



OPCW

Scientific Advisory Board

Nineteenth Session
10 – 12 September 2012

SAB-19/1
12 September 2012
Original: ENGLISH

**REPORT OF THE NINETEENTH SESSION OF THE
SCIENTIFIC ADVISORY BOARD**

1. AGENDA ITEM ONE – Opening of the session and election of the Vice-Chairperson of the Scientific Advisory Board

1.1 The Scientific Advisory Board (SAB) met for its Nineteenth Session from 10 to 12 September 2012 at the OPCW Headquarters in The Hague, the Netherlands. The session was opened by the Chairperson, Stefan Mogl.

1.2 At the beginning of the Nineteenth Session, Alejandra Graciela Suárez of Argentina was unanimously elected as the Vice-Chairperson of the SAB, replacing Mahdi Balali-Mood of the Islamic Republic of Iran, whose term of office on the SAB had come to an end.

2. AGENDA ITEM TWO – Adoption of the agenda

The SAB adopted the following agenda for its Nineteenth Session:

1. Opening of the session and the election of the Vice-Chairperson of the Scientific Advisory Board
2. Adoption of the agenda
3. *Tour de table* to introduce Scientific Advisory Board Members
4. Welcome address by the Deputy Director-General
5. Overview of developments at the OPCW since the last session of the Scientific Advisory Board
6. Establishment of a drafting committee
7. Developments in science and technology
 - (a) The SAB's report on developments in science and technology: Discussion of the final draft and adoption of the report



- (b) Convergence of chemistry and biology: Intersessional work and report from the second meeting of the temporary working group, including discussions on the topic of production by synthesis
 - (c) Incapacitating chemical agents
- 8. Education and outreach in science and technology
 - (a) Intersessional work since 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
- 9. Scientific and technological elements of verification methodologies, emerging technologies, and new equipment:
 - (a) Sampling and analysis
 - (i) Report from the seventh meeting of the temporary working group on sampling and analysis
 - (ii) Update on Secretariat action in regard to sampling and analysis
- 10. Scheduled chemicals and advice on the Annex on Chemicals
 - (a) Advice on situations where a Schedule 1 chemical is an unavoidable by-product in a reaction mixture (see Annex 6 of the report by the SAB on its Eighteenth Session)
- 11. Further scientific and technological advice relevant to the Convention
- 12. Future work of the Scientific Advisory Board
 - (a) Roadmap of SAB work
 - (b) Contributions to *OPCW Today*
- 13. Any other business
- 14. Adoption of the report
- 15. Closure of the session

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

The session was opened with a *tour de table* in order to introduce the members of the SAB. One new member, Mohammad Abdollahi from the Islamic Republic of Iran, attended his first session, and Robin Black was attending his last session of the SAB. A list of participants is contained in Annex 1.

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

- 4.1. The Deputy Director-General welcomed the members of the SAB on behalf of the Director-General, and congratulated Alejandra Graciela Suárez on her election as Vice-Chairperson. She also thanked Robin Black for his service to the SAB and welcomed Mohammad Abdollahi to his first session. The Deputy Director-General also conveyed her appreciation to the members of the temporary working groups (TWGs) for their contributions.
- 4.2. The Deputy Director-General noted that States Parties had begun 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”) and that the Open-Ended Working Group for the Preparation of the Third Review Conference had already met nine times. She informed the SAB that the Technical Secretariat (hereinafter “the Secretariat”) would issue a comprehensive review of the operation of the Chemical Weapons Convention (hereinafter “the Convention”) in October, and that the Director-General and States Parties looked forward to receiving the SAB’s report on developments in science and technology, which will assist preparations for the Third Review Conference.
- 4.3. The Deputy Director-General mentioned two key trends: The growing convergence taking place between chemistry and other scientific disciplines, and the need for a multi-disciplinary and multi-stakeholder approach to inputs on science and technology. She highlighted how these trends are reflected in the work of all three of the SAB’s TWGs.
- 4.4. Thanking the Chairperson and other members of the SAB for their regular briefings to the policy-making organs, the Deputy Director-General stressed the importance of robust engagement between the SAB and the other organs of the OPCW. Enhancing their understanding and appreciation of the SAB’s work will create greater receptivity for its recommendations. Future opportunities for such interaction include the Fourteenth Annual Meeting of National Authorities and the Seventeenth Session of the Conference of the States Parties, both in November 2012.
- 4.5. In conclusion, the Deputy Director-General reminded members of the existence of the SAB trust fund, which was created in 2006 to support the activities of the SAB. A call for voluntary contributions was issued earlier in 2012, and the Deputy Director-General thanked the Government of the United Kingdom of Great Britain and Northern Ireland for its contribution. She also thanked the European Union (EU)

for its Council Decision in support of the OPCW¹; this funding is used for meetings of the TWGs.

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

- 5.1 The Secretary of the SAB, Stian Holen, provided an overview of developments at the OPCW since the SAB's last session in April 2012. His presentation emphasised that science and technology underpin many Articles of the Convention, and thus are central to the OPCW's future work.
- 5.2 The Secretary informed the members of the Board on the progress being made in the context of informal consultations on issues related to the chemical industry, Articles VII and XI of the Convention, and the Draft Programme and Budget for 2013. The Secretary also informed the SAB about the commencement of preparations for the Third Review Conference, to be held in April 2013. He updated SAB members on developments relating to progress in the destruction of chemical weapons, preparedness under Articles IX and X, universality, and chemical safety and security.
- 5.3 The Secretary described activities by the Secretariat and the SAB to engage with States Parties and stakeholders to the Convention, including briefings by SAB members on the margins of the Executive Council and a side event at the Meeting of Experts on the Biological Weapons Convention (BWC) in Geneva in July 2012. In addition, the Secretariat has also organised three technical workshops in recent months on the following topics: The Secretariat's relations with civil society, chemical safety and chemical security, and the preparedness of the Secretariat to conduct challenge inspections (CIs) and investigations of alleged use (IAUs).
- 5.4 Looking forward, the Secretary made reference to the report of the SAB to the Director-General and to the Third Review Conference, which the SAB will finalise at this session. He also highlighted future events at which the SAB will engage with States Parties, including meetings of the Open-Ended Working Group for the Preparation of the Third Review Conference, the Fourteenth Annual Meeting of National Authorities, the Seventeenth Session of the Conference of the States Parties, and the Third Review Conference itself.

6. AGENDA ITEM SIX – Establishment of a drafting committee

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

¹ Council Decision 2012/166/CFSP of 23 March 2012 in support of activities of the Organisation for the Prohibition of Chemical Weapons (OPCW) in the framework of the implementation of the EU Strategy against Proliferation of Weapons of Mass Destruction

7. AGENDA ITEM SEVEN – Developments in science and technology

Subitem 7(a): The SAB's report on developments in science and technology: Discussion of final draft and adoption of the report

- 7.1 The SAB continued the discussions on its draft of the “Report of the Scientific Advisory Board on Developments in Science and Technology for the Third Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention,” which it had begun at its Eighteenth Session. The report was adopted by the SAB. It was transmitted to the Secretariat and will be circulated to all States Parties as an official document.

Subitem 7(b): Convergence of chemistry and biology: Intersessional work and report from the second meeting of the temporary working group, including discussions on the topic of production by synthesis

- 7.2 The Chairperson of the TWG on the Convergence of Chemistry and Biology, William Kane, provided an overview of its second meeting, which took place on 6 and 7 September 2012. The report of the TWG is contained in Annex 3. Based on feedback from the Director-General, the terms of reference were updated during the intersessional period. In addition to looking at the production aspects, the benefits of the convergence of chemistry and biology will be covered in the report.
- 7.3 There were two guest speakers at the meeting, Richard Johnson (Chief Executive Officer of Global Helix LLC, Maryland, the United States of America) and Scott Mohr (Director of the Bioinformatics Graduate Programme in the Department of Chemistry at Boston University in the United States of America). Richard Johnson provided an excellent presentation on emerging trends and drivers in the global biotechnology industry, and Scott Mohr gave a comprehensive presentation on the extent and implications of the convergence between chemistry and biology in the age of synthetic biology, a key point of which was that, insofar as living systems are concerned, the barriers between chemistry and biology have vanished.
- 7.4 The TWG continued its in-depth discussion on the topic of commercial bio-mediated processes. William Provine of DuPont, Delaware, the United States of America provided examples of such processes within his company that utilise metabolic engineering or synthetic biology as core technologies. DuPont has a full-scale commercial facility, operating since 2007, to make propanediol. He provided an explanation of the bio-mediated process and unit operations that are involved in the production of propanediol. He also explained how the company uses biotechnology to make a range of products, including biofuels (cellulosic ethanol and butanol), enzymes, biocatalysts, and Omega-3.
- 7.5 In his presentation, the Chairperson of this TWG highlighted the fact that there are major challenges in regard to the utilisation of new bio-mediated processes for large-scale production, including the need for considerable process development and scale-up, capital investment, start-up, and demonstration of the commercial facility. This normally requires a number of years to take a process from the laboratory phase to commercial production.

- 7.6 Robin Black made a presentation on bioregulators. Commentators on the Convention have been making increasing references to bioregulators as toxic chemicals or incapacitants. These chemicals of biological origin fall within the remits of both the Convention and the BWC. Bioregulators regulate a wide range of body functions, including blood pressure, airway compliance, sleep, mood, cognisance, and behaviour. They include a wide range of chemical classes, e.g., short chain peptides, polypeptides, nucleotides, lipid-derived metabolites, and small molecules such as neurotransmitters. Peptides are the largest group of bioregulators and have been the class for which most concern has been expressed. Robin Black provided a number of examples of peptides and reviewed some of the limitations of peptides with regard to their development as potential drugs. Although the Convention-related concern for bioregulatory peptides may be overstated by some commentators, it is recommended that the Secretariat increase and maintain in-house knowledge of bioregulators.
- 7.7 The TWG continued its review of the meaning of the term “produced by synthesis”. A key issue in the implementation of Part IX of the Verification Annex to the Chemical Weapons Convention (hereinafter “the Verification Annex”) is whether or not biologically-mediated processes are covered by this term. The TWG was of the view that any process designed for the formation of a chemical substance should be covered by the term “produced by synthesis”.
- 7.8 Discussion was initiated on the potential benefits to the Convention of the convergence of chemistry and biology. A presentation was made by Hua Li reporting on the progress that has been made in the area of medical countermeasures against chemical-warfare agent poisoning, with the development of new bio-based drugs for treatment including:
- (a) protein-based drugs developed for prophylactic treatment of nerve agent poisoning (such as the recombinant butyrylcholinesterase (BuChE) derived from the milk of transgenic goats); and
 - (b) custom-designed monoclonal antibodies that could effectively scavenge or hydrolyse nerve agents.
- 7.9 There was also a presentation by William Provine on the use of engineered enzymes for safer and easier decontamination. This topic will be reviewed in more detail at the TWG’s next meeting.
- 7.10 In terms of future developments, the TWG discussed such topics as the use of nanomaterials in gas mask canister adsorbents and for protective clothing—a development that could result in more effective personal protection while reducing the burden for the wearer (when compared to systems currently in use). This area will be explored in more detail by the TWG.
- 7.11 Djafer Benachour gave a presentation on the impact of nanotechnology on the convergence of chemistry and biology. As an illustration, he described the combination of nano-biocatalysis and microreactor technology and the benefits that may be derived from it in terms of safety, cost, yield and energy consumption.

7.12 The recommendations from the first meeting were reviewed by the TWG at its second meeting. Some of them were modified and a number of action items were agreed upon, so that the recommendations could be further addressed (see the full report of the TWG in Annex 2).

7.13 The SAB endorsed the report of the TWG.

Subitem 7(c): Incapacitating chemical agents

7.14 Three members of the SAB attended the second meeting of the International Committee of the Red Cross (ICRC) on incapacitating chemical agents (ICAs) in Montreux, Switzerland.² The Chairperson of the SAB reported on the programme and its focus on different legal frameworks, as well as on the different policy options that were discussed. Valeria Santori from the Secretariat summarised for the SAB the discussions during the ICRC meeting on policy issues relating to the treatment of incapacitating agents under the Convention, as well as under other legal frameworks; she also reported on the policy options that were discussed at the meeting. The SAB recalled that at the Montreux meeting it had been stated that an international legal framework for dealing with ICAs existed and could be used, if required. Following the meeting, the ICRC published a short summary, as well as a synthesis of what had been learned about ICAs through the different expert papers that had been distributed and workshops that had taken place.³ A comprehensive report of the meeting is forthcoming.

7.15 In the view of the SAB, the technical discussion on the potential use of toxic chemicals for law enforcement purposes has been extensive. The SAB may continue its discussion once technical information about specific candidates for ICAs and/or distribution systems for such agents are made available to it.

7.16 The SAB recommends that the Secretariat start preparations for verification activities that could be required during an IAU. Such preparations should include the development of analytical methods and procedures, as well as the collection of analytical reference data for the analysis of such chemicals. One development in analytical instrumentation that may contribute to the analysis of ICAs is high-resolution mass spectrometry (HRMS). The Secretariat should invite laboratories in Member States to contribute to the development of respective analytical methods and to the collection of analytical reference data.

² Expert meeting entitled: “Incapacitating Chemical Agents: Law Enforcement, Human Rights Law and Policy Perspectives”, from 24 to 26 April 2012, Montreux, Switzerland

³ International Committee of the Red Cross: “Toxic Chemicals as Weapons for Law Enforcement: A threat to life and international law? Summary” (September 2012); and International Committee of the Red Cross, “Toxic Chemicals as Weapons for Law Enforcement: A threat to life and international law? Synthesis”, (September 2012)

8. AGENDA ITEM EIGHT – Education and outreach in science and technology

Subitem 8(a): Intersessional work since the first meeting of the temporary working group on education and outreach in science and technology

- 8.1 Djafer Benachour, Chairperson of the TWG on education and outreach, reported on the intersessional work that had taken place since the TWG's first meeting in April 2012. One of the recommendations of the first meeting of the TWG was the implementation of codes of conduct at a national level. The TWG Chairperson, therefore, participated in a workshop held in Amman, Jordan, on 4 and 5 July 2012; the workshop aimed at inaugurating a code of conduct for chemists in North Africa and the Middle East. Eleven countries were represented, and a first version of a code of conduct was drafted. This version is currently being discussed by the chemistry communities in the respective countries. Djafer Benachour presented a brief report on this workshop to the SAB.
- 8.2 Another recommendation from the first meeting of the TWG was that the OPCW should cooperate in education and outreach with other international organisations and treaties (e.g. the International Atomic Energy Agency (IAEA), the BWC, and the World Health Organization (WHO)), and international scientific bodies (such as the International Union of Pure and Applied Chemistry (IUPAC) and the International Union of Toxicology (IUTOX)), as well as professional associations (such as the International Council of Chemical Associations (ICCA), the European Chemical Industry Council (CEFIC), and non-governmental organisations (NGOs)). For that purpose, the OPCW (represented by the TWG Chairperson) was invited to address the IUPAC Committee of Chemistry Education (CCE) on 15 July 2012 and to participate in a joint event, the "22nd International Conference on Chemistry Education" and the "11th European Conference on Research in Chemical Education", held in Rome, Italy, from 16 to 20 July 2012. The Director-General of the OPCW gave a keynote address at the opening of the conference.
- 8.3 Djafer Benachour presented a report on these important scientific events, with an emphasis on:
- (a) cooperation with IUPAC/CCE and other international scientific institutions;
 - (b) new educational techniques; and
 - (c) recent outreach tools related to chemistry education and outreach activities.
- 8.4 The SAB recommends future OPCW participation in such conferences.

Subitem 8(b): Outreach activities of the Secretariat

- 8.5 Daniel Feakes of the Secretariat gave an overview of recent outreach activities by the Secretariat. Since the Eighteenth Session of the SAB, the Secretariat has undertaken numerous activities to raise awareness of the Convention. For example, in July 2012 the Director-General addressed over 600 chemistry educators at the 22nd International Conference on Chemistry Education mentioned above, and travelled to Australia,

where he spoke at the Lowy Institute for International Policy and at Australian National University. The first module of a new e-learning series is available on the OPCW website covering “the history of the CWC⁴ and chemical disarmament”.⁵ Further modules will follow in the near future.

- 8.6 Daniel Feakes informed the SAB that, during the week of 3 September, the OPCW marked the fifteenth anniversary of the entry into force of the Convention, and the twentieth anniversary of the conclusion of the negotiations on the Convention. The occasion was marked by a series of public events, and two SAB members and one TWG member participated in an event on science and technology.

Subitem 8(c): Outreach activities by members of the SAB

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

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

Subitem 9(a): Sampling and analysis

Report from the seventh meeting of the temporary working group on sampling and analysis

- 9.1 The SAB received the report of the seventh and final meeting of the TWG on sampling and analysis (S&A), held on 4 and 5 September 2012 (see Annex 2). Robin Black, Chairperson of this TWG, presented the key findings, conclusions, and recommendations. The main topics discussed were: Sample preparation for toxin analysis; identification of ricin; an update on biomedical samples; criteria for trace analysis; protocols for analysing samples of mixed or unknown hazard; emerging mass-spectrometric techniques; chemical forensics (attribution); relevant activities of the Secretariat; analysis of Schedule 3 chemicals and perfluoroisobutene (PFIB), and use of mobile laboratories during the third OPCW exercise on the delivery of assistance (ASSISTEX 3).
- 9.2 The main conclusions and recommendations of the meeting were:
- (a) Samples suspected of containing ricin can be purified for analysis based on a combination of the molecular size, the electronic charge of the molecule, and specific affinity for antibodies and lactose.
 - (b) Identification of ricin for verification purposes should be based on two analytical techniques. The primary (confirmatory) technique should be based on the mass spectrometric identification of peptides formed on enzymatic digestion. The two techniques should be selected in such a manner that they provide evidence of an intact ricin molecule, i.e. with chains A and B

⁴ CWC = Chemical Weapons Convention

⁵ For more information, and to register for access to the e-learning modules, see <http://www.opcw.org/opcw-e-learning/>

connected by a disulfide bond. The TWG recommended criteria for identification.

- (c) The TWG noted that the second confidence-building exercise on biomedical samples, held in January 2012, demonstrated a broadening capability for metabolite analysis in urine. The quality of data and reporting was significantly improved over the first exercise, with a lower occurrence of system contamination and reporting of false positives. The exercise provided an opportunity to exercise draft criteria for trace analysis, based primarily on a system used by the European Commission (EC).
- (d) Trace analysis identification criteria required by both the EC guidelines for substances in animal products and those required by the World Anti-Doping Agency (WADA) for the identification of drugs in human urine appear to be appropriate for OPCW purposes. The TWG recommended that the OPCW adopt a system based on the flexible-point system used by the EC, with minor modifications adapted, so as to be consistent with OPCW proficiency-testing requirements.
- (e) A problem faced by many laboratories is how to handle samples where the nature of the hazard is unknown, particularly the elimination of any biological hazard prior to chemical analysis. The TWG was briefed on three protocols for mitigating or eliminating a biological hazard, based on isolation with remote handling, chemical sterilisation with paraformaldehyde, and physical separation of biological organisms using ultracentrifugation and filtration.
- (f) The TWG continues to endorse Secretariat efforts to reduce on-site analysis time. An instrumental development of possible relevance is the use of transportable mass spectrometers capable of direct sampling. One promising instrument has dual sources based on desorption electrospray ionisation (DESI) and direct analysis in real time (DART).
- (g) New developments in HRMS are having a substantial impact on off-site analysis. HRMS allows the determination of the molecular formula, e.g., in the case of analytes that are not in the OPCW Central Analytical Database (OCAD), thus narrowing down the number of possible structures. It also allows retrospective analysis of mass spectral data for analytes present at trace levels, rather than the selective analysis for predetermined analytes used in low-resolution instruments. HRMS was used with impressive results in the two OPCW confidence-building exercises on biomedical samples.
- (h) An additional aspect of verification analysis being explored by several laboratories is a methodology that allows attribution of a sample to a particular source. Proof of principle was demonstrated with samples of VX.
- (i) In exercises such as ASSISTEX 3, the TWG agreed that greater attention should be focused on screening samples to determine the most appropriate ones for further analysis, and to the management of the entire S&A process.

- (j) The Chairperson of the TWG expressed his appreciation to the members of the TWG for their hard work, to the Head of the OPCW Laboratory and his staff for their input into the TWG, and to the Secretariat for their support.

9.3 The SAB endorsed the report of the TWG.

Update on Secretariat action in regard to sampling and analysis

- 9.4 Hugh Gregg, Head of the OPCW Laboratory, updated the SAB on the technical status of S&A. He reported on a quality-review visit performed during a Schedule 2 industry inspection that involved S&A. The timelines and bottlenecks in the process have been documented. In this inspection, the gas chromatography-mass spectrometry (GC-MS) was set up on the afternoon of arrival and was ready for analysis the following morning, after the pre-inspection briefing. The analytical chemists were able to prepare three samples for analysis that same day (using standard sample-preparation protocols), and the analyses were able to run overnight. Had a larger autosampler been used, all the samples would have been ready for data analysis the following morning.
- 9.5 The Head of the OPCW Laboratory reported on the types of GC-MS instruments necessary for on-site inspections. A demonstration of an “all-in-one” GC-MS instrument at the OPCW Laboratory led to the conclusion that the current research-grade GC-MS instrument is still the best suited instrument for OPCW purposes.
- 9.6 Progress has been made on the improved sample-preparation procedures described in detail in the report of the sixth meeting of the TWG on S&A.⁶ Additionally, an explanation for why previous fast-GC methods appeared problematic was presented (most likely due to slightly different GC columns phases and/or manufacturing processes). Progress also continues on streamlining the on-site reporting that is required.
- 9.7 Hugh Gregg reported on several potential methods for the analysis of PFIB. A local company (DuPont, in Dordrecht, the Netherlands), has agreed in principle to assist the OPCW Laboratory by providing a dilute standard of PFIB in an inert gas. This will enable the laboratory to develop an analytical method that will most likely use Tenax® sorbent coated with a derivatising agent.
- 9.8 Following the Thirty-First Proficiency Test, the laboratories designated for the off-site analysis of samples were listed. The need for a technical arrangement to be executed between each designated laboratory and the Secretariat was emphasised.

⁶ See Annex 2 of SAB-17/1, dated 23 November 2011.

10. AGENDA ITEM TEN – Scheduled chemicals and advice on the Annex on Chemicals

Subitem 10(a): Advice on situations where a Schedule 1 chemical is an unavoidable by-product in a reaction mixture (see Annex 6 of the report from the SAB on its Eighteenth Session)

- 10.1 In relation to paragraph 14.2 of the report of the SAB at its Eighteenth Session (see SAB-18/1, dated 19 April 2012), in which the Director-General requested the SAB to provide advice on situations where a Schedule 1 chemical is an unavoidable by-product, the Chairperson of the SAB presented a study of the literature on this topic, which was carried out by the Spiez Laboratory in Switzerland. The objective of the study was to answer two questions: Are Schedule 1 chemicals possibly in use as intermediates in the chemical industry (captive use) and is it feasible that Schedule 1 chemicals are present as unavoidable by-products or impurities in reaction mixtures? The study included previous work carried out by members of the SAB.⁷
- 10.2 The approach taken to answer the two questions posed in paragraph 10.1 was to perform a particular study for which specific searches were designed for a database that contains reaction and patent information for industrial chemicals.⁸ No results could be found for the Schedule 1 chemicals 1A01-03 (phosphor-based nerve agents), 1B09-12 (phosphor-based direct precursors of nerve agents), and 1A05 chemicals (arsenic-based blister agents). The study then focused on 1A04 chemicals (sulfur mustards) and 1A06 chemicals (nitrogen mustards).
- 10.3 The study shows that it is technically feasible for sulfur and nitrogen mustards to occur in certain types of industry as impurities or by-products. This literature study has been limited to a search of open literature and there is no guarantee that synthesis routes were applied by industry exactly as they were described in the publications, or that they have not been changed since their publication and are still in use.
- 10.4 Based on the studies that have been presented to the SAB, the SAB is of the view that, from all the chemicals listed in Schedule 1, only the chemicals belonging to Schedule 1A04 (sulfur mustards) and the chemicals belonging to Schedule 1A06 (nitrogen mustards) may be formed as unwanted by-products in an industrial process. The starting materials or impurities used in these processes must have molecular structures that are similar to precursors of nitrogen mustards or sulfur mustards, and a chlorination reaction must be part of the designed process. A number of other factors may influence whether or not and how much of a Schedule 1 by-product is formed, including the quality of the raw materials being used, process-design features, reaction parameters, and so on. These can only be assessed on a case-by-case basis.
- 10.5 In paragraph 6 of Annex 6 to the report of the SAB at its Eighteenth Session, the Director-General posed three questions to the SAB. The questions are reproduced below, and the response from the SAB is provided after each question:

⁷ S/528/2005 dated 1 November 2005; and SAB-8/1, dated 10 February 2006 and Corr.1, dated 15 March 2006

⁸ See <https://www.reaxys.com/info/about-overview> for more information on the database.

- (a) “What is the technical feasibility for using a reaction mixture containing a Schedule 1 chemical for activities prohibited by the CWC?”
- The SAB replied that, if a reaction mixture contains 1A04 or 1A06 chemicals that are formed as a by-product during a process at an industrial facility, as described in paragraph 10.4 above, the SAB considers that it is impractical to utilise such a reaction mixture for activities prohibited by the Convention.
- (b) “Under which technical conditions can a Schedule 1 by-product be recovered?”
- The SAB replied that Schedule 1 by-products present as impurities in a reaction mixture could be isolated by processes such as distillation, chromatography, extraction, and crystallisation. However, the SAB considers this to be impractical, particularly taking into consideration that the direct synthesis of Schedule 1A04 or 1A06 chemicals would be technically much easier, more efficient, and far less expensive.
- Without knowing the details of a specific process, and the composition of the resulting reaction mixture, the SAB cannot assess the “technical conditions” that would be required to recover Schedule 1 by-products as described above.
- (c) “Is it possible on a technical foundation to determine 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?”
- The SAB replied that it views the recovery of Schedule 1A04 or 1A06 impurities that might be formed at a facility during an industrial process (as described in paragraph 10.4 above) to be an issue of little practical relevance, and considers it unlikely that such reaction mixtures could be utilised for activities prohibited by the Convention. However, there is insufficient technical information available to recommend a specific concentration limit above which this conclusion might not apply. The SAB will give this question further consideration.

11. AGENDA ITEM ELEVEN – Further scientific and technological advice relevant to the Convention

No discussion took place under this agenda item during this session of the SAB.

12. AGENDA ITEM TWELVE – Future work of the Scientific Advisory Board

During discussions in regard to its future work, the SAB raised the following points:

- (a) preparatory work for upcoming meetings of its TWGs;

- (b) the date for its Twentieth Session;
- (c) how it can enhance its engagement with States Parties; and
- (d) the intersessional work that needs to take place before its Twentieth Session.

Subitem 12(a): Roadmap of SAB work

- 12.1 The SAB tentatively decided that its Twentieth Session would take place from 10 to 14 June 2013.

Subitem 12(b): Contributions to *OPCW Today*

- 12.2 Members of the SAB were invited to submit articles for publication in the OPCW publication, *OPCW Today*. A number of members agreed to submit articles in the future.

13. AGENDA ITEM THIRTEEN – Any other business

The Chairperson of the SAB bade farewell to Robin Black, who would be completing his term of office on 30 November 2012, and thanked him for his invaluable contribution to the work of the SAB.

14. AGENDA ITEM FOURTEEN – Adoption of the report

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

15. AGENDA ITEM FIFTEEN – Closure of the session

The Chairperson closed the session at 18:00 on 12 September 2012.

Annexes:

- Annex 1: List of Participants in the Nineteenth Session of the Scientific Advisory Board
- Annex 2: (English only, unedited): Report of the Seventh Meeting of the SAB Temporary Working Group on Sampling and Analysis, The Hague, the Netherlands, 4 and 5 September 2012
- Annex 3: (English only, unedited): Report of the Second Meeting of the SAB Temporary Working Group on the Convergence of Chemistry and Biology, The Hague, the Netherlands, 6 and 7 September 2012

Annex 1

**LIST OF PARTICIPANTS IN THE NINETEENTH SESSION
OF THE SCIENTIFIC ADVISORY BOARD⁹**

	Participant	Institution
1.	Abdollahi, Mohammad	Tehran University of Medical Sciences, Islamic Republic of Iran
2.	Álvarez, Roberto Martínez	Complutense University, Madrid, Spain
3.	Baulig, Augustin	Secrétariat général de la défense et de la sécurité nationale, France
4.	Benachour, Djafer	Ferhat Abbas University, Ministry of Higher Education and Scientific Research, Setif, Algeria
5.	Black, Robin	Defence Science and Technology Laboratory (Dstl), Porton Down, United Kingdom of Great Britain and Northern Ireland
6.	Dubey, Devendra Kumar	Vertex Laboratory, Gwalior, India
7.	Fujiwara, Shuzo	National Institute of Advanced Industrial Science and Technology, Tsukuba, Japan
8.	Geist, Michael	BASF SE, Ludwigshafen, Germany
9.	Kane, William	Monsanto Company, Louisiana, United States of America
10.	Mogl, Stefan ¹⁰	Spiez Laboratory, Spiez, Switzerland
11.	Muhammad Zafar-Uz-Zaman	National Engineering and Scientific Commission (NESCOM), Islamabad, Pakistan
12.	Neffe, Slawomir	Military University of Technology, Warsaw, Poland
13.	Rybalchenko, Igor V.	Military Science Centre of the Ministry of Defence, Moscow, the Russian Federation
14.	Suárez, Alejandra Graciela ¹¹	Universidad Nacional de Rosario, Argentina
15.	Trifirò, Ferruccio	Faculty of Industrial Chemistry, University of Bologna, Italy
16.	Vanninen, Paula	VERIFIN, Department of Chemistry, Faculty of Science, University of Helsinki, Finland
17.	Vučinić, Slavica	National Poison Control Centre, Military Medical Academy, Belgrade, Serbia
18.	Zaitsev, Volodymyr	Taras Shevchenko National University of Kyiv, Ukraine
19.	Zhang, Nan	Ministry of National Defence, Beijing, China
20.	Zina, Mongia Said	Faculty of Sciences of Tunis, Tunisia

⁹ Flerida Arsciwals Cariño and Abdullah Al-Amri did not attend the Nineteenth Session of the SAB. Three seats are vacant.

¹⁰ Chairperson of the SAB

¹¹ Vice-Chairperson of the SAB

Annex 2

REPORT OF THE SEVENTH MEETING OF THE SAB TEMPORARY WORKING GROUP ON SAMPLING AND ANALYSIS, THE HAGUE, THE NETHERLANDS 4 AND 5 SEPTEMBER 2012

Introduction

1. The Temporary Working Group (TWG) on Sampling and Analysis (S&A) of the Scientific Advisory Board (SAB) held its seventh meeting on 4 and 5 September 2012 at the OPCW Headquarters in The Hague.
2. The meeting was chaired by Robin Black on behalf of the SAB.
3. The list of participants in the meeting is given in Appendix 1.
4. The following agenda was adopted:
 - (a) Opening of the meeting and adoption of the agenda
 - (b) Sample preparation for toxin analysis
 - (c) Ricin analysis
 - Immunoaffinity/enzymatic assay
 - Update & review of recommendations
 - (d) Overview and evaluation of the 2nd OPCW confidence building exercise on biomedical samples
 - (e) Criteria for trace analysis:
 - Relative merits of the EC and WADA identification criteria
 - Recommendations for the way forward
 - (f) Protocols for mixed/unknown sample analysis
 - (g) Emerging mass spectrometric techniques
 - Portable DESI/DART system
 - Impact of HRMS, recent developments
 - (h) Chemical forensics (attribution)
 - (i) Update on activities in S&A by the Technical Secretariat (TS)
 - (j) Potential methodologies for analysis of perfluoroisobutene (PFIB)

- (k) Schedule 3 chemical analysis
- (l) Review of recommendations
- (m) Any other business
- (n) Elaboration and adoption of the report from the meeting

AGENDA ITEM TWO – Sample preparation for toxin analysis

5. Sng Mui Tiang, of DSO, Singapore, provided an overview of the approaches to sample preparation for toxins being adopted in DSO. The isolation and purification of ricin are based on a combination of differences in molecular mass, the electronic charge of the molecule, and specific affinity for antibodies and lactose. The protocols for the extraction of ricin from water, milk and cotton swabs have been accredited. Work is in progress to improve the sensitivity of the methods, to reduce sample preparation time, and to extend the procedures to other matrices.

AGENDA ITEM THREE – Ricin analysis

Immunoaffinity/enzymatic assay

6. Anne Bossée, of DGA CBRN Defence, France, gave an overview of their work on a ribosomal functional assay based on immunocapture, enzymatic reaction with a partial ribosome sequence, and LC-MS. This method captures ricin by an antibody, immobilized on magnetic beads, targeted at the ricin B chain. The isolated ricin is incubated with a specific synthetic RNA substrate (5' CGCGCGAGAGCGCG 3') in a depurination buffer. The enzymatic N-glycosidase activity of the ricin A-chain releases adenine from the RNA substrate, which is identified by LC-MS/MS in selected reaction monitoring (SRM) mode. This method has the advantages of high sensitivity (0.1 ng/mL in water), specificity (resulting from the antibody used), and demonstrates the presence of functionally active ricin in the sample. The method, which is an indirect method of identification of ricin, requires a rigorous and time-consuming sample preparation. It has been tested in different matrices, including raw castor bean extract, tap water, milk, and wheat flour extract spiked with ricin D at 100 ng/mL.

Criteria for identification of ricin

7. The identification criteria for ricin were reviewed and updated by Sten-Åke Fredriksson of FOI (CBRN Defence and Security), Sweden. The consensus of the TWG was that identification of ricin should be based on two different analytical techniques and that the primary (confirmatory) technique should be based on mass spectrometry. The two methods should be selected such that they provide evidence of an intact ricin molecule, i.e. with chains A and B connected by a disulfide bond. This can be accomplished by a functional assay designed to use both the lectin properties of the B chain and the N-glycosidase activity of the A chain, as described in paragraph 3.1. Alternatively, determination of the molecular mass or detection of a disulfide linked peptide by MALDI-MS/MS or by LC-ESI-MS/MS can be used.

8. It was recommended that identification of ricin by mass spectrometric methods should be based on comparison with the isoform ricin D, using trypsin for digestion to characteristic peptides. Some analytical techniques were recommended for ricin, which are not in use for the analysis of other scheduled chemicals. These include immunological methods, e.g. enzyme linked immunosorbent assay (ELISA) or a Lateral Flow Assay (LFA), functional assays, e.g. based on the catalytic activity of ricin (see para 3.1), and polymerase chain reaction (PCR) which detects DNA remnants from the producing plant species. The analytical techniques and recommended criteria can be summarized as follows:
- (a) Mass spectrometric data, for proteolytic peptides, should demonstrate an amino acid sequence consistent with that of ricin D. A minimum of 4 peptides should be identified, selected from both the A and B chains, with a minimum 10% sequence coverage (i.e. 53 amino acid residues). The uniqueness of the peptides to ricin should be described in the method documentation (some tryptic peptides are observed with other proteins).
 - (b) The uniqueness of the peptide sequence ions for LC-MS/MS SRM transitions should also be described in the method documentation. Intensity ratios should be within the tolerance limits recommended by WADA¹² and the EC.¹³
 - (c) Supporting data is required from one of the following techniques: recognition by a ricin-specific antibody; positive response in a ricin functionality assay; PCR; molecular mass, or retention parameter, or peptide mass fingerprint consistent with a reference sample of ricin D.
9. It was noted that, as an alternative to the identification of intact ricin, some challenge inspections or investigations of alleged use might require identification of degradation products of ricin. The nature of these degradation products is a knowledge gap. The alkaloid ricinine, which is a stable molecule co-produced with ricin in the castor bean, is used as a marker for ricin in forensic investigations.

AGENDA ITEM FOUR – Report of the 2nd OPCW confidence building exercise on biomedical samples

10. Robin Black, Dstl, United Kingdom, provided an overview of the 2nd OPCW confidence building exercise on biomedical samples, held in January 2012. Twenty two laboratories participated including the preparation and evaluation laboratories. Samples were prepared by the TNO Health, Security and Safety Laboratory, Rijswijk, the Netherlands, and the results evaluated by Dstl, Porton Down, UK.
11. Samples of commercial human urine were spiked with urinary metabolites of nerve agents or sulfur mustard, the lowest concentrations being 5 ng/ml. Laboratories were asked to use a reporting format based on the format recently adopted for OPCW

¹² WADA Technical Document - TD2010IDCR. Identification criteria for qualitative assays incorporating column chromatography and mass spectrometry

¹³ Commission decision of 12 August 2002. Implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results. L221/8 17/8/2001

Proficiency Tests. Laboratories were informed that identification would be assessed against a system of identification points, based, with minor modifications, on the system used by the EC for identifying banned substances in food and animal products. The evaluation laboratory also assessed the results against the WADA criteria for trace levels of drugs in human urine.

12. As in the first exercise, held in 2010, the most sensitive and selective methods were provided by LC-MS/MS or GC-MS/MS in SRM mode, or high resolution single stage LC-MS in extracted ion mode. For GC-MS, perfluorinated derivatives gave lower limits of detection and greater selectivity than silyl derivatives. The level of identification, and limits of detection of analytical methods, will always be dependent on the equipment available. Laboratories with triple quadrupole instruments, other instruments capable of MS/MS, or alternatively high resolution (HR) (resolution >10,000), provided better quality data than those using single stage quadrupole instruments. The capabilities of time-of-flight (TOF) instruments, with their superior ability to acquire full mass spectra at low concentrations, and retrospective search of the data (see paragraph 7.2), have yet to be fully exploited in biomedical sample analysis.
13. This second confidence building exercise, like the first, successfully demonstrated a broader capability to analyze urine samples for metabolites of CW agents. The results have provided the basis for recommending analytical procedures. Many laboratories were able to meet the identification criteria as stipulated in the OPCW guidelines for the exercise. Encouragingly, system or sample contamination was less of a problem in this second exercise than in the first. Carry-over of analyte was a greater problem with GC-MS analysis than with LC-MS. It is important that this issue continues to be addressed through modifications to equipment used, protocols adopted, and derivatization procedures.
14. It has been provisionally recommended that the next exercise should address protein adducts in blood. These should be chosen from those adducts where the CW agent residue can be displaced from the protein by hydrolysis (e.g. sulfur mustard as thiodiglycol), by fluoride ion (nerve agent inhibited acetyl- or butyrylcholinesterase), or as a derivative (Edman degradation of mustard alkylated N-terminal valine on haemoglobin). An alternative view is that the third exercise should again use urinary metabolites, with reporting required to near proficiency test standards and applying the revised criteria for identification (see paragraph 5), or possibly a combination of metabolites and adducts.

AGENDA ITEM FIVE – Criteria for identification in trace analysis

15. Paula Vanninen of VERIFIN, Finland, gave an overview of criteria for identification using trace analysis, as may be applied to investigations of alleged use. The relative merits were discussed of the WADA criteria for drugs in urine, the EC criteria for monitoring of certain substances and residues in live animals and animal products, and the points system derived from the EC system drafted by the TS (OPCW/TS 2012) for the 2nd OPCW confidence building exercise.

16. Based on the report of an OPCW intern working in VERIFIN,¹⁴ on work performed from September to December 2011, both WADA and EC guidelines appear to be fit for OPCW purposes. The WADA and EC systems differ in values for maximum tolerance windows for relative ion abundances of diagnostic ions. Another difference is that in full scan spectra the EC requires a minimum number of four diagnostic ions (with $S/N \geq 3$), whereas WADA requires that all ions above 10% relative abundance must be reported. Based on the intern assessment, lower limits of quantitation were achieved using the EC criteria. It was noted that it is important to compare analyte and reference chemical at similar concentration levels, prepared in similar blank material as recommended by WADA. The TWG recommended adaption of the EC criteria with the following modifications:
- (a) The EC system requires 4 points for identification with a maximum of 3 techniques. It was agreed that 5 points is more appropriate for OPCW purposes for unequivocal identification. This can be achieved by using multiple techniques.
 - (b) Signal to noise ratio $S/N \geq 5:1$ should be adopted instead of $S/N \geq 3:1$, consistent with criteria used in OPCW Proficiency Tests. It was proposed that GC or LC combined with an elemental detector should be worth 1 identification point.
 - (c) Analysis should be by at least two different analytical techniques, one of these must be a spectrometric technique. This should also apply to HRMS in combination with GC or LC. It was noted that HRMS techniques are able to separate isobaric compound by acquiring accurate mass data, but are not always able to differentiate isomeric compounds.
17. It was agreed that the standard addition method (by spiking the analyte of interest in an aliquot of the sample) is a good method to demonstrate retention time. A reference chemical for comparison should be analysed in a similar matrix at similar concentration level.

AGENDA ITEM SIX – Protocols for unknown/mixed sample analysis

LLNL “All-Threats Forensic Receival Facilities”

18. Armando Alcaraz of the Lawrence Livermore National Laboratory (LLNL), USA, presented an overview of the LLNL “All-Threats Forensic Receival Facilities”. He discussed the different types of hazardous materials - Radiological (R), Nuclear (N), Chemical (C), Explosives (E) and Biological (B) and how they establish various co-located forensic analytical capabilities designed to analyze suspect samples. Examples were given of “real world” unknown samples and how they were analyzed to identify the threat material. Two radiological and two suspect chemical samples were discussed. In addition to analysis, various items of physical evidence, such as fingerprints, hair and fibres, need to be protected for law enforcement forensic examiners.

¹⁴ Che Nin Man (Toxicology Laboratory, National Poison Centre, University Sains Malaysia, Malaysia)

Unknown sample handling and processing at DGA CBRN Defence

19. Anne Bossée, of DGA CBRN Defence, France, described the protocol used at DGA CBRN Defence for managing unknown RBCE samples. After first screening the unopened parcel for R and C hazards, the parcel is transferred to a B and C filtered glove box in a BSL-3 laboratory. The parcel is opened by a mixed R, B and C expert team, and a second screening for R and C vapour hazards is performed on the sample. The absence of explosives may be demonstrated by Hazmat ID analysis after organic extraction. B and C risk mitigation is performed by physical separation using ultracentrifugation, the supernatant being analysed for C analysis and the pellet for B). The B risk in the supernatant is further mitigated by filtration (0.2 then 0.02 µm) prior to C analysis. For R analysis, the B and C risk is avoided by treatment with nitric acid during sample preparation. This protocol is still being validated with additional B and C materials in various matrices.

Protocols for mixed/unknown sample analysis at VERIFIN

20. Paula Vanninen, of VERIFIN, Finland, provided an overview of protocols used for mixed/unknown sample analysis suspected of containing C and B agents, for on-site and off-site laboratories. Little information is available on the effects of various sample treatment procedures on the analytes of concern and analytical results. In order to render the sample safe for C analysis in the C-laboratory, B agents must be inactivated. Most methods used for inactivation of B will induce at least partial degradation of C agents, particularly as the procedure should be capable of inactivating all biological agents (bacteria, viruses and spores).
21. A procedure has been developed for the Finnish deployable laboratory (on-site analysis) together with the Defence Forces Technical Centre. The protocol includes extraction of the sample, filtration, and irradiation with a UV light. The protocol destroyed most of the spores and viruses studied in the B-laboratory. The protocols are currently applied in the deployable laboratory.
22. Protocols for off-site laboratories, i.e. designated laboratories, are being explored in a collaboration between the SPIEZ Laboratory, Switzerland and VERIFIN. The protocols under study are based on existing decontamination methods for B agents, 10% paraformaldehyde (PFA) and 2 % peracetic acid (PAA). Preliminary results indicate that B decontamination with 10 % PFA still allows analysis for the presence of intact C agents. Conversely, the strong oxidizer 2 % PAA also destroys C agents and analysis of intact agents is not possible. Analysis for the degradation products of C agents in decontaminated samples requires development of sample preparation methods.

AGENDA ITEM SEVEN – Emerging mass spectrometric techniques

Portable DESI/DART system

23. Armando Alcaraz of the LLNL, US, presented an overview of a commercial Portable DESI/DART-MS/MS system and some applications utilizing the switchable Direct ElectroSpray (DESI)/Direct Analysis in Real Time (DART) sources. The system may have potential applications for on-site CWC inspections as it has a Level-1 “first responder operation mode” and “expert mode”. The system weighs 54 kg and is 38.6 cm (H) x 56.6 cm (W) x 60.2 cm (D) with a 300 W power requirement. One of the advantages of DESI and DART sampling sources is the ability to introduce a sample directly into the MS for analysis without any sample preparation.

Impact of HRMS, recent developments

24. Martin Schaer of the SPIEZ Laboratory, Switzerland provided a detailed presentation on recent developments in HRMS. HRMS opens new possibilities in screening for, and identification of, CWC-related compounds. Instruments such as the Orbitrap, QTOFs, and other newly available systems, though expensive, are being more widely used. The high resolution allows the measurement of the isotopic distribution of a molecule to yield high mass accuracy, which allows the molecular formula (or a very narrow choice) to be calculated. QTOF measurements have to be calibrated internally, and using a lock mass. The high mass accuracy also allows the use of very narrow windows when constructing extracted ion chromatograms providing very high selectivity. Within one LC run, full scan plus MS/MS or in-source CID data can be obtained. The completeness of this data set allows retrospective searching of the data, unlike MS/MS SRM where target analytes are pre-selected. HRMS libraries for target screening contain the molecular formula and (if available) the retention time. New compounds can easily be added. HR instruments were used with impressive results in the two OPCW Confidence Building Exercises on Biomedical Samples, providing data comparable to MS/MS SRM chromatograms at least down to spiking levels of 5 ng/ml.

AGENDA ITEM EIGHT – Chemical forensics (attribution)

Chemical profiling of chemical warfare agents for forensic purposes.

25. Daan Noort of the TNO Health, Security and Safety Laboratory, Rijswijk, Netherlands, presented on a collaborative project, between TNO and The Netherlands Forensic Institute (NFI), on attribution studies of chemical warfare agents. The goal of this project is to assist forensic investigations in attributing an agent found at the scene of an incident to a particular source. Key questions are:
- (a) can the synthetic route be deduced from the composition of the by-products in the CW sample?
 - (b) can a correlation be made between chemical profiles of crude samples, found in an improvised laboratory and at the site of the crime?

- (c) what is the stability of the chemical profile, over time, on various matrices and under various conditions?
26. Studies with VX were reported. VX was synthesised according to three different methods, but with no purification of intermediates or end-products. Analysis was performed with GC-MS and DART. The conclusions were:
- (a) Chemical profiles of crude VX samples remain more or less intact upon prolonged storage, and after spiking in/on various matrices.
- (b) Correlation of chemical composition of specific batches (crime scene *vs* laboratory) should be feasible.
- (c) Chemical profiles of crude VX samples are indicative for a particular synthetic route.

Similar results were obtained for sulfur mustard and sarin. It was noted that small changes in the synthesis protocol might have a large impact on the chemical profile of the end product.

27. Robert Mathews stated that similar results were obtained in a DSTO study of the recovery of amiton (VG) from various matrices, including painted surfaces, soil, rubber and concrete.

Identification and attribution profiling of mushroom toxins in food

28. Sten-Åke Fredriksson, FOI Sweden, reported an investigation into the identification and attribution of amanita mushroom toxins in food. Using a two stage approach,¹⁵ a generic screen was performed by LC-MS/MS SRM to detect toxins based on a list of 87 selected intoxicants, followed by a second LC-MS analysis applying accurate mass determination and generation of an attribution profile. To demonstrate the potential of the methodology, mushroom stews containing either *Amanita phalloides* (Death Cap) or *Amanita virosa* (Destroying Angel) were analysed. By combining the screening method with accurate mass LC-MS, the attribution profile for 17 amanita toxins was established and used to identify the mushroom species in question. The analytical data was consistent with the fact that the *A. virosa* specimens used in this study were of European origin. This adds an important piece of information that allows geographic attribution, thus strengthening the attribution profile.

AGENDA ITEM NINE – Update on sampling and analysis by the TS

29. Hugh Gregg of the TS reported on a quality review performed during a Schedule 2 industry inspection. The timelines and bottlenecks in the process were documented. In this inspection, the GC-MS was set up on the afternoon of arrival, and was ready for analysis the following morning, after the pre-inspection briefing. The analytical chemists were able to prepare three samples for analysis (using standard sample

¹⁵ Jansson *et al.* Forensic Science International, 221 (2012) 44–49

preparation protocols) on the same day as the pre-inspection briefing, and the analyses were run overnight. Had a larger autosampler been taken on-site, all the samples would have been ready for data analysis the following morning.

30. The TS reported on the types of GC-MS instruments necessary for on-site inspections. A demonstration of an “all-in-one” GC-MS instrument at the OPCW Laboratory led to the conclusion that the current research-grade GC-MS instrument is still the best suited for OPCW purposes.
31. Progress has been made on the improved sample preparation procedures described in detail to the sixth meeting of the TWG on S&A. Additionally, an explanation for why previous fast-GC methods appeared problematic was given (slightly different GC columns phases and/or manufacturing processes). Progress continues on streamlining on-site reporting.

AGENDA ITEM TEN AND ELEVEN – Potential methodologies for analysis of PFIB and Schedule 3 chemicals

32. Hugh Gregg described several potential methods for analysis of the Schedule 2 chemical PFIB that are reported in the literature. A local company (DuPont, in Dordrecht, The Netherlands), has agreed in principle to assist the OPCW laboratory by providing a dilute standard of PFIB in an inert gas. This will enable the laboratory to develop a method, most likely using Tenax sorbent on which a derivatizing agent is absorbed, along similar lines to a method reported from the Dstl laboratory in the UK. The GC-MS analysis of some reactive Schedule 3 chemicals, e.g. phosphorus halides, remains a capability gap. One laboratory expects to publish some results in the near future.

AGENDA ITEM THIRTEEN – Any other business

How to improve S&A in assistance and protection exercises

33. Francesco Pilo of the Firefighters Public Rescue and Civil Defence Department, Italy, presented proposals to improve S&A in exercises such as Assistex 3, held in Tunisia in 2010. Some critical points from this exercise were highlighted and revolved mainly around the time taken to analyse samples, plus the high number of samples that were unsuitable for analysis. This restricted the maximum number of samples analysed in a day to 15. It was proposed that more time be allocated to S&A in the next Assistex exercise to improve the quality of S&A, and to trial new procedures. Methods for screening samples to determine the most appropriate for further analysis should be trialled, and attention should be paid to the management of the entire process.

Summary and conclusions

34. Samples suspected of containing ricin can be purified for analysis by a combination of separation on the basis of molecular mass, the electronic charge of the molecule, and specific affinity for antibodies and lactose.

35. The consensus of the TWG was that identification of ricin for verification purposes should be based on two analytical techniques and that the primary (confirmatory) technique should be based on mass spectrometric identification of peptides formed on enzymatic digestion. The two techniques should be selected such that they provide evidence of an intact ricin molecule, i.e. with chains A and B connected by a disulfide bond. The TWG has recommended criteria for identification.
36. The TWG has previously recommended criteria for the identification of saxitoxin.
37. The second confidence building exercise on biomedical samples, held in January 2012, has demonstrated a broader capability for metabolite analysis in urine. The quality of data and reporting was significantly improved over the first exercise, and the occurrence of system contamination and reporting of false positives was encouragingly less than in the first exercise. The exercise provided an opportunity to exercise draft criteria for trace analysis, based primarily on a system used by EC.
38. The criteria required by the EC guidelines for substances in animal products, and WADA criteria for the identification of drugs in human urine, both appear to be fit for OPCW purposes. The TWG recommends that the OPCW adopt a system based on the flexible points system used by the EC, with minor modifications to be consistent with OPCW Proficiency Test requirements.
39. A problem faced by many laboratories is how to handle samples where the nature of the hazard is unknown, particularly the elimination of any biological hazard prior to chemical analysis. The TWG was briefed on three protocols for eliminating a biological hazard, based on isolation with remote handling, chemical sterilisation with paraformaldehyde, and physical separation of biological organisms using ultracentrifugation and filtration.
40. The TWG continues to endorse TS efforts to reduce on-site analysis time. An instrumental development of possible relevance is the use of transportable mass spectrometers capable of direct sampling. One promising instrument has dual sources based on desorption electrospray ionisation (DESI) and direct analysis in real time (DART).
41. New developments in HRMS are having a substantial impact on off-site analysis. HRMS allows the determination of the molecular formula, e.g., in the case of analytes that are not in the OPCW Central Analytical Database (OCAD), thus narrowing down the number of possible structures. It also allows retrospective analysis of mass spectral data for analytes present at trace levels, rather than the selective analysis for predetermined analytes used in low resolution instruments. HRMS was used with impressive results in the two OPCW confidence building exercises on biomedical samples.
42. For verification analysis, the TS is concerned primarily with identification of scheduled chemicals. An additional aspect being explored by several laboratories is methodology that allows attribution of a sample to a particular source. Proof of principle was demonstrated with samples of VX.

43. In exercises such as Assistex 3, greater attention should be focused on screening samples to determine the most appropriate ones for further analysis, and to the management of the entire S&A process.

Closure of the meeting

44. The members of the TWG expressed their gratitude to the chairperson Robin Black for acting as chair for six sessions of the TWG.
45. The Chairperson closed the meeting at 17:45 on 5 September 2012.

Appendix 1: List of participants

Appendix 1

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

4 – 5 SEPTEMBER 2012

	Participant	Institution
1.	Alcaraz, Armando	Lawrence Livermore National Laboratory, United States of America
2.*	Black, Robin	Defence Science and Technology Laboratory (Dstl), Porton Down, United Kingdom of Great Britain and Northern Ireland
3.	Bossée, Anne	Centre d'Etudes du Bouchet, France
4.	Cermak, Jiří	Research Institute for Organic Syntheses, Czech Republic
5.	Coleman, Philip	Protechnik Laboratories, Lynnwood Glen, South Africa
6.	Fredriksson, Sten Åke	Swedish Defence Research Agency, Sweden
7.	González Chávez, José	Universidad Nacional Autónoma de México, Mexico City, Mexico
8.*	Martinez-Alvarez, Roberto	Complutense University, Madrid, Spain
9.	Mathews, Robert	Defence Science and Technology Organisation, Melbourne, Australia
10.	Noort, Daan	TNO Defence, Security & Safety, The Netherlands
11.	Pilo, Francesco	Italian Fire Brigade, Italy
12.	Schär, Martin	Spiez Laboratory, Switzerland
13.	Sng, Mui Tang	DSO National Laboratories, Singapore
14.	Tabet, Jean-Claude	University of Pierre & Marie Curie, France
15.	Trapp, Ralf	Independent consultant
16.*	Vanninen, Paula	VERIFIN, Department of Chemistry, Faculty of Science, University of Helsinki, Finland

* members of the SAB

Annex 3
REPORT OF THE SECOND MEETING OF THE SAB TEMPORARY
WORKING GROUP ON THE CONVERGENCE OF
CHEMISTRY AND BIOLOGY
THE HAGUE, THE NETHERLANDS
6 AND 7 SEPTEMBER 2012

AGENDA ITEM ONE – Opening of the meeting and adoption of the agenda

1. The Temporary Working Group (TWG) on the Convergence of Chemistry and Biology of the Scientific Advisory Board (SAB) held its second meeting on 6 and 7 September 2012 at the OPCW Headquarters in The Hague.
2. The meeting was chaired by William Kane on behalf of the SAB.
3. The list of participants in the meeting is given in Appendix 1.
4. The following agenda was adopted:
 - (1) Opening of the meeting and adoption of the agenda
 - (2) Revised Terms of Reference
 - (3) Biologically mediated synthesis of chemicals:
 - (a) The processes that are used in the biologically mediated synthesis of chemicals;
 - (b) The extent of use of biologically mediated synthesis in commercial chemical production;
 - (c) The utility of biologically mediated techniques for the synthesis of toxic chemicals;
 - (d) The application of biologically mediated processes for the synthesis/production of toxins and bioregulators, and future trends;
 - (4) Chemical synthesis of agents of biological origin (e.g. toxins, bioregulators) and of replicating systems:
 - (a) Nature and potential threats of these agents to the CWC
 - (5) Whether any biotechnological processes exist, other than biologically mediated synthesis, that are of relevance to the implementation of the CWC;

- (6) The meaning of “production by synthesis”
- (7) The potential benefits to the CWC of the convergence of chemistry and biology (which might include e.g. protective measures, medical countermeasures, and diagnostics).
- (8) Whether there are other scientific disciplines, apart from biology, that are converging in a significant way with chemistry, and whether it is possible to identify triggers or early-warning indicators for potential game-changing events that might have implications (whether positive or negative) for the CWC:
 - (a) Impact of nanotechnology (such as nano-catalysts that could be used in bio-processes)
 - (b) Other disciplines
- (9) Recommendations, intersessional work and date of next meeting
- (10) Any other business
- (11) Elaboration and adoption of the report from the meeting

AGENDA ITEM TWO – Revised Terms of Reference

5. The Chairman introduced some revisions to the TWG’s terms of reference based upon requests from the Director-General. Noting that the TWG’s main focus is the convergence of chemistry and biology, members of the TWG recognised that care will need to be taken when exploring other disciplines which might be converging with chemistry. The TWG approved the revised version of its terms of reference (see Appendix 2).

AGENDA ITEM THREE – Biologically mediated synthesis of chemicals

6. Guest presenter Richard A Johnson of Global Helix LLC gave a presentation on emerging trends and drivers in the global biotechnology industry. He identified 10 key biotechnology trends and drivers: The Century of Grand Synthesis; Disruptive Innovation directed at Societal Grand Challenges and Value Creation; Biotechnology increasingly is an Information Business; Who is Us? Redrawing the Boundaries of Biotechnology in the “New Biology”; Engineering Biology Increasingly Transforms Biotechnology; Robust 21st Century Biotechnology Toolkit as a Driver of Economic Inflection Points; New Biotechnology Transforms the Therapeutic and Diagnostic Spectrum in Health and our Understanding of Basic Biology; Biotechnology Moves Beyond Health; Convergent 21st century Infrastructure Spans Boundary Domains and; the Globalization of Biotechnology Capacity.
7. Guest presenter, Scott Mohr of the Bioinformatics Graduate Program and the Department of Chemistry at Boston University gave a presentation on the

extent and implications of the convergence between chemistry and biology in the age of synthetic biology. Dr Mohr made a number of key points: Insofar as living systems are concerned, the barriers between chemistry and biology have vanished; Whole-genome DNA sequencing and synthesis give “molecular life scientists” extraordinary control over the biosphere; Under the banner of “synthetic biology” this control is now being exerted by a world community of scientists, including especially the younger generation; The possibility for perverse abuse of this new-found power is very real and; failure to recognize this threat and act now poses a real danger to all humans on the planet.

8. William Provine of DuPont reviewed industrial examples that utilize metabolic engineering or synthetic biology as a core technology in those commercial developments. He reviewed how industry is utilizing the broad field of biotechnology and how this presents important opportunities that should be explored and developed to identify those safe and commercially viable applications that bring significant benefits to society. These opportunities arise in areas including food, energy generation, and protection of life. Benefits may include lower cost, higher quality products and reduced reliance on fossil fuels along with other environmental benefits.
 - (a) A key technology being employed is the use of metabolic engineering which is defined as the targeted and purposeful alteration (using genetic engineering techniques) of an organism's metabolic pathways in order to better understand how the pathways work or to redesign them to produce a different set of products. Such microbes are then utilized in fermentation-based production processes.
 - (b) Enzymes/Biocatalysts: DuPont develops biobased solutions using innovative enzymes, peptides and performance proteins to help improve performance, productivity, and environmental footprints in markets such as animal health and nutrition, cosmetics and personal care, laundry and dishwashing detergents, food and beverage production, pulp and paper and textiles processing.
 - (c) Cellulosic Ethanol: is a renewable, advanced biofuel produced by converting the starch extracted from cellulose - the cell walls of plants – into sugars and fermenting the sugars into ethanol. Agricultural byproducts such as corn stover and cereal straws are the most commonly used renewable feedstocks today. Genetic engineered yeasts and bacteria are being used in large-scale development plants today around the world.
 - (d) Biobutanol: Butanol (C₄H₉OH) that is produced from agricultural feedstock rather than petroleum. Butanol has properties that make it an excellent high performance fuel.
 - (e) Omega-3: Aquaculture, including salmon production, currently uses about 50 percent of the fishmeal and 80 percent of the fish oil produced from the global catch of feeder fish. DuPont has developed

an innovative yeast through metabolic engineering that is rich in long-chain Omega-3s to replace the fish oil in the salmon diet, greatly reducing the need for feeder fish. Today, typically about four kilograms of feeder fish are used to produce the fish oil needed to raise one kilogram of farmed salmon. The new diet requires only one kilogram of wild fish per kilogram of salmon, or 75 percent fewer feeder fish, while maintaining the levels of Omega-3s required for the salmon to be healthy and nutritious.

9. William Kane gave a brief presentation on the commercialization of biomediated processes. The major challenges of utilizing a new process for large scale production were highlighted including the need for considerable capital investment, process development and scale-up, startup and demonstration of commercial facility. This normally requires a number of years to take a process from the lab stage to commercial production. The range of products that are currently being produced (or will be produced in the next few years) with a biomediated process include the following categories: organic acids (e.g. lactic acid, succinic acid), alcohols, surfactants (for soaps and detergents), rubber chemicals, pharmaceuticals, plasticizers, polymers, lubricants, cosmetics, flavours and fragrances, biofuels. It was noted that the new production facilities for bio-based chemicals should be studied in more detail so their relevance to the CWC can be further assessed (need to compare to Other Chemical Production Facilities).

AGENDA ITEM FOUR – Chemical synthesis of agents of biological origin (e.g. toxins, bioregulators) and of replicating systems

10. Robin Black made a presentation on bioregulators. Commentators on the CWC are making increasing reference to bioregulators, as toxic chemicals or incapacitants. These chemicals of biological origin fall within the remits of both the CWC and BWC. Bioregulators regulate a wide range of body functions, including blood pressure, airway compliance, sleep, mood, cognisance and behaviour. They include a wide range of chemical classes, e.g., short chain peptides, polypeptides, nucleotides, lipid-derived metabolites and small molecules such as neurotransmitters. Peptides are the largest group of bioregulators and have been the class for which most concern has been expressed.
11. Some commentators have suggested that bioregulatory peptides offer prototypes for incapacitants. However, most peptides have inherent disadvantages if they are intended to target the central nervous system. They are inefficient in penetrating biological membranes, such as the lung and blood brain barrier, the natural bioregulator is rapidly metabolised by proteases, and the stability of peptides towards weaponisation and dissemination are unknown. These shortcomings can be overcome, e.g. large numbers of metabolically resistant analogues have been screened by drug companies, and new formulations, particularly associated with liposomes or nanocarriers, are being explored to enhance penetration of the blood brain barrier. However, all of these modifications add to the complexity and cost of the end product.

12. Other types of bioregulator should also be noted, for example some of those derived from lipid pathways such as eicosanoids (prostanoids etc), leukotrienes and platelet activating factor, have high biological activity and in some cases toxicity.
13. Although the concern for bioregulatory peptides may be overstated, it is recommended that the TS increase and maintain in-house knowledge of bioregulators.

AGENDA ITEM FIVE – Whether any biotechnological processes exist, other than biologically mediated synthesis, that are of relevance to the implementation of the CWC

14. It was noted that the meaning of “biologically mediated process” has not been defined for the purposes of addressing this agenda item. As a way forward, Robert Mathews will research the meaning of the term as it was used in the context of the CWC negotiations and will share his analysis with the TWG prior to the next meeting. It will then be possible to frame the question more clearly to the life science community to see if there are any other types of processes that should be considered by the TWG. Piers Millett offered to seek further input from members of the life science community and report back to a future TWG meeting.
15. The meeting was advised of past work in engineering enzymes which could be relevant. Scott Mohr will provide a summary of this work at a future TWG meeting.

AGENDA ITEM SIX – The meaning of “production by synthesis”

16. A key issue in the implementation of Part IX of the Verification Annex is whether or not biologically-mediated processes are covered by the term “production by synthesis”. The TWG was of the view that any process designed for the formation of a chemical substance should be covered by the term “production by synthesis”.

AGENDA ITEM SEVEN – The potential benefits to the CWC of the convergence of chemistry and biology (which might include e.g. protective measures, medical countermeasures, and diagnostics).

17. Hua Li reported that progress has been made in the area of medical countermeasures against CWA poisoning by convergence of chemistry and biology, including:
 - (a) protein-based drugs developed for prophylactic treatment of nerve agent poisoning, for instance the recombinant butyrylcholinesterase (BuChE) derived from goats milk;

- (b) monoclonal antibodies obtained based on the synthetic haptens could effectively bind to the nerve agents or hydrolyze the agents; and
 - (c) penetration of antidote (HI-6) through blood brain barrier was significantly increased by either a formulation with nano carriers, or modulation of the transporters located on the blood brain barrier.
 - (d) A new class of chemical and biological agent detectors based on molecular recognition by aptamers consisting of single-stranded DNA or RNA molecules was highlighted. They have a recognition format similar to antibodies and antigens. Published applications include the detection of ricin and abrin.
18. Robert Mathews provided a presentation on the benefits from the convergence of chemistry and biology for protection against chemical weapons. With respect to detection equipment and alarm systems, he referred to the development of bio-based detection systems (including systems designed to utilise sensor proteins used in animal olfactory processes). Such systems offer the potential to provide both “broad spectrum” detection, and “specific agent class” detection with reduced interfering responses. With respect to protective equipment, Dr Mathews referred to S&T efforts to develop nanomaterials as gas mask canister adsorbents and for protective clothing, which may be more effective and have reduced burden for the wearer than current systems. Developments in enzymes offer improved decontamination. Likewise, the development of potentially useful therapeutic agents and enhanced drug delivery systems may result in more effective medical countermeasures. The convergence of chemistry and biology is also resulting in improvements in chemical analysis (including bioforensics) which will facilitate more sensitive analysis of samples associated with investigations of alleged use of chemical weapons. There is anticipation of applications based upon these developments becoming available within the next decade.
19. William Provine noted that enzymatic approaches to decontamination of toxic substances are being developed to respond to chemical and biological attacks, as they lend logistical and environmental advantages over chemical and physical approaches. Current commercial enzymes include DuPont’s DEFENZ 120, which is highly specific to G-type nerve agents such as sarin, soman, and other organophosphate materials; and DEFENZ 130, which is highly specific to VX, Russian-VX, and pesticides such as parathion. Both products contain an industrial-grade enzyme and a buffering mixture in one small package and are non-toxic and non-corrosive, easy to use, and water soluble. Both products can also be formulated with other solutions.
20. Piers Millett introduced recent research which reports relevant advances in improving enzymatic hydrolysis of nerve agents. Rational design and directed evolution has been used to make structural changes to phosphotriesterase (PTE) and manipulate the binding pockets. A range of PTE mutants has been produced which demonstrates a strong preference for the Sp enantiomers (more toxic form) of sarin, soman, cyclosarin VX and VR agents. This range

of PTE mutants also demonstrates a significant increase in their ability to detoxify nerve agents. One enzyme with 11 mutations proved 15,000 times more effective than wild type PTE in breaking down cyclosarin. Other advances in biological enabling technologies relevant to both rational design and directed evolution not applied in this research, such as Conjugative Assembly Genome Engineering (CAGE) and Multiplex Automated Genome Engineering (MAGE), might provide opportunities to further improve the efficiency and selectivity of enzyme activity.

AGENDA ITEM EIGHT – Whether there are other scientific disciplines, apart from biology, that are converging in a significant way with chemistry, and whether it is possible to identify triggers or early-warning indicators for potential game-changing events that might have implications (whether positive or negative) for the CWC

21. Djafer Benachour gave a presentation on the impact of nanotechnology on the convergence of chemistry and biology. One of the many developments of nanotechnology is the production of nanomaterials. Among these materials, nanocatalysts are now commonly used in industrial processes, resulting in much higher yields, no side products, lower energy consumption, as well as lower costs. When these catalysts are used in microreactors, a scaling down of the equipment by a factor of 10^{-5} could be achieved, making biological and chemical reactions easier to perform. This microreactor technology, combined with nanocatalysts could be extended to biologically-mediated methods of chemical production currently under development, e.g. biocatalysis, synthetic biology and biopharming.

AGENDA ITEM NINE – Recommendations and intersessional work

22. The TWG reviewed the recommendations emanating from its first meeting (see subparagraphs 10.1-10.7 of Annex 3 of SAB-17/1 dated 23 November 2011).
23. Furthermore, the TWG agreed the following actions to follow-up the recommendations in the next intersessional period:
 - (a) Recommendation 10.1 was addressed at this TWG meeting and will continue to be addressed at future TWG meetings.
 - (b) Regarding recommendation 10.2, the TWG noted that it and its reporting to the SAB already provide a structured monitoring process for the near term. Additionally, the TWG recommended that the issue of convergence should be addressed on a periodic basis in other relevant fora which bring together experts from both the CWC and BWC, including practising scientists. In this regard, the TWG encourages the TS to continue its dialogue and interaction with the BWC Implementation Support Unit (ISU).

- (c) On recommendation 10.3, the TWG noted that it remains as an active part of the agenda as long as the TWG exists. For example, Robert Mathews will report to the next meeting of the TWG on the negotiating history of the term “biologically-mediated processes”.
- (d) With regard to recommendation 10.4, members of the TWG have conducted an informal review using scientific and business journals and the TWG is of the view that a formal survey should not be a priority at this time. Future consideration of this recommendation will be addressed under 10.3. In addition, relevant additional information will be gathered by: inviting guest speakers from the pharmaceutical industry and specialty chemicals sector to a future meeting; and TWG members attending relevant meetings such as the Biotech Industry Organization annual convention.
- (e) The TWG decided to revise the wording of recommendation 10.5. It now reads: “While the technical capability to synthesise many toxins, bioregulators and peptides exists today (through both traditional chemical synthesis and through synthetic biology methods), practical limitations currently exist. These areas need to be assessed regularly by the SAB and relevant TWGs. This issue will remain as a standing agenda item for future meetings of this TWG.”
- (f) On recommendation 10.6, Scott Mohr offered to conduct a detailed technical feasibility analysis of the production of bioregulators, peptides and toxins (including Saxitoxin and Ricin) via synthetic biology and/or biopharming, and to report back to the next TWG meeting. The TWG also suggested that a researcher working with saxitoxin will be invited to attend a future meeting of the TWG. Hua Li offered to explore current research involving ricin.
- (g) The TWG decided to revise the wording of recommendation 10.7, so that it now reads: “Other aspects of the convergence of chemistry and biology of potential relevance to the CWC should continue to be studied, including the development of improved protective measures, and analysis of biologically active compounds. These areas also need to be assessed regularly by the SAB and relevant TWGs. This issue will remain as a standing agenda item for future meetings of this TWG.” In addition, Robert Mathews will research the meaning of “biologically-mediated processes” as it was used in the context of the CWC negotiations and will share his analysis with the TWG prior to the next meeting. Piers Millett offered to seek further input from members of the life science community and report back to a future TWG meeting. The meeting was advised of past work in engineering enzymes which could be relevant. Scott Mohr will provide a summary of this work at a future TWG meeting.
- (h) As a follow-up to William Provine’s remarks on enzymatic approaches to decontamination of toxic substances (see paragraph 19 above), he

agreed to provide a presentation on DuPont's line of enzymes at the next meeting of the TWG.

AGENDA ITEM NINE – Date of next meeting/s

24. Members tentatively agreed to hold the third meeting of the TWG on 3 and 4 April 2013. In order to engage States Parties the fourth meeting could usefully be held in November 2013 in conjunction with the annual meeting of National Authorities.
25. The TWG recommended that the TS investigate the possibility of its members visiting a relevant plant site during a future TWG meeting. TWG members with suggestions will send them to the TWG Chairman by 1 October 2012.
26. Members also encouraged the discussion of convergence topics during the Third Review Conference in April 2013, for example in the form of side-events and poster sessions.

AGENDA ITEM TEN – Any other business

27. A side-event was organised at the Meeting of Experts to the Biological Weapons Convention in July at which the Chairman and two other TWG members made presentations about the work of the TWG to meeting participants. Robert Mathews described the side-event which was attended by approximately 60 participants from the BWC Meeting of Experts.
28. The Synthetic Biology 6.0 meeting in London in July 2013 could be a good opportunity for TWG members to get additional input on new relevant developments.

AGENDA ITEM ELEVEN – Elaboration and adoption of the report from the meeting

29. The report was adopted and the meeting was closed at 17:45.

Appendices:

Appendix 1 List of participants

Appendix 2 Revised Terms of Reference

Appendix 1

**LIST OF PARTICIPANTS IN THE SECOND MEETING OF THE SAB
TEMPORARY WORKING GROUP ON THE CONVERGENCE OF
CHEMISTRY AND BIOLOGY
6 AND 7 SEPTEMBER 2012**

	Participant	Institution
1.	Balali-Mood, Mahdi	Medical Toxicology Centre, Imam Reza Hospital, University of Medical Sciences, Mashhad, Islamic Republic of Iran
2.*	Benachour, Djafer	Ferhat Abbas University, Ministry of Higher Education and Scientific Research, Setif, Algeria
3.*	Black, Robin	Defence Science and Technology Laboratory (Dstl), Porton Down, United Kingdom of Great Britain and Northern Ireland
4.	Coleman, Philip	Protechnik Laboratories, Lynnwood Glen, South Africa
5.	Flower, Roderick	William Harvey Research Institute at Barts and the London School of Medicine and Dentistry, United Kingdom of Great Britain and Northern Ireland
6.*	Kane, William	Monsanto Company, United States of America
7.	Li, Hua	Chinese Academy of Military Medical Sciences, China
8.	Mathews, Robert	Defence Science and Technology Organisation, Melbourne, Australia
9.	Millett, Piers D	United Nations, Switzerland
10.*	Mogl, Stefan	Spiez Laboratory, Spiez, Switzerland
11.	Provine, William D.	DuPont Central Research & Development, United States of America
12.*	Rybalchenko, Igor	Military Science Centre of the Ministry of Defence, Moscow, Russian Federation
13.*	Zafar-Uz-Zaman, Muhammad	National Engineering and Scientific Commission (NESCOM), Islamabad, Pakistan
14.	Mohr, Scott (guest speaker)	Bioinformatics Graduate Program and the Department of Chemistry at Boston University, United States of America
15.	van Boheemen, Pieter (guest speaker)	Dutch DIY Bio community, The Netherlands
16.	Johnson, Richard (guest speaker)	Global Helix LLC, United States of America

* members of the SAB

Appendix 2

TEMPORARY WORKING GROUP ON THE CONVERGENCE OF CHEMISTRY AND BIOLOGY

TERMS OF REFERENCE¹⁶

- 1) The objective of the temporary working group (TWG) on the convergence of chemistry and biology is to further explore this convergence and the potential implications for the implementation of the Chemical Weapons Convention (CWC), as recommended by the Scientific Advisory Board (SAB) at its Sixteenth Session (see paragraph 14.3 of SAB-16/1, dated 6 April 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 Dr Robert Mathews as the Chair of the TWG. The first meeting was held in November 2011. After Dr Mathews had finished his term on the SAB in 2011, the Director-General appointed Mr Bill Kane as the new Chair of the TWG.
- 2) The TWG should consist of individuals with expertise in: chemistry; biotechnology and biological sciences; relevant research; relevant commercial/industrial production; and trends in other relevant scientific disciplines. Qualified members of the Scientific Advisory Board may join the TWG. Members of relevant international scientific organisations and key scientific unions in the life sciences, and international organizations maybe also be invited to join the group. Guest speakers may be invited from time to time. The TWG may also, when necessary, draw upon the expertise of the Technical Secretariat.
- 3) The TWG should consider both risks and benefits to the implementation of the CWC that arise from the convergence of the sciences. The TWG will report to the Scientific Advisory Board on:
 - a) Biologically mediated synthesis of chemicals:
 - i) The processes that are used in the biologically mediated synthesis of chemicals;
 - ii) The extent of use of biologically mediated synthesis in commercial chemical production;
 - iii) The use of biologically mediated techniques for the synthesis of toxic chemicals;
 - iv) The application of biologically mediated processes for the synthesis/production of toxins and bioregulators, and future trends;

¹⁶ Version 2, 22 June 2012

- b) Chemical synthesis of agents of biological origin (e.g. toxins, bioregulators) and of replicating systems;
 - c) Whether any biotechnological processes exist, other than biologically mediated synthesis, that are of relevance to the implementation of the CWC; (i.e. whether the types of production equipment and processes may pose a significant risk to the object and purpose of the Convention)
 - d) The meaning of “production by synthesis”;
 - e) The potential benefits to the CWC of the convergence of chemistry and biology (which might include e.g. protective measures, medical countermeasures, and diagnostics).
 - f) Whether there are other scientific disciplines, apart from biology, that are converging in a significant way with chemistry, and whether it is possible to identify triggers or early-warning indicators for potential game-changing events that might have implications (whether positive or negative) for the CWC.
- 4) The temporary working group will also advise on how to bring together expertise on the Biological Weapons Convention and Chemical Weapons Convention in order to discuss areas of common interest between the two Conventions and share knowledge related to convergence.
- 5) The temporary working group will exist for a period of two 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 further revised.