

**NOTE BY THE DIRECTOR-GENERAL****REPORT OF THE SCIENTIFIC ADVISORY BOARD ON
DEVELOPMENTS IN SCIENCE AND TECHNOLOGY****1. Introduction**

- 1.1 Following the practice adopted by the First Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention (hereinafter “the First Review Conference”),¹ the Director-General has asked the Scientific Advisory Board (SAB) to again prepare a report on relevant developments in science and technology that States Parties to the Chemical Weapons Convention (hereinafter “the Convention”) may wish to take into account in their review of the operation of the Convention, as provided for in paragraph 22 of Article VIII. The Director-General hereby forwards this report, which is annexed to this Note, to the States Parties.
- 1.2 In order to assist States Parties in their review, particularly with regard to any relevant scientific and technological development to be taken into account, the Director-General, again following established practice, provides in this Note his own assessments of the issues covered by the SAB in its report.
- 1.4 The Director-General wishes to use this opportunity to express his gratitude to the SAB for its valuable and thoughtful contribution to preparations for the Second Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention (hereinafter “the Second Review Conference”). The Director-General notes that this report was the result of extensive deliberations within the SAB, using a wide range of input from the global scientific community.
- 1.3 The SAB has organised its findings under six main headings, which, for ease of reference, are followed in this Note by the Director-General.

2. Advances in science and technology (paragraphs 2.1 to 2.14 of the attached SAB report)

- 2.1 In its report, the SAB draws the attention of the States Parties to the fact that science and technology are advancing rapidly in areas that are relevant to the Convention. These advances are expected to bring numerous benefits to humankind, for example

¹ See RC-1/DG.2, dated 23 April 2003.



in the form of new medicines and diagnostics, improved means of pest control, or new materials. They will open new avenues for international cooperation in the peaceful uses of chemistry, which could be taken up by the OPCW International-Cooperation Programme. They are also expected to help improve protection against toxic chemicals—improvements that are important given that there remain certain States not Party to the Convention, a fact that gives rise to particular concerns. Such improvements may also help counter the threat of non-State actors acquiring chemical weapons.

- 2.2 But these developments also pose potential risks to the Convention. With advances in chemistry and the convergence of chemistry and biology, many more chemical compounds are being synthesised and tested for their biological activity; some of which might have utility for weapons purposes. Advances in particle engineering and nanotechnology may lead to more effective delivery systems. The SAB concluded, however, that a major offensive programme would be required to convert a new biologically active toxic chemical into a chemical weapon. This, in the view of the Director-General, underlines the necessity to continue working towards the universal adherence to, and full compliance with, the Convention. The SAB considerations may provide useful background for the Second Review Conference when it addresses issues related to universality, national implementation, and verification.
- 2.3 The SAB noted again the question of the use of incapacitating chemicals for law enforcement, pointing to the possibility that new compounds might be discovered that more closely fit the profile required of such agents. The SAB remarked, however, that in the past, only two types of chemicals acting on the central nervous system appear to have been developed into chemical-warfare agents or incapacitating agents for use in law enforcement. The Director-General wishes to add that some aspects of the development of means of delivery of such incapacitants for law-enforcement purposes might be difficult to distinguish from aspects of a chemical weapons development programme. If States Parties find it desirable to evaluate the broader implications of the use of incapacitants for law-enforcement purposes, the Second Review Conference could offer an opportunity to initiate such an evaluation, and the SAB's observations might help in such an endeavour.
- 2.4 The SAB noted that significant changes are under way in the chemical industry: advances in chemical manufacturing (new processes, equipment, and technologies), structural changes (new production locations and changes in trade patterns), and a convergence of chemistry and biology. These trends make chemical manufacturing more effective and versatile. At the same time, the global map of chemical manufacturing and trade is changing, with many more plants in many more countries capable of a rapid changeover from one chemical to another. The Director-General believes that these trends underline the need to continue working towards full and effective national implementation of the Convention, and to ensure that the national implementation measures adopted by the States Parties appropriately reflect the comprehensive nature of the Convention's prohibitions (the "General Purpose Criterion"). The First Review Conference has already highlighted this point, and States Parties may wish to come back to it, in particular, as they review the implementation of Articles VI and VII of the Convention.

- 2.5 Trends in the chemical industry also call for a further evolution of the Convention's verification system under Article VI. The SAB observed that the verification regime for other chemical production facilities (OCPFs) was included in the Convention as a dynamic system that would take into account advances in chemical production technologies. The SAB concluded that this regime needs to evolve further in terms of the number of inspections conducted, the selection of OCPFs for inspection, and how inspection objectives are determined with regard to unscheduled chemicals in order to ensure compliance. The States Parties may wish to consider this point as they review the implementation of Article VI of the Convention. The SAB also noted that inspectors, as well as National Authorities, need to be kept informed about the changes occurring in production technologies. The Director-General wishes to call the attention of National Authorities to these technological advances; he will also ensure that the Technical Secretariat (hereinafter "the Secretariat") take the necessary measures to maintain in the Inspectorate an appropriate knowledge base about these developments.
- 2.6 The growing convergence between chemistry and biology is an issue that may need further reflection. These trends clearly have an impact on the scientific basis of the Convention, but it is less clear at this stage how the implementation process should be adapted. An obvious aspect is the need to ensure that the implementation process, at both the national and the international level, is firmly based on the premise that all toxic chemicals and their precursors are chemical weapons unless they are intended for purposes not prohibited, and so long as their types and quantities correspond to such purposes. At the practical level, however, more study is required. While the further development of the OCPF verification regime, in principle, seems an appropriate direction in which to proceed, the differences between the design criteria underlying that regime and the characteristics of the facilities in industry and academia that are at the forefront of the cross-over between chemistry and biology need to be recognised. There are also legal issues arising, on the one hand, from the overlap between the regimes of the Convention and the Biological and Toxin Weapons Convention, and, on the other hand, from the regime differences between those two treaties. The Director-General is of the view that this matter warrants further study and that additional advice might be sought from the SAB, from States Parties that have assessed these developments, and from stakeholders in industry and academia. Such additional advice would facilitate the consideration of this issue by the policy-making organs in due course.

3. The schedules of chemicals (paragraphs 3.1 to 3.14 of the SAB report)

- 3.1 The SAB again addressed the question of "captive use or production" of Schedule 1 chemicals.² The SAB reported that this issue has no practical relevance; it should therefore not be pursued any further.
- 3.2 The practice of States Parties is that salts of scheduled chemicals, if not specifically listed in the schedules, are not considered to be covered under the respective schedule.

² This issue was brought to the SAB's attention by the Executive Council's facilitator for chemical-industry issues in 2005 (see paragraph 9.1 of SAB-7/1, dated 11 March 2005), after a decision had been taken by the Conference regarding the concept of captive use regarding Schedule 2 and 3 chemicals (C-9/DEC.6, dated 30 November 2004).

The SAB recalled that there may nevertheless be cases where the production of a salt of a scheduled chemical involves first the production of the free base (i.e., the scheduled chemical), and that depending on the amounts involved, declarations may be required. The SAB also pointed out that in the case of nitrogen mustard (HN-3) (a Schedule 1 chemical), the hydrochloride salt may be isolated as a precursor. The Director-General wishes to draw the attention of States Parties to this advice, so that they can take it into account when preparing their declarations under Article VI.

- 3.3 The SAB again addressed the role of Chemical Abstracts Service (CAS) Registry Numbers. The SAB advice remains that these are practical tools for identifying scheduled chemicals, but they should not in themselves be considered to have regulatory power. The Director-General concurs and at the same time agrees that the OPCW Declaration Handbook should provide references to the various CAS numbers corresponding to the entries in the schedules.³
- 3.4 The SAB reviewed the question of what constitutes “Saxitoxin, CAS registry number 35523-89-8”. It observed that the nomenclature of saxitoxin has evolved since the Convention was negotiated, reflecting a more refined understanding of its molecular structure. Saxitoxin, it seems, is a case where the CAS Registry Number contained in the Convention is unhelpful: The structure that was weaponised in the past is different from the one that corresponds to the CAS Registry Number given in Schedule 1. States Parties are advised to take account of this when preparing declarations under Article VI of the Convention. As a separate issue, the SAB stated its intention to review the appropriateness of listing saxitoxin in Schedule 1 or Schedule 2A. The Director-General is looking forward to any technical advice that the SAB may submit on the matter in the future.
- 3.5 The SAB recalled its previously recorded understanding of what, within the meaning of the Convention, constitutes ricin. The SAB noted, however, that there are problems regarding the analysis of ricin. The Director-General is awaiting any further technical advice that the SAB may submit on the matter.
- 3.6 In the broader context of the composition of the schedules of chemicals of the Convention, the SAB advised that the number of known toxic compounds that could potentially be abused for chemical weapons purposes will steadily increase, and pointed out that advances in the life sciences will create new risks in this regard given the dual-use potential of many chemicals. However, the SAB advised against adding new chemicals to the schedules as this would create additional burdens on reporting requirements and verification. Instead, the SAB emphasised the need to ensure the comprehensive nature of the concept of “chemical weapons” in implementing the Convention (including national implementation and self-governance by industry and academia). The Director-General concurs with that recommendation. The First Review Conference has already affirmed the comprehensive nature of the concept of “chemical weapons” in the context of its review of the general provisions of the Convention as well as of issues related to national implementation; when the Second Review Conference returns to these issues, the SAB’s advice may again be useful.

³ The Secretariat has already undertaken the identification of such CAS Registry Numbers in a project jointly carried out with the European Chemical Industry Council (CEFIC) and intends to include these in the next version of the Declaration Handbook to be issued in April 2008.

3.7 The SAB highlighted the need for transparency in chemical-defence programmes, and for a careful assessment of the compatibility with the Convention of the development of weapons that employ toxic chemicals (incapacitants) for law-enforcement purposes. It also addressed issues related to transparency and confidence building. As for the first issue, the Second Review Conference may wish to take this up when it addresses issues related to the annual submission by States Parties of information on their national protective programmes, using the adopted formats and in accordance with the requirements of the Convention and the procedures adopted by the Conference of the States Parties (hereinafter “the Conference”). As for the second issue, the Director-General’s views have already been set out in paragraph 2.3 above.

4. Verification (paragraphs 4.1 to 4.13 of the SAB report)

4.1 In its report, the SAB focussed on two issues related to verification: sampling and analysis, and the question of biomedical samples.

4.2 With regard to sampling and analysis, the SAB was of the view that the current procedures used for on-site analysis (gas chromatography-mass spectrometry (GC-MS) in combination with the OPCW dual-mode software containing the OPCW Central Analytical Database (OCAD)) remain fit for purpose. It provided useful commentary on the present capabilities of the Secretariat, outlined trends that should be monitored, and made suggestions for how certain logistical aspects could be further improved. It also reflected on the work of designated laboratories and the current system of OPCW proficiency testing. The Director-General welcomes this advice, which the Secretariat will take into account as it further improves its capabilities to conduct sampling and analysis.

4.3 With regard to analysis of toxins, the SAB observed that the OPCW has a requirement to secure access to methods for their identification. Problems remain with regard to suitable analytical methods. There are also uncertainties about which designated laboratories have the capability to undertake toxin analysis. The SAB also noted that the OPCW has not yet addressed trace analysis of environmental samples, which may be important in investigations of alleged use (IAUs). Both issues remain under the purview of the SAB, and the Director-General is looking forward to receiving the SAB’s advice on them in due course.

4.4 The SAB also pointed out that in certain inspection scenarios, there is a need for OPCW inspectors to analyse samples in order to establish the identity of riot control agents, or of chemicals contained in old and abandoned chemical weapons (OACWs). The SAB recommended that the spectral data for these chemicals be included in the OCAD. The Director-General endorses this recommendation—these analytical data are essential for certain types of inspections. He hopes that the policy-making organs can agree on guidance on the inclusion of riot control agents and chemicals contained in OACWs in the OCAD.

4.5 With regard to the analysis of biomedical samples—an essential tool for the conduct of IAUs—the SAB recalled that the OPCW has yet to establish a capability to handle or analyse such samples, and that there is no system of designated laboratories for their analysis. The SAB has been working on this issue for several years now. As a

first step, the OPCW Laboratory, with support from the Netherlands Organisation for Applied Scientific Research (TNO), plans to organise a first confidence-building exercise in 2008. From the perspective of the Director-General, it would be desirable for the Second Review Conference to encourage States Parties to engage in the process and help in setting up an OPCW capability to analyse biomedical samples, as required by the Convention. Progress in this respect would also facilitate cooperation among States Parties, and between them and the Secretariat, in this important area.

5. Destruction of chemical weapons (paragraphs 5.1 and 5.2 of the SAB report)

5.1 The SAB noted that the technologies used in the destruction of declared chemical weapons stockpiles appear to have matured to a point where the implementation of the requirements of the Convention requires no further technological innovation or development. With regard to OACWs, on the other hand, the SAB noted that further research and development are needed for their safe recovery, and that there is a continuing need for innovation in, and new approaches to, the destruction of recovered items.

5.2 The First Review Conference encouraged international cooperation in the destruction of chemical weapons, including OACWs, among States Parties. As the Second Review Conference returns to these issues, it may wish to take the SAB's observations into account.

6. Assistance and protection against the effects of chemical weapons, and international cooperation (paragraphs 6.1 to 6.4 of the SAB report)

6.1 The SAB observed that the advances in science and technology have the potential to help States Parties improve the level of protection they can offer against chemical weapons. Effective defence should discourage the development and use of chemical weapons. Enhanced international cooperation in this field can act as an incentive for States not Party to join the Convention. The SAB described in some detail the current state of affairs with regard to detection and field analysis, medical countermeasures, and decontamination.

6.2 The Second Review Conference may wish to take these observations into account when it addresses the implementation of Article X of the Convention, and in this context, when it addresses the Secretariat's activities (such as the OPCW Databank on Protection, the OPCW Protection Network, training courses and exercises) to render advice to States Parties who wish to enhance their protective capacity, as provided for under paragraph 5 of Article X.

7. Education and outreach in the context of the Convention (paragraphs 7.1 and 7.2 of the SAB report)

7.1 The SAB recalled the progress made since the First Review Conference, in collaboration with the International Union of Pure and Applied Chemistry (IUPAC), in raising awareness in the chemical profession about the Convention. Educational material has been developed and evaluated in a number of pilot studies; further such trials are envisaged and plans are being made for the material to be made available on the IUPAC website.

7.2 The Director-General welcomes these and similar initiatives and is of the view that further collaboration between the OPCW and the scientific and chemical-industry communities is important for the effective implementation of the Convention. In this context, the adoption of professional codes of conduct and other governance measures can help promote compliance with the requirements of the Convention by all professionals and institutions that deal with chemicals. When the Second Review Conference addresses issues related to the implementation of the Convention, it may also wish to address these and other awareness-raising and outreach activities, and provide guidance for future goals and activities in this field.

Annex:

Report of the Scientific Advisory Board on Developments in Science and Technology for the Second Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention (Second Review Conference)

Annex

**REPORT OF THE SCIENTIFIC ADVISORY BOARD ON DEVELOPMENTS IN
SCIENCE AND TECHNOLOGY
FOR THE
SECOND SPECIAL SESSION OF THE CONFERENCE OF THE STATES PARTIES
TO REVIEW THE OPERATION OF THE CHEMICAL WEAPONS CONVENTION
(SECOND REVIEW CONFERENCE)**

1. INTRODUCTION

- 1.1 Pursuant to Article VIII, paragraph 22, of the Convention, the Second Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention (hereinafter “the Second Review Conference”) will take place from 7 to 18 April 2008.
- 1.2 The Scientific Advisory Board (SAB) was established by the Director-General in accordance with Article VIII, subparagraph 21(h) and paragraph 45, of the Chemical Weapons Convention (hereinafter “the Convention”), so that he could offer to the of the States Parties (hereinafter “the Conference”), the Council, and States Parties specialised advice in those areas of science and technology that are relevant to the Chemical Weapons Convention (hereinafter “the Convention”). In keeping with this mandate, and as its contribution to the preparations for the Second Review Conference, the SAB has prepared this report, which analyses relevant developments in science and technology over the past five years and presents recommendations and observations that the SAB considers to be important to both the review of the operation of the Convention and its future implementation.
- 1.3 This report provides updates on issues identified in the SAB’s report to the First Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention (hereinafter “the First Review Conference”) and sets forth several additional issues for consideration. It discusses the following topics:
 - (a) advances in science and technology:
 - (i) the convergence of chemistry and biology;
 - (ii) the accelerated discovery of chemicals;
 - (iii) nanotechnology;
 - (iv) technologies for delivery systems; and
 - (v) production technologies;
 - (b) schedules of chemicals:
 - (i) captive use of Schedule 1 chemicals;
 - (ii) salts of scheduled chemicals;

- (iii) Chemical Abstracts Service registry numbers;
 - (iv) saxitoxin;
 - (v) ricin; and
 - (vi) new toxic compounds;
- (c) verification:
- (i) on- and off-site sampling and analysis; and
 - (ii) analysis of biomedical samples;
- (d) destruction of chemical weapons;
- (e) assistance and protection against the effects of chemical weapons, and international cooperation; and
- (f) education and outreach in the context of the Convention.

2. ADVANCES IN SCIENCE AND TECHNOLOGY

- 2.1 Science and technology are advancing at an increasing rate in areas directly relevant to the Convention. It is important that the OPCW take note of these developments in order to ensure that the Convention, and in particular its verification regime, continue to be implemented effectively.

Convergence of chemistry and biology

- 2.2 An important trend in the life sciences is the increasing convergence of chemical and biological systems, which results from an increasing understanding of complex life processes in the post-genomic era, along with the emerging ability to replicate life processes. These advances will undoubtedly lead to major benefits to humankind in the medical and other sciences, but there is also a clear potential for abuse. These developments reinforce the overlap between the Convention and the Biological and Toxin Weapons Convention, as does the increasing number of toxins and potentially toxic bioregulators being characterised.

Accelerated discovery of chemicals

- 2.3 New biologically active molecules are being discovered at an unprecedented rate. For example, parallel synthesis and high-throughput screening are producing data on millions of compounds. The tools for such techniques are becoming widely available and could be selectively targeted at toxic molecules. Pharmaceutical and pesticide companies now hold huge databases of biological data that could be a source of prototypes for new chemical-warfare agents. It should, however, be noted that most of this data is now being generated through the use of *in vitro* assays and that relatively few investigations progress to the study of a compound's toxicity *in vivo*. It should also be noted that the discovery of large numbers of biologically active compounds before high-throughput screening was introduced has had relatively little

impact on the development of new chemical-warfare agents. Moreover, a major offensive programme would be required in order to convert a new biologically active toxic compound into a chemical weapon.

- 2.4 One area in drug research that is causing some concern involves compounds that could be developed legitimately within the constraints of the Convention as non-lethal agents for law-enforcement purposes. Such compounds clearly have dual-use potential. The accelerated discovery of drugs has resulted in the identification of many new compounds that act very selectively on the central nervous system, both regionally and with regard to receptor subtypes. It remains to be seen what challenge, if any, one or another of these compounds could pose to the Convention. It should be noted here, too, that although many extremely potent compounds that act on the central nervous system were discovered in period from the 1950s to the 1970s, only two types, anticholinergics and opioids, appear to have been developed into chemical-warfare agents or non-lethal agents for use in law-enforcement.

Nanotechnology

- 2.5 Developments in the rapidly expanding field of nanotechnology and particle engineering offer new opportunities to develop defensive countermeasures against chemical weapons—for example, in the delivery of drugs, in the development of new sensors, in diagnostics, and in the development both of improved filtration systems for respirators and protective clothing and of new decontaminants.
- 2.6 Advances in nanotechnology and aerosol technology are being explored with a view to achieving more-effective, better-targeted delivery of biologically active compounds. Many of the considerations that promote the design of particles for the delivery of drugs via the respiratory system could also have a bearing on the dissemination of aerosolised chemical-warfare agents. Nanotechnology is being exploited to engineer or design biologically active systems and so-called “smart materials” that respond to specific stimuli and deliver active ingredients to targets in the body. Nanoparticulates could provide a new means of facilitating entry into the body or cells, particularly in the brain, in order to achieve selective reactions with target proteins or genes, or to overcome any immune reaction in the target organism. Some nanoparticulates show greater toxicity than micronised material. It should, however, be recognised that the sophisticated engineering of a high-value drug for targeted delivery might not be appropriate for a chemical weapons delivery system, where as much as 99.9% of the toxic chemical disseminated will not reach its target organ within the human body.

Technology for delivery systems

- 2.7 Pharmaceutical companies are showing an increasing interest in administering drugs by inhalation as an alternative non-invasive method of delivery. In the case of drugs with a low molecular mass, many of which are readily absorbed by the lungs, this route circumvents the extensive metabolism that occurs in the intestinal tract following ingestion. Larger molecules, such as proteins, are also absorbed through the lung membrane, albeit at a slower rate. A major goal of pharmaceutical companies has been the development of devices that would deliver insulin as an

inhalable aerosol and that would thus obviate the need for millions of diabetics to inject insulin. Some drug companies are also focussing on the lungs as a point of entry for the rapid administration of drugs to the central nervous system. The physical properties that promote rapid absorption through the lungs are similar to those that promote the penetration of the blood-brain barrier, and a number of devices have been developed for administering such drugs as opioids, anti-migraine drugs, and anti-convulsants as aerosols.

- 2.8 Many of the considerations that promote the design of particles for the effective and targeted delivery of drugs via the respiratory system would be applicable to the dissemination of a chemical-warfare agent as an aerosol. The efficiency of absorption has been improved, for instance, through the use of large porous aerosol particles that allow the delivery of drugs into the deep alveolar regions of the lungs and promote their absorption there. The spray-drying equipment needed to create such particles is relatively inexpensive and widely available, although the optimisation of a well-engineered particle requires expertise and considerable effort. This type of technology can be combined with nanotechnology to deliver nanoparticulate aggregates that will, once absorbed, disperse in the body, where their design (e.g., multifunctional polymeric design) could facilitate improved and more-selective delivery and targeting of drugs.

Production technologies

- 2.9 As noted in the report of the SAB to the First Review Conference (RC-1/DG.2, dated 23 April 2003), major developments relevant to the implementation of the verification regime under Article VI of the Convention are taking place in the production of industrial chemicals.
- 2.10 Technological innovations continue to make chemical manufacturing more versatile and more efficient. The flexibility of the chemical industry is increasing with the widespread use of multipurpose production equipment, and the emerging use of microreactors, which was noted in the SAB's report to the First Review Conference, may create an additional dimension. Microreactors exhibit many potential advantages for the manufacture of a number of fine chemicals, and they eliminate the problems associated with the scaling-up of production processes from laboratory to industrial-scale volumes. Microreactor systems would not exhibit the traditional signatures if adapted to the manufacture of highly toxic compounds and could significantly reduce the time required to make the transition in the development of highly toxic new compounds from the research to the production stage. However, although these systems have become more prevalent in research-and-development laboratories, including industrial research-and-development laboratories, they are not yet widely used in industry, and they are being integrated into industrial-scale production more slowly than some had predicted. This development clearly requires a watching brief to assess what impact it might have on the verification regime under the Convention.
- 2.11 Significant advances are also being made in the application of chemical and bio-catalysis to industrial production. Approximately 85% of industrial chemical

processes are catalytic. Nanotechnology offers new approaches to the design of catalysts that will increase reactivity, selectivity, and efficiency.

- 2.12 The increasing globalisation of the chemical industry means that chemical production is spreading to new, non-traditional countries, and the trend in optimising what is known as “scale of production” is leading to the creation of so-called world-scale plants—a phenomenon whereby a single plant supplies a significant part of the total world production of a given chemical. This is leading in turn to an increase in the international trade in chemicals. A number of countries in Asia, Eastern Europe, and South America, including China and India, the Russian Federation, and Brazil, are becoming major players in the production of chemicals, including fine chemicals.
- 2.13 As production technologies change and the number of potential chemical-warfare agents increases, the General Purpose Criterion for the definition of chemical weapons and for verification at other chemical production facilities (OCPFs) becomes more important.⁴ The OCPF verification regime was included in the Convention as a dynamic system that would take into account advances in chemical-production technologies. This regime needs to evolve further in terms of the number of inspections conducted, the selection of OCPF plant sites, and how inspection objectives are determined with regard to unscheduled chemicals in order to ensure compliance.
- 2.14 It is essential in this respect for inspectors and National Authorities to be kept informed of changes in production technologies.

3. SCHEDULES OF CHEMICALS

- 3.1 Both the definition of chemical weapons and the schedules of the chemicals themselves have been the object of extensive discussions by the SAB. Many of the chemicals that are listed in Schedules 1, 2, and 3 have been used, stored, or weaponised as chemical-warfare agents.
- 3.2 The Convention contains a mechanism to amend the schedules. Chemicals can be added to, or deleted from, the schedules subject to agreement by States Parties. They can also be moved from one schedule to another should the States Parties consider this beneficial for verification purposes.

Captive use of Schedule 1 chemicals

- 3.3 The SAB was asked by the Director-General to consider the issue of the “captive use or production” of Schedule 1 chemicals, in which the chemical is not isolated but is an intermediate in an industrial process. Under the only possible scenario known to the SAB in which such a process could take place, nitrogen mustard (HN-3), a Schedule 1 chemical, would be formed as an impurity in the synthesis of pethidine-like compounds, because of the presence (at approximately 1%) of triethanolamine in the diethanolamine used as a precursor. However, the nitrogen mustard would be present

⁴ Among the definitions of “chemical weapons” given in Article II, paragraph 1, of the Convention, is the following, in subparagraph 1(a):

“Toxic chemicals and their precursors, except where intended for purposes not prohibited under this Convention, as long as the types and quantities are consistent with such purposes”. Some States Parties and commentators refer to this condition as the “General Purpose Criterion”.

at such a low concentration that it would be impractical to isolate it from the reaction mixture. The SAB considers this to be a purely academic issue that does not require adjustments to Schedule 1.

Salts of scheduled chemicals

- 3.4 The SAB was asked by the Director-General to review its observations on salts of scheduled chemicals. These salts are chemically distinct from their parent compounds, and have different physical and chemical properties, as well as their own CAS Registry Numbers. Their inherent toxicity usually differs little from that of the parent compound, although the physical hazard is different. The salt can easily be retransformed into the base (with the exception of quaternary salts). In industry, a base is often converted to a salt if it is more convenient to handle in this form or, in the case of drugs, to administer. Normally, from the standpoint of the end user, there is no essential difference between the free base and the corresponding salt.⁵ The SAB notes that, on regulatory grounds, States Parties have disagreed with its recommendation that all salts of scheduled chemicals be treated in the same way as their corresponding free bases. Consequently, salts of scheduled chemicals are to be treated differently from their corresponding free bases in relation to, for example, the Convention's provisions on the trade in scheduled chemicals. It should be noted that there are cases where scheduled chemicals are an intermediate in the production of such salts. Even though these bases are not isolated or captured from the equipment, they could be removed from the production equipment if that were so decided. Declarations might thus still be due, depending on the amounts produced.⁶ In the case of nitrogen mustard (HN-3), the hydrochloride salt may be isolated as a precursor to the free base.

Chemical Abstracts Service Registry Numbers

- 3.5 One issue that the SAB noted in the context of its previous recommendations on salts is the role of the Chemical Abstracts Service (CAS) Registry Numbers indicated in the schedules of chemicals. The SAB has come to the view that, while the CAS Registry Numbers are a useful aid to identification, they were intended as specific identifiers of scheduled chemicals. There appears to be a question among States Parties about whether these numbers have a regulatory value. The SAB would like to caution against such a view, because there is not necessarily a one-to-one relationship between CAS Registry Numbers and chemical structures. While these numbers are useful in the identification of chemical compounds, this usefulness should not lead to the assumption that they should have any regulatory power within the context of the Convention. At the same time, it could be helpful if the OPCW Declaration Handbook were to provide references to the various CAS numbers that are related to an entry in the schedules (for example, for different isomers of a scheduled chemical and for mixtures containing a scheduled chemical).

⁵ See paragraph 2.10 of SAB-II/1, dated 23 April 1999.

⁶ Examples of such "captive use" of a scheduled chemical in the production of a corresponding salt that is not listed in the schedules can be found in Schedule 1 (e.g., the production of HN-2 hydrochloride), as well as in Schedule 2 (e.g., the captive use of 3-quinuclidinyl benzilate (BZ) in the production of clidinium bromide).

Saxitoxin

- 3.6 Related to the issue of salts is the question of what constitutes saxitoxin, which is listed in Schedule 1 together with the CAS Registry Number of the dihydrate (free base). This situation is of little help when it comes to considering which form or forms of the molecule are considered to be included in the schedules of chemicals.
- 3.7 A survey of the literature shows how the understanding of the nomenclature and molecular structure of saxitoxin has evolved in recent decades. Since the elucidation of the structure, the term “saxitoxin” has been used variously to describe the dihydrochloride of the molecule, or the free base, or its cation. In the natural environment, saxitoxin exists exclusively in cationic form. More recently (and since the conclusion of the Convention), the nomenclature has become more specific, distinguishing between saxitoxin dihydrochloride and saxitoxin (di)hydrate. From the record of negotiations, it appears that what negotiators wanted to include in the schedules was the form of saxitoxin that had been weaponised in the past (the agent TZ, which is a salt), and other forms of weaponisable saxitoxin. Problems related to this question became apparent after the entry into force of the Convention, when Part VI of the Verification Annex to the Convention (hereinafter “the Verification Annex”) had to be adjusted to take account of practical realities. The notification regime for transfers of saxitoxin for medical and diagnostic purposes was changed so that it required notification at the time of transfer instead of in advance.⁷ It should be noted that the issue of what constitutes saxitoxin again shows that the CAS Registry Numbers given in the Convention cannot be considered to have regulatory power and that they are essentially aids to identification.
- 3.8 There were also discussions, based on the guidelines in the Convention, of whether Schedule 1 or Schedule 2A would be more appropriate for saxitoxin. In this regard the SAB agreed to take the matter up at a future Session.⁸

Ricin

- 3.9 The SAB was also asked by the Director-General to consider what, within the meaning of the Convention, constitutes “ricin”. Such an understanding may be helpful to States Parties and could be incorporated into the OPCW Declaration Handbook. The SAB recommends the following definition of ricin:

“All forms of ricin originating from *Ricinus communis*, including any possible variations in the structure of the molecule arising from natural processes or manmade modification, are to be considered ricin as long as they conform to the basic ‘native’ bipartite molecular structure of ricin (A-S-S-B) that is required for mammalian toxicity. Once the inter-chain S-S bond is broken or the protein denatured, it is no longer ricin.”

⁷ EC-MII/DEC.1, dated 15 January 1999. A first change was notified by the Depositary in notification C.N.916.1999.TREATIES-7, issued on 8 October 1999; a second, in C.N.157.2000.TREATIES-1, issued on 13 March 2000.

⁸ The following arguments were given for placing saxitoxin in Schedule 2A: that it would greatly reduce the administrative burden, and that, with reference to subparagraph 1(c) of the Annex on Chemicals, saxitoxin is of quite some use in very small quantities for purposes not prohibited under the Convention.

- 3.10 It should be noted that this understanding is consistent with a Conference decision that plants that process castor oil should not be subject to the Convention's reporting procedures under Schedule 1 (C-V/DEC.17, dated 18 May 2000).
- 3.11 The SAB is of the view that the analysis of ricin poses a number of problems. Ricin is a glycosylated protein that exists in a number of isoforms, and new mutations occur that will create additional isoforms in the future. There is also the possibility that the A-S-S-B linkage may be intact, but with the loss of the three-dimensional conformation of the ricin molecule the ricin might thus be rendered inactive.

New toxic compounds

- 3.12 The number of known toxic compounds that could potentially be abused will steadily increase. The advances in the life sciences described above will create new risks in this regard, given the dual-use potential of many chemicals. States as well as non-State proliferators may alternatively opt for toxic industrial materials as less-effective chemical weapons. The importance of the comprehensive nature of the definition of "chemical weapons" in the Convention, and of its implementation by States Parties, is consequently reinforced. Non-proliferation efforts, including measures to control access to relevant chemicals, equipment, and technologies, remain important. At the same time, effective self-governance by the scientific community must complement these safeguards.
- 3.13 The SAB continues to hold the view that adding a large number of new toxic compounds to the schedules of chemicals would introduce additional burdens on reporting requirements and verification.
- 3.14 The potential risks to the Convention associated with advances in science and technology would increase significantly, should dedicated chemical weapons programmes exist and should they take advantage of new toxic chemicals. There is therefore good reason to call for transparency in chemical-defence programmes, and to assess carefully the compatibility with the Convention of the development of weapons that employ toxic chemicals for law-enforcement purposes (including so-called non-lethal weapons). From the standpoint of promoting transparency and building confidence, there will, inter alia, be advantages in considering an extension of the Convention's declaration requirements so that States Parties would have to declare all chemicals they have stockpiled for law-enforcement purposes (types, quantities, and delivery systems). However, such non-lethal chemicals require thorough study. The terminology surrounding so-called non-lethal incapacitants also needs further elaboration.

4. VERIFICATION

On- and off-site sampling and analysis

- 4.1 After a gap of four years, the SAB has reconvened its temporary working group (TWG) on sampling and analysis. This group is addressing methods and procedures used for on- and off-site analysis, particularly the unresolved problem of the analysis of toxins.

- 4.2 The SAB is of the view that the current procedures used for on-site analysis, based around gas chromatography-mass spectrometry (GC-MS) in combination with the OPCW dual-mode software containing the OPCW Central Analytical Database (OCAD), are fit for purpose. It is, however, commonly acknowledged that the logistic burden posed by the equipment required for the preparation of samples, and the time for analysis, remain greater than is desirable. The SAB notes the development of more-portable and miniaturised GC-MS systems, but believes that none of these is yet likely to meet the technical specifications for on-site inspections.
- 4.3 The analysis of aqueous samples is particularly time-consuming because of the need to evaporate aqueous extracts or samples to dryness prior to derivatisation of polar analytes (e.g., degradation products). This requirement also adds significantly to the weight of the sample-preparation equipment. The (TWG) on sampling and analysis is reviewing recent developments in the preparation of aqueous samples and will assess their possible applicability to on-site analysis. A number of approaches use extractive derivatisation, thus removing the need to concentrate aqueous samples to dryness.
- 4.4 The use of liquid chromatography-mass spectrometry (LC-MS) would allow the direct analysis of aqueous samples and would expand the number of analytes (e.g., toxins) that could be analysed on-site. However, LC-MS is not regarded as a substitute for GC-MS but as a complementary technique: for example, vesicants are difficult to analyse by LC-MS. Furthermore, the OPCW Inspectorate seeks to decrease the logistic burden of on-site analysis, not increase it. The TWG has reviewed developments in LC-MS technology and concluded that LC-MS instrumentation has yet to be developed into rugged portable systems. An additional factor is that the OCAD does not at present contain spectra acquired through LC-MS. It is recommended that developments in LC-MS be closely monitored by the SAB and the Technical Secretariat (hereinafter “the Secretariat”), and that the Validation Group take up the issue of LC-MS data.
- 4.5 The SAB notes the success of the current system of proficiency testing used for designated laboratories and those seeking designation. However, some of the samples provided in these tests do not accurately reflect the samples that would be submitted for off-site analysis. Current proficiency-test protocols require that spiked samples and blank samples be labelled as such. In a real case requiring off-site analysis, there would be nothing to indicate which are the collected samples, which the spiked positive controls, and which the blank negative controls. It is therefore imperative that a reporting system be developed that takes this situation into account. The SAB fully supports the current plans to change the format of proficiency tests in order to more accurately reflect how real samples would be handled. This new format was given a successful trial run in 2005 and will be introduced in 2008.
- 4.6 The proficiency-testing scheme regularly practices the analysis of samples in designated laboratories. The SAB notes that other components of off-site analysis, as documented in OPCW standard operating procedures, have rarely been practiced. The SAB recommends that the OPCW consider establishing a process whereby all the procedures relating to off-site analysis of samples, including sample transport, accounting of sample material and waste, issues relating to confidentiality, and so on, are practised more regularly.

- 4.7 Toxins have long posed a problem for sampling and analysis. Ricin and saxitoxin are listed in Schedule 1; the OPCW therefore has an obligation to secure access to methods of identification. These toxins present a number of problems for the existing system of designated laboratories. Firstly, neither can be identified through the use of GC-MS analysis because of the polar, involatile nature of each and, in the case of ricin, because of its high molecular mass. Well-established methods exist for analysing saxitoxin in the context of paralytic shellfish poisoning, through the use of LC combined with MS or fluorescent detection, and commercial immunoassay kits are available. A number of laboratories, both designated and non-designated, have developed expertise in the analysis of ricin and other proteinaceous toxins, based on mass spectrometry, immunoassays, and functional assays (i.e., assays that demonstrate biological activity).
- 4.8 The TWG on sampling and analysis is currently addressing toxin analysis. Issues that need to be considered include the status of immunoassays, the degree of mass accuracy that is required for determining molecular mass, and the percentage of the structure that needs to be identified by amino acid sequencing. A possible requirement to demonstrate biological activity is also being discussed.
- 4.9 The SAB has requested the OPCW Laboratory to determine which designated laboratories have the capability to identify toxins, particularly ricin and saxitoxin. If the overall capability is deemed to be inadequate, then laboratories outside the current system could be considered by the Director-General for the analysis of Schedule 1 toxins, in accordance with Part II, subparagraph 56(b), of the Verification Annex.
- 4.10 In certain scenarios, particularly those involving allegations of use, the capability to analyse riot control agents and degradation products of scheduled compounds is extremely important in the context of verification. The SAB therefore strongly recommends that the Council approve the addition to the OCAD of spectroscopic data on such compounds. These data have already been validated by the Validation Group. The SAB also recommends the inclusion of spectroscopic data relevant to old and abandoned chemical weapons (OACWs), for some of the arsenicals weaponised in the early part of the twentieth century, for instance.
- 4.11 Finally, the SAB notes that the OPCW has not yet addressed the matter of the trace analysis of environmental samples, which may be important in investigations of alleged use (IAUs). The TWG on sampling and analysis has been asked to consider trace analysis and make recommendations regarding its possible implementation by the OPCW Laboratory.

Analysis of biomedical samples

- 4.12 The Convention provides for the collection of biomedical samples from suspected human and animal casualties in cases of IAUs. Such samples may provide the best evidence of alleged use, particularly in remote areas where no munitions residues can be found. At present, the OPCW has no capability to handle or analyse such samples, and there is no system of designated laboratories for the analysis of biomedical samples. The requirement for analyte- or class-specific trace-analytical methods, the detection and identification of biological markers of exposure (which may include

simple degradation products) rather than agents, and the increased sophistication of equipment (GC-MS, GC-MS-MS, and LC-MS-MS) that may be required are areas in which this type of analysis differs from the environmental type of analysis now carried out in designated laboratories. Furthermore, some of the analytical standards are not widely available. The SAB convened a TWG to address the issue of biomedical samples. The group has held three meetings and fully met its terms of reference as defined by the SAB. The key recommendations it has made are:

- (a) that the OPCW Laboratory, with assistance from experts from States Parties, now move forward on the issue of biomedical sampling and analysis;⁹
- (b) that the SAB request the Director-General to make sufficient resources available to the OPCW Laboratory to initiate and maintain this process;
- (c) that the OPCW Laboratory, with the assistance of experts from States Parties, compile details of analytical methods and of synthetic methods or commercial sources for analytical standards;
- (d) that confidence-building exercises begin as soon as is practically possible; and
- (e) that proficiency tests proceed only when a minimum level of expertise has been achieved by a number of laboratories.

4.13 The OPCW Laboratory, with support from the Netherlands Organisation for Applied Scientific Research (TNO), plans to organise the first confidence-building exercise in 2008. Issues that will be addressed in these exercises include criteria for identification, and operating procedures.

5. DESTRUCTION OF CHEMICAL WEAPONS

5.1 The SAB noted that the technologies used in the destruction of declared chemical weapons stockpiles appear to have matured to a point where implementation of the requirements of the Convention requires no further technological innovation or development.

5.2 With regard to non-stockpile problems, such as those posed by OACWs, the SAB noted that further research and development are needed for the safe recovery of OACWs both by excavation and by removal from the sea at relatively shallow depths. It also noted that there is a continuing need for innovation in, and new approaches to, the destruction of recovered items.

6. ASSISTANCE AND PROTECTION AGAINST THE EFFECTS OF CHEMICAL WEAPONS, AND INTERNATIONAL COOPERATION

6.1 Advances in the life sciences, information technology, materials science, and nanotechnology have the potential to help States Parties improve the level of protection they can offer against chemical weapons. Effective defence should

⁹ The Council noted the Secretariat's intention to develop a proposal on the establishment of an OPCW capability to analyse biomedical samples (paragraph 6 of EC-44/2, dated 17 March 2006).

discourage the development and use of chemical weapons. Enhanced international cooperation in this field can act as an incentive for States not Party to join the Convention.

- 6.2 With regard to detection devices, the SAB recognised that it takes a considerable amount of time and effort to transfer a new detection technology from laboratory instrumentation to a reliable and robust field-detection device. Technologies that have already matured will continue to play a key role in the detection of chemical-warfare agents over the next five years. Portable and miniaturised versions of devices that feature mature technologies and that are capable of detecting chemical-warfare agents, such as gas chromatography-flame photometric detection, GC-MS, and ion-mobility spectrometers, are now becoming commercially available. New ionisation methods that enhance the ability of mass spectrometers to interrogate surfaces (liquids and solids) may greatly expand the effectiveness of inspections in the future, if devices that use these methods can be miniaturised and reduced in cost. Other trends that may lead to new detection devices include those involving lab-on-a-chip,¹⁰ DNA arrays, protein arrays, and biosensors for chemical-warfare agents. New methods of detection based on quantum-dot technology still lack sensitivity, but once this problem has been solved, they could lead to inexpensive personal detectors.
- 6.3 In the field of medical countermeasures, improvements are necessary both in the available treatments (for example, antidotes that can be used against a broader range of agents), and in the planning of medical countermeasures and the management of casualties. The search for more-effective antidotes, such as enzyme reactivators for nerve-agent intoxication, is continuing. Some beneficial effects of oximes in the treatment of soman poisoning appear to be caused not by reactivation of inhibited cholinesterase, but by some effect on ion channels. Current emergency-response procedures can be time-consuming and can delay the treatment of victims. Best practices need to be identified and followed, and more-effective antidotes need to be found and used. Training and exercises are essential to maintaining the required levels of preparedness.
- 6.4 In the area of decontamination, requirements are taking account of the changing nature of such operations, which are more likely to take place in urban areas and to affect civilians directly. Standard military decontamination technology is often not appropriate under such conditions or for decontamination of some industrial chemicals. There is a need for smaller and easier-to-transport decontamination equipment that requires fewer personnel to operate it. Decontamination materials should be environmentally friendly, less corrosive, and less aggressive. Progress has been made with new materials for skin decontamination. Advances in science and technology are expected to contribute to further improvements in the field of decontamination and the medical treatment of intoxication by chemical-warfare agents.

¹⁰

A lab-on-a-chip aims to scale down the elements of the chemical and processing worlds. This scaling down involves flow and transport necessary for multiple chemical analyses, mixing, detection, separation, and so on.

7. EDUCATION AND OUTREACH IN THE CONTEXT OF THE CONVENTION

7.1 The ongoing project between the OPCW and the International Union of Pure and Applied Chemistry (IUPAC) on Convention education and outreach, which was begun in 2004, aims to increase awareness of the Convention and its benefits. The three main events that are associated with the steps recommended under the project to further chemical education, outreach, and codes of conduct in light of the obligations of the Convention, are summarised below:

- (a) A workshop on education and outreach in Oxford, the United Kingdom of Great Britain and Northern Ireland, in 2005, concluded that the OPCW should continue to support IUPAC in awareness raising, educational initiatives, and codes of conduct. It also stressed IUPAC's position as a link to national associations. Furthermore, the workshop highlighted the role that National Authorities could play, both in this regard and by generating and maintaining support among governments for including appropriate references to the Convention and its requirements in university and school curricula, as well as by providing ethical guidance in this area to students and teachers alike. The SAB also noted the important role that IUPAC and national chemical societies could play in promoting and developing codes of conduct (or in advocating the incorporation of elements relevant to the Convention into existing codes).
- (b) A conference held in Moscow, the Russian Federation, in October and November 2005, addressed, inter alia, chemical ethics and issues in education relevant to the Convention. It recognised both the lack of attention given to these issues by national associations and the need for further action at the national level, especially in the area of public awareness.
- (c) A seminar on chemical education and outreach that was held in Bologna, Italy, in September 2006, brought together members of the SAB and IUPAC. In this meeting, the general ethical principles of chemistry were discussed, as were various existing codes of conduct. It was concluded that States Parties should be encouraged to become actively involved in the promotion of these issues.

7.2 Four sets of written material have been prepared on the issue of the multiple uses of chemicals and the ethical questions it gives rise to. These materials include information on codes of conduct and sample case studies that could be used by chemistry teachers and students. Two further papers are being prepared. The SAB has been informed that, according to the leader of the joint OPCW-IUPAC project, Professor Alistair Hay of the University of Leeds, successful pilot studies have been conducted at IUPAC meetings that were held in October and November 2005 in Moscow, the Russian Federation (the aforementioned conference on science education and responsible stewardship), and in August 2006 in Seoul, the Republic of Korea. These studies have confirmed the validity of the educational concept and the usefulness of these materials, which have subsequently been improved. Further pilot studies are being considered, and plans are being made for the written materials to be translated into the six official languages of the OPCW and to be made available on the IUPAC website.