

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16 Ezan E, Duriez E, Fenaille F and Becher F. Functional assays for ricin detection, in, *Detection of Biological Agents for the Prevention of Bioterrorism*, Banoub J (ed), NATO Science for Peace and Security Series A - Chemistry and Biology, 131-147, 2010.

17 Musshoff F and Madea B. Ricin poisoning and forensic toxicology. *Drug Testing & Analysis*, 1, 184-191 (2009).

18 Report of the Sixth Meeting of the SAB Temporary Working Group on Sampling and Analysis, The Hague, The Netherlands, 17-18 November 2011. SAB-17/1, Annex 2.

19 Johnson R C, Lemire S W, Woolfitt A R et al., Quantification of ricinine in rat and human urine: a biomarker for ricin exposure. *Journal of Analytical Toxicology*, 29, 149-155 (2005)

crude ricin preparations. It is readily isolated from biological fluids and can be identified using LC-MS/MS at least up to four days following an intoxication.

12. DECONTAMINATION

Ricin can be detoxified by heating at 80°C for 10 min or 50°C for 60 min.[20] Hot pressing denatured ricin completely in the seed mash as indicated by non-responsiveness to an antibody.[21] Cold pressing generally leaves residual ricin. Treatment with sodium hypochlorite (bleach) also rapidly deactivates the toxin. It was almost completely detoxified by Chlorox domestic bleach within 15 minutes. [22]

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20 Mackinnon P and Alderton M. An investigation of the degradation of the plant toxin, ricin. *Toxicon,* 38, 287-291 (2000).

21 Barnes D J, Baldwin B S and Braasch D A. Degradation of ricin in castor seed meal by temperature and chemical treatment. *Industrial Crops & Products*, 29, 509-515 (2009).

22 Cole K, Gaigalas A and Almeida J, Process monitoring the inactivation of ricin and model proteins by disinfectants using fluorescence and biological activity. *Biotechnology Progress,* 24, 784-791 (2008).

Annex 6

DIRECTOR-GENERAL'S REQUEST TO PROVIDE ADVICE ON SITUATIONS WHERE A SCHEDULE 1 CHEMICAL IS AN UNAVOIDABLE BY-PRODUCT

1. When addressing the issue of occurrences of captive use of Schedule 1 chemicals[1], the SAB reported at its eight session[2] (in 2006) that "*there was a possibility that a Schedule 1 chemical (HN-3) would be formed as an impurity in the synthesis of pethidine-like compounds, for example, because of the presence (at approximately 1%) of triethanolamine in the diethanolamine used as a precursor".*

2. The SAB thereby pointed out the possibility of the production of unavoidable Schedule 1 by-product due to the presence of an impurity in the raw materials. In the example considered by the SAB previously, the impurity forms, after the reaction of chlorination, a Schedule 1 product which is present at a low concentration level in the reaction mixture.

3. Although it was not explicitly mentioned by the SAB, the Technical Secretariat assumes that (since the example was provided in the context of a study about captive use) the Schedule 1 chemical was considered to be immediately consumed in the production process.

4. The Director General would now like to seek the advice of the SAB where no consumption occurs of the unavoidable Schedule 1 by-product that has been produced. Such a case may occur since:

   a. many reactions resulting in the formation of a Schedule 1 chemical are common reactions (such as chlorination), widely used in chemical plant sites; and
   b. Schedule 1 direct precursors (such as triethanolamine) have many applications and can be found as additives or traces in several products.

5. Technical views are sought from the SAB by the DG in accordance with paragraph 21 h of Article VIII, especially if such cases could affect the operation of the CWC.

6. The Director General would like to ask the SAB to address the type of situation described in paragraph 4:

   a. What is the technical feasibility for using a reaction mixture containing a Schedule 1 chemical for activities prohibited by the CWC?
   b. Under which technical conditions can a Schedule 1 by-product be recovered?
   c. When addressing the example mentioned in paragraph 1, the SAB also stated: "*However, the nitrogen mustard would be present at such a low concentration*

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1 In the note S/528/2005 dated 1 November 2005 from the Technical Secretariat, the Executive Council's facilitator on Industry-Declaration submitted two questions to the SAB through the Director-General. These questions inquired as to 1) examples of Schedule 1 chemicals produced as intermediates, by-products, or waste products that are produced and consumed, are stable, and can possibly be isolated, but are not isolated, and 2) if the captive use exists, does it occur above the quantitative limits in VA Part VI?

2 Paragraph 2.2 of SAB-8/1, dated 10 February 2006.

[at approximately 1%] *that it would be difficult to isolate it from the reaction mixture."*[3] If it is possible to determine on a technical foundation, is there a concentration level under which it is considered so difficult to isolate a Schedule 1 chemical from the reaction mixture that this would not constitute a realistic technical possibility for activities prohibited by the CWC?

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[3] Ibid.