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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

Introduction

1. The Scientific Advisory Board (SAB) was established by the Director-General in accordance with subparagraph 21(h) and paragraph 45 of Article VIII of the Chemical Weapons Convention (hereinafter "the Convention"), so that he could offer to the Conference of the States Parties (hereinafter "the Conference") and the Executive Council (hereinafter "the Council") specialised advice in those areas of science and technology that are relevant to the Convention. In keeping with this mandate, and as its contribution to the preparations for the Third Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention, to be held in April 2013, 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.

2. This is the third report by the SAB on developments in science and technology relevant to the Convention. The SAB's two earlier reports were presented to the First Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention[1] (hereinafter "the First Review Conference"), as well as to the Second Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention[2] (hereinafter "the Second Review Conference").

3. For the preparation of this third review, the SAB has drawn on several sources of insight, including:

   (a) its two earlier reports for the Review Conferences;

   (b) the workshop that was organised by the International Union of Pure and Applied Chemistry (IUPAC) in February 2012, in Spiez, Switzerland, to

1 RC-1/DG.2, dated 23 April 2003.

2 RC-2/DG.1, dated 28 February 2008 and Corr.1, dated 5 March 2008.

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review advances in science and technology (S&T) with regard to their impact on the Convention;

(c) the deliberations of the SAB and its temporary working groups (TWGs) since the Second Review Conference (documented in the reports from the Twelfth to Nineteenth Sessions of the SAB);[3]

(d) the report of the Advisory Panel on Future OPCW Priorities;[4]

(e) a range of literature; and

(f) the individual expertise of the current members of the Board.

4. This report has been structured into three sections: Part A, Part B, and Part C. Part C contains a detailed analysis regarding developments in science and technology that in the view of the SAB may affect the implementation of the Convention. Parts A and B are summaries based on the analysis in Part C: Part A raises issues that may impact the scope of the implementation of the Convention and Part B summarises issues related to the work of the Technical Secretariat (hereinafter "the Secretariat").

PART A: ISSUES THAT MAY IMPACT THE SCOPE OF THE IMPLEMENTATION OF THE CONVENTION

5. The convergence of the sciences, and in particular the convergence of chemistry and biology combined with the rapid advances in the life sciences, may affect the future implementation of the Convention. The convergence of chemistry and biology is evident in the increasing commercial production of chemicals through biologically mediated processes, and the chemical synthesis of simple replicating organisms, biological parts, and agents of biological origin such as bioregulators and toxins. "Synthetic biology" is a rapidly expanding part of convergence, which enables the design and construction of new biological systems and components, and the redesign of existing ones for specific purposes. These new technologies have the potential to simplify the production of certain classes of chemicals such as toxins and bioregulators. In the view of the SAB it seems unlikely that advances collected under the "umbrella" term of convergence will be applied to the production of classic chemical-warfare agents, that is, the nerve and blistering agents listed in Schedule 1 of the Annex on Chemicals. The SAB requires more information to assess the applicability of biologically mediated processes to precursor-type chemicals and will obtain this information through its TWG on the convergence of chemistry and biology. The Board expects many benefits from the convergence of the sciences in the areas of protection against chemical weapons. The SAB considers the convergence of chemistry and biology an important area to keep under review. It will continue to inform the Director-General and States Parties about future trends.

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3 See SAB-12/1, dated 26 November 2008; SAB-13/1, dated 1 April 2009; SAB-14/1, dated 11 November 2009; SAB-15/1, dated 14 April 2010; SAB-16/1, dated 6 April 2011; SAB-17/1, dated 23 November 2011; SAB-18/1, dated 19 April 2012; and SAB-19/1, dated 12 September 2012.

4 S/951/2011, dated 25 July 2011.

6. The convergence of chemistry and biology is leading to an increased overlap between the Convention and the Biological Weapons Convention (BWC), for example, in the areas of toxins and bioregulators, which risk falling between the two conventions. The SAB has initiated an exchange between experts on the Convention with experts from the BWC in its TWG on the convergence of chemistry and biology. The Board recommends that the interaction between experts on the two treaties, and between the Secretariat and the Implementation Support Unit of the BWC is strengthened. Discussions on the effects of convergence on these two conventions should be supported by technical reviews in other fora.

7. Nanotechnology is an equally important emerging technology that potentially might have an impact on the Convention. Nanotechnology is being applied in many areas that will benefit humankind (diagnostics, pharmaceuticals, textiles, water purification, catalysis, and many others) as well as in the development of improved countermeasures against chemical-warfare agents, for example in detection, diagnostics, physical protection, and decontamination. While the application of nanotechnology and the use of nanomaterials are expected to provide many benefits, there have been concerns for the potential toxicity of nanoparticulate material, about which relatively little is known. At present, concerns for enhanced acute toxicity of nanoparticulates are unconfirmed, but this aspect should remain under periodic review. Nanomaterials are being widely investigated for the "smart" delivery of drugs for therapeutic purposes, and this aspect could possibly be applied to the delivery of toxic chemicals.

8. The changing nature of drug design, combined with high throughput screening, is producing ever larger databases of new chemicals, some of which could have high toxicity. However, most of the screening for biological activity, including preliminary toxicity testing, is today based on in vitro[5] testing and not directly transferrable to human toxicity. Furthermore, a significant effort would be required to develop a new toxic chemical into a chemical weapon. The SAB is of the view that the larger databases of biologically active chemicals, as they may exist today in pharmaceutical companies and related institutions, do not represent a proportionally higher risk to the Convention in comparison to the smaller databases that existed prior to the Convention, when much of the testing was performed on experimental animals.

9. In its discussions on the Annex on Chemicals, the SAB was of the view that the definition of toxic chemicals in the Convention, the "general-purpose criterion", encompasses all potential candidate chemicals. In relation to salts of scheduled chemicals the SAB reaffirms its earlier conclusion from 1998 that, from a technical perspective, there should be no differentiation between the treatment of the free base and the corresponding protonated salt. Regarding the allocation of chemicals presently on the schedules, the Board discussed the placing of saxitoxin and ricin in Schedule 1 based on the technical "Guidelines for the Schedules" and concluded that this is still appropriate. Regarding the existence and properties of an allegedly new class of nerve agents under the name "Novichoks",[6] the Board had insufficient peer reviewed scientific information in order to perform a technical assessment.

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5 "In vitro" refers to test tube experiments, whereas "in vivo" refers to testing with living organisms.

6 Novichok = "newcomer".

10. 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 the term "produced by synthesis". In the view of the SAB, any process designed for the formation of a chemical substance should be covered by the term "produced by synthesis".

11. The SAB recommended in the report of its Fifteenth Session (SAB-15/1) to extend the exemption from the 30-day notification period currently in place for quantities of five milligrams or less of saxitoxin for medical/diagnostic purposes (paragraph 5bis of Part VI of the Verification Annex) to include analytical purposes as well, both for saxitoxin and ricin. The SAB also recommended that retransfers to other States Parties of quantities of five milligrams or less of saxitoxin and ricin should be permitted for medical/diagnostic and analytical purposes, without being subject to a 30-day notification requirement. This will help facilitate the conduct of analytical exercises for saxitoxin and ricin, and simplify the procuring of reference standards for verification analysis.

12. The SAB, at its Sixteenth Session, discussed some of the scientific aspects of chemical incapacitants intended for "law enforcement" and has received briefings on three international meetings held on this subject.[7] The Board considers the term "non-lethal" as inappropriate when referring to chemicals intended for use as incapacitants, because for all chemicals toxicity is a matter of dosage. The Board noted that chemicals considered having high safety margins in the context of controlled pharmaceutical use can have very low safety margins in the context of incapacitants when factors such as uneven dissemination, variability in human response, and the possible need for a rapid onset are required. It was also emphasised that the issue is not just what incapacitating chemical is used for law enforcement purposes, but how it is used, and the consequences such a use may have. The types of chemicals and pharmaceuticals, known to have been considered as incapacitants from open literature sources, were discussed. Most are centrally acting compounds that target specific neuronal pathways in the brain. All of them emerged from drug programmes undertaken from the 1960s to the 1980s, as far as can be judged by the research that has been published.

13. In the view of the SAB the technical discussion on the potential use of toxic chemicals for law enforcement purposes has been exhaustive. It may continue its discussions once technical information about specific candidate chemicals and/or dissemination systems is made available. The SAB recommends that the Secretariat start preparations for verification activities, relevant to incapacitating chemicals, that could be required in an investigation of alleged use (IAU). Such preparations should include developing analytical methods and procedures, as well as collecting analytical reference data for the analysis of such chemicals. The Secretariat should invite laboratories in Member States to contribute to this effort.

14. In relation to captive use of Schedule 1 chemicals, the SAB considers that it is technically feasible that Schedule 1 chemicals are being used as captive intermediates, in particular nitrogen mustards, but potentially also sulfur mustards. The Board

7 Two meetings organised by the International Committee of the Red Cross (ICRC) (in 2010 and 2012) and one organised jointly by VERIFIN and the Spiez Laboratory (in 2011).

recommends that States Parties assess the scale of such use in their respective industries.

15. The Board also discussed the technical feasibility of Schedule 1 chemicals being formed through impurities during industrial production. The SAB assesses it to be technically feasible that certain Schedule 1 chemicals, nitrogen mustards and sulfur mustards, could be formed if starting materials contain precursor chemicals for nitrogen and sulfur mustards, or if starting materials contain respective impurities, and the synthetic process includes a chlorination step. While such Schedule 1 by-products are detectable using state-of-the-art analysis methods, they may go unnoticed if not actively looked for by chemical analysis. As long as such Schedule 1 by-products remain in low concentrations, it is impractical to isolate them, and they therefore pose no threat to the Convention. They may, however, have to be taken into consideration from a regulatory perspective. The SAB recommends that States Parties assess if certain Schedule 1 chemicals could occur in certain types of their industries or whether this remains merely an academic possibility.

16. The OPCW has made significant progress since the Second Review Conference in its ability to verify the presence or absence of toxic chemicals through on- and off-site analysis. Progress has been achieved, both in the types of chemicals that can be verified (for example, saxitoxin and ricin) as well as in the types of samples that can be analysed (environmental and biomedical, including trace analysis). The identification of non-scheduled or novel toxic chemicals remains unaddressed, which may be important, for example, for an IAU, when there is evidence that a toxic chemical has been used for prohibited purposes, but no scheduled chemicals can be found. OPCW inspection teams are not in a position to analyse for toxic chemicals that are outside of the Annex on Chemicals without sending the samples to designated laboratories. From a technical perspective this is a weakness in detecting the re-emergence of chemical weapons.

17. The OPCW proficiency testing programme has been instrumental in establishing a system of expert-designated laboratories, which the Director-General can request to undertake off-site analysis. The current status is that 22 laboratories have been designated from a broad geographical area. This system of designated laboratories has been very costly to establish, is equally costly to maintain, and makes demands on resources from the laboratories and from the Secretariat. It should also be noted that no off-site analysis has yet been undertaken in a designated laboratory. At the present time, the Secretariat is also seeking to establish a capability for biomedical sample analysis in cases of IAUs, and the SAB has made recommendations for the broader application of trace analysis in an IAU. It has also recommended analytical methods and identification criteria for the verification of the two Schedule 1 toxins, saxitoxin and ricin. The SAB recommends that a review of the entire proficiency-testing programme be undertaken, taking into consideration these additional aspirations for verification.

18. The OPCW's methods for on-site and off-site analysis focus on the unambiguous identification of scheduled chemicals, their precursors, and degradation products. An additional capability being pursued in several chemical defence and verification laboratories is attribution of a toxic chemical or precursor to a particular source or production route. Developing such a capability would require substantive research

cooperation between laboratories, which could be coordinated through the OPCW. The OPCW would enhance its capabilities, for example, during an IAU, while the laboratories of Member States would benefit from improving their individual capabilities.

19. Education and outreach in science and technology relevant to the Convention is important to the Convention's future implementation. In the view of the SAB and its TWG on education and outreach, it is a critical element in the prevention of the re-emergence of chemical weapons and the misuse of toxic chemicals. Education and outreach serves a number of purposes, such as raising awareness about the Convention among the global scientific community, relevant industry, as well as civil society. Education and outreach should become a stronger element of national implementation of the Convention, but this will require concerted efforts by all stakeholders of the OPCW and should be assisted by, and coordinated through, the Secretariat, in cooperation with National Authorities. Effective interaction with the scientific communities will require engagement of a broader range of stakeholders, especially on a national level.

PART B: ISSUES RELATED TO THE TECHNICAL SECRETARIAT

20. Advances in production technologies and the ensuing changes in the chemical industry will necessitate that the Secretariat enhance its technical expertise in areas such as biologically mediated production processes, green chemistry, and microreactors, all of which may affect industry verification activities. Advances in production technology may also affect how certain types of toxic chemicals—such as toxins, bioregulators, or other classes of chemicals, including incapacitating agents—can be produced, a development that will necessitate adjustments to current verification practices. The Secretariat, therefore, should strengthen its efforts to stay abreast of technological developments in these areas.

21. Substantive progress has been achieved through the work of the SAB's TWG on sampling and analysis (S&A), in cooperation with the OPCW Laboratory, on issues that the SAB had reported to the Second Review Conference in relation to on- and off-site analysis, as highlighted above (analysis of ricin, saxitoxin, biomedical samples, trace analysis, and shortening on-site analysis time). This progress must now be integrated into the procedures of the Secretariat and its designated laboratory network.

22. OPCW proficiency testing has established a worldwide network of designated laboratories. The process of transferring authentic samples from an inspection for off-site analysis at designated laboratories, however, has been practised on a few occasions only. The SAB is of the view that the entire process of off-site analysis should be practised more regularly, and that funding should be made available for this. The capability to transport samples off site for independent analysis will be an important element in any challenge inspection (CI) or IAU, as well as in the case of inconclusive findings during routine on-site analysis.

23. The OPCW Central Analytical Database (OCAD) is a critical element for OPCW on-site analysis. The Secretariat must ensure that the content of this database is adequate to allow the OPCW to meet future verification challenges.

24. OPCW inspectors are required to operate a wide variety of equipment in different scenarios. It is important that inspectors have equipment available that allows them to execute their tasks in an efficient and safe manner. The SAB wishes to emphasise the importance of training for inspectors to ensure that equipment is properly utilised, and of inspectors gaining practical experience across the breadth of operational challenges (routine inspections, CIs, and IAUs).

25. While there have been advances in relation to assistance and protection against chemical weapons, many challenges still remain. Through the increasing concern for non-State actors employing toxic chemicals, additional technical challenges have arisen in relation to detection, medical countermeasures, and decontamination. Systems and technologies developed for military use are not always fully transferable to an urban civilian environment. For example, there remain deficiencies in the detection of toxic chemicals in relation to selectivity and sensitivity, as well as ease of operation. There also is limited knowledge available regarding the efficacy of methods for the decontamination of public urban environments. The Secretariat should consider the establishment of a mechanism for the sharing of best practices among States Parties as part of its international-cooperation activities.

PART C: ANALYSIS OF DEVELOPMENTS IN SCIENCE AND TECHNOLOGY RELEVANT TO THE CHEMICAL WEAPONS CONVENTION

ADVANCES IN SCIENCE AND TECHNOLOGY

Overview

26. Science and technology continue to advance at an accelerating pace in areas that may impact on the Convention. Advances in the life sciences, the material sciences, and enabling technologies offer potential far-reaching benefits to humankind in areas such as renewable energy sources, health care, food production, and eliminating environmental pollution. A number of these advances are also being exploited for the improvement of defensive countermeasures against toxic chemicals, e.g. in medical treatment, detection, protection, decontamination, and verification technology. While the outcomes are overwhelmingly likely to be beneficial to humankind, it is recognised that these advances may also offer opportunities for malevolent exploitation, some of which may pose challenges to the implementation of the Convention. Five major subject areas, which are considered to have particular relevance to the Convention, are discussed in paragraphs 26 to 61:

(a) the convergence of chemistry and biology (paragraphs 28 to 46);

(b) accelerated discovery of chemicals (paragraphs 47 to 49);

(c) nanotechnology (paragraphs 50 to 55);

(d) technologies for delivery (paragraphs 56 to 58); and

(e) production technologies (paragraphs 59 to 61).

27. Advice on the Annex on Chemicals is discussed in paragraphs 62 to 86; the impact of recent advances on verification technology is discussed in paragraphs 87 to 115; destruction of chemical weapons is briefly addressed in paragraphs 116 and 117; assistance and protection is discussed in paragraphs 118 to 124; and education and outreach in science and technology is discussed in paragraphs 125 to 131.

Convergence of chemistry and biology

28. There has always been an interdependent relationship between the fundamental sciences of chemistry and biology. At the molecular level, biological systems obey the laws of chemistry, which is the basic premise that underpins the pharmaceutical and pesticide industries. What is changing is the unprecedented growth in our understanding of the fundamental chemistry and genetics of living systems, a result of interdisciplinary research teams using ever more sophisticated and powerful instrumentation and experimentation. Key enabling factors have been the availability of increasing computing power at steadily decreasing cost, the efficiency of automated second generation DNA sequencing and synthesis, and the development of instrumentation capable of imaging down to the molecular and atomic level. Major advances have occurred in neuroscience, expanding our knowledge of how endogenous chemicals (bioregulators, including neurotransmitters, hormones) regulate normal homeostatic function and how, in the brain, they modulate cognition, mood, and behaviour. In order to address these important developments, the SAB has convened a TWG, comprised of chemical and biological experts, on the convergence of chemistry and biology.

29. A number of subject areas have been included under the general umbrella of the "convergence of chemistry and biology",[8] most of which have existed, at least at a low level, for many years. These include:

(a) biologically mediated processes (employing biological catalysts, naturally occurring organisms or genetically modified organisms) for the production of chemicals;

(b) recombinant DNA technology that allows replacement of the original genome in bacterial, yeast, and other cells with synthetically produced genomes, to produce organisms with new capabilities;

(c) chemical (DNA) synthesis of replicating systems which, to date, has been limited to small viruses and a simple bacterial genome; and

(d) toxins and bioregulators, naturally occurring chemicals that may have high toxicity, or provide prototypes for new incapacitants.

8 Jonathan B. Tucker, "The convergence of biology and chemistry: implications for arms control verification", *Bulletin of the Atomic Scientists*, 66 (2010) 56-66.

30. The first three of these subject areas are encompassed by a relatively new term "synthetic biology".[9] This is defined as:

(a) the design and construction of new biological components and systems that do not already exist in the natural world; and

(b) the re-design of existing biological systems for specific purposes.

31. Synthetic biology aims to apply engineering principles to the design of biological systems. An analogy is the construction of electronic systems through the combination of standard components.

32. The main relevance of convergence to the Convention could be simply stated as the biological synthesis of toxic chemicals, and the chemical synthesis of replicating systems, biological parts, or chemicals of biological origin. In this area, there is considerable overlap with the BWC.

33. Biologically mediated production of bulk chemicals: The production of bulk chemicals using biologically mediated processes is increasing, driven by the increasing cost of petroleum-based feedstock and the shift towards greener chemistry. Ethanol has long been a prime example of this process, but a number of chemical companies have developed, or are developing, pilot plant or full-scale production facilities for other commodity chemicals. Some examples are lactic acid, acetone-butanol-ethanol, and 1,3-propanediol, which are now manufactured using biological processes on a scale greater than 45,000 tonnes per year. These processes start from a naturally occurring feedstock abundant in carbohydrates (sugars), which incorporate the basic carbon skeleton of the product. Some of these new routes are very efficient and are expected to compete economically with petroleum-based routes.

34. Biocatalysis in bulk and fine chemical production: Enzymes (nature's catalysts) have been used to promote chemical reactions for many years, for example, during the commercial production of the artificial sweetener aspartame. With a growing capability to modify enzymes (an example of synthetic biology), their use is predicted to increase in high-volume manufacturing of commodity chemicals, and in low-volume production of specialty chemicals and pharmaceuticals.

35. Biologically mediated production of toxic chemicals: The SAB has provisionally concluded that for Schedule 1 nerve and blister agents, there is no apparent advantage in production through biological processes. The chemical synthesis of these chemicals is relatively simple, and the presence of elements such as sulfur and phosphorus limit the availability of suitable naturally occurring feedstock. The use of modified enzymes is a possibility. In order to assess the feasibility and practicability of synthesising precursor chemicals by biological processes, the SAB endorses the ongoing efforts of the TWG on the convergence of chemistry and biology to study the biotechnology and chemical industry to better understand the types of biological processes being used commercially, as well as the range of chemicals produced.

9 www.syntheticbiology.org

36. Biological production of more complex chemicals: As a result of advances in recombinant expression systems, important developments are occurring in the production of more complex chemicals in modified biological systems, predominantly for application in the pharmaceutical industry. These are conveniently divided into the biological production of proteins, and the production of low molecular mass non-protein natural products.

37. Recombinant proteins can be produced by genetically modified yeast and bacteria in a conventional bioreactor. In recent years, some protein-based pharmaceuticals, and other proteins such as spider silk, have been produced in transgenic plants or animals. This technology, termed biofarming, offers a potentially cheaper and abundant source of these proteins. It requires insertion of a foreign gene (a defined DNA sequence) into plant or animal cells. Examples are the cost-effective production of vaccines, therapeutic antibodies, and microbiocides. Spider silk has been produced in the milk of transgenic goats.

38. The production of non-protein complex chemicals in foreign organisms, termed metabolic pathway engineering, is much more difficult. Multiple genes are required to produce the enzymes that sequentially promote each stage of the biosynthetic pathway. The exemplar of this emerging technology has been the production in a genetically modified bacterium (E. coli) of artemisinic acid, a precursor for the plant-derived antimalarial drug artemisinin. Isolation from the plant source is complex and very expensive.

39. Application of synthetic biology to the production of toxic chemicals: Genetically modified organisms could be adapted to the production of protein toxins such as ricin, or non-protein toxins such as saxitoxin. In the case of ricin, and bacterial toxins such as botulinum, production from culture of the natural organism is reasonably efficient. This is not the case for saxitoxin, which must be harvested from marine organisms. In theory, metabolic pathway engineering could be used to produce saxitoxin but, at the present, would require an extensive and covert research programme.

40. Chemical (DNA) synthesis of replicating systems: Modern DNA sequencers and synthesisers have advanced to the point where genes and entire microbial genomes can be readily sequenced and reconstructed by automated coupling of the four chemical units of DNA. A number of simple pathogenic viruses, and a bacterial genome consisting of more than 1 million base pairs, have been synthesised. This technology has advanced to the point where non-scientists can experiment with commercially available DNA-based building blocks (for example, Biobricks^{TM}) to construct novel systems. As synthetic biology matures it could lead to the development of "designer microbes" for the production of chemicals ranging from bio-fuels to therapeutic peptides and bioregulators.

41. Toxins and bioregulators: Toxins and bioregulators are chemicals of biological origin. Their production and use for prohibited purposes is controlled under both the Convention and the BWC. Two toxins, saxitoxin and ricin, are included in Schedule 1 of the Convention for verification purposes; no bioregulator is included in the schedules.

42. The only current practical method of moderate- to large-scale production of proteinaceous toxins such as ricin would be through culturing of a natural organism, or a genetically enhanced organism. Small molecule toxins such as saxitoxin can be isolated from the naturally producing organisms, or one that accumulates the toxin (such as shellfish), or by chemical synthesis. In reality, biological and chemical synthesis of these small molecule toxins in moderate quantities would be difficult and very expensive, and the threat to the Convention from such toxins is assessed as low by many observers. Metabolic pathway engineering may offer a future alternative, but at present this is emerging technology.

43. Peptides, composed of short chains of amino acids, comprise the largest group of bioregulators. Advances in neuroscience, driven by the increasing occurrence of neurodegenerative diseases such as Alzheimer's and debilitating conditions such as depression, have identified numerous new pathways and their associated bioregulators. Observers have frequently associated peptide bioregulators with the possible development of incapacitants. However, peptides are rapidly degraded by enzymes in the body, are usually poorly absorbed through the blood-brain barrier, and are relatively expensive to manufacture (though costs have fallen in recent years). Their potential for development as incapacitants may, therefore, be overstated. Pharmaceutical companies tend to focus on longer-lived (and potentially more toxic) metabolically resistant analogues, or on non-peptide mimics of the bioregulator. Although peptide bioregulators could be produced in genetically modified organisms, the pharmaceutical industry regards chemical synthesis as the most cost-effective method for small peptides, using combinations of solid phase and solution synthesis. This requires specialist equipment.

44. Beneficial applications to chemical defence: The convergence of chemistry and biology (and related aspects of nanotechnology) has the potential to improve protection against toxic chemicals. Examples of beneficial applications of synthetic biology in chemical defence include the production of recombinant human butyrylcholinesterase in transgenic goats as a potential bioscavenger for nerve agents (see paragraph 122), and the development of modified enzymes that efficiently catalyse the hydrolysis of nerve agents for medical treatment or for decontamination purposes. Many other applications in detection and diagnostics are being explored.

45. Implications for verification: Other chemical production facilities (OCPFs): The term "produced by synthesis" is used in Part IX of the Verification Annex ("Regime for Other Chemical Production Facilities"). A facility producing an unscheduled chemical ("produced by synthesis") is declarable and the facility is subject to inspection, if the annual inspection threshold is reached. A key issue in the implementation of Part IX is whether biologically mediated processes should be considered to be synthesis within the above definition. At present, this is open to interpretation. Some States Parties declare OCPFs employing biologically mediated processes, some do not. A report prepared by the SAB in 1999 concluded that "produced by synthesis" should include synthesis by biological means. However, at that time there were few discrete organic chemicals (DOCs) that were manufactured in declarable quantities through the use of biological processes. The SAB notes that this situation has changed, with an increasing trend towards commercial production of bulk chemicals by means of biological processes. The SAB reaffirms its 1999 recommendation that "produced by synthesis" should include biologically mediated

processes. There may be a number of differences in the type of equipment used in a biomediated process when compared to a classical chemical reaction. Further study of these commercial-scale facilities (including reaction, separation, and purification operations) is needed to determine their degree of relevance to the Convention.

46. Summary: Advances considered under the general term "convergence of chemistry and biology" are accelerating at an unprecedented rate, particularly in synthetic biology. A feature of the technology is that it overlaps the remits of the Convention and the BWC, and some aspects, for example, bioregulators and their analogues, risk falling between the two. The SAB considers it important that the Secretariat expands its in-house knowledge of these developments. The SAB recommends that regular assessments of the implications for implementation of the Convention should be undertaken, using expertise within the SAB, the TWG on the convergence of chemistry and biology, and the Secretariat. The SAB further recommends that the Secretariat establish a process for increasing the interaction of the Secretariat and SAB with experts associated with the BWC, in particular with its Implementation Support Unit.

Accelerated discovery of chemicals

47. In its 2008 report on advances in science and technology[10] in preparation for the Second Review Conference, the SAB referred to the rapidly changing nature of drug design and development (and other chemicals), particularly technology that allows the rapid synthesis and screening of many thousands of compounds. The tools for such techniques have become widely available. Combinatorial and other forms of parallel multi-compound synthesis, combined with simultaneous high-throughput screening for biological activity against in vitro test systems, has produced data on millions of chemical compounds. Combinatorial libraries containing thousands of "drug-like" chemicals are now commercially available for screening. Such techniques could be directed towards the discovery of new toxic chemicals, including incapacitants. It is, therefore, of interest to note that this "shotgun" or non-targeted approach to drug discovery is now falling out of favour because of a number of disadvantages, including a limited success in discovering new drugs.

48. More rational and focused approaches towards screening for new lead compounds are now being preferred, based on knowledge of the three-dimensional structure of the receptor or enzyme ("structure-based design"), or a computer-generated model based on molecules that bind to the presumed receptor ("ligand-based design"). The first approach has been facilitated by the increasing number of biological targets that have been identified through molecular genomics and proteomics, and the large number of proteins whose structure has been determined through the use of X-ray crystallography and nuclear magnetic resonance (NMR) techniques. Candidate molecules computed to have high affinity for the target are synthesised and tested for activity in suitable in vitro assays. A third approach that is now being widely applied is "virtual" (that is, *in silico*) high-throughput screening, in which libraries of virtual compounds are "docked" against a model of the three-dimensional receptor using advanced computational techniques. This approach has been facilitated by the ready availability of software, some of it freely available on the internet, by global sharing

10 Annex of RC-2/DG.1 and Corr.1.

of data, and by the availability of computing power of desk-based personal computers (PCs). In a chemical-defence context, these approaches have been applied to mechanistic studies of nerve agent inhibition of the enzyme acetylcholinesterase, and the design of new therapeutic reactivators of acetylcholinesterase.

49. There has been some concern that amongst the millions of compounds that have been screened in drug-discovery programmes there will be prototypes for new toxic chemicals. This may be the case, but nearly all of these data are generated using in vitro screening and may not reflect toxicity in vivo. Comparatively little testing is now undertaken in animals other than for lead compounds. This contrasts with the much smaller number (thousands) of compounds that were screened during the 1950s to the 1970s. For a large percentage of these compounds, toxicity testing was performed in small animal species. The SAB is of the view that the existence today of large in-house databases in pharmaceutical companies and related institutions poses no greater risk to the purposes of the Convention than the much smaller databases that existed before entry into force of the Convention. For example, all of the centrally acting chemicals known to have been seriously studied as potential incapacitants are products or extensions of "traditional" drug research programmes of the 1950s to the 1970s. All of the scheduled nerve agents, plus the newer ones referred to in paragraph 82, can be traced to prototypes from the pesticide industry from the 1930s to the 1970s. As noted in the 2003 SAB report on science and technology[11] in preparation for the First Review Conference, a major (and covert) offensive programme would be required in order to develop a new toxic compound into a chemical weapon.

Nanotechnology

50. The term "nanotechnology" applies to functional components and materials that are smaller in size than 100 nanometres in at least one dimension. Most nanomaterials have physical, chemical, or biological properties that differ significantly from those at a larger scale. Nano-sized particles have a high surface area to mass ratio, which may impart higher chemical reactivity, increased strength, and modified electrical properties. Nanoparticles may also exhibit altered optical and magnetic properties.

51. As reflected in the 2008 SAB report on science and technology, nanotechnology is a rapidly expanding technology that may have significant implications for the Convention. One estimate puts the global value of commercial applications to be around at least USD 1,000 billion by 2015. Nanotechnology is contributing to major advances in materials science, medicine, electronics, and energetics.

52. A notable example in material science is carbon nanotubes (CNTs), graphite-like structures that self-organise into a lattice-like tubular form. CNTs exhibit much higher mechanical strength than steel, are 30% lighter than aluminium, and conduct electricity. In medicine, nanoparticle-based formulations are being widely explored for enhanced or "smart" drug delivery. Examples are controlled drug release, enhanced penetration of the blood-brain barrier (e.g. for therapeutic peptides), and targeting specific organs or cells (e.g. cancer cells). Allied to these advances in therapeutics, nanotechnology is contributing to major developments in diagnostics.

11 Annex of RC-1/DG.2.

53. Risks of nanotechnology: A general concern for nanomaterials is their potential to enhance the acute (short-term) or chronic (long-term) toxicity of chemical substances, and materials that are normally considered to be inert. This concern arises primarily from their altered chemical reactivity, combined with an ability to penetrate membranes. For example, inhaled nanoparticles have been demonstrated in several areas of the brain. This has led to occupational and environmental health concerns. There are considerable knowledge gaps in this area. It should be noted that humans have long been exposed to nanoparticulates from the burning of fossil fuels, and common materials that contain nanoparticulates include paint and cosmetics.

54. Beneficial applications to chemical defence: Nanotechnology is contributing to the development of improved defensive countermeasures against toxic chemicals. Applications are under investigation for improving the delivery of therapeutic drugs (see paragraphs 51 and 52). Developments in diagnostics have led to prototype point-of-care devices for diagnosing exposure to nerve agents, and a range of biological agents and toxins. The electronic and optical properties of nanomaterials are being explored in the development of new detectors. Novel decontaminants, based on the increased reactivity and high absorptive capacity of nanoparticles, are in development. Nanofibres are being incorporated into new lightweight protective clothing, and into more effective materials for respirator filters.

55. As with advances in synthetic biology, nanotechnology has the potential for application to purposes prohibited by the Convention. The enhanced delivery of therapeutic drugs to their biochemical target could be exploited for the delivery of toxic chemicals. The concern for nanoparticles with significantly enhanced acute toxicity compared to larger particles has not been substantiated, although this is still under investigation. No nanomaterials are currently known to have an intrinsic toxicity that might make them attractive for use in chemical weapons. The risk to the Convention posed by nanomaterials is, therefore, currently regarded as low. The prevailing view of the SAB is that nanotechnology is unlikely to provide a dramatic improvement in the military utility of existing chemical agents, but it could be exploited in the development of new agents.

Technologies for delivery of toxic chemicals and drugs

56. Munitions: The SAB notes with concern isolated reports of the commercial availability of munitions apparently designed to deliver large amounts of riot control agents over long distances. Devices that might be attractive for the dissemination of chemical weapons and biological-weapons agents by non-State actors continue to receive attention. While the few instances of the release of toxic chemicals by non-State actors have used crude devices, spray and fogging devices developed by the pesticide industry or developed for veterinary treatment of large-scale animal farms are of concern.

57. Drug delivery: In its 2008 report on science and technology, the SAB highlighted interest within the pharmaceutical industry in administering drugs by inhalation, as an alternative non-invasive method of delivery. This route circumvents the extensive metabolism that may occur in the intestinal tract following administration by ingestion, and can deliver drugs with suitable physical properties, or in appropriate formulations, rapidly 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. A number of devices have been reported for aerosol administration of drugs such as insulin, opioids, anti-migraine drugs, and anti-convulsants. As reported above, a major growth area is the application of formulations based on nanoparticles. These may be designed to control drug release, to protect the drug from rapid metabolism, to enhance penetration of membranes such as the blood-brain barrier, and to target specific organs or types of cells.

58. Features that promote the effective and targeted delivery of drugs via the respiratory system would be applicable to the dissemination of a toxic chemical, especially a solid disseminated as a particulate aerosol. One development has been the use of porous nanoparticles as carriers composed, for example, of silica or L-lactide, that allow delivery of drugs into the deep alveolar regions of the lungs. The equipment needed to create such particles is relatively inexpensive, although the optimisation of a well-engineered particle requires expertise and considerable effort. The technology could be exploited in the design of incapacitants. However, the sophisticated engineering of a high-value drug for targeted delivery may not be appropriate for chemical-warfare agent delivery.

Production technologies

59. As noted in the 2008 SAB report on science and technology, 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. Technological innovations continue to make chemical manufacturing more versatile and more efficient. Computerised control systems allow for greater automation, resulting in better process control with fewer manual operating steps. Integrated industrial parks with multiple companies and product lines have become common on a global scale. Flexibility is facilitated with the widespread use of multipurpose production equipment that maximises asset utilisation with quick product changeovers.

60. The emerging use of microreactors and small-scale flow reactors continues to be monitored by the SAB. The advantages in the manufacture of fine chemicals include the following: increased efficiency of reaction, resulting from the large area to mass ratio and efficient mixing, and the capability of increasing the scale of production simply by increasing the number of parallel microreactors ("numbering up"). This avoids the considerable effort and some of the problems associated with traditional scaling-up from laboratory to industrial-scale volumes. If adapted to the manufacture of toxic chemicals, microreactor systems, by themselves, would not exhibit the traditional physical signatures of larger-scale industrial plants. However, for moderate- to large-scale production processes, microreactors would most likely have to be coupled with raw-material handling systems, downstream processing equipment, and end-product storage capability, and there would still be a signature from precursor chemicals. These features, common to a traditional manufacturing facility, would make it more difficult to hide illicit production capability.

61. Microreactors and small-scale flow reactors have become more prevalent in research-and-development laboratories, and the technology has undoubtedly made significant advances in the last five years. Although use is increasing, microreactors are not yet widely used in industry, and they are being integrated into industrial-scale

production more slowly than some observers have predicted. At this point in time, microreactors should not be considered to be generic reactors. They are mostly designed and custom-built for a specific chemical process, although microreactors constructed on a modular concept are also available. They do not provide a simple "off-the-shelf" solution to chemical production. Although the time required to make the transition in the development of a highly toxic new chemical from the research to the production stage could be significantly shortened, the development of a viable process would still require lead time, experienced technical staff, and considerable investment in research. Microreactors also have limitations for handling solids, which makes them less flexible in regard to the handling of a broad range of chemical processing steps. While there are a number of limitations to the use of microreactors, the technology clearly requires monitoring in order to assess the impact it might have on the verification regime under the Convention.

SCHEDULES OF CHEMICALS AND ADVICE ON THE ANNEX ON CHEMICALS

Captive use of Schedule 1 chemicals

62. In the chemical industry, captive use is the production and consumption of a chemical intermediate that is confined to the company's own manufacturing needs. Depending on the process, the chemical may be isolated, or consumed in situ without leaving the reactor.

63. Declarations of captive use under the Convention are required to provide assurance that scheduled chemicals cannot be diverted for prohibited purposes. At its Ninth Session, the Conference approved for declaration purposes Schedule 2 or 3 chemicals produced and/or consumed as intermediates, by-products, or waste products.[12] At its Tenth Session, the Conference approved the same approach for Schedule 1 chemicals.[13]

64. Most examples of the captive use of Schedule 1 chemicals have concerned nitrogen mustards as intermediates. In 2010, one State Party identified an undeclared process in use at a pharmaceutical company, employing bis(2-chloroethyl)methylamine (HN2) as a captive intermediate in the production of the analgesic drug ketobemidone. The SAB was asked to consider if there might be other processes that still use nitrogen mustards as intermediates, or other commercially significant processes that produce other Schedule 1 chemicals as captive intermediates.

65. The study identified 87 patented (since 1940) processes that use HN1, HN2, or HN3 as intermediates. However, patents do not provide a true indication of captive use, and the processes described may not be utilised. In the case of ketobemidone, alternative production routes exist, although changing processes for pharmaceuticals can incur high costs when toxicity tests for impurities have to be repeated. More accurate indicators for pharmaceutical production are government licences (such as from the European Medical Association for Pharmaceuticals), which contain a full description of the process used and the impurity profile. It is therefore difficult to

12 C-9/DEC.6, dated 30 November 2004.

13 C-10/DEC.12, dated 10 November 2005.

obtain a full picture of captive use without a comprehensive search of the licence databases of States Parties.

66. Efforts should be made to ensure that the chemical industry (via the National Authorities) in each State Party is informed on the issues related to captive use of scheduled chemicals. National Authorities have been asked to report any other examples of captive use to the Secretariat.

67. Following a request by the Director-General to the Eighteenth Session of the SAB to provide advice on situations where a Schedule 1 chemical is an unavoidable by-product, the SAB continued its study, which began in 2010. The study focused on 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 performed by the Board.[14]

68. Searches were performed in a database that contains reaction and patent information for industrial chemicals (Reaxys®[15]). The study confirmed earlier findings of potential uses of nitrogen mustards as intermediates in captive use and indicated also potential cases of use of sulfur mustards. In a second step, the study searched for patents and published reaction-starting materials that contain substructures of precursors of nitrogen and sulfur mustards combined with known chlorinating agents as part of the published information. This was a result of the fact that, if the industrial starting material contains a substructure of sulfur or nitrogen mustards, a chlorination reaction may have the potential to form related Schedule 1 chemicals. In a last step, the study focused on starting materials (ethanolamines) that contain known impurities that form nitrogen mustards through chlorination. The results of this literature study confirm earlier findings that Schedule 1 chemicals may be in use as intermediates in captive use. The study furthermore shows that it is technically feasible for sulfur and nitrogen mustards to occur in certain types of industry as impurities or by-products. The SAB is, however, not in a position to assess if this is actually the case in practice.

69. The Board considers it highly unlikely that Schedule 1 chemicals, formed as by-products as described above, could be extracted from the reaction mixture or that such a process would be utilised for the synthesis of Schedule 1 chemicals. Efforts, however, should be made to advise industry of the technical feasibility of the formation of Schedule 1 chemicals, because such chemicals may be detected during inspections.

Salts of scheduled chemicals

70. Some scheduled chemicals that contain a basic nitrogen atom can exist as free bases, or in protonated form as salts. The production of the salt may proceed via the free base, or vice versa in the case of nitrogen mustards. Free bases and salts generally have similar intrinsic toxicity, but may present different hazards according to their physical form (free bases may be liquids and salts are usually crystalline solids).

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

15 See https://www.reaxys.com/info/about-overview.

Acids such as benzilic acid and hydrogen cyanide also form salts. In aqueous solution, the two forms are in equilibrium, depending on the pH. Following protracted negotiations on the schedules of chemicals, the wording "and corresponding salts" was included in some cases, but in other cases it was not. For example, it is included for V-type nerve agents, but not for nitrogen mustards. There are, therefore, ambiguities as to whether salts of some chemicals should be covered by the provisions of Article VI.

71. In 1998 the majority of SAB members recommended that "there should be no differentiation between the treatment of a free base and the corresponding salt".[16] This recommendation was not supported by meetings of government experts in 2000 and 2004. The First Review Conference in 2003 encouraged the Council to include the matter on its list of outstanding issues.

72. In January 2011, the Secretariat prepared a non-paper on salts of scheduled chemicals for the Industry Cluster.[17] It reported that "modest amounts" of nitrogen mustard HN2 hydrochloride salt are produced for pharmaceutical purposes (as an anticancer agent) and very small amounts of saxitoxin salts are produced for diagnostic/analytical kits. The paper discussed the risks posed to the Convention by salts of scheduled chemicals and the implications for declaration and verification activities. The paper concluded that the greatest impact on declaration obligations, if salts were covered by the schedules, would be for Schedule 3 chemicals, because of their widespread and diverse industrial use (e.g. the salts of triethanolamine and hydrogen cyanide).

73. The SAB remains of the view that, on scientific grounds, there should be no differentiation between the treatment of the free base and the corresponding salt, and reaffirms the recommendation it first made in 1998.

Chemical Abstract Service (CAS) registry numbers

74. The Secretariat has worked with the European Chemical Industry Council (CEFIC) and the European Union on creating an updated (2009) *Handbook on Chemicals*. This publication has been made available to Member States and individual companies via the Internet. The *Handbook* was developed to facilitate the efforts of National Authorities, customs authorities and industry to identify and declare individual scheduled chemicals. It has undergone a major revision and incorporates information on all 1329 scheduled chemicals and riot control agents declared to the Secretariat from 1997 until February 2009. The *Handbook* is not a comprehensive list of all declarable chemicals and as such should only be used as a tool to assist in the identification of chemicals.

75. The SAB recognises the importance of the *Handbook on Chemicals* and requests the Secretariat, with the support of States Parties, to update the *Handbook* at regular intervals. A helpful addition would be to provide references to the various CAS

16 Page 4 of SAB-II/1, dated 23 April 1999.

17 Secretariat non-paper: "Salts of Scheduled Chemicals", dated 18 January 2011 (written by the Industry Cluster).

registry numbers that are related to an entry in the schedules, for example for different isomers of scheduled chemicals and for mixtures containing a scheduled chemical.

76. The SAB reaffirms its 2008 view[18] that the CAS registry numbers are a useful aid to identification; they were intended as specific identifiers of scheduled chemicals. There appear to be different views among States Parties about whether CAS numbers have a regulatory value. The SAB cautions against such a view, because there is not necessarily a one-to-one relationship between CAS registry numbers and chemical structures. They should be viewed as aids to identification.

Saxitoxin

77. An example of ambiguity resulting from the assignment of CAS numbers is saxitoxin. During its Thirteenth Session, the SAB revisited a previous discussion[19] on the CAS registry number (35523-89-8) given for saxitoxin hydrate (as listed in Schedule 1 of the Convention). This differs from the CAS number (35554-08-6) for saxitoxin hydrate dihydrochloride salt, which is the form of saxitoxin that was previously weaponised on a small scale (as TZ). In fact seven CAS numbers have been assigned to saxitoxin hydrate (free base), its optical isomers, and various salts.

78. A summary of the history of the negotiations to include saxitoxin in the schedules, and the various forms of saxitoxin and their CAS numbers, is provided in a fact sheet prepared by the SAB.[20] The view of the SAB was that the form of saxitoxin that was weaponised (dihydrochloride salt) should be covered by Schedule 1, and that all salts should be declarable. It should be noted that it is the salts of saxitoxin that have good long-term stability, but the hydrate free-base does not.

79. The SAB also discussed issues relating to the transfer provisions for saxitoxin and ricin, following difficulties that have been experienced in the transfers of samples for analytical purposes, including during a recent international round-robin exercise on ricin analysis. The SAB recommends that the exemption from the 30-day notification period, currently in place for quantities of five milligrams or less of saxitoxin for medical/diagnostic purposes (paragraph 5bis. of Part VI of the Verification Annex),[21] should be extended to cover chemical analysis for verification and related purposes for saxitoxin and ricin. The SAB further recommends that retransfers to other States Parties of quantities of five milligrams or less of saxitoxin and ricin should be permitted for medical, diagnostic, and analytical purposes, without being subject to a 30-day notification requirement.

Ricin

80. The proteinaceous plant toxin ricin differs from other scheduled chemicals in that there are a number of variants of the structure. The SAB was asked to clarify this situation by defining what constitutes ricin. The initial definition proposed by the SAB, and included in its 2008 report on S&T, was later revised in order to exclude

18 Page 13 of the annex to RC-2/DG.1.

19 Page 4 of SAB-8/1 and Corr.1.

20 "Saxitoxin Fact Sheet", pages 34 to 40 of Annex 4 of SAB-18/1.

21 Paragraph 5bis of Part VI of the Verification Annex.

ricin-like molecules that were under investigation as anticancer agents. These materials have an additional linkage between recombinant A and B chains, in the form of a short peptide chain, and are several orders of magnitude less toxic than naturally produced ricin. The view of the SAB was that the inclusion of such materials within the definition of ricin did not serve the object and purpose of the Convention.[22] The SAB proposed the following modified definition:

> "All forms of ricin originating from *Ricinus communis*, including any variations in the structure of the molecule arising from natural processes, or man-made modification designed to maintain or enhance toxicity, are to be considered ricin as long as they conform to the basic 'native' bipartite molecular structure of ricin that is required for mammalian toxicity, i.e. A and B chains linked only by a disulfide bond (A-S-S-B). Once the inter-chain S-S bond is broken or the protein denatured, it is no longer ricin."

81. The SAB has compiled a fact sheet on ricin which summarises the structure, the sources of ricin, its toxicity, its mechanism of action, clinical features of ricin poisoning, the medical treatment that should be given, military interest in this toxin, history of weaponisation, detection, verification, and decontamination.[23]

Non-scheduled toxic chemicals that may pose a risk to the Convention

82. In 2008, a book authored by Vil Mirzayanov, a former Soviet scientist, reported that Soviet scientists had investigated a new class of nerve agents commonly referred to as "Novichoks" (newcomers), which were suitable for use as binary weapons. The structures shown in the book incorporated an acetamidine or guanidine group into a sarin-like structure in place of the alkoxy group. While some of these structures fall within the generic definition of Schedule 2B(4) chemicals, it was reported that some were non-scheduled analogues, wherein the alkyl group attached directly to phosphorus was replaced by an alkoxy group. The compounds were reported to have high toxicity and no recorded industrial use. There is very little information available on those compounds in open-source literature, and the existence and properties have not been verified in peer reviewed literature. The SAB is therefore not in a position to make further comments.

Incapacitants

83. Many observers, particularly non-governmental organisations (NGOs), are expressing increasing concern for the development of chemical incapacitants for "law enforcement".[24] Particular points of concern are the absence of a definition of the terms "law enforcement" and "incapacitants", the misleading impression of high safety margins associated with known potential incapacitants, and the clear potential for dual use of such chemicals, including for purposes that are prohibited by the Convention. The SAB has received briefings on three international meetings on

22 Page 6 of SAB-14/1.

23 "Ricin Fact Sheet", pages 34 to 40 of Annex 4 of SAB-18/1.

24 Subparagraph II(9d) of Article II of the Convention, section entitled "Purposes Not Prohibited Under this Convention".

incapacitants—two organised by the International Committee of the Red Cross in 2010[25] and 2012[26], and one organised jointly by VERIFIN and the Spiez Laboratory in 2011.[27]

84. The SAB discussed some of the scientific aspects of incapacitants at its Sixteenth Session. It was acknowledged that the term "non-lethal" is inappropriate when referring to chemicals intended for use as incapacitants. For all chemicals, toxicity is a matter of dosage. It was further noted that chemicals considered to have high safety margins (on the basis of therapeutic ratios (LD_{50}/ED_{50}) in the context of controlled pharmaceutical use) can have very low safety margins when factors such as uneven dissemination, variability in human response, and the possible need for a rapid onset are required. Furthermore, pharmaceutical companies commonly publish toxicity data that have been obtained from experimentation on small rodent species, and this may not extrapolate to higher species. In particular, there are large species differences in the reaction to morphine-like drugs such as the fentanyls, which appear to have attracted the greatest attention as potential incapacitants. It was also emphasised that it is not simply a matter of precisely what incapacitating chemical is used for law enforcement purposes, but how it is used. In one incident, pepper spray (a riot control agent) was used to break up a fight in a crowded night club, which resulted in 19 deaths as people panicked and tried to escape.

85. The types of chemicals and pharmaceuticals known to have been considered as incapacitants from open-literature sources have been discussed. Most are centrally acting compounds that target specific neuronal pathways in the brain. All of them emerged from drug programmes undertaken from the 1960s to the 1980s.

86. In the view of the SAB, the technical discussion on the potential use of toxic chemicals for law-enforcement purposes has been exhaustive. The SAB may continue its discussions once technical information about specific candidate chemicals and/or dissemination systems is made available to the Board. The SAB recommends to the Secretariat that it start preparations for verification activities that could be required in an IAU. Such preparations should include developing analytical methods and procedures, as well as collecting analytical reference data for the analysis of such chemicals. The Secretariat should invite Member States' laboratories to contribute to this effort.

VERIFICATION TECHNOLOGY

Inspection equipment

87. The Second Review Conference requested the Secretariat to seek advice from the SAB when reviewing requirements and specifications for inspection equipment. The SAB, together with the Secretariat, has since reviewed the list of equipment approved

25 International Committee of the Red Cross, "Incapacitating Chemical Agents: Implications for International Law", held in Montreux, Switzerland, 24 to 26 March 2010.

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

27 Technical Workshop on Incapacitating Agents, held in Spiez, Switzerland, 8 and 9 September 2011.

by the Conference at its First Session. An updated list of operational requirements and technical specifications was approved by the Conference at its Fifteenth Session.

88. The SAB is of the view that the Secretariat, with its operational inspection experience, is best suited to identify changes or additions to equipment needs. The SAB would, however, wish to remain active on such issues and requests that it be briefed by the Secretariat on substantial changes. The SAB will inform the Secretariat if it identifies new technologies that have matured to a level that could be of interest, and will provide any other advice requested in relation to inspection equipment.

89. Inspectors are required to operate a wide variety of equipment in different scenarios. The SAB wishes to emphasise the importance of training for inspectors, to ensure that equipment is properly utilised, and to gain operational experience across the breadth of operational challenges, that is, during routine inspections, CIs, and IAUs.

On-site sampling and analysis

90. The SAB is of the view that the Secretariat, with its operational inspection experience, is best suited to modify on-site analytical methods and procedures. The SAB would, however, emphasise that modifications should be validated to demonstrate that methods and procedures remain fit for purpose. The SAB will assist the Secretariat in advising on new methods and procedures that might be applicable to on-site analysis.

91. The 2008 SAB report on science and technology discussed a number of outstanding issues relevant to on-site and off-site S&A. Issues discussed in regard to on-site analysis were the logistics of transporting and setting up analytical equipment, and the time constraints that influence analyses.

92. The OPCW Inspectorate (INS) undertakes verification activities on site using approved equipment and documented protocols for S&A. Ideally, equipment should be readily portable and easy to set up, procedures must be fit for purpose, and consistent with the time constraints of the inspection. Above all, on-site analysis must be rugged and reliable. The following paragraphs highlight areas where, in the view of the SAB, an effective capability has been reached, progress has been made, or where further improvement is desirable.

93. From September 2006, the Secretariat introduced on-site analysis for inspections of declared Schedule 2 facilities. These inspections have demonstrated that equipment and procedures are fit for purpose; however, on average, only two to three samples were analysed within the 96-hour time constraint of the inspection. The SAB and the Secretariat recognise that it is desirable to have procedures that allow for a greater throughput of samples. With this objective, the OPCW Laboratory procured autoinjectors, which permit analysis overnight, and modified procedures are being developed in order to:

(a) decrease the time needed for gas chromatography-mass spectrometry analysis (GC-MS) by using “fast GC”; and

(b) shorten sample preparation time, particularly in regard to aqueous samples.

94. These topics have been addressed by the TWG on S&A, and are also relevant if on-site analysis is conducted during Schedule 3 or OCPF inspections.

95. Fast GC employing currently approved equipment, but using a faster temperature programme and narrower, shorter columns, should allow a modest reduction (about one half to one third) of the time required for gas chromatographic separation of chemicals. A limitation on the degree of reduction in separation time is that some problems have been experienced with variability in retention indices (RIs) compared to those in the OCAD. The OPCW Laboratory, in collaboration with the VERIFIN laboratory (Finland), is currently evaluating ways of modifying the procedure.

96. The TWG initially considered that liquid phase microextraction using hollow-fibre membranes was the most promising technique for simplifying the lengthy procedure currently used for aqueous sample preparation by inspectors and by many designated laboratories during proficiency tests. However, the TWG has now endorsed an alternative procedure developed by the OPCW Laboratory, which involves injection of the sample onto a tube containing Tenax® adsorbent, derivatisation in the tube, and thermal desorption GC-MS. This procedure takes considerably less time than the one currently being used. A description of this process has been published in a peer-reviewed journal and is currently being evaluated for robustness by some designated laboratories. This procedure, however, is not amenable to autoinjection, a disadvantage that should be resolved.

97. In the last five-year period, the OPCW has conducted exercises in scenarios involving a supposed IAU and a CI. S&A was conducted during the CI exercise (Thailand, November 2011), and in the exercise ASSISTEX 3 (Tunisia, September 2010). The technical challenges for S&A in these scenarios may differ from those presented during routine inspections and may require adaptations of existing procedures. Furthermore, depending on the scenario, on-site analysis may have to satisfy different mission objectives, not only in evidence gathering and verification but also in supporting response teams in fast identification in support of health and safety.

98. The SAB has reiterated the importance of the OCAD for S&A, a fact that the Board emphasised in its 2008 science and technology report. If a chemical is not included in the OCAD, an inspection team may fail to identify it during on-site S&A. This is important, not only for scheduled chemicals, but also for relevant non-scheduled chemicals—for example, a non-scheduled degradation product of a Schedule 1 chemical (as a possible indicator of production or use) or a non-scheduled toxic chemical, such as a riot control agent that has been used for activities prohibited by the Convention.

99. The content of the OCAD has increased significantly under the period of review. This has been the result of the many contributions of data from Member States' laboratories, as well as the work of the Validation Group and its untiring efforts, together with the OPCW Laboratory, to expand the content of this unique database for chemical weapons-related analysis. However, a new practice has created a difference in the content of the database for on-site analysis during inspections, and the content available to designated laboratories for off-site analysis. The Secretariat distributes all data validated by the Group to the designated laboratories. If approval of this data by the Council is deferred, it is not available for the conduct of inspections.

100. The TWG on S&A has reviewed the current status of portable liquid chromatography-mass spectrometry instrumentation, and direct sampling MS techniques, such as desorption electrospray ionisation (DESI) and direct analysis in real time (DART), which minimise or eliminate the need for sample preparation and extend the range of analytes that can be accommodated. The TWG concluded that it will be several years before portable and rugged instrumentation that might be applicable to on-site analysis would be commercially available, although DESI is already being used successfully for Convention-related analysis in some vehicle-based mobile laboratories. The TWG also concluded that the use of molecularly imprinted polymers (MIPs, which are sometimes referred to as "synthetic antibodies") and solid phase microextraction (SPME) for sample preparation had limitations with regard to the generic-type analysis required for on-site inspections. Both techniques are useful in more targeted applications. SPME is being used successfully in mobile laboratories.

Off-site analysis

101. The 2008 SAB report on science and technology referred to changes being proposed in proficiency testing, and noted major capability gaps for off-site analysis with regard to IAUs of chemical weapons, where the analysis of environmental and biomedical samples at trace levels may be required, and with regard to Schedule 1 toxin analysis. These issues have been further addressed by the SAB through the TWG on S&A, and by the OPCW Laboratory. Substantial progress has been made over the past five years. Off-site laboratory analysis is much more likely to adopt new instrumentation and techniques in comparison to on-site analysis. The SAB and its TWG have maintained a watching brief on new developments in analytical instrumentation and methodology that may be relevant to Convention-related analysis.

102. The SAB noted in the above-mentioned report that the samples then used in OPCW proficiency testing did not accurately reflect samples that might be submitted for off-site analysis. A modified format, introduced by the Secretariat for the Twenty-Third OPCW Proficiency Test, has removed this shortcoming and proven to be effective. The current status of 22 designated laboratories provides the Director-General with good flexibility to select laboratories for off-site analysis, but it remains desirable to have designated laboratories available from all regional groups.

103. Other aspects of off-site analysis, as documented in the OPCW standard operating procedures (SOPs), have rarely been practised. This was noted by the SAB in its 2008 report. The SAB would like to reiterate the importance of regularly practising the complex process of off-site analysis, which includes such activities as sample transport, accounting of sample material and waste, issues relating to confidentiality, reporting of results to the Director-General, and evaluation of these results by the Secretariat.

104. Current OPCW proficiency testing does not address the identification of non-scheduled or novel toxic chemicals. This may, for example, be important for an IAU, when there is evidence that a toxic chemical has been used for prohibited purposes but no scheduled chemical can be found. The SAB recommends that the Secretariat, with the support of designated laboratories and other relevant experts, evaluate a possible approach for such a scenario.

105. An important aspect of IAUs is the possible requirement for trace level analysis (i.e. at parts per billion), for environmental samples and almost certainly for biomedical samples. Historical precedence, before entry into force of the Convention, suggests that MS techniques targeted at specific analytes (single stage, tandem, and high-resolution MS, using selected ion or selected reaction monitoring), are likely to be required. Identification using these techniques will differ from the generic techniques used in OPCW proficiency tests, where analytes are spiked at parts per million and where full spectral data can be obtained. If the Secretariat wishes designated laboratories to apply trace analytical techniques in off-site analysis, it is important that written criteria for identification are stipulated, in line with other regulatory bodies, such as the World Anti-Doping Agency (WADA) and the European Commission (EC). The SAB TWG on S&A has addressed this issue and made recommendations to the Secretariat. Identification criteria for trace analysis were evaluated as part of the second OPCW confidence-building exercise on biomedical samples. After considering the results of this exercise, the TWG on S&A, at its seventh meeting (Annex 2 of SAB-19/1), recommended that the Secretariat adopt, with minor modifications, identification criteria based on the EC identification points system.

106. The OPCW proficiency testing programme has been instrumental in establishing a system of expert designated laboratories, which the Director-General can request to undertake off-site analysis. The current status is that 22 laboratories are designated from a broad geographical base. This system of designated laboratories has been very costly to establish, is equally costly to maintain, and is demanding on resources from the laboratories and the Secretariat. It should also be noted that no off-site analysis has yet been undertaken in a designated laboratory. At the present time, the Secretariat is also seeking to establish a capability for biomedical sample analysis in cases of IAUs, and the SAB has made recommendations for the broader application of trace analysis in an IAU, and for the verification of the two Schedule 1 toxins, saxitoxin and ricin. Whilst not wishing to hinder the future designation of additional laboratories, the SAB believes that it is now appropriate that a review of the entire proficiency testing programme be undertaken.

107. The OPCW and its designated laboratories have attained a high technical competence in identifying scheduled chemicals and their degradation products at the levels required in OPCW proficiency tests, and have developed robust procedures applicable to different scenarios. An additional capability being pursued in several chemical defence and verification laboratories is attribution of a toxic chemical or precursor to a particular source or production route. Approaches include the identification of certain impurities, statistical comparison of complex GC-MS chromatograms, and isotope ratio MS. Should the Secretariat seek to establish such a capability to identify attribution signatures for toxic chemicals in designated laboratories and/or in-house, extensive collaboration between institutions and laboratories would be required. The major problem with attribution is the lack of reference data for comparison.

Biomedical samples

108. In cases of IAUs, the Convention provides for the collection of biomedical samples from suspected human and animal casualties. Such samples may provide the best evidence of use of chemical-warfare agents, particularly in remote areas where no

munition residues can be found. Following the recommendations of the TWG on biomedical samples, which were endorsed by the SAB, the Secretariat initiated a series of confidence-building exercises with the following objectives:

(a) to broaden the expertise across laboratories;

(b) to compare and evaluate different methods for the identification of biomarkers of exposure;

(c) to evaluate identification criteria at trace levels; and

(d) to identify problems, such as trace-level contamination of equipment.

109. The first exercise (held from December 2009 to January 2010), in which metabolites of nerve agents and sulfur mustard were spiked into synthetic urine at levels down to 10 ng/ml, demonstrated an encouraging capability in one half of the 22 participating laboratories.[28] A similar level of proficiency was demonstrated in the second exercise (held from February to March 2012), where spiking levels were as low as 5 ng/ml, and with improved quality of the data and reporting.[29] The SAB fully supports these exercises, which have significantly broadened the capability to analyse biomedical samples across Member States. It is recommended that the exercises progress towards the more difficult analysis of longer-lived biomarkers of exposure, such as protein adducts.

Toxin analysis

110. The protein toxin ricin and the marine toxin saxitoxin are included in Schedule 1 of the Annex on Chemicals. The OPCW Secretariat, therefore, has an obligation to develop or have access to methods of verification. These toxins present problems for the current system of designated laboratories and proficiency testing. Neither can be identified using GC-MS, because of their polar and involatile nature and, in the case of ricin, its high molecular mass. Well-established methods exist for the analysis of saxitoxin in the context of paralytic shellfish poisoning. A number of laboratories, mostly government-affiliated and including some OPCW designated laboratories, have developed expertise in ricin analysis in the context of chemical and/or biological defence or counter-terrorism.

111. The TWG on S&A has reviewed the various methods that can be used to detect and identify saxitoxin and ricin, and has submitted recommendations to the Secretariat on those methods considered most appropriate for verification purposes.[30, 31] It was recommended that, for both toxins, a screening technique, for example based on immunoassay, combined with a confirmative technique based on liquid chromatography-tandem mass spectrometry (LC-MS-MS), be used. In the case of ricin, the protein (molecular mass ~62-65 kDa) would need to be enzymatically

28 Evaluation of the First Confidence-Building Exercise for Biomedical Samples, June 2010.

29 Evaluation of the Second Confidence-Building Exercise for Biomedical Samples, June 2012.

30 Report of the sixth meeting of the TWG on S&A, Annex 2 of SAB-17/1, pages 15 to 23.

31 Annex 2 of SAB-19/1.

digested to a series of low-molecular mass peptides, and these would be sequenced and identified using LC-MS-MS.

112. The TWG, through the efforts of the Spiez Laboratory, Switzerland, held an informal exercise on saxitoxin analysis, which has assisted in providing firm proposals for identification. Several laboratories participated in an international round-robin exercise on ricin analysis, which was co-ordinated by the Robert Koch Institute, Germany, under the auspices of the Global Health Security Action Group. In addition to providing valuable data, this exercise facilitated consultation with expertise outside of the TWG and the designated laboratories.

New techniques relevant to Convention-related analysis

113. Analytical instrumentation continues to evolve with improved capabilities for Convention-related analysis. Nuclear magnetic resonance spectroscopy (NMR) has continued to become more sensitive and can be more readily applied to complex mixtures and aqueous samples. Raman spectroscopy is continuing to improve, although mainly in regard to applications in detection rather than identification. Arguably the most important development over the past five years has been the increasing availability (though at high cost) of high-resolution mass spectrometers capable of routine, accurate mass measurements. These have found application in OPCW proficiency tests in determining the molecular formula of unknown chemicals whose spectra were not present in the OCAD. Accurate mass measurement also provides substantial advantages in the analysis of proteinaceous toxins, such as ricin. Time-of-flight and other high-resolution instruments are finding increasing application in trace analysis, where full spectral data can be acquired and searched retrospectively at high resolution using extracted ion monitoring. This contrasts with scanning instruments, where ions to be monitored at trace levels must be pre-selected, thus restricting the number of pre-determined analytes that can be detected.

114. The analytical procedures used by OPCW inspectors and designated laboratories evolved from a manual entitled "*Recommended Operating Procedures for Analysis in the Verification of Chemical Disarmament*", the so-called "Blue Book", published in 1994 by the VERIFIN Laboratory, Finland. Starting in 2009, the recommended operating procedures (ROPs) have been updated through international collaboration with expert laboratories working in the field of Convention-related analysis, and have been published in a new edition.[32] These methods provide guidelines for designated laboratories, or laboratories applying for designation. The ROPs are also used to train personnel working in the field of defence against chemical-warfare agents.

115. The SAB has maintained a watching brief on methods and equipment for field detection of chemical-warfare agents. Advances are being made in miniaturisation of detection equipment and devices, using a number of different technological approaches. Nanotechnology is playing a significant part in these developments. Nevertheless, most field-detection systems still lack sensitivity in terms of them being used as alarm devices, many lack selectivity and show cross sensitivities leading to false positive identifications, and some show lack of robustness during field use.

32 *Recommended Operating Procedures for Analysis in the Verification of Chemical Disarmament*. 2011 Edition. Vanninen, P. (ed). The Ministry for Foreign Affairs of Finland, University of Helsinki.

Considering the increased demand and interest from first-responder organisations for such detection systems, the SAB anticipates further progress on field detection devices for chemical-warfare agents.

DESTRUCTION OF CHEMICAL WEAPONS

116. The SAB stated in its 2008 science and technology report that the technologies and processes for the destruction of declared chemical weapons stockpiles had matured. Using various destruction technologies, over 70% of the currently declared stockpile has been irreversibly destroyed. Progress and development in destruction technology has been shared between Member States in different fora and, to a significant part, through a series of chemical demilitarisation conferences, organised jointly by the Russian Federation, the United Kingdom of Great Britain and Northern Ireland, and the United States of America, and held annually from 1998 to 2012. The expertise to monitor and verify destruction of chemical weapons stockpiles is an important technical capability developed by the Secretariat.

117. For non-stockpile munitions, destruction processes for old chemical weapons (OCWs), and old and abandoned chemical weapons (OACWs), have been further developed during the period under review. The safe recovery, identification, and destruction of such chemical munitions still pose different technical challenges, depending on the circumstances and the number and condition of the discovered munitions. The discovery of non-stockpile munitions will continue for many years, possibly long after the completion of the destruction of declared stockpiles. The OPCW will need to assist Member States and maintain the necessary technical expertise. The SAB will continue to keep a watching brief on the development of new destruction technologies and assist where required.

ASSISTANCE AND PROTECTION

118. Advances in science and technology provide opportunities for better assistance and protection against chemical weapons. Research is advancing in all areas of chemical defence, although the development of these advances into robust fieldable and affordable devices, and acceptance by the military, is generally slow. In the last decade, much of the focus has been on first responders, in addition to military requirements.

119. The first and essential line of defence against chemical weapons is detection. The requirements differ according to the purpose of the detector. The initial requirement is to warn of the presence of a toxic hazard; the second requirement is the identification of the type or particular chemical-warfare agent or toxic industrial chemical for initial medical management of casualties. Thereafter, monitoring is required to determine the extent of the hazard, to direct and monitor decontamination, and to assess when it is safe to remove protective equipment. Most in-service detectors and hand-held monitors are based on ion mobility spectrometry, flame photometry, surface acoustic wave devices, Raman spectroscopy, and portable GC-MS and Fourier transform infrared spectroscopy (FTIR). Improvements are being sought in all of these techniques, and many newer types of rapid response detectors are under investigation; these detectors use various types of nanomaterial (e.g. carbon nanotubes, zirconia nanoparticles, and quantum dots) as transducers, and molecular

recognition technologies including molecularly imprinted polymers and immunoassays. Notable progress is being made in portable, point-of-care diagnostic devices, much of it exploiting aspects of nanotechnology and lab-on-a-chip technology. Prototype devices have been developed for diagnosing exposure to a nerve agent, more reliably than simply measuring cholinesterase levels. The SAB will continue to monitor the development of new portable instruments for the rapid detection of chemical-warfare agents and toxic industrial chemicals.

120. Considerable effort continues to be directed towards the development of improved medical countermeasures against nerve agents, although translation into fieldable therapeutic drugs has been slow. A new drug would have to undergo rigorous testing, which would include studies on non-human primates, before it could be licensed. The current medical treatment for nerve-agent poisoning employs atropine or another anticholinergic drug, an oxime to reactivate inhibited acetylcholinesterase (AChE), and an anticonvulsant drug, such as diazepam or its prodrug avizafone, to minimise neuropathological damage to the brain. Some armed forces use pre-treatment with the reversible cholinesterase inhibitor pyridostigmine to improve protection, particularly against soman.

121. The search continues for an effective broad spectrum oxime reactivator of nerve-agent inhibited cholinesterase. Each of the fielded oximes has limitations, as illustrated by the range of different oximes that are included in military medical kits (e.g. pralidoxime (2-PAM), trimedoxime (TMB-4), methoxime (MMB-4), obidoxime (LüH-6), and HI-6). All these oximes are effective against poisoning by sarin and VX. Trimedoxime, methoxime, and particularly obidoxime are effective reactivators of tabun-inhibited AChE, but effective reactivation of soman-inhibited enzyme remains a problem. HI-6 shows some therapeutic efficacy against soman poisoning in experimental animals, but this appears to result from a direct action on nicotinic receptor ion channels and not from reactivation. Efforts are also being directed at protection and reactivation of AChE in the central nervous system, and improved neuroprotection following delayed therapy.

122. An alternative approach to pretreatment and immediate therapy for nerve-agent poisoning is the use of a scavenger to detoxify the nerve agent before it reaches its biochemical target. Human plasma-derived and recombinant human butyrylcholinesterase (BuChE) have been investigated as candidates for a number of years. Effectiveness has been demonstrated in experimental animals, but there are problems relating to the supply and pharmaceutical use of BuChE. A disadvantage to BuChE as a scavenger is that it forms a stoichiometric 1:1 adduct with the nerve agent which, like inhibited AChE, is irreversible in the short term, thus requiring a relatively large mass of the proteinaceous enzyme to be administered. Attempts are in progress to find or engineer an acceptable catalytic scavenger. Enzymes that hydrolyse nerve agents (phosphatases) are also being explored, including the application of synthetic biology to engineer improvements over the naturally occurring enzymes. Gene therapy might be a future direction for therapy against nerve-agent poisoning, offering the possibility of transitory production of scavengers or degrading enzymes in the body.

123. Some attention is being directed at improved or controlled delivery of therapeutic drugs, for example enhanced penetration of the blood-brain barrier, or slow release

formulations, such as skin patches for treatment following percutaneous exposure, where the agent is absorbed much more slowly.

124. In other aspects of defensive countermeasures, improved physical protection against chemical-warfare agents is being developed, for example lighter suits, self-decontaminating suits, respirators with a lower physiological burden, and improved canister materials. As referred to in paragraph 54, nanomaterials are being incorporated into these new designs. Improved decontaminants are in development, which are based, for example, on alkaline peroxide formulations and microemulsions. One of the problems is that most fielded decontaminants are too aggressive to be used on sensitive equipment. Hydrolysing enzymes (e.g. phosphatases and phosphotriesterases) are under intensive investigation, including modified enzymes produced in recombinant organisms (an example of synthetic biology). A skin decontaminant, RSDL®, has been adopted by some armed forces.

EDUCATION AND OUTREACH IN SCIENCE AND TECHNOLOGY

125. Education and outreach in science and technology is important to the future implementation of the Convention. Education and outreach serves a number of purposes including:

(a) raising awareness of the Convention among students, educators and the global scientific community;

(b) educating on the risks associated with multiple uses of chemicals;

(c) contributing to national implementation of the Convention;

(d) contributing to the prevention of the misuse of toxic chemicals;

(e) facilitating chemical safety and chemical security; and

(f) building skills and capabilities relating to the peaceful uses of chemistry.

126. Several programmes associated with education and outreach have been conducted by the OPCW International Cooperation and Assistance Division (ICA) in collaboration with the IUPAC and other organisations, and joint IUPAC/OPCW workshops have been held. A number of publications are available from the IUPAC and other publishers, in particular, a final version of a proposed code of conduct and a number of teaching modules based on the general ethical principles of chemistry.

127. The Secretariat has accepted opportunities to make presentations to the scientific community on outreach activities under Article XI of the Convention, for example at the OPCW Conference on International Cooperation and Chemical Safety and Security, held on 12 and 13 September 2011. These outreach activities include the Associate Programme, the Conference-Support Programme, the Internship-Support Programme, Support for Research Projects, the Analytical-Skills-Development Course, and the course on Chemical-Safety Management. The International Year of Chemistry in 2011 offered an opportunity for the OPCW to build closer ties with the

global chemical community. Various outreach events were held, mainly at national levels. The SAB commends the Secretariat for these activities.

128. The SAB also stresses the importance of targeting professional bodies and academic institutions, with the aim of encouraging institutions to include a module on the Convention in their academic curricula. The Board would like to emphasise that persuading institutions to include education on the Convention into already crowded courses can be difficult. The SAB believes the National Authorities should have a role to play in encouraging such activities.

129. The SAB recommends that outreach activities should consider the particular requirements or region and that appropriate support be provided accordingly. Assistance should be provided primarily to support institutions in States Parties, rather than to individuals.

130. In accordance with the Note by the Director-General in response to the report of the Seventeenth Session of the SAB[33], and in view of the important role that education and outreach plays in chemical safety, chemical security, and awareness of the Convention, the SAB has convened a TWG on education and outreach.

131. The SAB endorsed the recommendations made at the first meeting of the TWG, which include the preparation of educational materials, the cooperation of the OPCW in education and outreach with other international organisations and in regard to other treaties (for example, the International Atomic Energy Agency (IAEA), the BWC, the World Health Organization (WHO)) and international scientific bodies (e.g. the IUPAC and the International Union of Toxicology (IUTOX)), as well as professional associations (the International Council of Chemical Associations (ICCA) and CEFIC), and NGOs. The Board also recommends more engagement from States Parties in the teaching of ethics and responsible science, as well as in the drafting of national codes of conduct, and in offering support in regard to other forms of outreach. These activities will require adequate funding to remain sustainable.

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33 EC-67/DG.11, dated 9 February 2012, paragraph 22.