OPCW

Review Conference

Fifth Session
15 – 19 May 2023

RC-5/DG.1
22 February 2023
Original: ENGLISH

REPORT BY THE DIRECTOR-GENERAL

REPORT OF THE SCIENTIFIC ADVISORY BOARD ON DEVELOPMENTS IN SCIENCE AND TECHNOLOGY TO THE FIFTH 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 render to the Conference of the States Parties (hereinafter "the Conference") and the Executive Council (hereinafter "the Council") specialised advice in areas of science and technology relevant to the Convention. In keeping with this mandate, and as its contribution to the Fifth Review Conference,[1] to be held from 15 to 19 May 2023, 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 for the review of the operation of the Convention and its future implementation.

2. This report contains an executive summary and recommendations addressing issues that may impact the implementation of the Convention and the work of the Technical Secretariat (hereinafter "the Secretariat"). The analysis of developments in science and technology that inform these recommendations is provided in Annex 1.

3. This is the fifth report for a Review Conference by the SAB on developments in science and technology relevant to the Convention. The four earlier reports were presented to the First Review Conference,[2] the Second Review Conference,[3] the Third Review Conference,[4] and the Fourth Review Conference.[5]

1 Review Conference = Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention.

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

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

4 RC-3/DG.1, dated 29 October 2012.

5 RC-4/DG.1, dated 30 April 2018.

4. To guide the scientific review, the SAB has drawn insights from sources that include:

(a) its four earlier reports to the First, Second, Third, and Fourth Review Conferences;

(b) the deliberations of the SAB during regular sessions of the Board since the Fourth Review Conference (documented in the reports from its Twenty-Eighth through its Thirty-Sixth Sessions);[6]

(c) the deliberations of the SAB's Temporary Working Groups (TWG) on the Convergence of Chemistry and Biology[7] (from November 2011 to November 2013), Education and Outreach[8] (from November 2012 to September 2014), Verification[9] (from March 2013 to May 2015), Investigative Science and Technology[10] (from February 2018 to December 2019), and the Analysis of Biotoxins, which held its first six meetings prior to the publication of this report;[11]

(d) two workshops, co-organised by the SAB and external partners and funded by the European Union; these workshops addressed artificial intelligence (AI)-assisted chemistry (held in The Hague, the Netherlands, in June 2022) and emerging developments in the chemical industry (held in Antwerp, Belgium, in June 2022);

(e) intersessional responses from the SAB to requests for advice from the Director-General on different topics: One request and response on new types of nerve agents was considered and completed since the Fourth Review Conference.[12] Previous requests considered medical countermeasures and longer-term treatment for victims of chemical agent exposure,[13] isotopic labels

---

6 SAB-28/1, dated 14 June 2019; SAB-29/1, dated 2 September 2020; SAB-30/1, dated 12 November 2020; SAB-31/1, dated 4 March 2021; SAB-32/1, dated 17 June 2021; SAB-33/1, dated 18 November 2021; SAB-34/1, dated 17 March 2022; and SAB-35/1, dated 16 June 2022. Note that while the report for the Thirty-Sixth Session of the SAB has yet to be released, the content of the session has been taken into account for this report.

7 The final report of the TWG on the Convergence of Chemistry and Biology was published as SAB/REP/1/14, dated 27 June 2014, which is available at: https://bit.ly/TWGCBCon. A quick reference guide to its recommendations is available at: https://bit.ly/TWGCBConRec.

8 The final report of the TWG on Education and Outreach was published as SAB/REP/2/14, dated 25 November 2014 and is available at: https://bit.ly/TWGEO.

9 The final report of the TWG on Verification was published as SAB/REP/1/15, dated June 2015, and is available at: https://bit.ly/TWGVER. A quick reference guide to its recommendations is available at: https://bit.ly/TWGVERRec.

10 The final report of the TWG on Investigative Science and Technology was published as SAB/REP/1/19, dated December 2019. Available at: https://bit.ly/TWGIST.

11 Meeting reports are available at https://www.opcw.org/resources/documents/subsidiary-bodies/scientific-advisory-board.

12 SAB-28/WP.1, dated 3 July 2018.

13 SAB-21/WP.7, dated 29 April 2014; and SAB-22/WP.2/Rev.1, dated 10 June 2015.

and the stereochemistry of scheduled chemicals,[14] sample storage and stability,[15] and riot control agents (RCAs);[16]

(f) the participation of members of the SAB in scientific conferences and workshops, including Spiez CONVERGENCE workshops held in 2018, 2021, and 2022,[17] and engagement with other scientific advisory mechanisms;

(g) a range of scientific literature and patents across diverse areas of relevance; and

(h) the individual expertise of the members of the Board, all of whom have contributed to the scientific review process.

5. With regard to subparagraphs 4(b) to (e) above, 21 meetings and workshops were held with a combined participation of 546 people (from 50 States Parties), 19 reports were produced, and 227 presentations and briefings were received.

6. For clarity, the references to all scientific literature and open-source information drawn from in the preparation of this report have been removed. A fully referenced version may be made available to States Parties upon request. Furthermore, all abbreviations used throughout this report are listed in Annex 2.

7. The SAB's detailed analysis of developments in science and technology relevant to the Convention is found in Annex 1. Based on this analysis, the SAB has provided advice and made a number of recommendations. In some cases, a recommendation may not relate to a single section within Annex 1 but is based on information from several sections. After each recommendation, the principal section(s) in Annex 1 to be consulted for more information is provided; additional information contributing to the recommendation may also be discussed elsewhere.

EXECUTIVE SUMMARY

8. The SAB notes that the Convention is shaped by developments in science, especially as rapid technological innovations increase the accessibility of modern scientific tools to new actors and domains. The implementation of the Convention is increasingly transdisciplinary in the modern era, necessitating collaboration across disarmament regimes and scientific disciplines to continue to carry out the OPCW's mandate effectively. As the end of the destruction of declared stockpiles nears, the focus of the OPCW's work must shift towards preventing the re-emergence of chemical weapons, the misuse of chemistry, and the weaponisation of science, both literally and rhetorically. The convergence of different fields of science, within the context of a volatile social and political landscape, presents an ever-changing set of challenges to and opportunities for the implementation of the Convention.

---

14 SAB-23/WP.1, dated 28 April 2016.

15 SAB-23/WP.2, dated 25 May 2016.

16 SAB-25/WP.1, dated 27 March 2017.

17 Spiez CONVERGENCE: report of the Third Workshop, 2018, available at: https://bit.ly/SpiezCON3; report of the Fourth Workshop, 2021, available at: https://bit.ly/SpiezCON4; and report of the Fifth Workshop, 2022, available at: https://bit.ly/SpiezCON5.

9. At the time of the Fourth Review Conference, the Fourth Industrial Revolution, was only in its initial phases. Since then, the last few years have witnessed a significant blurring of the boundaries between the physical, biological, and digital realms, with technologies developing and advancing at a rapid pace. A number of notable advances relating to AI, additive manufacturing (also known as 3D printing or AM), and biotechnology have been observed.

10. AI is a highly disruptive cross-cutting technology with an unparalleled flexibility of application, and features in many sections of this report. In organic chemistry, it is being utilised for the discovery of new compounds, the identification of novel synthetic routes, and the prediction of properties, such as toxicity. It is also being coupled with automated platforms, so-called "laboratory robots", for more effective, streamlined, and safer processes. Furthermore, the application of AI in chemical safety may help identify less hazardous chemicals for substitution in production processes and lead to reductions in waste, or even determine novel processes for its reuse.

11. The SAB notes the significant potential this technology presents, and the many opportunities it may afford in terms of strengthening the verification regime, streamlining certain chemical weapons-related research activities, and possibly leading to breakthroughs in research on medical countermeasures to chemical weapons exposure. However, developments should be monitored closely, such as the ease and speed with which new toxic non-scheduled chemicals may be designed, as well as the ease and speed with which the synthetic routes to them can be identified.

12. There has been a clear shift in the use of AM—from a simple rapid prototyping tool at the time of the Fourth Review Conference, to its integration into production processes in many sectors today. The range of printed materials has increased considerably, and now includes a variety of metals and alloys, chemically resistant polymers, biocompatible materials, and even energetic materials. A variety of components may be printed, such as for dispersal systems or chemical reactors. This technology is becoming increasingly affordable, technically accessible, and widely available.

13. AM has also been used in drug delivery to produce microneedle arrays, transdermal patches, implantable devices, and bio-inks. Coordination cages and encapsulation techniques are also increasingly being used in drug delivery, and could be harnessed for medical treatments following exposure to chemical weapons.

14. The potential misuse of these technologies, including in contexts beyond the Convention, has been highlighted over the last few years. The need for ethical codes of conduct or guidelines is becoming increasingly apparent. This is especially the case for converging technologies and transdisciplinary work, in which the awareness of dual-use applications is often limited. The SAB therefore encourages States Parties to raise awareness within their scientific communities, either by promoting existing codes of conduct (such as The Hague Ethical Guidelines[18]) or developing their own.

15. The information available on the aforementioned technologies is a stark contrast to the paucity of information available to date on the newly scheduled chemicals (NSCs) in Schedule 1.A.13 to 1.A.16. Review of the open-source data on the NSCs has revealed a

---

18 https://www.opcw.org/hague-ethical-guidelines.

significant number of information gaps impacting activities such as verification, protection, and capacity building, limiting the work of the Secretariat and designated laboratories. A full understanding of all Schedule 1 chemicals is paramount in preventing the re-emergence of chemical weapons; sharing information on this topic is strongly encouraged.

16. The analytical capabilities of the designated laboratory network play a significant role in the implementation of the Convention. It is therefore of vital importance that these capabilities continue to develop with the emergence of new threats and challenges, such as complex sample matrices. To this end, the OPCW Central Analytical Database (OCAD) and the Validation Group Working Database should be as comprehensive as possible and include information on NSCs, central nervous system-acting chemicals (CNS-acting chemicals), and other relevant chemicals.

17. It is acknowledged that biotoxins pose investigative challenges, stemming principally from their great diversity. They may be loosely divided into low molecular weight biotoxins (such as saxitoxin) and high molecular weight biotoxins (such as ricin), but vary significantly within these classes in terms of size and chemical properties. Consequently, there is no single analytical technique that can be applied to them universally. Indeed, analyses of low molecular weight biotoxins require very different methods than those of high molecular weight biotoxins, and relatively few laboratories are skilled in both types of analysis. The TWG on the Analysis of Biotoxins has been considering this issue in detail, and has determined that designated laboratories should continue to improve their analytical capabilities with respect to the scheduled biotoxins ricin and saxitoxin. The SAB notes that cooperation and knowledge sharing is key in capacity building, and that the expertise of other laboratories, such as those listed in the roster under the United Nations Secretary-General's Mechanism (UNSGM) for Investigation of Alleged Use of Chemical and Biological Weapons, should be leveraged to develop a non-scheduled biotoxin analytical capability, and that regular exercises should be undertaken. Similarly, exercises would also be beneficial in developing knowledge and capability in terms of the analysis of trace levels of biotoxins in biomedical samples.

18. A promising biomedical technique based on dried blood spots (DBS) has emerged as a suitable alternative to traditional blood tubes. The technique provides a number of advantages over existing blood sampling techniques, including increased sample storage time. The SAB agrees that this merits further exploration, possibly as part of a biomedical sample confidence-building exercise.

19. More broadly, sampling is required for the safe and effective management of chemical incidents. In the case of a deliberate release of a persistent chemical warfare agent, the challenge is not only to detect and identify the contaminant, but also to assure decision makers that the agreed decontamination goals have been met. Statistical sampling and analysis strategies could be particularly effective in achieving these goals, in addition to providing an improved level of confidence.

20. The TWG on Investigative Science and Technology highlighted the need to develop and strengthen forensic capabilities, particularly in chemical profiling. Chemical profiling may provide valuable information about the production process of a particular chemical, as well as information about its provenance. It can also be used to create linkages among different incidents involving chemical weapons. This work would offer a number of

benefits, including supporting the identification of non-State actors, as well as assisting States Parties in combatting terrorism and other criminal activities. The topic of chemical profiling warrants an in-depth review for comprehensive understanding.

21. Green chemistry and digitalisation are two driving factors that are transforming the chemical industry. Developments in green chemistry, especially the substitution of hazardous chemicals and low-waste-generating processes, are directly benefiting the chemical safety and security of the chemical industry. The Fourth Industrial Revolution in the chemical industry has not been confined only to the incorporation of new technologies in production processes and supply chain management. Connected devices, such as wearable sensors and smart personal protective equipment (PPE), are enhancing chemical safety, while immersive technologies, such as virtual reality and digital twins are transforming learning and development across the chemical sector and are proving remarkably beneficial for chemical safety training. The SAB notes the importance of education and training for improving chemical safety and security, and the value that can be brought through engagement with a range of technical experts, including at international organisations, within the chemical industry, and in industry associations. Strengthening chemical safety and security through cooperation and the adoption of risk-based approaches and best international practices will benefit the chemical industry as a whole and be particularly useful to those States Parties with developing and transitional economies. As chemical safety and chemical security are complementary, strengthening chemical safety will also often enhance chemical security.

22. As the final destruction of the remaining declared chemical weapon stockpiles draws near, the OPCW's expertise may be refocused on the remaining chemical weapons that exist outside of declared stockpiles, such as those dumped at sea. The SAB recognises that in order for the OPCW to be sufficiently prepared to address this issue effectively and assist States Parties in the future, a range of scientific and technological information would need to be compiled and reviewed.

23. The threat of non-State actors acquiring and using chemical weapons persists, either by their use of more readily accessible technologies to develop their own weapons, or by their opportunistic acquisition. This highlights the need for the OPCW to continue supporting the development of national-level capacities for responding to chemical weapons attacks.

24. The SAB regards the OPCW's new Centre for Chemistry and Technology (ChemTech Centre) as an important nucleus for facilitating activities related to research, analysis, training, information exchange, and capacity building. The establishment of this flagship facility will create unprecedented opportunities for the OPCW to support States Parties, engage with other important stakeholders on developments in science and technology, and develop additional capabilities for taking action on the recommendations set out below as its mission evolves post-destruction.

25. Developments across scientific disciplines since the publication of the SAB's report to the Fourth Review Conference have the potential to greatly impact the OPCW's work moving forward; they could be leveraged to more effectively implement the Convention, but could equally be misused and exploited for harmful purposes. The SAB re-emphasises the importance of continuing to monitor science and technology in this regard, and submits the following recommendations for consideration.

RECOMMENDATIONS

Advice on chemicals

26. The SAB notes that significant information gaps remain regarding NSCs. Maintaining a full understanding of all Schedule 1 chemicals plays a critical role in preventing the re-emergence of chemical weapons. The SAB notes that these information gaps continue to challenge traditional inspection, enforcement, verification, and capacity-building activities. The SAB recommends that States Parties share any information they can regarding NSCs, along with all scheduled chemicals, to ensure that the OPCW remains fit for purpose. This could be by sharing information directly with the Secretariat, but could also be in the form of peer-reviewed publications and other scientific literature. In particular, the following information would be of value:

(a) analytical data on the NSCs themselves, as well as on specific precursors and degradation products, to aid in the detection and identification of these compounds. These data are also critical for keeping the OCAD and the Validation Group Working Database updated (for further consideration, see "Sampling and analysis" and specifically "Newly scheduled chemicals" in Annex 1);

(b) property information for the NSCs; physical properties such as vapor pressure, chemical properties such as reactivities, and information related to their toxicity to humans and the environment, as well as other hazards (for further consideration, see "Decontamination and remediation");

(c) information on chemical degradation pathways and products, which will assist with any chemical profiling work associated with NSCs, and provide information about reasonable storage conditions (for further consideration, see "Forensic and investigative science and technology" and "Sample storage and stability");

(d) human and plant biomarkers associated with exposure to NSCs (for further consideration, see "Off-site analysis – Biomedical" and "Chemical detection – Plant-based sensors");

(e) information related to the effectiveness of protective equipment and decontamination techniques for these compounds, particularly if the equipment and approaches are utilised by the Secretariat in its work. This information is critical for inspectors to continue to do their work safely (for further consideration, see "Personal protective equipment" and "Decontamination and remediation"); and

(f) any information related to appropriate medical countermeasures for these compounds. This information is needed not just for Secretariat staff who may need to handle these compounds, but can also be shared with States Parties to support current assistance and protection capabilities (for further consideration, see "Medical countermeasures").

27. In order to facilitate the exchange of information on NSCs, the SAB highly encourages the Secretariat to organise workshops focused on the aforementioned topics.

28. The SAB recommends that the Secretariat continue to request and add analytical information related to other relevant chemicals including RCAs, CNS-acting chemicals, Schedule 1 biotoxins, and other materials relevant to the Convention (such as precursor chemicals to the NSCs) to the OCAD and Validation Group Working Database, as appropriate, for verification and forensic activities performed by the designated laboratories. (For further consideration, see "Sampling and analysis" and "Forensic and investigative science and technology").

29. The SAB and Secretariat should continue to review advances in technologies related to drug preparations and delivery systems that may potentially be applicable to using CNS-acting chemicals as chemical weapons. (For further consideration, see "Delivery of toxic chemicals and drugs").

30. The SAB notes that no compounds were added to the schedules with the recent adoption of decision C-26/DEC.10 (dated 1 December 2021) at the Twenty-Sixth Session of the Conference. While no compounds were added, the SAB encourages States Parties to share technical information on CNS-acting chemicals of concern, particularly information for inclusion in the Validation Group Working Database and the OCAD, as appropriate. Information sharing is vital for the successful implementation of the Convention. (For further consideration, see "Central nervous system-acting chemicals" and "Sampling and analysis").

31. The SAB recommends that the Director-General consider establishing a TWG to study current developments concerning CNS-acting chemicals, and it is further recommended that this TWG include the participation and expertise of other relevant international institutions (e.g., the United Nations Commission on Narcotic Drugs). (For further consideration, see "Central nervous system-acting chemicals").

Advice on technology convergence

32. One exciting area of advance over the past five years has been the use of AI and machine learning in many areas of the chemical and biological sciences. While there is a lot of focus on the potential for computers to greatly augment drug design, retrosynthesis, and the identification of synthetic pathways, both for chemicals and biologicals, there are also enormous gains to be had in areas such as property and hazard prediction, as well as by automating synthesis, formulation, and other experimental processes. The OPCW should closely monitor the rapid development in this field and consider not just the potential risks that it poses, but also the opportunities it presents. (For further consideration, see "Informatics and predictive analytics").

33. The Secretariat should consider the potential risks that AI-assisted chemistry and machine learning may pose to the Convention and the work of the OPCW. In particular, focus should include the ease and speed with which new toxic compounds may be discovered and novel synthetic routes to toxic compounds can be identified, as well as the possibility to automate, via robotic platforms, both the design and production aspects of chemical synthesis. (For further consideration, see "Informatics and predictive analytics").

34. Conversely, AI and machine learning will also provide opportunities to streamline certain types of chemical weapons-related research and strengthen the verification regime. AI could also be used to identify and promote a decreased use of toxic chemicals in academia and industry, or may even pave the way to understanding how

chemicals can be reused in the chemical life cycle, ensuring that less waste is generated. In addition, AI may help kick-start new approaches to the design and discovery of medical countermeasures for exposure to chemical weapons. It is recommended that the OPCW consider how the application of AI and machine learning can be harnessed to enhance these areas. (For further consideration, see "Informatics and predictive analytics" and "Chemical safety and security").

35. AM allows for weapons of mass destruction-related equipment and components to be designed and produced in non-traditional ways. The SAB recommends that the Secretariat continue to seek information from experts and liaise with other international bodies (e.g., the Missile Technology Control Regime (MTCR) and Wassenaar Arrangement, amongst others) to stay apprised of the risks that AM may pose with regard to the Convention and its implementation. (For further consideration, see "Additive manufacturing").

36. The SAB suggests the Secretariat consider looking into how AM techniques can assist with research and experimentation. For example, they may facilitate rapid testing of materials designed to be resistant to chemical agents, or may help streamline certain types of chemical weapons-related experimentation. (For further consideration, see "Additive manufacturing").

37. The SAB recommends that the OPCW continue to investigate the effects that the rapidly advancing technologies related to synthetic biology and metabolic engineering may have on the future of verification as the Organisation moves beyond its disarmament mission and increases its focus on preventing the re-emergence of chemical weapons. (For further consideration, see "Biotechnology").

Advice on science and technology relevant to verification

38. The Secretariat should continue to evaluate next-generation analytical techniques to determine their applicability to the mission of the OPCW. These include core technologies such as GC-MS,[19] LC-MS[20] including HRMS,[21] and NMR[22] spectroscopy for the analysis of Convention-related chemicals, as well as PS-MS,[23] IMS,[24] and MS-IMS[25] technologies, among others. (For further consideration, see "Sampling and analysis" and "Forensic and investigative science and technology").

39. The OPCW Laboratory should determine whether the identification of scheduled chemicals can be done with HRMS and MS/HRMS[26] and without the use of a reference standard for data comparison. (For further consideration, see "Sampling and analysis – Biomedical").

---

19 Gas chromatography-mass spectrometry.

20 Liquid chromatography-mass spectrometry.

21 High resolution mass spectrometry.

22 Nuclear magnetic resonance.

23 Paper spray mass spectrometry.

24 Ion mobility spectrometry.

25 Mass spectrometry-ion mobility spectrometry.

26 Mass spectrometry/high resolution mass spectrometry.

40. The Secretariat should continue to evaluate equipment (both existing within the Secretariat, as well as commercially available) for rapid on-site detection and tentative identification of all scheduled compounds. In addition, in light of expanding mission needs, understanding the potential to detect or identify other compounds that may be misused, such as CNS-acting chemicals, RCAs, malodorants, biotoxins, toxic industrial chemicals, etc., would be useful. This is particularly important for inspectors who may be in environments where the chemical that is present is unknown. (For further consideration, see "On-site analysis").

41. The Secretariat should consider integrating emerging imagery technologies (satellite, hyperspectral, and thermal imagery, and unmanned aerial vehicles (UAVs)) with existing chemical detection or sampling equipment to obtain diverse datasets for verification and monitoring activities. (For further consideration, see "Detection systems").

42. The Secretariat should organise workshops with experts and equipment manufacturers to review new technologies used in sampling, detection, and off- and on-site identification related to operational needs. The ChemTech Centre could provide an excellent forum for an ongoing series of workshops in this area. (For further consideration, see "Chemical detection" and "Sampling and analysis").

43. The SAB recommends the Secretariat provide a forum where the results of the Plant Biomarker Challenge can be showcased, with follow-up discussions on other research needed in the promising field of vegetation markers. (For further consideration, see "Plant-based sensors").

44. The OPCW should continue the organisation of optional biomedical sample confidence-building exercises with a broader scope to address analogues of sulfur mustard, nitrogen mustards, different organophosphate chemicals and NSCs. The OPCW Laboratory could also then update its documentation of relevant biomarkers and its reporting criteria,[27] based on the results of these additional exercises and the performance and specifications of modern instrumentation. (For further consideration, see "Sampling and analysis – Biomedical").

45. The SAB recommends that the OPCW build and maintain relationships with laboratories outside the designated laboratory network that may have expertise in the analysis of non-scheduled toxic chemicals such as toxic industrial chemicals, CNS-acting chemicals, and biotoxins. (For further consideration, see "Sampling and analysis – Biotoxins").

46. The SAB recommends that the OPCW and its designated laboratories continue to look into novel methods to determine exposure to chlorine gas in environmental, biomedical, and plant samples. This may include research on chlorine gas markers with a focus on approaches that differentiate exposure to chlorine gas versus other chemical species of reactive chlorine. (For further consideration, see "Off-site analysis – Chemical" and "Off-site analysis – Biomedical: Chlorine").

47. The Secretariat should continue to strengthen its capabilities in chemical profiling. This may include arranging workshops for designated laboratories, with an emphasis on the requirement of the technique (i.e., the use of very stringent quality control measures for the performance of analytical instrumentation, the need to report non-scheduled

---

[27] QDOC/LAB/WI/BioPT04.

chemicals, and the requirement of the use of supervised machine-learning tools for unknown sample classification). It should also stay apprised of the work of the Chemical Forensics International Technical Working Group. The Director-General may consider establishing a new TWG on this subject. (For further consideration, see "Forensic and investigative science and technology").

48. The Secretariat should consider how to engage with reference laboratories and laboratory networks (e.g., the UNSGM laboratory network) capable of analysing a broader range of toxins than the two biotoxins (ricin and saxitoxin) included in Schedule 1 of the Convention. (For further consideration, see "Sampling and analysis – Biotoxins").

49. The Secretariat should consider establishing an ongoing OPCW-UNSGM Working Group to discuss and harmonise analytical techniques and reporting criteria requirements in relation to biotoxins. (For further consideration, see "Sampling and analysis – Biotoxins").

50. The OPCW Laboratory should continue biotoxin confidence-building exercises by exploring different scenarios (various concentrations and matrices) with ricin, saxitoxin, and their analogues, culminating in the launch of a biotoxin proficiency test. (For further consideration, see "Sampling and analysis – Biotoxins").

51. The Secretariat should better define the performance and reporting criteria for biochemical methods such as immunological or functional methods that are relevant to the analysis of high molecular weight biotoxins. It should also revise mass spectrometry (MS) criteria to take into account current use in the proteomics field and the capabilities of modern instrumentation. (For further consideration, see "Sampling and analysis – Biotoxins").

52. The SAB advises the Secretariat to study the possibility of implementing DBS sampling to increase sample storage time and the stability of biomedical samples. This may then facilitate a future biomedical sample confidence-building exercise, in which DBS and liquid blood samples can be analysed in parallel in order to test the limits of the technique and enhance the capabilities of the designated laboratories. (For further consideration, see "Sample storage and stability – Biomedical samples").

53. The SAB notes that destruction activities related to declared stockpiles of chemical weapons is on track for completion in 2023. The Secretariat may then turn to applying its knowledge and expertise to remaining chemical weapons, such as sea-dumped chemical weapons, as well as old and abandoned chemical weapons. In this regard, the SAB recommends that the Secretariat collect information related to the science and technology relevant to sea-dumped chemical weapons (as well as old and abandoned chemical weapons), to include destroying them and rendering them safe on-site, as well as safe sampling, collection, and analysis methods. This will help ensure that the Organisation is prepared to assist States Parties as needed in future. (For further consideration, see "Destruction of chemical weapons").

54. The SAB recognises that non-State actors are often opportunistic; they will use the resources at their disposal when creating threat devices. As such, they may utilise old or classical munitions such as rockets, mortars, or pyrotechnic devices in order to deliver and perhaps disseminate chemical threats. The SAB therefore recommends the Secretariat consider including the topic of disposal and neutralisation of munitions with chemical payloads in their capacity-building activities to help ensure States Parties are capable of properly handling and disposing of such materials. (For further consideration, see "Destruction of chemical weapons" and "Munitions and spraying devices").

Advice on technologies for the delivery and dissemination of toxic chemicals and drugs

55. The continued development of unmanned platforms (such as UAVs) to deliver payloads for permitted purposes (such as in agricultural settings) and the development of (semi-)autonomous weapons systems should be monitored to assess the risk of development for chemical weapons-delivery purposes. Continuing to monitor and assess the technological advances in this area will be critical to ensure that any potential risk of misuse can be minimised. The SAB recommends that the Secretariat maintain regular contact with other international bodies that more thoroughly consider and monitor these technologies. (For further consideration, see "Munitions and spraying devices").

56. It is recommended that the Secretariat monitor the development of the different technologies used to encapsulate chemicals for drug delivery, such as DNA[28] origami, nanostructured organic or inorganic carriers, or molecular cages—including organelles. This technology may be misused to increase the penetration capability of selected chemical agents, for example. Conversely, these technologies may offer opportunities for treatment after exposure to chemical agents. The OPCW may consider investigating or supporting research related to gaining a better understanding of how these technologies may be used for therapeutic purposes. (For further consideration, see "Drug delivery").

Advice on assistance and protection

57. The SAB encourages the Secretariat to continue to make use of risk-based decision making when it comes to hazard mitigation and management, especially for toxic chemicals where not all the properties are well known, such as the NSCs. (For further consideration, see "Decontamination and remediation").

58. Another recommendation is to strengthen awareness of chemical weapons among the general population, and the chemical weapons emergency response capabilities of first responders and experts in States Parties. Several initiatives and training courses have been conducted in recent years to strengthen these capacities, and it is recommended that these efforts be continued (such as with IUPAC[29]). An additional course of action could be to perhaps partner with other international organisations and entities to increase their breadth and impact (for example, the European Union Chemical, Biological, Radiological, and Nuclear (CBRN) Risk Mitigation Centres of Excellence Initiative and INTERPOL,[30] among others). This includes strengthening CBRN risk assessment at a national level, and developing standard operating procedures for chemical incidents, including food poisoning and the improper use of hazardous chemical waste materials.

59. The SAB recommends that the OPCW continue to develop statistical sampling and analysis strategies to boost confidence in the characterisation of potentially contaminated areas and provide decision makers with the necessary assurance that identified decontamination goals have been met. The development of appropriate training programmes may be useful in imparting knowledge to States Parties. (For further consideration, see "Decontamination and remediation").

---

28 Deoxyribonucleic acid.

29 International Union of Pure and Applied Chemistry.

30 The International Criminal Police Organization.

60. The Secretariat should consider supporting the further development of clinical treatments related to nerve agent poisoning, noting the NSCs as well as continued gaps in information about other existing nerve agents. (For further consideration, see "Medical countermeasures").

61. The SAB advises that the Secretariat, perhaps through a panel of subject matter experts, determine additional equipment and capabilities that will continue to allow inspectors to operate safely in environments where NSCs or CNS-acting chemicals may be present.

Advice on science and technology of relevance to chemical safety and security

62. The SAB encourages the Secretariat to continue engaging with technical experts in the chemical industry and at international organisations in order to strengthen its continued assistance to States Parties in the area of chemical safety and security. This is important not only to share and discuss relevant issues and the measures implemented to prevent the acquisition and weaponisation of toxic chemicals by non-State actors, but also to recognise and mitigate the risk of either the unintentional or deliberate release of toxic industrial chemicals that could cause grave damage to human populations and the environment. The SAB recalls that chemical safety complements and benefits chemical security. Adopting the concepts of inherent safety is a part of building an effective safety culture in any chemical facility, whether it be in industry, government, or academia. The SAB recommends that the Secretariat continue to promote chemical safety in order to also strengthen approaches to chemical security. (For further consideration, see "Chemical safety and security").

63. The SAB recommends that the Secretariat survey and evaluate state-of-the-art approaches to chemical safety assessment. This may be an appropriate topic for funded research activities. Cooperation on this topic with industry and industry associations could be beneficial, and might also include the practical implementation of chemical safety assessment methodologies in chemical industry work processes. The SAB encourages the Secretariat to communicate with States Parties, especially those with developing and transitional economies, about state-of-the-art information on chemical safety assessments. (For further consideration, see "Chemical safety and security").

64. The reduction of harmful chemicals in products and processes is pivotal in attaining sound management of chemicals—including waste—and thus towards meeting the goals of the United Nations 2030 Agenda for Sustainable Development. The SAB recommends that the Secretariat explore the framework and tools available for hazardous chemical substitution in order to facilitate its efforts to assist States Parties in reducing hazardous chemical inventories by finding effective alternatives to chemicals of concern. (For further consideration, see "Chemical safety and security").

65. The SAB recommends that the Secretariat consider collating property and hazard data associated with toxic industrial chemicals to best understand the risks associated with their potential misuse. (For further consideration, see "Chemical safety and security").

Advice on scientific literacy and scientific advice

66. Scientific literacy is paramount when it comes to the application of scientific advice. For scientific advice to be effective, the understanding of the recipient is very important. The Advisory Board on Education and Outreach (ABEO) has been contributing

excellent work to the Organisation in this regard. A closer collaboration between the SAB and the ABEO will enhance the synergy between scientific advice and literacy relevant to the effective implementation of the Convention. Collaboration between these two Boards at side events—during Conferences, for example —may be helpful in pushing forward a combined agenda of effective scientific advice and literacy in science. The SAB suggests the two Boards offer webinars and other learning opportunities on chemical ethics, the dual use of new and emerging technologies, and safe-by-design chemicals and processes, among other topics. (For further consideration, see "Scientific advice and science communication").

67. In addition to scientific literacy, vetting the information used in scientific advice from journals, books, and other source materials is important to ensure that the advice is sound. In particular, information gleaned from social media and even certain news sources may be fraught with misinformation, or even disinformation, about science. The Secretariat should consider strengthening the trustworthiness of its own science and technology offerings to ensure that fact-based, objective information on science and technology associated with the Convention and the work of the OPCW is widely available and referenceable. Addressing misinformation in a timely manner via OPCW institutional media channels should also be considered an important strategy in mitigating the adverse effects of biased information. Time is essential, particularly when countering social media misinformation, given the speed at which social media can disseminate such misinformation. (For further consideration, see "Scientific advice and science communication").

68. Identifying and then later sharing best practices in implementing scientific advice will help assist many States Parties. This does not just apply to advice from the SAB, but all types of scientific advice, such as from national or regional technical reachback mechanisms available to frontline officers. This will help identify gaps in the implementation of the Convention, and in turn aid in customising scientific advice so that it is understandable and useful to policymakers and other stakeholders. (For further consideration, see "Scientific advice and science communication").

69. Case studies have shown that long-term education and outreach programmes are effective in enhancing scientific literacy among the youth. The current work of the OPCW in partnering with other organisations, such as IUPAC, has proven to be effective. This approach should be continued and expanded to include partnerships with other relevant organisations and institutions, such as national or international societies of chemistry or chemical industry associations. This may aid in providing long-term education and outreach activities, in addition to awareness-raising initiatives at the ChemTech Centre. (For further consideration, see "Scientific advice and science communication").

70. The use of social media and e-learning systems are proven effective in imparting scientific knowledge, and the OPCW should continue to pursue these approaches. During the COVID-19 pandemic, online modules and examinations provided avenues for learning during lockdowns. In the "new normal", blended learning—such as hyflex, which is a combination of virtual and in-person learning modes—is more efficient and economically viable. Activities that cannot be done virtually and that require hands-on experiences must be preserved as in-person sessions. However, the use of gamification tools, augmented reality, and virtual reality will be useful in learning simulations, such as for laboratory work. These may be used as pre-learning sessions before in-person

laboratory-based activities, such as those to be implemented at the ChemTech Centre. It should also be noted that development of this technology at the OPCW will be helpful in training Secretariat staff serving in complex mission environments. (For further consideration, see "Scientific advice and science communication").

Annexes (English only):

Annex 1 Analysis of Developments in Science and Technology Relevant to the Chemical Weapons Convention

Annex 2 Abbreviations

Annex 1

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

TABLE OF CONTENTS

Chemicals **18**

Changes to Schedule 1 of the Annex on Chemicals 18
Riot control agents 18
Central nervous system-acting chemicals 18

Production: Scientific developments **19**

Chemical synthesis of biological substances 19
Biological production of chemicals 20

Production: Technological developments **21**

Informatics and predictive analytics 21
Continuous flow chemistry 24
Additive manufacturing 24
Biotechnology 26

Delivery of toxic chemicals and drugs **28**

Drug delivery 28
Munitions and spraying devices 29

Chemical detection **30**

Chemical sensors 30
Biological sensors 30
Insect-based sensors 31
Plant-based sensors 31
Detection systems 32

Sampling and analysis **33**

On-site analysis 33
Chemical 33
Biomedical 34
Off-site analysis 35
Chemical 35
Biomedical: nerve agents 36
Biomedical: unknown organophosphate nerve agents 36
Biomedical: mustards 37
Biomedical: chlorine 38
Biomedical: newly scheduled chemicals 39
Biotoxins 40

Sample storage and stability **42**

Toxic chemicals and environmental and material samples 42
Biomedical samples 42

Forensic and investigative science and technology 44

Temporary Working Group on Investigative Science and Technology 44
Chemical profiling of chemical warfare agents 46

Decontamination and remediation 47

Risk-based operational decision making 47
Acceptable percutaneous dose 48
Decontamination considerations 49
Predicative decontamination models 50
Catalysts for decontamination 50

Destruction of chemical weapons 51

Chemical safety and security 53

Chemical security 53
Chemical safety 54
Green and sustainable chemistry 55

Personal protective equipment 56

Medical countermeasures 57

Newly scheduled chemicals 57

Scientific advice and science communication 58

Social media and scientific advice 59
Ethics and peer review 59
Science education and outreach 60

Acknowledgements 61

CHEMICALS

Changes to Schedule 1 of the Annex on Chemicals

1. Expertise on Schedule 1 chemicals—specifically their analysis, synthesis, and safe use—must be maintained in order to prevent the re-emergence of chemical weapons.

2. The Scientific Advisory Board (SAB) notes its advice on new types of nerve agents (SAB-28/WP.1, dated 3 July 2018) in response to a request by the Director-General following a review of the findings of the March 2018 technical assistance visit requested by the United Kingdom (TAV/02/18). In light of its review of these chemicals, the SAB recommended that consideration be given as to whether any changes to the Schedules would be warranted.

3. At its Twenty-Fourth Session, the Conference of the States Parties (hereinafter "the Conference") adopted decisions C-24/DEC.4 and C-24/DEC.5 (both dated 27 November 2019), in which it approved certain changes to Schedule 1 of the Annex on Chemicals to the Chemical Weapons Convention (hereinafter "the Convention"). The SAB notes that these changes, which entered into force on 7 June 2020, have significantly expanded the list of Schedule 1 chemicals, which now includes four new entries: 1.A.13, 1.A.14, 1.A.15, and 1.A.16.

4. Since the Fourth Review Conference,[31] validated data on both scheduled (including the new additions to Schedule 1) and non-scheduled chemicals relevant to the Convention have been included in the OPCW Central Analytical Database (OCAD). Annual releases of the database have been made available (v.20_2018, v.21_2019, v.22_2020, v.23_2021, and v.24_2022).

Riot control agents

5. Riot control agents (RCAs) are chemical compounds that, under appropriate conditions such as in open spaces in low to moderate concentrations, usually cause temporary disablement in individuals. These agents act primarily on the sensory nerves of the peripheral nervous system in the eyes, nose, respiratory tract, and skin, having limited or no effect on the central nervous system itself.

6. The SAB has repeatedly considered issues related to RCAs[32] and the advice provided on this topic in its report to the Fourth Review Conference remains unchanged.[33]

Central nervous system-acting chemicals

7. The SAB recognises that central nervous system-acting chemicals (CNS-acting chemicals) are not RCAs, as they do not meet the definition set out in paragraph 7 of Article II of the Convention.[34] CNS-acting chemicals can be understood to be different

---

31 Review Conference = Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention.

32 S/1177/2014, dated 1 May 2014; SAB-21/1, dated 27 June 2014; and SAB-25/WP.1, dated 27 March 2017.

33 RC-4/DG.1, dated 30 April 2018.

34 "Riot Control Agent" means: Any chemical not listed in a Schedule, which can produce rapidly in humans sensory irritation or disabling physical effects which disappear within a short time following termination of exposure.

from RCAs in that their effects are not usually confined to temporary sensory irritation, and they affect the central nervous system.

8. When CNS-acting chemicals are disseminated in an airborne form, the delivered dose cannot be controlled. There have been examples of the use of CNS-acting chemicals in law enforcement that have resulted in permanent harm and death due to an irreversible action on life processes. No CNS-acting chemicals with a sufficient margin of safety adequate for use for riot control or law enforcement purposes have been identified.

9. The risks posed by CNS-acting chemicals have been highlighted by the SAB on many occasions. The Board has assessed that certain CNS-acting chemicals are extremely toxic, with some as lethal as nerve agents.

10. In its report to the Fourth Review Conference, the SAB stated that because the scientific facts had not changed since first considering the issue, and technical discussions on CNS-acting chemicals were exhausted, there was no value in revisiting this topic. It noted that this was an important issue relevant to the Convention, and regarded it to be in the policy domain.

11. At its Twenty-Sixth Session, the Conference adopted a decision on CNS-acting chemicals (C-26/DEC.10, dated 1 December 2021), deciding that, inter alia, the aerosolised use of CNS-acting chemicals is understood to be inconsistent with law enforcement purposes as a "purpose not prohibited" under the Convention.

12. The SAB notes that the term "aerosolised" specifically refers to small solid particles or liquid droplets dispersed in a gas. The term does not, however, cover gases or vapours, and wording would need to be revised to extend the understanding to cover all possible airborne formulations.

13. The decision adopted by the Conference requested that the Director-General task the SAB with continuing its review of relevant developments in science and technology related to CNS-acting chemicals, and provide updates to the Conference as appropriate. The SAB therefore remains watchful of the rapidly evolving pharmaceutical and chemical industries, with the incorporation of new technologies such as artificial intelligence (AI) and machine learning, and will remain vigilant for any consequent impact on this topic.

14. Although CNS-acting chemicals are unscheduled, an understanding of the analysis, synthesis, and safe handling of these chemicals would aid in the prevention of CNS-acting chemicals emerging as chemical warfare agents (CWAs).

PRODUCTION: SCIENTIFIC DEVELOPMENTS

Chemical synthesis of biological substances

15. The number of substances of biological origin that can be produced by chemical synthesis—such as proteins, peptides, and biotoxins—continues to increase. Recently, synthesis protocols have been published for the divergent chemical synthesis of saxitoxin (one of the two Schedule 1 toxins), which will also allow for the synthesis of saxitoxin derivatives.

16. Chemical synthesis of large, complex proteins can be accomplished first by synthesising smaller peptide subunits by solid phase peptide synthesis. However, joining two or more large peptide fragments into a more complex protein can only be accomplished through native chemical ligation due to a variety of structural factors. This method has been successfully applied to the chemical synthesis of Shiga toxin components and the toxin of the long-chain scorpion, resulting in a toxin material with high biological activity in high yield. In a similar way, the chemical synthesis of functional α-bungarotoxin (a snake venom) has been undertaken, leading to a fully functional toxin.

17. Peptide-based structures are another class of small-molecule toxins that are synthetically accessible. For instance, α-amanitin is an extremely toxic bicyclic octapeptide isolated from the death-cap mushroom, and highly toxic to eukaryotic cells. A multistep synthesis method for this toxin has been published, and can also be used for the construction of endless numbers of variants with different properties. A concise synthesis of tetrodotoxin was recently reported.

18. Synthetic infectious horsepox virus, a large DNA[35] virus, was constructed starting from chemically synthesised DNA fragments. Noteworthy in this case is the phenomenon of so-called "reverse genetics", in which infectious viruses are generated without the need for a nucleic acid. More recently, the reconstruction of a bacterial genome of a Caulobacter species through chemical synthesis has been reported, highlighting the promise of chemical synthesis for decoding fundamental genome functions and its concurrent utility for the construction of tailor-made organisms for industrial purposes and health benefits.

Biological production of chemicals

19. The continued focus on more efficient, cost-effective, and—most importantly—sustainable manufacturing routes, is making the microbial production of chemicals an increasingly attractive route. Rapid developments in biotechnology are being leveraged to enable the production of a growing range of chemicals from cheap and renewable feedstocks.

20. Advances in metabolic engineering have enabled the use of organic carbon sources to produce target chemicals via common model microorganisms such as *Escherichia coli* (*E. coli*). With an increased focus on a circular economy, a number of major chemical companies are also employing microorganisms to convert their waste to fuels or useable chemicals.

21. Enabled by innovative metabolic modelling and advances in platform -omics technologies, synthetic biology, and genome editing tools, the production of chemicals in microorganisms is no longer restricted to products arising from native metabolic potential, and microbial cell factories may produce value-added chemicals directly. The integration of these analytical developments has offered new knowledge and manifold strategies to unravel biological cellular networks, modify biological systems, and create synthetic bio-devices or biosynthesis platforms.

---

35 Deoxyribonucleic acid.

PRODUCTION: TECHNOLOGICAL DEVELOPMENTS

Informatics and predictive analytics

22. Informatics is a wide scientific discipline that includes a number of rapidly developing fields such as AI, machine learning, and deep learning. Although these terms are often used interchangeably, deep learning is a specific type of machine learning, which in turn is a branch of AI.

23. In machine learning, systems learn and improve through experience, thereby programming themselves. Machine-learning algorithms allow difficult-to-perceive patterns to be identified from large and complex datasets. In deep learning, algorithms are produced in a similar manner, but are present in many more layers, creating artificial neural networks. These neural networks mimic the behaviour of the human brain and allow deep learning to resolve more challenging issues than machine learning. Although not a new concept, neural networks have only seen rapid developments in recent years.

24. The overarching field of AI has grown tremendously, with a surge in journal and patent publications, especially since 2015. Its application in the chemical sciences has seen a similar increase in growth, with the analytical chemistry and biochemistry sectors integrating AI to the greatest extent.

25. This recent growth is primarily attributed to three advances: increased availability of small-molecule libraries; the development of algorithms capable of exploiting the big data resources of these libraries; and increased computing power, along with leverage of cloud-based graphics processing units to rapidly build models using libraries and algorithms. The chemical sciences can also benefit from developments in other application domains of machine learning, such as natural language processing, thus increasing the potential of this technology further still.

26. AI has found applications in a large number of chemical fields; of particular interest are drug discovery, property prediction, virtual high-throughput screening (vHTS), synthesis route planning, reaction optimisation, small-molecule analysis, and retrosynthesis. Moreover, deep learning has recently emerged as one of the most promising tools in pharmaceutical research.

27. Many pharmaceutical and biotechnology companies are leveraging AI, either by developing in-house capabilities or working in partnership with AI start-ups. Recently, the Machine Leaning for Pharmaceutical Discovery and Synthesis Consortium was established, which is a collaboration among the Departments of Chemistry, Chemical Engineering and Computer Science at the Massachusetts Institute of Technology, and the pharmaceutical and biotechnology industries. Its objective is to facilitate the design of software to automate small-molecule discovery and synthesis.

28. Drug discovery is traditionally a complex, expensive, and time-consuming process, involving *in vitro* and *in vivo* testing. Deep learning can accelerate this process considerably by decreasing cost and removing the need for some of the extensive testing processes. In 2020, AI algorithms were leveraged to accelerate design, development, and manufacture of a COVID-19 vaccine. In early 2022, the first AI-discovered and AI-designed drug entered Phase 1 clinical trials in under 30 months, demonstrating significant cost and time savings over a traditional preclinical programme.

29. The advent of the era of big data has shifted AI approaches in the drug discovery field from machine learning to deep learning, a more powerful and efficient tool for handling the huge quantities of complex data generated. Neural networks have been used to identify chemical structures of medicinal relevance, although data on chemical compounds, functional groups, and possible biological activity need to be acquired as a first step in order to successfully train the networks. The development of deep neural networks has seen renewed interest in their application in medicinal chemistry.

30. Machine-learning methods have been used extensively to predict the biological, chemical, and physical properties of novel compounds, and are well established.

31. When discussing biotoxins, it is important to recognise that large, high molecular weight biotoxins are most often proteins, the shape and structure of which are chiefly responsible for how they interact with the body. Recognising this, researchers have been working towards a model for understanding how DNA instructions are translated into a 3D protein structure. These efforts have largely focused on developing models that predict how translated amino acid sequences become folded into specific protein shapes. Successful predictive capabilities, as demonstrated in competitions like the "Critical Assessment of Structure Prediction", and successful models like AlphaFold and ColabFold, have broad-ranging implications for toxicity prediction, drug development, genetic engineering, and much more.

32. Chemical toxicity prediction continues to move away from *in vivo* and *in vitro* methods towards computational—or "*in silico*"—methods thanks to significant advances in the field of computational toxicology. Methodologies that were considered state-of-the-art at the time of the publication of the SAB's Workshop on Chemical Warfare Agent Toxicity report in 2016 are quickly being phased out by AI and machine-learning models.

33. Despite the rapid development of new, advanced machine-learning models, they do not yet have the same regulatory recognition as better-tested models (such as quantitative structure-activity relationship models), which retain an important place in toxicity prediction.

34. More recent models are able to elucidate complex adverse outcome pathways, toxicity mechanisms, and specific mechanistic interactions between toxic substances and the body without the need for *in vivo* or *in vitro* testing, with numerous examples performing exceptionally well. One example of a novel *in silico* approach to toxicity prediction is the quantitative adverse outcome pathway. This differs from other adverse outcome pathway models by quantifying the physiological conditions and dose at which a "biological tipping point" is exceeded and adverse outcomes occur.

35. Whilst there is a paucity of information available on NSCs, the application of machine-learning techniques may generate useful data. A machine-learning model has recently been developed to predict the vapour pressure and toxicity of more than 10,000 structural variants of some NSCs and their derivatives. This model could be further developed to predict vapour pressures and toxicities of unknown nerve agents and could be useful in informing decisions on protection, decontamination, and remediation following a possible chemical weapon attack in the future.

36. From a medicinal chemistry perspective, there are clear benefits to being able to predict toxicities. However, the potential for misuse was recently explored, and a proof-of-concept experiment demonstrated that a drug discovery machine-learning model could also be used to deliberately generate, in a short time frame, large numbers of chemical structures with properties similar to known CWAs.

37. Selecting compounds based on specific predefined characteristics is an important aspect of drug discovery and process design. This is a tedious task that involves working through a large number of candidate molecules and rigorously testing them in a process that could take months to years. Instead of physically testing each molecule using *in vitro* high-throughput screening assays, virtual screening takes advantage of developments in machine learning to greatly increase the number of molecules that can be screened from chemical compound libraries.

38. Virtual high-throughput screening now sees regular use in the drug development process and allows pharmaceutical companies to screen millions of molecules for bioactivity, toxicity, and other specific characteristics in a fraction of the time needed for traditional methods. There has already been demonstrated commercial success, with numerous drugs identified via vHTS currently on the market or in clinical trials.

39. Machine learning is also being applied to organic chemistry, in synthesis route planning, and catalyst and reaction optimisation, with a number of companies employing *in silico* synthetic planning into their overall approach to accessing target molecules.

40. The last three years have witnessed renewed interest and rapid developments in machine learning and retrosynthesis planning. The synthesis of some organic targets involves a counterintuitive strategy comprising a sequence of steps that initially increase molecular complexity. Such complexifying sequences are known as “tactical combinations”, and until recently, only 500 had been catalogued by machine-learning approaches. A recent algorithmic discovery has led to over 46,000 viable tactical combinations being identified based on reaction classes, and almost five million based on specific reaction variants.

41. The application of models in organic chemistry could stimulate innovation and lead to discoveries in the vast unexplored chemical space. However, the available data in organic chemistry remains small, and the success of models in synthesis predictions correlates directly with the quantity and the quality of available databases.

42. AI is also being incorporated in automated systems. There are a number of examples of “laboratory robots” that have been developed by start-ups or in academia, designed to produce chemicals more reproducibly and efficiently, as well as to accelerate development and vastly increase productivity.

43. AI continues to advance at an incredibly rapid pace, and is being increasingly leveraged throughout the chemical sciences, both in academia and industry. Given the advances witnessed to date, further major progress is expected, with new trends and breakthroughs continuing to push the boundaries of this technology.

44. In spite of the benefits, AI also has significant potential to be weaponised. Companies are increasingly employing ethical approaches and frameworks to ensure that AI systems are built to benefit society. Furthermore, codes of conduct are being developed for the responsible use of AI.

Continuous flow chemistry

45. Continuous flow chemistry presents a number of manufacturing benefits: faster, safer, and more environmentally sustainable reactions that have a smaller footprint, produce a better quality product, and, critically, can perform chemistry that is difficult or impossible to do in batch mode. Continuous flow manufacturing is gaining momentum within the pharmaceutical and chemical industries.

46. Despite efforts to develop the manufacturing flexibility of and robust processes for continuous chemical production, the application of flow technology to commercially relevant examples remains a challenge. Barriers to commercialisation include issues associated with the versatility of system modules and complications with utilising or producing solids. However, technological advances in other fields are rapidly solving these and other challenges, making continuous flow chemistry one of the most promising emerging technologies in the chemical and pharmaceutical industries.

47. AI is playing an increasingly important role in the widespread adoption of continuous flow chemistry by providing economically viable alternatives to batch production. It has proved invaluable in overcoming the difficulties associated with reworking established reaction pathways into new pathways that are better suited to continuous flow chemistry, as AI-based systems are better able to identify unintuitive intermediate steps. In a combination of technologies, a robotic platform for the flow synthesis of organic compounds has been developed and demonstrated for 15 medicinally relevant small molecules. AI, in the form of a retrosynthesis prediction algorithm, was also leveraged by the platform.

48. Of particular relevance to the Convention are the modularity and mobility of continuous flow systems. These characteristics, in conjunction with the greatly improved safety of continuous flow systems, makes continuous flow chemistry a versatile asset for rapid, on-site destruction of CWAs.

49. Conversely, continuous flow chemistry has recently been used to produce organophosphorus compounds. The electrochemical phosphorylation reaction, which requires only mild conditions, afforded a 70% yield—almost twice that achieved for the same reaction in batch mode.

50. The increased safety—and often higher yields—afforded by flow reactors could be exploited by non-State actors, enabling hazardous chemical reactions to be successfully carried out, leading to the large-scale production of toxic or energetic materials.

Additive manufacturing

51. Additive manufacturing (AM), or 3D printing, is a production process that differs significantly from conventional methods, which are normally based on subtractive manufacturing. Using instructions from a computer-aided design file, AM builds up liquid or solid materials, layer by layer, to create three-dimensional components.

52. AM processes are divided into seven categories,[36] and these allow for highly customised components to be produced. Fused deposition modelling and fused filament fabrication—both material deposition methods—are the most commonly employed processes due to their low cost, simple operation, and non-toxic feedstock.

53. Solid starting materials for printing are commonly metals and polymers, in powder or wire form, but ceramics may also be used. A number of liquid silicone AM printers have been commercialised over the last five years, and some work has been carried out on printing glass, but this remains a challenge.

54. Developments in AM over the last few years include increased layer thickness and laser power, leading to quicker build times. In some industries, AM has shifted from simply being a rapid prototyping technique to being incorporated in production processes. AM is now routinely used in many industrial sectors, including aerospace, automotive, robotics, consumer products, energy, pharmaceutical and medical, and even the food industry.

55. It is also possible to print larger components. The construction industry has used AM to 3D print houses and bridges. Furthermore, gas metal arc welding has been used to build large metal parts such as the key components of excavators, which weigh almost 200 kg when printed.

56. AM is also used in the chemical industry where one of its principal applications is in the fabrication of "reactionware": laboratory-scale 3D-printed chemical reactors. AM has greatly reduced the cost of producing prototype systems for testing new reaction pathways, as well as the cost of scaling those prototypes up to industrial-scale outputs.

57. Prior to 2016, flow reactors were usually made from polydimethylsiloxane and glass, and were specially designed to possess excellent heat transfer capabilities and handle both high and low temperatures and pressures. However, they were difficult to make and only experts in the art were capable of manufacturing them to the necessary standards.

58. Now, small-sized flow reactors, printed from a variety of materials and capable of handling a diverse range of chemical transformations, can be 3D printed easily and affordably. They provide a realistic alternative to traditional large-scale batch reactors and offer advantages for process safety and for achieving elevated yields.

59. The range of polymers and metals that can be printed has increased significantly. Superalloys are being developed for AM processes, and a "crash-proof" aluminium alloy was recently developed for the automotive industry. Like superalloys, some polymeric substances used in AM are chemically resistant; for example, polypropylene reactionware has been printed and used to handle hydrogen fluoride (HF) reagents.

60. Other 3D-printed reactionware for organic synthesis has also been developed, including catalyst-embedded 3D-printed stirrers and miniature gadgets to facilitate the *in situ* monitoring of chemical reactions.

---

[36] Powder bed fusion, material extrusion, vat photopolymerisation, material jetting, binder jetting, sheet lamination, and directed energy deposition.

61. In terms of detection, identification, and monitoring equipment, AM could potentially be used to produce components resistant to CWAs or aggressive decontamination equipment, or to generate replacement parts in the field. The technology could also be used to produce complex components of sensitive equipment in a way that makes them less vulnerable to contamination, such as by encapsulation.

62. On the other hand, AM could be misused to produce improvised devices for terrorist purposes. These could be prefabricated in a way in which openings are accurately cut to install necessary components, such as detonators, while making it easy to add the payload (chemical or biological agents and/or explosives). Explosives and other energetic materials such as solid rocket fuel can also be 3D printed.

63. Although AM cannot be used to produce CWAs and toxic chemicals directly, it can be used to print some chemical production equipment. It can also be used in the fabrication of delivery and dissemination devices, such as unmanned aerial vehicles (UAVs) and spraying equipment. Components that fall within the purview of the Missile Technology Control Regime (MTCR) can be produced via 3D printing.

64. Some countries have added AM technologies to their export control regimes. For example, specific AM equipment[37] has been added to the European Union Dual-Use Control List.[38]

65. Materials may be printed and used to encapsulate hazardous or toxic materials by non-State actors for ease of handling as well as avoiding cross border detection. Furthermore, non-State actors can access academic or design expertise through numerous online platforms to acquire complex 3D-print files for malicious purposes. Awareness should be raised within the scientific and industrial communities for the purpose of identifying such attempts and reporting them, where possible, to the relevant authorities.

Biotechnology

66. Advances in biotechnology have made the isolation and synthesis of biotoxins much more accessible. Aside from Schedule 1 toxins—saxitoxin and ricin—a number of other biotoxins have been identified as having the potential for misuse, making them a growing area of concern. These include abrin, aflatoxins, botulinum toxins, epsilon toxin, staphylococcal enterotoxins, T-2 toxin, and tetrodotoxin. Furthermore, the availability and use of dual-use biotechnologies have now been extended to a growing number of individuals and organisations, making external monitoring and verification of their application and end use exceedingly difficult.

67. The emergence of CRISPR/Cas9[39] and other genome-editing technologies has had tremendous effects on the field of synthetic biology. This technology enables precise edits to be made to the genetic material of virtually any living cell, and allows those changes

---

37 Directional-solidification or single-crystal additive-manufacturing equipment and some categories of A machine tools with an additive manufacturing capability in addition to a turning, milling, or grinding capability.

38 EU Regulation 2021/821 – PE/54/2020/REV/2 (http://data.europa.eu/eli/reg/2021/821/oj).

39 Clustered regularly interspaced short palindromic repeats and CRISPR-associated protein 9.

to be passed on to subsequent generations. The key implication of modern genetic engineering techniques of relevance to the Convention is the ability to transform cells into biofactories for the production of chemicals, either for peaceful or malicious uses.

68. The genetic sequences of highly pathogenic bacteria and viruses can now be downloaded freely from websites, such as GenBank, EMBL,[40] and DDBJ.[41] Various viral, prokaryotic, and eukaryotic genomes can be synthesised, at low cost, using commercial services. Few formal regulatory constraints exist to prevent these services from producing these sequences; however, many informal and industry-specific controls are in place to screen orders and outputs to prevent dangerous sequences from being widely disseminated. The technical barriers for the artificial design and chemical synthesis of dangerous bacteria or a viral genome, toxin, or bioregulator chemical, are falling quickly due to advances in synthetic biology technologies that have reduced the cost and increased accessibility. Special attention should be paid to the commercialisation of benchtop DNA synthesisers that could be misused to covertly print dangerous sequences that code for the bioproduction of toxic chemicals. In addition, international biological academic competitions such as the International Genetically Engineered Machine and the rapid expansion of amateur biological groups have made it easy to find and utilise relevant professional knowledge and skills.

69. Genetic engineering of live cells *in vivo* is still the most widely utilised format for the bioproduction of specific proteins in small quantities, particularly for research purposes. However, the rapid modernisation of cell-free (or *in vitro*) protein synthesis (CFPS) in recent years has created many new opportunities for large-scale production of specific proteins, including those that cannot be found in nature. Recently developed CFPS systems boast two major attributes of relevance to the Convention. First, by eliminating the need to sustain life, CFPS can be used to manufacture proteins that are novel, difficult to produce, or would otherwise be highly toxic to the host cell. Second, CFPS systems are scalable, enabling reactions from 10 µL up to 100 L to be performed. There are still limitations to overcome, such as difficulties producing large proteins or ensuring that synthesised proteins are folded into the correct conformation, but these difficulties are quickly being overcome by developments in continuous flow chemistry and AI.

70. Many of the challenges at the forefront of biology have to do with either inadequately small datasets or overwhelmingly large datasets. AI can solve both of these problems in different ways. When it comes to inadequately small datasets, AI can be used to build models of living systems (human, animal, plant, and microbe) that can serve as digital (*in silico*) proxies for testing when live organism (*in vivo*) testing is not feasible or not possible. This capability will have major implications for the pharmaceutical and chemical industries, cutting costs and enabling testing that would be unethical to perform on live organisms. Overwhelmingly large datasets, such as datasets originating from hospital systems or high-throughput DNA sequencing, can be collated and analysed quickly utilising data harmonisation and text mining. These AI-driven tools can extract insightful trends and data points from these enormous datasets to inform researchers, medical practitioners, and policymakers. There are numerous other AI applications that can be used in biotechnology, such as major breakthroughs in protein folding prediction, that are discussed elsewhere in this report.

---

40 European Molecular Biology Laboratory.

41 DNA Data Bank of Japan.

71. One particular "big data" challenge in biology that has seen major advances is the study of -omics. This emerging field derives its name from the word endings used to describe a variety of fields of studies within biology, such as: genomics (the study of the genome), proteomics (the study of the proteins produced by an organism), transcriptomics (the study of the RNA[42] instructions produced by reading DNA), metabolomics (the study of the biochemical interactions within and between the cells of an organism), and many more. High-throughput screening assays and machine-learning algorithms have unveiled critical understandings of pathogen-host relationships, aging, and drug discovery and targeting, to name just a few examples. These novel insights into the complexities of cellular biochemistry are already impacting medicine, but will also be leveraged for innumerable other applications, such as more efficient bioproduction of useful chemicals, the development of medical countermeasures to CWAs, and toxicity prediction for as-of-yet undiscovered chemicals.

72. The SAB notes that there is limited available information about the analysis, generation, synthesis, and safe handling of biotoxins, bioregulators, and other chemicals of biological origin or biological inspiration. The ability to rapidly synthesise, modify, and produce large quantities of these materials may exacerbate safety and security related to this problem. Advances in technologies at the convergence of biology and chemistry increase the risk of a novel toxin or bioregulator that evades traditional defensive countermeasures (including medical and protective countermeasures and detection technologies) that are rapidly emerging and creating a proliferation concern. Significant advances in the fields of nanotechnology, proteomics, nanomaterials, polymers, liposomes, encapsulation sciences, and AI can be leveraged in the production of not only new defensive countermeasures and vaccines, but also organisms, biotoxins, and bioregulators with characteristics that render them more useful for carrying out a biochemical warfare attack.

73. Further investigation and discussion of relevant regulations or oversight rules will be necessary in the future, as biosafety, biosecurity, and ethical issues are not limited by national boundaries. Extensive discussions and exchanges of ideas should be encouraged within and among the scientific community, international organisations, and national governments, with the goal of formalising a suitable international governance system to prevent the misuse and abuse of synthetic biology and other technologies that exist at the convergence of biology and chemistry.

DELIVERY OF TOXIC CHEMICALS AND DRUGS

Drug delivery

74. AM is enabling new directions in drug product design by expanding the types and performance of the drug delivery systems that can be designed and fabricated. Supporting the trend towards personalised medicine, some pharmaceuticals may be 3D printed in small batches, providing control over dosage and pill geometries—commercial hardware is now available to do so. AM can provide greater control over drug distribution within the product and can be leveraged to fabricate drug delivery systems with unconventional release profiles that are currently difficult or even impossible to achieve using traditional manufacturing techniques.

---

42 Ribonucleic acid.

75. In the 1990s, the development of microneedle-based devices was constrained by the high cost and limitations associated with microfabrication technology. However, these barriers have been overcome with the recent developments in AM. Fabricated devices consist of arrays of microneedles ranging from 25 – 2000 µm in height and 50 – 250 µm in diameter. The microneedles can be solid, coated, dissolvable, or hollow, and may be self-administered—no clinical expertise is required. The array of tiny needles can be used for the delivery of various chemicals through the skin, bypassing the stratum corneum, thus prompting increased bioavailability and rapid action of the drug.

76. AM has also been applied to the production of transdermal patches and a range of implantable drug delivery devices, including intracranial, intraocular, subcutaneous, and intravaginal implants. These implantable systems are currently used in cancer and central nervous system disorder treatments, as well as for pain control. High-resolution AM enables intricate, sophisticated, and miniaturised drug delivery systems to be produced.

77. 3D bioprinting, a form of AM using cells and biomaterials, is also being used for drug delivery and a number of hydrogel bio-inks have been developed. These bio-inks can absorb large amounts of water, facilitating the release of drugs or proteins over specific time frames.

78. The development of encapsulation technologies has continued towards optimised drug delivery. DNA origami technology allows for the production of self-assembled and well-defined nanostructures, ranging from nanometres up to sub-micrometres. DNA nanostructures can be designed to penetrate human skin with size-dependent efficacies, with potential applications in transdermal drug delivery.

79. Coordination-based delivery mechanisms, including nano-sized extended metal-organic frameworks (MOFs) and discrete coordination cages, are attracting increasing attention in drug delivery due to their numerous benefits, such as remarkable biocompatibility, *in vivo* stability, and high encapsulation efficiency.

Munitions and spraying devices

80. The continued development, testing, production, and promotion of diverse munition systems capable of disseminating RCAs on a large scale or over a long distance remain areas of concern. A review of developments and specifications of commercial products shows that a large variety of delivery systems and ammunition carrying chemical payloads are now available. Moreover, the capabilities being developed increasingly resemble military equipment. These systems could be repurposed and filled with other chemicals including CWAs, CNS-acting chemicals, and bioregulators.

81. Since the Fourth Review Conference, there has been a surge in the use of electrostatic sprayers and foggers for the disinfection of surfaces contaminated by COVID-19. Although this is not a new technology and is commonly used to apply pesticides to crops, devices are more widely and readily available than ever before. They can be person-portable, cordless, and compact, or even integrated in a UAV or an unmanned ground vehicle (UGV) to decontaminate large areas such as offices, schools, airports, and arenas.

82. Incorporation of AI into agricultural sprayers, both manned and unmanned, is now gaining traction and is leading to targeted application of chemicals. Facial recognition technology integrated within UGVs or UAVs could be exploited by non-State actors to direct a targeted release of toxic chemicals at specific people. Although access to facial recognition technology was very limited a decade ago, it is now widely available through various online platforms.

83. The use and availability of UAVs to spray crops has also increased, with better battery life and payload capacity. This legitimate use requires monitoring, or at least certain codes of conduct applied to the sale of these commercially available products.

84. Non-State actors are often resourceful and creative. Conventional munitions or old chemical weapons could be modified and exploited to fabricate a threat device. Indeed, such an approach was already used by Daesh when it created its own munitions to deliver homemade sulfur mustard. The SAB notes that although all declared chemical stockpiles will be destroyed in the near future, information on how these weapons are constructed is still available.

CHEMICAL DETECTION

Chemical sensors

85. Compared to classical laboratory-based instrumental techniques and large expansive field detectors, molecular sensors are emerging as a comparatively cheaper, faster, and more easily deployable alternative. These miniaturised sensors, commonly deployed in a network, are based on either a covalent or supramolecular approach. In a covalent approach, the sensor reacts with an analyte, forming a covalent bond—colorimetric sensors are a typical example of this approach. A supramolecular approach involves a non-covalent interaction between the sensor and an analyte.

86. Paper-based sensors are receiving increasing attention for a range of applications due to their many benefits: portability, low cost, ease of use, reagent-free nature, high accuracy, and low detection limits. Recently, a robust and low-cost microfluidic paper-based analytical device has been developed for the colorimetric detection of nerve agents. Detection assays for on-site samples can be conducted with a very small sample volume. The device developed demonstrated adequate sensitivity with a limit of detection for VX in solution at 0.1 µg/mL, and a required volume of only 2.5 µL.

87. With similar advantages to paper-based sensors, molecular probes remain attractive tools for the detection of CWAs. Graphene is an increasing focus of research and development in many scientific fields, including its application in sensors; some graphene-based CWA sensors have recently been reported.

Biological sensors

88. Biosensors are powerful analytical tools that can achieve real-time quantitative analysis with high accuracy using low sample volumes. They have the potential to be integrated with other technologies to create on-site and highly integrated monitoring platforms.

89. Photoluminescence sensors based on silicon quantum dots and fluorescent proteins, and enzyme-based colorimetric sensors have been developed, integrated, and employed to detect and differentiate between nitroaromatic compounds and nerve agents. This approach uses both materials chemistry and biochemistry to accurately detect chemical hazards.

Insect-based sensors

90. Olfactory receptors (OR) in living systems significantly outperform current sensors using artificial materials. Whilst animals are able to detect a range of volatile organic chemicals, including drugs and explosives, insect olfactory systems are capable of detecting specific chemicals at extremely low concentration levels, even down to a single molecule. As a result, insect ORs are attracting increased interest in research, with a view to developing biosensors. Insects may be trained to show a behavioural response. Other insect-based approaches include inserting chips in locusts and creating biosensors using insect OR *in vitro*. A better understanding of the insect olfactory system will be helpful in the development of bio-mimetic olfactory systems for detecting specific chemicals of interest.

91. In an alternative approach that also utilises insects, blow flies have recently been used as environmental chemical sample collectors. Blow flies sample their environment and store chemical samples in their gut. In this study, flies were exposed to CWA simulants (dimethyl methylphosphonate (DMMP) and diethyl phosphoramidate), as well as the pesticide dichlorvos, and then captured in baited traps. An LC-MS/MS[43] method was established to detect CWA simulants or their hydrolysis products from extracted fly guts. Overall, it was observed that, after exposure, the quantity of CWA simulant in fly guts diminishes with time. However, exposure was detectable even after 14 days, providing an extended detectability window.

Plant-based sensors

92. Although traces of CWAs and their degradation products may be found in environmental samples of soil and water, certain chemicals—such as chlorine gas—dissipate quickly, while others are rapidly removed through leaching into groundwater. Furthermore, in aqueous environments—and especially under alkaline conditions—alkyl methylphosphonates (AMP) are relatively readily hydrolysed to form methylphosphonic acid (MPA), thus preventing a specific nerve agent from being identified. Plants, however, could be used as potential sentinels of exposure, as they may absorb chemicals through their roots or leaves, thereby preserving the chemicals present or producing associated biomarkers. Their wide abundance and fixed location make them particularly useful.

93. Studies have shown that plants are able to store and concentrate AMP markers (at the subparts per million level, in the case of garden cress) for at least five weeks, both in the roots and in the leaves. Higher concentrations in the roots prevent the hydrolysis of AMP to MPA, ensuring a high retrospectivity for analysis. This makes it possible to identify the type and possible origin of the nerve agent used. MPA was detected after five weeks in the roots, but after no more than one week in the leaves.

---

43 Liquid chromatography-tandem mass spectrometry.

94. Degradation products and/or synthesis impurities related to V agents, nitrogen mustard, sulfur mustard, and its analogues have been studied in garden cress, with markers seen to accumulate and concentrate for at least five weeks. V-agent impurities and nitrogen mustard hydrolysis products were better accumulated by the roots, while markers of sulfur mustard accumulated mainly in the aboveground parts of the plants.

95. Using environmental samples to confirm chlorine exposure remains a challenge due to chlorine's rapid dissipation after release, high reactivity, and the large number of naturally occurring chlorinated compounds in the environment. It has recently been observed that exposure of plants to chlorine not only results in a visual "pixelated" bleaching pattern in the tissues, but also in the formation of a variety of chlorinated sugars, metabolites, and lipids. The chlorinated compound 2,4,6-trichlorophenol, which does not occur naturally in plants, has been detected up to a week after exposure to a low concentration of chlorine gas and is one potential indicator.

96. Furthermore, post-exposure analysis of ribulose-1,5-bisphosphate carboxylase-oxygenase (rubisco), an enzyme common to all green-plant tissue, revealed the presence of peptides with chlorinated tyrosine amine acids (3-chlorotyrosine or 3,5-dichlorotyrosine). It remains difficult to unambiguously confirm chlorine gas exposure on the basis of these markers due to the potential environmental availability of a chlorine source.

97. To bolster research in this useful yet underexplored area, the OPCW, with funding from the European Union, launched the Plant Biomarker Challenge to develop new approaches to utilising plants as sentinels of toxic chemical exposure.[44] A total of 15 proposals, spanning all regional groups, were submitted to the first phase of the challenge; of these, six were awarded a 12-month contract. Two of these projects were selected to undertake follow-up research over a six-month second phase.

98. The projects have explored a range of plants—both cultivated crops and weeds—and fungi, and challenged them with a range of chemical agents, including scheduled chemicals, toxic industrial chemicals (TICs) and organophosphate (OP) pesticides. A range of on-site and off-site analytical methods have been utilised and developed.

Detection systems

99. Under the SIGMA+[45] project, automated and distributed networks of sensors using AI analytics have been developed. These sensors are designed for the long-range, real-time detection of both chemical and biological substances. During the testing process, highly sensitive chemical and biological sensors that were mounted on law enforcement vehicles were able to characterise real environmental background data. AI-supported algorithms were then employed to refine detection of chemical simulants against that background, leading to a reduction in false alarms by 75%. This mobile network has provided real-time analysis of potential chemical, biological, radiological, and nuclear (CBRN) threats via remote link to a tablet.

100. Integrating sensors, cameras, and even sampling equipment into UGVs and UAVs can provide a number of benefits over traditional monitoring systems.

---

44 https://www.opcw.org/biomarker.

45 https://www.darpa.mil/program/sigma-plus.

101. Chemical capacitance carbon nanotube-based chip sensors mounted on a quadrotor UAV have been shown to detect and map DMMP, a sarin (GB) simulant. The system, which was tested under both realistic indoor and outdoor conditions, demonstrated fast and accurate DMMP detection and provided concentration profiles both indoors and outdoors.

102. In 2019, the manufacturer Teledyne FLIR launched the MUVE C360: a multi-gas detector completely integrated with a UAV. The sensor block includes a photo-ionisation detector, lower explosive limit detector, and six sensors for Cl_2, CO, O_2, SO_2, NO_2, and H_2S, providing real-time detection. An important design feature is the ability to sample from unperturbed air.

103. Similarly, researchers from Poland and Austria have developed and tested a flexible gas detector that can be mounted on a UAV or UGV. A miniaturised vacuum pump samples the surrounding air and immediately distributes gas to the sensors for a rapid response. This allows Cl_2, H_2S, NO, NO_2, NH_3, and H_2O_2 to be measured in real time. A two-meter flexible tube allows samples to be drawn from any areas inaccessible to the UGV or UAV. In this detector, the downwash effect has been reduced by using a long-distance probe.

104. To achieve efficient, effective, and fail-safe detection of CWAs and TICs using UAVs and UGVs, a number of practical technology barriers need to be overcome:

(a) the quality of monitoring data is dependent on weather conditions, target chemical concentration, chemical interferents (such as from a UAV engine exhaust), and other operating parameters;

(b) electrically powered UAVs have limited flight time and payload capacity;

(c) downwash from the UAV rotor blades affects the mounted sampling and detection system; and

(d) increasing the speed of the UAV often negatively impacts sampling times, in turn affecting detection limits and efficiency.

SAMPLING AND ANALYSIS

On-site analysis

Chemical

105. Detection and identification of CWAs—and TICs to a lesser extent—is usually performed by instrumental analysis techniques (GC,[46] HPLC,[47] IC,[48] GC-MS,[49] LC-MS,[50] and NMR[51] spectroscopy) due to the high sensitivity and selectivity they offer. The instruments are primarily used in a laboratory environment due to their high cost, need for skilled operators, size, and other operational aspects that limit their use in the field.

---

46 Gas chromatography.

47 High performance liquid chromatography.

48 Ionic chromatography.

49 Gas chromatography-mass spectrometry.

50 Liquid chromatography-mass spectrometry.

51 Nuclear magnetic resonance.

106. Recently, some field-based GC-MS and MS[52] instruments were developed, such as the FLIR Griffin G510, Inficon Hapsite, and MX908 HPMS. These instruments provide reasonably reliable capability for in-the-field identification of chemical threats with sufficient sensitivity and selectivity. However, they remain inferior to laboratory-based GC-MS instruments in terms of mass range, resolution, and GC oven temperature range. The identification of chemicals with low vapour pressures (such as the chemicals listed in Schedule 1.A.13 to 1.A.16 chemicals and V-series nerve agents) is therefore challenging in the field—especially in cold weather conditions—if no additional sampling devices are used.

107. Inconsistencies in the performance of field portable GC-MS systems (e.g., variations in internal standard peak areas and daily response) have been addressed by the use of focusing agents. These are target-based thermal absorption standards used to determine relative response factors. More accurate and reliable quantification of different nerve agents has been achieved with the use of focusing agents, compared with the use of traditional internal standards, such as bromopentafluorobenzene.

108. Trace-level quantification of analytes and enhanced selectivity in field portable GC-MS systems have been enabled with the use of miniaturised pre-concentrators.

109. There have been some recent advances in portable Raman spectroscopy, but no increase in sensitivity. Raman spectroscopy is only used for on-site analysis, and its utility is limited to relatively simple matrices.

110. Current portable and hand-held detectors can still only provide provisional or confirmed identification of a chemical; unambiguous identification is provided by off-site analysis, using orthogonal measurement methods.

Biomedical

111. The most common method for rapid point-of-need diagnosis of exposure to nerve agents is based on nerve agent-induced changes on acetyl- or butyrylcholinesterase (AChE or BChE) activity in blood. However, the large inter- and intra-individual variation of cholinesterase (ChE) activity in blood remains a drawback to this approach. In order to draw firm conclusions about possible exposure, the AChE inhibition level needs to be at least 40%. In this regard, the baseline values of individuals are of utmost importance.

112. A selection of assays and devices based on AChE or BChE inhibition are commercially available (e.g., Testmate, ChECheck mobile), or will soon be available (e.g., Scentmate). A simple lateral flow assay or other immune-chromatographic strip test would be ideal for rapid point-of-need diagnosis of nerve agent exposure. Unfortunately, specific antibodies against nerve agent-phosphorylated ChE are lacking, because the phosphorylated site in inhibited AChE or BChE is not accessible for antibody recognition.

113. A number of new technologies and approaches that do not require the availability of specific antibodies have been reported. Typical examples include an integrated lateral flow test strip with an electrochemical sensor device, a disclosure test, and an enzyme

[52] Mass spectrometry.

ticket. Point-of-need diagnostics for sulfur mustard exposure, such as a lateral flow assay product that employs antibody-based detection of sulfur mustard adducts, have been demonstrated. Using this approach, field detection of skin exposure to sulfur mustard should be possible. The Immunochemical Detection Kit has been reported to detect DNA-sulfur mustard adducts in blood and skin. Nevertheless, none of these devices are currently commercially available.

114. Currently, the majority of these technologies—if in service—are being used in dedicated, well-equipped laboratories. It is therefore important to further test the ability to use these devices in the field under realistic operational conditions. Point-of-need devices could then be considered as indicative tests for use in the field. Verification of the results, and therefore proof of exposure, would require subsequent biomedical sample analysis, using methods developed by the OPCW's designated laboratories (DLs).

Off-site analysis

Chemical

115. Sample preparation, methods, and instruments have continued to evolve and improve Convention-related off-site analysis for both environmental and biomedical samples.

116. There have been significant advances in Convention-related analysis of chemicals by HRMS.[53] These have enabled accurate molecular mass determination and generated empirical molecular formulae (both of which are important factors in determining the structure of small unknown chemicals); this technology is now used by the DLs. It has also enhanced sensitivity for biotoxins. The SAB notes that there are currently limited HRMS data available on Convention-related chemicals. This necessitates the comparison of acquired HRMS data with low resolution data, or comparison with a chemical reference analysed under the same conditions, which is currently the preferred approach.

117. Advances in GC-MS instrumentation, such as the use of low-thermal mass resistively heated columns, enables the analysis of low volatile compounds.

118. Equipment based on micro- and nanotechnologies is emerging, enabling miniaturisation. However, this equipment is less robust and suffers from poor selectivity and a high false positive detection rate. Research efforts are under way to eliminate these issues and ensure more reliable performance.

119. The development of methods to verify chlorine releases using environmental sample matrices is progressing. The reaction of chlorine gas with organic chemicals to produce their chlorinated analogues was extensively investigated when environmental pollutants, such as dioxins and chlorinated phenols, were discharged in industrial effluents. Chlorinated phenols are only produced by man-made reactive chlorine species, such as chlorine gas and sodium hypochlorite (the active ingredient in bleach). Both of the highly chlorinated phenols (trichlorophenol (TCP) and tetrachlorophenol (TeCP)) were produced when chlorine gas was used as a bleaching agent in the production of bleached kraft pulp. However, the chlorination of phenol by sodium hypochlorite in aqueous solutions only produced TCP. Chlorine gas is five orders of magnitude more reactive than

53 High-resolution mass spectrometry.

sodium hypochlorite when used for the chlorination of aromatic ethers. This may explain the observed selective production of TeCP by chlorine gas. Thus, the presence of TeCP in environmental matrices has the potential to be specific to chlorine gas exposure.

Biomedical: nerve agents

120. Nerve agent exposure assessment relies on the analysis of biomarkers, which are either free metabolites in urine or adducts with proteins or DNA in blood. Biomarkers in biomedical samples can be analysed using GC-MS/MS[54] and LC-MS/MS techniques, or with MS/HRMS.[55] To enhance throughput in biomedical sample analysis, 96-well plates have been introduced, thus making it possible to simultaneously prepare a large number of plasma or serum samples when using immunoaffinity, or alternately, solid-phase extraction for urine samples. This could facilitate high-throughput analysis in cases of mass casualties.

121. In order to reduce the incubation time, columns containing immobilised enzymes required for protein adduct proteolysis have been developed. Automation has been introduced thanks to an immobilised enzyme reactor (IMER) coupled online prior to LC-ESI-MS/MS[56] analysis for nerve agents (pepsin IMER for BChE-OP digestion) and for sulfur mustard (trypsin IMER for haemoglobin-sulfur mustard adducts digestion).

Biomedical: unknown organophosphate nerve agents

122. Recent analytical developments have been published in order to augment the toolbox of methods available to laboratories for investigating exposure to an unknown OP nerve agent. The trend observed has been to leverage HRMS, which allows non-targeted analyses thanks to its sensitivity and mass accuracy. Using LC-Q-Orbitrap[57] and LC-QTOF[58] instrumentation, HRMS technology makes it possible to screen unknown OP nerve agent samples—at subparts per thousand to parts per billion levels—in a non-targeted or semi-targeted analysis mode. This methodology is complementary to the traditional targeted methods used in multiple reaction monitoring mode that are usually focused on specific OP nerve agents. It is also possible, in the same analytical run, to perform an analytical LC-HRMS[59] scan followed by automatic LC-MS/HRMS[60] scans on the most abundant peak(s) detected, thus yielding additional information, such as on the structure of a V agent side chain, for example. Finally, several complementary MS/HRMS and/or MS/MS[61] scans, requiring further sample injections, can then be performed with higher sensitivity thanks to the structural determination of the biomarker obtained in the first non-targeted analyses.

---

54 Gas chromatography-tandem mass spectrometry.

55 Mass spectrometry/high resolution mass spectrometry.

56 Liquid chromatography electrospray ionisation tandem mass spectrometry.

57 Liquid chromatography hyphenated with quadrupole-Orbitrap mass spectrometry.

58 Liquid chromatography hyphenated with quadrupole-time of flight mass spectrometry.

59 Liquid chromatography-high resolution mass spectrometry.

60 Liquid chromatography with tandem mass spectrometry experiments performed by low resolution isolation of ions of interest followed by high resolution analysis of those ions.

61 Tandem mass spectrometry at low resolution.

123. Unknown OP poisoning can also be identified at low resolution by LC-MS/MS in precursor ion scan mode on a triple quadrupole MS based on the characteristic fragmentation pathway of the BChE-OP adduct-derived nonapeptide. Employing this specific precursor ion mode, it is possible to identify the mass of the BChE-OP adduct-derived nonapeptide. Nevertheless, the significantly lower sensitivity of the precursor ion mode, compared to the multiple reaction monitoring mode, constitutes a limitation of the analytical method.

124. The side chain of 1.A.13 and 1.A.14 chemicals and V agents can be identified by MS/HRMS analysis using the information-rich, low-mass region of the spectra. A complete structural interpretation of the particular agent can be performed thanks to the ability to use exact mass measurement. With this increased selectivity, identification of an unknown OP nerve agent can be performed without a reference standard. Contrary to the classical V agents, the entire moiety of the 1.A.13 or 1.A.14 chemical, covalently bound to the serine of the BChE catalytic site peptide, is released during the collision-induced dissociation process in the ion source, or in the collision cells of MS/MS instruments. In addition, it can be observed in its hydrolysed form (for example A230[62]-OH, where the fluoride functional group is replaced by a hydroxyl group), thus facilitating its identification.

125. New developments are focusing on biomarker derivatisation, which is performed to improve detection limits—for example, by inducing a shift of the biomarker retention time into a retention time region with less matrix interferences. It may also be performed to enhance the sensitivity by improving the ionisation efficiency of analytical LC-MS/MS or LC-MS/HRMS methods. This approach comes from the proteomics field, where the derivatisation of proteins and peptides at nucleophilic amino acids or at the peptide N-terminus is often used to improve ionisation properties.

Biomedical: mustards

126. The long-lived human serum albumin (HSA)-sulfur mustard adducts are usually successfully analysed, after proteolysis, as an alkylated tripeptide or dipeptide, with no derivation. The on-line nicotinylation on the N-terminus of the HSA-sulfur mustard derived dipeptide biomarker leads to a 34% higher LC-MS/MS response due to its less hydrophilic properties, compared to non-derivatised peptides. The liquid chromatography retention time shift (which could also be an advantage in cases of matrix interference observed in the LC-MS/MS retention time window of the non-derivatised peptide) was also recently published for propionic anhydride and benzyl chloroformate for the same HSA-sulfur mustard-derived dipeptide biomarker.

127. The HSA-nitrogen mustard (HN1, HN2, HN3) and HSA-sesquimustard adducts can also be analysed by LC-MS/MS in multiple reaction monitoring mode, or by LC-MS/HRMS after proteolysis, as an alkylated tripeptide, with no derivation, and with the same methodology as for HSA-sulfur mustard adducts.

128. Other sulfur mustard-adducts are still being investigated, notably from red blood cells, by searching for several alkylated peptides derived from haemoglobin in order to improve the sensitivity of the analytical method, as compared to the alternative N-terminal valine method.

---

62 Open-source publications indicate that A230 is the abbreviated name given to the Schedule 1.A.13 chemical methyl-(1-(diethylamino)ethylidene) phosphonamidofluoridate.

Biomedical: chlorine

129. Development methods for the verification of chlorine exposure are progressing. There are three different classes of chlorine adducts with biomolecules that have been presented as potential biomarkers for chlorine exposure:

(a) 3-chlorotyrosine and 3,5-dichlorotyrosine: produced by the chlorination of tyrosine residues in proteins;

(b) 2-chloro fatty acids: produced by the chlorination of plasmalogen lipids; and

(c) phosphatidyl lipid chlorohydrins: produced by the chlorination of unsaturated phosphatidyl lipids.

130. The verification of chlorine exposure is made difficult by the production of reactive chlorine species and hypochlorous acid by neutrophilic inflammatory cells in the human body. Inflammatory diseases consequently produce background levels of all suggested chlorine biomarkers from the hypochlorous acid that is released by inflammatory cells. In a case of alleged exposure to chlorine, the relative increase of the biomarker compared to common background levels has to be calculated. The presence of chorine biomarkers at low levels in blank samples will require the reporting criteria to be modified appropriately. Indeed, biomarkers of classical CWAs are usually absent in the blank samples from non-exposed humans.

131. The principal sample source of these chlorinated biomolecules is tissue from the lungs and the airways. Lung fluid samples are a good source of all the biomarkers listed above. However, as sampling requires advanced medical equipment and skilled medical staff, alternative biomedical sample types are preferred.

132. Blood serum and hair are easy to sample, and elevated levels of chlorinated tyrosines were reported in samples from chlorine-exposed mice. Elevated biomarker levels were found in blood serum samples up to 24 hours after exposure, and in hair samples after 30 days. However, the results acquired from the chlorine exposure of mouse muzzle hair may not be fully comparable to the passive exposure of human scalp hair of victims from a chlorine attack.

133. Nasal lavage fluid has been presented as a new biomedical matrix for phosphatidyl lipid chlorohydrin biomarker detection in the nasal mucosa of exposed animals. Medical expertise is not required for sampling this fluid, which can be performed quickly and easily following a chlorine attack. Furthermore, the nasal mucosa is known to contain a low level of inflammatory cells reducing the background level of the phosphatidyl lipid chlorohydrins.

134. It is important to provide evidence that the biomarkers identified are specific to chlorine gas alone, and are not from other agents containing reactive electrophilic chlorine, such as bleach. However, bleach is a liquid solution of sodium hypochlorite, and inhalation of a bleach aerosol is a possible chemical attack scenario to be considered. Bleach is highly unlikely to give rise to biomarkers in biomedical samples of internal tissues, such as blood serum and lung fluid, but could potentially produce chlorine biomarkers in human skin epidermis and hair. Chlorine-containing chemicals such as

chloropicrin, phosgene, and cyanogen chloride do not produce reactive electrophilic chlorine species if inhaled, and would not therefore produce any of the chlorine biomarkers listed above.

Biomedical: newly scheduled chemicals

135. To date, there have been relatively few studies published on the newly scheduled OP families (1.A.13 to 1.A.15). Any existing publications on NSC biomarkers have focused on the families of chemicals listed in 1.A.13 and 1.A.14.

136. Hydrolysis products of 1.A.13 and 1.A.14 chemicals have been studied by spiking human urine with their degradation products *in vitro*. Several sample preparation methods for alkyl alkylphosphonic acids (conventional nerve agent hydrolysates) in urine have been used, including liquid, liquid extraction, solid-phase extraction, and derivatisation. The analytical performance of hydrophilic interaction liquid chromatography and reverse-phase liquid chromatography coupled with tandem mass spectrometry were compared for some NSC hydrolysis products and alkyl methylphosphonic acids (urine biomarkers of G and V nerve agents). Open-source data suggest that extraction recovery for the hydrolysis products of the chemicals listed in 1.A.13 to 1.A.15 is lower than for alkyl methylphosphonic acids.

137. To achieve the same subparts per billion level of sensitivity attained for the non-derivatised alkyl methylphosphonic acids, derivatisation prior to LC-MS/MS analysis has been proposed: the 4-(4,6-dimethoxy-1,3,5-triazin-2-yl) derivatives of 1.A.13 and 1.A.14, and the pentafluorobenzyl derivative of 1.A.15 have been successfully detected.

138. It has been observed that the NSCs listed in 1.A.13 and 1.A.14, unlike G and V nerve agents, are stable in human urine spiked *in vitro* for at least one month. This indicates the theoretical possibility of detecting these agents intact in human urine.

139. Similar to the other OP nerve agents, the newly scheduled chemicals listed in 1.A.13 and 1.A.14 form adducts with proteins—principally ChEs; additionally, depending on the concentration of the intoxication, they can form adducts with human albumin, which is the most concentrated protein in plasma. Therefore, the same methodology used for OP nerve agents can be applied.

140. Several studies have demonstrated that the BChE-OP nerve agent protocol also works for BChE-1.A.13/1.A.14 adducts. As with the other OP nerve agents, potassium fluoride (KF) has been used to reverse the binding in the protein A234[63] (a 1.A.14 chemical) adduct, thus regenerating the toxic A234. However, KF regeneration was significantly longer for this NSC than for the classical OP nerve agents (3 hours vs 30 minutes at room temperature).

141. The A234 regenerated from the adduct can be either analysed by LC-ESI-MS/MS (the most sensitive) or by GC-MS/MS. However, neither the KF regeneration method nor the analysis of the nonapeptide can be used to verify the original leaving group on the original nerve agent. This limitation also applies to V-series agents.

---

63 Open-source publications indicate that A234 is the abbreviated name given to the Schedule 1.A.14 chemical ethyl (1-(diethylamino)ethylidene)phosphoramidofluoridate.

142. In the case of the human albumin A234 adduct, *in vitro* adduction was observed after over-handed shaking incubation for 48 hours, compared to the usual 1 to 2 hours for classical OP nerve agents. During sample treatment of A234-spiked human plasma, extraction of the tyrosine A234 chemical obtained by proteolysis of albumin A234 also required longer incubation compared to the classical OP nerve agents (18 hours vs 2 hours).

143. Despite the small number of publications currently available on NSCs, the SAB notes that the number of these publications has been on the rise since 2021, demonstrating that work is in progress at several DLs in a number of States Parties. In order to improve the capabilities of the DLs, it is necessary to share the results of these recent and future studies, in addition to updating the 2017 Recommended Operating Procedures with the sample preparation and analytical methods for these NSCs.

144. The SAB notes that there are currently no publications available on biomarkers of exposure to the chemicals listed in 1.A.15 and 1.A.16.

Biotoxins

145. A biological toxin—or simply, biotoxin—is any toxic chemical that is produced by a living organism, such as a microorganism, plant, or animal. Some biotoxins, such as saxitoxin, ricin, staphylococcal enterotoxin B, and botulinum toxins have been weaponised in the past.

146. In many cases, a number of closely related but distinct toxins possess very similar properties and pose particular investigative challenges, since they are at the intersection of chemical and biological agents. Although methods have been developed to detect ricin and saxitoxin (i.e., the two Schedule 1 biotoxins) with multiple screening techniques and confirmatory analyses using LC-MS/MS, the detection and quantification of protein toxins remains challenging in complex matrices, especially at pg/mL and ng/mL levels.

147. Since very low quantities of these agents can be lethal, detection methods should apply both high sensitivity and selectivity, and properly discriminate interferences and contaminations. The high complexity and diversity of the samples is one of the main obstacles. Conventional detection methods rely on bioassays or analytical methods, such as nucleic acid-based analyses (e.g., PCR[64]) or immunological assays (e.g., ELISA[65]). Although they are fast analyses, they have limitations in some cases, such as a lack of selectivity, which can yield false positives.

148. In early 2021, the Temporary Working Group (TWG) on the Analysis of Biotoxins was established. Its objective is to review the science and technology relevant to the analysis of biotoxins, as well as the considerations that need to be taken into account in investigations of their alleged use. The overall work of the TWG is intended to identify the skill sets and equipment that can augment and strengthen the Secretariat's capabilities.

149. There is great diversity in the field of biotoxins. They can loosely be divided into low molecular weight toxins, such as saxitoxin, and high molecular weight toxins, such as botulinum neurotoxins or ricin. All are toxic and have a biological organism as their origin, but beyond that, they are extremely different in terms of size and chemical properties like stability and polarity.

---

64 Polymerase chain reaction.

65 Enzyme-linked immunosorbent assay.

150. Small molecular toxins are organic molecules that often act as inhibitors of human enzymes, thereby mediating their toxicity. In contrast, most of the relevant high molecular toxins are proteinaceous enzymes, and their toxicity is linked to their own enzymatic activity. A wide range of biochemical processes in the human body may be impaired by the activity of a toxin. Consequently, parameters such as the rapidity of disease onset, clinically relevant concentrations, and symptoms of exposure may differ between classes of toxins. Since biotoxins include very different types of chemical molecules, there is not one overall analytical technique that can be applied universally to biotoxins.

151. Furthermore, analyses of low molecular weight biotoxins, such as saxitoxin, require very different methods from analyses of high molecular weight biotoxins, such as ricin. Relatively few laboratories are skilled in both types of analyses.

152. For many low molecular weight biotoxins, traditional MS methods prove quite useful, with some consideration given to solubility and chromatographic retention of the biotoxins. The molecular masses of low weight biotoxins (100 –3,000 Da) are within the mass range of modern mass spectrometers, and selective LC-MS/MS methods can be used to detect toxins. However, this technique is susceptible to ion suppression by the sample matrix, and polar toxins like saxitoxin can be difficult to detect if present at low levels in samples of complex matrices (e.g., food or biomedical matrices).

153. The chemical analysis of high molecular weight biotoxins such as protein toxins (50,000 – 500,000 Da) is mainly based on the digestion of proteins to peptides and subsequent MS/MS analysis of the digests. Tryptic fragments of proteins are well characterised, and peptide sequences can be matched to protein sequence databases, thereby covering a large part of the toxin-producing organisms of the world.

154. Often, immunology and MS are combined to enhance the specificity and the sensitivity of MS methods by on-line or off-line sample enrichment with antibodies. If the toxin is present at a low concentration in a sample containing a high protein matrix (e.g., biomedical samples), the sensitivity of the LC-MS/MS technique may be a limiting factor. The use of immunoaffinity-based enrichment of a selected toxin (or toxins) prior to digestion and LC-MS/MS analysis of the tryptic peptides can significantly increase toxin detection in such complex samples.

155. In the case of high molecular weight toxins in particular, important orthogonal approaches to MS include ELISA and functional assays, providing unambiguous identification. Alternative techniques to detect high molecular weight toxins include polyacrylamide gel electrophoresis (PAGE), 2D-PAGE, DNA sequencing (using DNA traces from source organism), and cytotoxicity assays. However, none of these individual assays should stand alone as unambiguous identification. The use of some of these alternative approaches should take into consideration that the rigorous characterisation of reagents such as antibodies is necessary for accurate biotoxin identification.

156. The SAB also notes that some analytical techniques that are very reliable for biotoxins—like LC-QTOF, MALDI-TOF[66] or MALDI-TOF-TOF, ELISA, and *in vitro* cell assays—are not used for any other chemicals related to the Convention (except ricin).

---

66 Matrix-assisted laser desorption/ionisation-time of flight.

SAMPLE STORAGE AND STABILITY

Toxic chemicals and environmental and material samples

157. In response to a request for advice from the Director-General, the SAB communicated best practices for sample storage and the impact of sample stability on analytical results.[67] There have been no fundamental scientific or technological developments in this domain and the advice provided in 2016 remains current.

158. The SAB notes that there is little additional information available in open literature on the NSCs listed in 1.A.13 to 1.A.15.

159. Some data on the theoretical and experimental stabilities of the chemical families listed in Schedule 1.A.13 and 1.A.14 have been published, and that the degradation products of A234 in aqueous solutions at different pH levels have been determined experimentally. It was demonstrated that the same degradation products are formed in neutral, acidic, and basic aqueous conditions. The main degradation product formed is the hydrolysis product of A234 (i.e., the loss of HF). The hydrolysis rate of A234 was fastest under acidic conditions. This study also indicated that A234 is not easily hydrolysed in aqueous matrices and could be found two months after spiking at neutral and basic pH, and after one week at acidic pH.

160. A study of the extraction and analysis of the newly scheduled OP chemicals indicated that the compounds listed in Schedule 1.A.13 and 1.A.14 are relatively stable in aqueous media, as well as in wet or dried solid matrices such as sand, soil, and wipes. Open literature data indicate that the 1.A.13 and 1.A.14 chemicals were found to be stable in human urine for at least one month. On the contrary, the compound listed under 1.A.15 is not stable in aqueous media.

161. The SAB notes that there are currently no publications related to the stability (or indeed many other properties) of the newly scheduled carbamate family (1.A.16). Any publications on carbamates are not related to the types of structures in 1.A.16, but instead relate to smaller carbamates (such as the oximes pyridostigmine and physostigmine, as well as the pesticides carbaryl and aldicarb). Based on the structure of carbamates with an ammonium salt, they are hydrophilic and should be stable in aqueous media.

Biomedical samples

162. The diagnosis of exposure to toxic chemicals traditionally involves sampling blood and urine from the victims, transporting those biological samples to a laboratory—usually located far from the scene of the incident—and analysing them. In mass casualty incidents, sampling and analysis may be required on a large scale. Considering that biological samples are very sensitive to storage conditions, the preservation of large batches of samples—especially in hot climates—may be problematic.

---

67 SAB-23/WP.2, dated 25 May 2016.

163. Additionally, blood biomarker concentrations in the victims decrease over time, therefore prompt sample collection is critical. Alternatives to invasive, labour-intensive blood draws are needed to accelerate and simplify the sample collection process.

164. A promising new technique using dried blood spots (DBS) could be exploited and provide a suitable alternative to traditional blood tubes. This technique significantly simplifies the stability, transfer, and handling of blood samples, which are of high importance for the analysis of biomedical samples.

165. DBS involves the application of a drop of whole blood onto a filter card. The blood drop is obtained from a heel or toe prick (newborns and infants) or finger prick (children and adults) with a single-use safety lancet. After collection, the blood is left to dry at room temperature before being sent to a laboratory for analysis. Typically, small discs (with a diameter of 3 mm) are punched out from the dried blood card and an extraction is carried out for 30 minutes. Most often, concentrations of the analytes of interest are subsequently determined by LC-MS/MS, or by immunoassays.

166. There are multiple advantages to using DBS over traditional blood collection techniques:

(a) collecting dried blood samples is generally faster and less invasive than a blood draw;

(b) a smaller volume of blood is required;

(c) the risk of infection and blood haemolysis is minimised;

(d) minimal training is required, and the drop does not necessarily need to be collected by medical personnel, meaning self-sampling may be possible;

(e) blood spot cards can be kept at ambient temperature with desiccant and do not require cold storage; and

(f) since blood is dried on the collection cards, samples are considered stable and biologically non-hazardous during storage and transport.

167. This technique has been tested to detect exposure to nerve agents. The exposure to OP nerve agents can be confirmed by the identification of specific biomarkers, including BChE-OP and albumin-OP adducts. After exposure to VX and GB, the activity of BChE and the concentrations of nonapeptide derived from BChE-OP adduct in DBS remain the same after storage for 40 days at 22°C, whereas in liquid samples, BChE activity increases over time and the concentrations of BChE-OP adducts decrease, probably as a result of spontaneous reactivation.

168. Alkyl alkylphosphonic acid metabolites, readily formed by hydrolysis in the body, can be used as secondary biomarkers to diagnose OP nerve agent poisoning. They have been measured in DBS samples following human exposures to VX and GB, as well as in animal studies with GB and cyclosarin (GF).

169. This DBS technique has also been applied to identify a sulfur mustard biomarker in dried plasma samples. When simulating possible storage conditions, it was observed that exposure to moderate, hot, or dry climate conditions over a nine-day period did not affect the subsequent biomarker identification.

170. Finally, this DBS technique has also been proven useful in the sensitive monitoring of ricin and abrin exposure through the methanol/water extraction of the DBS card, followed by LC-MS/MS analysis of ricinine and L-abrine. Ricinine, a small molecule present as an impurity in ricin samples, may serve as provisional biomarker for assessing exposure to ricin that has not been fully purified. Using this technique, the detection limit of ricinine was 50 pg/mL in a DBS of whole blood, and the ricinine was stable on the paper even after four months at room temperature. As ricinine may be present in other materials, such as cosmetics and dietary products, this method is only intended for preliminary identification; in cases of a positive result, verification by analysis of the ricin itself should be conducted. The DBS collection, sample preparation, and analytical method were also successfully demonstrated for the rapid identification of L-abrine, a small molecule present in *Abrus precatorius* beans, as a specific biomarker of exposure to abrin (a ribosome-inactivating protein II biotoxin, and a proteic toxin analogue to ricin) with a detection limit of 100 pg/mL in a DBS. Similar to ricinine, L-abrine was also stable on the paper after four months of storage at room temperature.

171. No study on the longevity of DBS storage for CWAs has been reported.

FORENSIC AND INVESTIGATIVE SCIENCE AND TECHNOLOGY

172. Since 2013, there has been an ongoing requirement to conduct contingency operations, such as the OPCW Fact-Finding Mission in Syria, with an increasing focus on investigations and fact-finding, involving the collection and evaluation of a range of evidence related to the use of chemical agents. These non-routine missions are more demanding from a technical and forensic perspective than the missions described in Articles IX and X of the Convention.

173. This highlighted the need for the OPCW to evaluate technologies and adopt methods—both current and emerging—applicable to investigative work, especially for validating and determining the provenance of evidence, as well as for integrating multiple, diverse inputs in order to reconstruct a past event of chemical use.

Temporary Working Group on Investigative Science and Technology

174. Following the SAB workshop on chemical forensics in 2016 and the ensuing recommendations, the Director-General requested the SAB to establish a TWG to consider practical applications of investigative scientific methods and technologies for use by OPCW inspectors during contingency operations, with the aim of further enhancing capabilities.

175. The resultant TWG on Investigative Science and Technology met five times in 2018 and 2019 to consider this issue in detail, and focused on six key areas. Its detailed report and associated recommendations are available in a separate document,[68] and an overview of the topics discussed and noteworthy recommendations are reproduced below.

---

68 The final report of the TWG on Investigative Science and Technology was published as SAB/REP/1/19, dated December 2019. Available at: https://bit.ly/TWGIST.

(a) Forensic methods and capabilities

A review of methods and capabilities used in the forensic sciences that could be developed and/or adopted for Chemical Weapons Convention-based investigations.

TWG recommendation 1:
Appoint a forensic advisor with broad experience in forensic science, forensic examinations, and international law to provide advice to the Director-General and the OPCW.

(b) Data collection and management

Consideration of best practices and analysis tools used in the forensic sciences for effectively cross-referencing, validating, and linking together information related to investigation sites, material collected and analysed, and individuals interviewed. In addition, best practices for management of data collected in investigations were addressed.

TWG recommendation 4:
Review existing Recommended and Standard Operating Procedures (R/SOP). These should be reviewed together with an expert forensic consultant to ensure that they are forensically sound and fit for purpose, suitable for inclusion in a forensic case file and able to meet the requirements of the end user.

(c) Sampling, detection, and analysis

This section addresses the detection and analysis of toxic chemicals, with a focus on the point-of-need and non-destructive measurements at an investigation site to guide evidence collection. In addition, it reviews available methods for the sampling and analysis of environmental and biomedical materials for the verification of toxic chemical use and exposure. A wide range of chemicals are covered, including scheduled chemicals, TICs, CNS-acting chemicals, and biotoxins.

TWG recommendation 13:
Enhance capabilities for the on-site detection of chemical warfare agents and related compounds, including newly scheduled agents, TICs, CNS-acting chemicals, and biological toxins, from a variety of environmental matrices, including gaseous, liquid, and solid forms, to offer a broad coverage of possible scenarios.

(d) Integrity of the scene and evidence collection

This section considers the task of maintaining the integrity of an investigation site and the collection of evidence, with a focus on best practices for the handling, curating and storing, and annotating evidence. Furthermore, it also explores new technologies and methodologies that may be used to ensure the chain of custody and verify authenticity.

TWG recommendation 10:
The Secretariat should ensure that forensic issues are included in R/SOPs and Working Instructions including those related to on-site sample collection, handling, curation and storage, and annotation in accordance with forensic best practices.

(e) Provenance of chemicals

This section provides a review of the chemical profiling techniques used to determine the provenance of chemicals and material samples collected in an investigation (also referred to as "source profiling"). This would include the acquisition of chemical profiles or physical objects in a retrospective chemical weapons-related analysis to support the investigators in a retrospective review.

TWG recommendation 18:
Consider establishing a new TWG on the provenancing of samples of chemicals relevant to the Convention.

(f) Methodologies, procedures, technologies, and equipment

This section addresses additional considerations, and provides advice on Secretariat proposals for methodologies, procedures, technologies, and equipment for investigative purposes. The priority areas included considerations on topics such as non-traditional options for data collection, and situations where the traditional best practices may not fit the situational needs, among other aspects. Furthermore, approaches to understanding the factors related to technical investigative assistance, including possible legal issues, were considered.

TWG recommendation 33:
Strengthen the ability to evaluate and adopt new technologies and equipment to meet the Secretariat's evolving needs.

176. While the aforementioned recommendations are considered to be some of the most important proposed by the TWG, a total of 36 recommendations were issued. Implementation of these recommendations will better prepare the OPCW to effectively carry out non-routine missions by adopting new approaches, developing additional tools, and using methodologies suited to new and unfamiliar scenarios.

Chemical profiling of chemical warfare agents

177. The chemical attribution profiling of a CWA sample can be performed using common chemical analytical technologies to acquire data on chemical profiles consisting of a set of impurities, degradation products, or additives (organic and inorganic) in CWA samples. Such extrinsic chemical attribution signatures (hereinafter "signatures") can be by-products from chemical synthesis, or impurities from the precursors used. Another type of chemical profile is based on intrinsic signatures, such as stable isotope profiles within the CWA itself. A stable isotope profile consists of the site-specific abundance of stable isotopes within a CWA.

178. There are good analytical tools available for the chemical profiling of CWAs (e.g., GC-HRMS[69] and LC-HRMS) that are well suited to detecting the presence of contaminants in and traces of starting materials, by-products from synthesis, and stabilisers and other components of a CWA sample. In addition, there are methods for acquiring intrinsic signatures such as stable isotope ratios of selected elements present in a CWA (IRMS[70] or PSIA-NMR[71]).

179. Chemical profiles can be used in sample matching in order to link samples with a suspected common origin. Similarities in chemical impurity profiles can be used to link precursors to a specific CWA suspected to be produced from the analysed precursor(s). Such methods based on deuterium or carbon-13 profiles have been established to link specific precursor batches to batches of produced soman or GB, respectively. Furthermore, batch-specific impurity profiles of the nerve agent precursor methylphosphonic dichloride (DC) have been characterised in a large number of production batches, making it possible to link produced nerve agents to the starting material used for their production. In a recent inter-laboratory DC chemical profiling exercise, low between-lab variation in the chemical profiles was observed. This study highlights the potential for OPCW DLs to successfully perform chemical profiling using instrumentation and methods common to the OPCW laboratory network.

180. A second application of chemical profiling is determining the provenance of one or more CWA samples from a single seizure, with the aim of gaining information on a probable origin of the agent, the route of production (route sourcing), the technical competence of the perpetrator, etc. Classification models based on reference samples are needed in order to link an authentic sample to a synthesis route. In the case of route sourcing, the reference data must be comprehensive and cover a wide range of routes. Route-sourcing methods have been published for sulfur mustard and V-series agents.

181. In order to successfully match chemical profiles, the samples generally need to be comparable in both concentration and matrix. It would be difficult to assess the link between different types of samples (i.e., a highly concentrated sample of a neat substance and environmental or material samples collected at the scene) based on the comparison of attribution profiles. Attribution markers present as traces in the concentrated sample may not be detectable in the environmental sample, and the difference in sample matrices may make the comparison difficult.

DECONTAMINATION AND REMEDIATION

Risk-based operational decision making

182. Following the deliberate release of a persistent CWA in an urban environment, a decision on the level of residual hazard that constitutes a minimal health risk to the general population, or in other words “how clean is safe”, is required in order to facilitate the use of potentially contaminated equipment and vehicles, and to permit re-entry into contaminated buildings and areas.

---

69 Gas chromatography-high resolution mass spectrometry.

70 Isotope-ratio mass spectrometry.

71 Position specific isotope analysis-nuclear magnetic resonance.

183. Primarily, it is necessary to understand how and when contamination "hot spots" become "cool" enough to be considered safe. More formally, at any contaminated location, it is necessary to determine the amount of residual agent that can be tolerated: contamination levels greater than this will require some form of remedial action.

184. Risk-based operational decision making is key to providing informed advice on assistance and protection and allowing the OPCW to fulfil its mission objectives. It is the cornerstone of setting requirements for:

(a) the type and level of personal protection;

(b) hazard management strategies, including the selection of fit-for-purpose decontamination methods and technologies; and

(c) decontamination assurance sampling and analysis protocols to allow unrestricted entry to contaminated areas.

185. In relation to NSCs, several key knowledge gaps have been identified and outlined below. These gaps currently prevent setting decontamination and remediation goals.

186. Limited published data exists on the chemical, physical, and toxicological properties of NSCs, and available data on their environmental fate is confined to theoretical computational studies. However, when this is viewed alongside available information from recent real-world remediation operations, it suggests that a number of NSCs may present long-lived percutaneous hazards to unprotected individuals entering contaminated environments or handling contaminated items.

Acceptable percutaneous dose

187. Since the 1940s, there has been a growing body of literature describing how to determine the doses of different chemicals that cause a range of health effects. This has been accompanied by the development of increasingly stringent regulations prescribing acceptable occupational exposure limits (OELs). However, this has predominantly focused on exposure by respiratory routes.

188. There are no equivalent numerical regulatory limits for exposure via percutaneous routes. Currently, the state of the art is to attempt to harmonise the considerable range of "skin notation" approaches in use in different countries. For a given substance, the skin notation code is simply appended to inhalation OELs.

189. With regard to contact hazard, the appropriate penetration rates are those pertaining to how rapidly liquid contaminants penetrate skin. There is a large body of data relating to this phenomenon. This suggests that in future work, there is a possibility that contact hazard doses for CWAs might be derived from OELS for the vapour hazard, for which a substantial body of literature exists.

190. Current programmes within the international CBRN research community seek to mathematically model the physics and chemistry of exposure in an effort to address the contact hazard issue. However, this research is in its infancy and is unlikely to attain a sufficient degree of consensus in the short term.

191. It is noted that identified approaches stop short of demonstrating how to calculate acceptable surface contamination levels vis-à-vis the contact hazard. Alternative approaches—relating the acceptable percutaneous dose to acceptable surface contamination densities to which unprotected personnel may be exposed—are required.

192. In defining an acceptable dose, it is necessary to consider two factors: what health effects are acceptable, and what fraction of the population experiencing those health effects is acceptable. There is very limited information upon which to base any estimate of tolerable dosage for NSCs. At this time, it is not possible to have a quantitative estimate of the dose in humans that will produce adverse effects on health from low-level exposure in the long term.

193. Experimental investigations are very difficult or impossible due to the length of time required, dosage control, and the ill-defined nature of the toxicological effect. This means that any estimate must be derived working from what is known, to what is not known—in this case, from short-term toxicity to long-term, low-dose toxicity. Better *in silico* models are currently being developed that will make it possible to accurately extrapolate existing data to generate the insights that previously were only possible through experimental investigations.

194. For nerve agents like VX, this extrapolation is reasonable because nerve agents react with ChEs in the blood very quickly, so any dose that does not inhibit blood ChE after long-term exposure (weeks) is unlikely to get past the blood into the tissues and produce long-term effects on health.

195. In addition to identifying a tolerable dose, an exposure assessment needs to be conducted in parallel to understand how an unprotected individual would accumulate that mass in a contaminated environment.

Decontamination considerations

196. It is important to compare large-scale release scenarios (e.g., those involving the passage of a vapour or aerosol cloud over a wide area) with a situation more akin to the use of nerve agent in Salisbury (where a few individuals interacted with a primary contamination hot spot). In a large-scale release scenario, relatively high contamination densities are expected, comprising drops with a distribution of sizes.

197. When a material is contaminated with CWA, various agent-material interactions and mass transfer processes determine the redistribution of the agent in and on the material. The quantity of agent that strongly interacts with a material is dependent on the physical and chemical properties of both the agent and the material. Typical materials of interest include polymers or paint systems, for which absorption occurs via molecular diffusion. For a decontaminant to remove or neutralise agent from a material, the decontaminant must access the agent from these different distributions.

198. In the Salisbury scenario, contamination was found over a wide area, and at a considerable distance from the initial point of deposition. Effective access controls to a contaminated area are critical in order to minimise the spread of contamination in a large-scale scenario.

199. Related publications on the spread of liquids have shown that it is possible to determine the numbers of hot spots generated by fixed-fraction mass transfer. Understanding the spatial distribution of primary and higher order hot spots is an aspect of "crowd dynamics". Interestingly, recent studies on the spread of saliva containing Sars Cov-2 using similar mass transfer mechanisms has shown that these effects can be quantitatively predicted.

200. For the remediation of contaminated equipment, vehicles, buildings, and infrastructure, it is important to be able to translate the determined acceptable dose (the mass accumulated over a given time period) to acceptable contamination density on a surface (mass per surface area). This calculation determines the technical approach to remediation and informs sampling and analysis strategies, which are needed to provide decision makers with the necessary assurance that identified clearance goals have been met.

Predictive decontamination models

201. Recent research has demonstrated that the development of optimised decontamination procedures delivers significant performance gains, with consequent reduction in the time taken and consumables used to achieve "clean". However, identifying an optimal decontamination approach requires an understanding of a much greater number of physical and chemical factors than traditionally considered, including those relating to the nature of the contamination, the contaminated surface, and the decontaminant itself.

202. In order to understand the relative importance of these factors and how they interact, fluid mechanics and mathematical models need to be developed. Validated models of this type could make it possible to predict the performance of a wide range of commercially available and emerging decontamination products and facilitate the *a priori* development of optimised procedures.

203. Fundamental research on NSCs is needed for the following:

(a) to gain a better understanding of "how clean is clean enough";

(b) to establish the levels of "clean" that can be achieved practically;

(c) to ascertain the required resources (manpower and consumables); and

(d) to determine the risks associated with operating in areas that are not considered to be "clean enough".

Catalysts for decontamination

204. In the drive towards greener and safer processes, catalysts have continued to attract attention as alternatives to the traditional decontamination and destruction methods of incineration, neutralisation, and explosive systems. There has been significant focus on developing catalysts such as enzymes, MOFs, polyoxometalates (POM), nanocatalysts, and polymers, especially for the degradation of OP compounds.

205. Recent work includes the enzymatic degradation of G- and V-series nerve agents, as well as the newly scheduled OP chemicals (1.A.13 to 1.A.15). The hydrolysis rates of the OP NSCs that were tested were determined to be between zero and three orders

of magnitude slower than traditional nerve agents. An enzyme-based filtration device for the hydrolysis of OP compounds has been developed by immobilising *E. coli* cells that express a hydrolytic enzyme into alginate beads. With further development, this device may have an application in remediation.

206. In some cases, low catalytic activity, instability, and reusability can limit the practical application of enzymes. To overcome these issues, enzymes may be immobilised on a suitable support; yet whilst this increases stability, it often also reduces activity. An alternative approach is to immobilise the enzyme on a flower-like hierarchical three-dimensional nanostructure, a "hybrid nanoflower". Enzyme-based hybrid nanoflowers exhibit both increased stability and activity over the free enzyme. Cobalt-manganese multi-metallic phosphotriesterase hybrid nanoflowers used in a pump-flow reactor have been shown to be highly effective in degrading both GB and VX.

207. Advances in synthetic biology and genetic engineering are being leveraged to design enhanced enzymes with optimised performance for CWA degradation. Certain enzymes are much better at degrading specific OP compounds, and genetic engineering may be used to broaden their applicability. Despite these advances, a number of factors—including high purification cost, stability, and storage of enzymes—remain challenging. In contrast, nanozymes—nanomaterials with enzyme-mimetic catalytic activity—are emerging as an effective alternative to enzymes for the degradation of toxic chemicals.

208. MOFs—a type of nanozyme—are porous materials, the extended structure of which consists of organic ligands and inorganic clusters. In addition to being notable for having the highest ratio of surface-area-to-mass of any known material, their tuneable pore size and functionality afford advantages over other porous materials. They are a highly promising class of catalysts for the degradation of toxic chemicals, including CWAs and TICs, and research in this area is gaining traction. The degradation of some OP NSCs with a zirconium-based MOF has been investigated.

209. Whilst possessing a number of key characteristics for effective catalysis, such as tunability, MOFs also have a number of limitations, such as poor selectivity. To overcome this, hybrid approaches are starting to be explored, such as the incorporation of a POM (another type of nanozyme) into a MOF, or the integration of two or more different types of MOFs (MOF-on-MOF). The resultant materials have unique sets of properties with an enriched composition and structural diversity, and their combined performance surpasses that of the individual components alone.

210. Following the trend of data-driven chemistry, computational approaches are being used to understand structure-function-property relationships in MOF catalysis and to elucidate reaction mechanisms. Furthermore, vHTS is being used to identify MOFs of interest for specific applications.

DESTRUCTION OF CHEMICAL WEAPONS

211. In its report to the Second Review Conference, the SAB found that technology relating to the destruction of existing chemical weapons was sufficiently well developed to complete the destruction of declared stockpiles. This finding was reaffirmed in the SAB's reports to the Third and Fourth Review Conferences. As the complete destruction of all declared chemical weapons stockpile draws near, the OPCW will

continue to prevent their re-emergence, but may also focus its expertise on the remaining chemical weapons that exist outside of declared stockpiles, such as those that have been abandoned or dumped at sea. Successful execution of this latter activity would likely require additional tools, as well as greater utilisation of portable destruction facilities.

212. Destroying or isolating sea-dumped chemical weapons has been investigated by multiple stakeholders, with many finding that disturbing otherwise settled munitions presents a greater environmental and human health risk than maintaining the status quo. Even in cases where the location of munitions is known—which is not always the case—it may be impractical to safely recover and destroy those munitions. More research is needed to inform future mapping, assessment, and safe neutralisation. A few innovations in recent years may help alleviate identified problems.

213. One significant development comes from the analysis of benthic microbiomes around ocean dumping sites. Researchers have discovered that some bacteria species are able to utilise sulfur mustard hydrolysis products as a carbon source, while others are suspected to be converting CWAs into novel degradation products. The future direction of these discoveries could involve introducing genetically modified bacteria at dumping sites to accelerate decomposition without disturbing munitions, or locating unmarked dumping sites by searching for the novel degradation products produced by unique microbial communities that populate the seabed around leaking munitions.

214. Unmarked sites and leaking munitions present significant hazards to any potential recovery and destruction activities. Ensuring that those missions—when they are necessary—are safe for those involved is an important concern. Significant advances in robotics have proven to be a highly effective solution for limiting human exposure to hazardous conditions. In this case, robotic submersibles could take the place of human divers in potentially contaminated waters around sea-dumping sites.

215. When humans do have to interact with recovered munitions, minimising the risk of exposure is a key consideration. New developments in personal protective equipment (PPE) and portable destruction solutions can enhance the safety of smaller-scale missions, which will become an ever-greater part of the OPCW's mission in the post-destruction phase. There are also improved tools available to limit the amount of transport necessary for destroying small quantities of CWA, such as those utilised by the United States in the ongoing destruction of its own chemical weapons, as well as in its support of the OPCW's work to destroy the Syrian Arab Republic's chemical weapons. Alternative approaches to on-site destruction are being investigated that would allow for easier degradation and decontamination of contaminated materials other than munitions. The main benefits of these newer methods, such as atmospheric pressure plasma jets and cone spray ionisation, include reduced costs relative to existing explosive destruction chambers and the integration of sensor technologies to confirm the complete destruction of CWAs internally.

CHEMICAL SAFETY AND SECURITY

216. Whilst often considered together, chemical safety and chemical security have key differences and separate definitions. Chemical safety is the practice of using chemical substances in a manner that ensures the safety of human health and prevents damage to the environment. For the chemical industry, it comprises disciplines such as occupational safety, process safety, and transport safety and aims to ensure the safe handling of hazardous chemicals during production and transport. It also includes risk assessments relevant to consumer and environmental safety.

217. Chemical security refers to preventing the misuse of chemicals or chemical infrastructure, such as the diversion of chemicals for terrorist purposes, or malicious attacks on chemical plants. While chemical safety is about protecting people and the environment from chemicals, chemical security focuses on protecting chemicals from people.

218. Both chemical safety and security are highly regulated within the chemical industry. The legal framework for these areas is adjusted continuously, in line with new developments and knowledge in science and technology. Regulations also aim to ensure transparency of existing data, mainly concentrated on chemical safety themes. Besides legal requirements for chemical safety and security, the chemical industry is improving its processes with the objective of becoming more sustainable and energy efficient. Automation and digitalisation therefore play a major role in enhancing chemical safety and security processes.

Chemical security

219. Within chemical security management, several different areas can be considered: enhancement of physical site protection, material control, supply chain protection, and protection of intellectual property, among others.

220. Physical site protection helps prevent the unintended loss of hazardous chemicals. Many chemical companies use modern surveillance technology and have implemented strict access controls. This often extends beyond the production plants and includes other critical areas, such as warehouses.

221. Material control starts with the maintenance of automated systems, which support a transparent chemical inventory to track the purchase, production, use, sale, and disposal of hazardous chemicals. Radio-frequency identification (RFID), a passive data collection technology, is being used increasingly for traceability applications. RFID tags and innovative “smart labels” allow chemicals to be tracked throughout their lifecycle from production to storage, and onwards through the supply chain.

222. Infiltration of supply chains by criminals has triggered the development of a number of intelligent solutions that collect meaningful data to identify and target risks in more resilient supply chains. Based on collated incident information, trucking security databases and global risk maps have been developed. They help identify hot spots, support risk analysis, and determine safe and secure transport routes, thus preventing the theft of hazardous chemicals. The use of these data by trade companies and the police can further enhance supply chain security.

223. In this context of data exchange, blockchain infrastructure is a new technology with a wide range of applications, enabling data integrity with identical data and simultaneous data access in real time for all authorised parties involved along the supply chain. This ensures consistency, transparency, and traceability of data in a legally compliant manner and provides sustainable data quality.

224. Another important aspect of chemical security is the protection of sensitive electronic data, known as cybersecurity. Cybercrime is an increasing risk and is considered to be the highest risk to the chemical industry. Cyber tactics, techniques, and procedures are increasingly being used as weapons by both governments and non-State actors. An increasing landscape of cyber regulations can be observed globally. Companies are investing huge efforts to defend their data and intellectual property, including sensitive technology that can be misused by terrorists to produce hazardous substances. Collaboration between technology partners and companies is essential to keep up with the speed of advanced attackers. Protection approaches include awareness campaigns with employees, permanent software adaptation, and sound digital asset management.

Chemical safety

225. The management and control of chemical safety in the western world is achieved through the implementation of primary legislation, which has continued to become more stringent over the last few years. This has resulted in a strong safety culture in chemical companies with rigorous safety protocols. Many countries with developing or transitional economies are now implementing similar rules and regulations to enhance chemical safety in different areas of relevance.

226. The sound management of chemicals draws heavily on toxicology, ecotoxicology, and the process of chemical risk assessment. An emerging tool in toxicology is the use of so-called “new approach methodologies” to reduce animal testing and replace it with alternative *in vitro* and *in silico* studies. Use of these alternative methodologies in chemical risk evaluations provides a number of benefits (including the generation of increased quantities of more robust data), but their availability and regulatory acceptance remain a bottleneck.

227. The trend towards computational approaches seen in many areas of chemistry has also been observed in hazard identification, with examples of the use of AI in chemical safety assessment recently emerging. Complex computational modelling is being applied to new approach methodologies where high quality input data and human expertise is important in order to achieve a reliable outcome. Furthermore, the manufacturing trend towards automation is also being applied in the chemical industry, enhancing safety by removing the operator from the process and reducing exposure to potentially hazardous chemicals.

228. Industry 4.0—part of the Fourth Industrial Revolution being driven by automation, the Internet of Things, and the use of data analytics—is revolutionising the manufacturing sector and has led to the development of “connected safety”. This enables maintenance workers and operators working remotely in dangerous environments to share data in real time, allowing safety hazards to be identified and quickly addressed. Connected devices include wearable sensors and smart PPE. High resolution cameras ensure that photos of hard-to-reach places in industrial plants can be captured, so that frontline workers can leverage the devices for hands-free verification and visual documentation.

229. Immersive technologies are transforming learning and development across the chemical industry and academia, providing a number of benefits and—importantly—bridging the gap between theoretical knowledge and practical skills. Digital twin technology, virtual reality (VR), and augmented reality (AR) in particular are being used to train plant operators in the chemical industry and are making it possible to simulate hazardous environments and risk scenarios. VR is also being used in academia to educate students about laboratory safety.

230. Education and training are fundamental to raising awareness of and improving chemical safety. Manifold national and international educational programmes already exist. Some are promoted by international organisations and chemical associations, such as the International Programme on Chemical Safety, a collaboration among three United Nations bodies that seeks to establish a scientific basis for the safe use of chemicals and strengthen national capabilities and capacities for chemical safety. The COVID-19 pandemic has also led to an increased availability of e-learning training solutions on chemical safety.

231. Process safety is a vital part of every chemical industry; governments and communities will not allow companies to operate if they pose, or are perceived to pose, a significant risk. Identification of hazards early in the design phase of chemical plants is key to developing a sound concept for process safety. The process hazard assessment includes the elimination, reduction, or mitigation of identified hazards, while applying technical standards and requirements to achieve the safe, reliable, and efficient operation of chemical processes.

Green and sustainable chemistry

232. The application of the principles of green and sustainable chemistry in production is increasing chemical safety. The requirement to comply with increasingly stringent regulations, combined with the emergence of new technologies, is driving the shift towards alternative processes and materials in the chemical industry.

233. The elimination of hazardous raw materials through chemical substitution, one initiative of the cleaner production approach, is being employed more frequently to reduce the risks of chemicals that are harmful to human health and the environment. A variety of methods, software tools, and databases have been developed to facilitate this chemical substitution process. However, their utility is diminished by the lack of available data—especially toxicity data—in chemical databases, and the challenges associated with organising large quantities of data with software tools. There are, nevertheless, promising developments in AI and machine-learning tools that could create alternative approaches to data generation and organisation that could overcome existing challenges.

234. Whilst desirable, chemical substitution is not always a practical or implementable solution. Substitution may affect the quality of the final product, may not be economically viable, or may lead to technical issues during production scale-up. In some cases, it is simply not possible to identify a suitable substitution. For example, the highly toxic Schedule 3 chemical phosgene is used in the manufacture of coatings, adhesives, sealants, elastomers, plastics, a wide variety of pharmaceuticals, agricultural chemicals, and specialty chemical intermediates. It is almost impossible to find appropriate substitutes in each of these applications. In such cases, adequate engineering controls, safety measures, and mitigation strategies must be in place to minimise the risk.

235. When hazardous substances can be safely handled in established large-scale production processes and risks are mitigated, there is often little incentive or benefit to seek out substitutions. This applies to processes involving phosgene and hydrogen cyanide, which are used in closed systems or are produced and consumed *in situ*. Technological advances, such as continuous flow reactors with on-line analysis, are also contributing to improved process control and safety in the chemical industry.

236. Under the cleaner production approach, new low-waste processes and technologies are being developed, and the concept of circular chemistry is also gaining traction. One of the steps in circular chemistry is the collection and use of waste. Using AI, waste-to-valuable-chemicals algorithms such as the Allchemy platform are being leveraged to accelerate the productive reuse of chemicals that would otherwise incur storage or disposal costs, or even pose environmental hazards.

PERSONAL PROTECTIVE EQUIPMENT

237. Available information on the OP NSCs (listed in Schedule 1.A.13 to 1.A.15) indicates that existing PPE is likely to be adequate for providing respiratory and dermal protection against these chemicals when encountered as vapours and small quantities of liquid. The activated carbon adsorbents present in accredited respirator canisters and chemical and biological protective clothing should readily adsorb the vapours associated with these liquids. Likewise, the structural similarity with other OP nerve agents would indicate that their surface tensions are sufficiently high to prevent them from wetting and penetrating air-permeable protective suits treated with an appropriate fluoropolymer finish. Although currently employed adsorbents make for effective barriers against many CWAs, more advanced materials are currently being developed and integrated into PPE that are more effective at inactivating captured CWAs, as well as keeping PPE flexible and comfortable for the wearer.

238. MOFs are a class of well-studied organometallic compounds that can trap and chemically inactivate CWAs. They can be synthesised into a variety of 2D and 3D structures in strands or sheets, making them ideal materials for incorporation into PPE. There is a significant and growing body of work investigating how best to integrate MOFs into PPE. Much of this work is focused on determining which combinations of MOFs provide protection against the broadest spectrum of CWAs, which synthesis routes are most efficient for the production of MOF textiles, and how to make these textiles flexible and durable enough to be suitable for reusable PPE.

239. Recent developments in wearable devices and smart PPE materials have made rapid and selective real-time field identification of chemical agents possible. Leaps in adjacent technologies, such as nanotechnology and flexible computers, have opened new possibilities for wearable sensors designed to protect inspectors in the field, simplify verification activities, and improve chemical safety and security.

240. A particularly popular approach involves incorporating nanosensors into existing safety equipment to produce visual changes that alert the wearer to the presence of specific chemicals in their environment. For example, an enzymatic sensor built into the index finger of a glove allows the wearer to detect the presence of OP agents following sample collection on their thumb by swiping it across a surface. These gloves also incorporate an electronic interface that automatically transmits the results of the “lab-on-a-glove”

test to a wireless device. Similar advances have made it possible to detect a broad range of chemicals, including nerve agents, fentanyl, and potentially other CWAs. Another recent example incorporates a microsensor into safety glasses that, upon interacting with volatile gases in the environment, changes the polarity of light passing through the sensor to produce a vivid hologram visible to the wearer.

241. There are many innovations on the horizon that will shape the capabilities and adoption of wearable sensors in diverse settings. Novel applications of adjacent technologies—including AI—and innovative uses of existing wearable sensors, such as by food workers handling potentially contaminated foodstuffs, are currently outside the scope of this report. It is imperative, however, to continue monitoring how wearable sensors are used in other contexts to inform their future use in support of the Convention.

MEDICAL COUNTERMEASURES

242. In its report to the Fourth Review Conference, the SAB had noted that while efforts continued towards the development of improved medical countermeasures against CWAs, their translation into therapeutic drugs had been slow. The SAB reaffirms this finding.

Newly scheduled chemicals

243. Based on very limited data, it is considered likely that existing medical approaches to the treatment of patients exposed to OP AChE inhibitors are likely to be effective for the chemicals listed in Schedule 1.A.13 to 1.A.15. Both pharmacological therapy and intensive clinical management are likely to be required. In a single case review, pharmacological, antimuscarinic (atropine), and neuroprotective (anaesthetic agents and midazolam) approaches, in combination with intensive medical management, were required over a relatively long period to achieve a successful outcome for the patient. Following nerve agent exposure in the United Kingdom in 2018, media reports of survival in four out of five hospitalised patients also suggest that treatment can be effective, although no details of specific interventions in these cases have yet been published.

244. The treatment of OP poisoning commonly relies on an oxime to reactivate the OP-inhibited AChE. Based on the limited data available for the chemicals listed in Schedule 1.A.13 to 1.A.15, oximes are not expected to be particularly effective. Oxime reactivation of AChE inhibited by a surrogate agent was ineffective and, in the case study above, obidoxime failed to reactivate AChE and was discontinued after one day. Molecular modelling and experimental studies suggest that although oximes are not particularly effective, trimedoxime may be the most effective commercially available oxime for reactivating AChE that has been inhibited by these compounds.

245. The structures of the newly scheduled carbamates (Schedule 1.A.16) differ considerably from the other scheduled OP-based nerve agents. Although information on these nerve agents remains scarce in scientific literature, this structural variance is likely to give rise to different properties, including toxicological effects. More information is required on all NSCs to build a fuller understanding of their properties and enable the development of medical countermeasures, should the current ones prove ineffective.

246. As more relevant information becomes available, it would be prudent for the OPCW to seek assurance that advice on PPE and medical countermeasures remains credible, and to consider the need to conduct a more formal assessment of equipment.

SCIENTIFIC ADVICE AND SCIENCE COMMUNICATION

247. During the establishment of modern industrialised countries from the 19th century to the present date, the emergence of scientific advice—which is interdisciplinary in approach, impartial, and free from political, cultural, economic, ethnic, or religious interests—has been invaluable in the formulation of public policies.

248. Pressing issues and crises of the 21st century, such as climate change, security threats, and the COVID-19 pandemic, have defined the need for policy infrastructures that are evidenced-based, well assessed, constantly reviewed or monitored for effectiveness, and most importantly, developed through reliable scientific advice.

249. Those providing scientific advice need to adapt to rapidly changing political, economic, environmental, and human health conditions. Scientific advisors are adopting new methods to ensure its effectiveness in today's society, such as engaging critical stakeholders from the outset to clearly define boundaries between science, scientific advice, and politics. Multidisciplinary committees of experts have been established in order to guarantee the quality of advice in tackling emerging issues, and the comprehensive and rigorous synthesis of evidence-based scientific advice has been promoted.

250. Scientists need to be viewed as reputable and objective to earn the trust of the community. Scientific advice needs to be transparent, not only in terms of presenting evidence, but also in terms of its limitations, to sustain public trust, and to ensure a sustainable relationship between scientific advice and policymaking. The pandemic has cemented the international dimension of scientific advice and made it a global endeavour. However, at the same time, it has highlighted how scientific advice must compete against political self-interest, ideologies, well organised lobby groups, national agendas, and political bargaining. Political dissent between nations may also lead to a gap or a bias in the dissemination of knowledge and information, as well as the transfer of scientific advice.

251. Gender balance and cultural diversity is critical. Any chosen group of experts needs to be culturally diverse and maintain gender balance. Specific studies have shown that diversity leads to better science and contributes to the robustness of scientific advice. Cultural diversity enhances sensitivity in addressing issues and lessens suspicions and alienation among groups.

252. Most recently, the global societal disruption caused by the COVID-19 pandemic has put scientific advice to the test, and a number of different scientific expert advisory groups emerged to deal with specific aspects of the health emergency. Governments have turned to scientists to seek guidance in managing the pandemic, and the public has demanded that experts explain the basis for implemented policies.

253. Scientific literacy for the public and the non-scientific community does not mean acquiring a certain degree of knowledge, skills, and ability for each person. It means that there is sufficient shared information that is organised and distributed according to the abilities of the community members to effectively contribute to addressing problems and arrive at decisions.

254. Scientific diplomacy makes use of scientific cooperation not only to address global problems of the 21st century, but also to improve international relations. It hinges on the value of science and its practitioners as peacebuilding instruments. In scientific diplomacy, science is the impartial and neutral common language, free of ideological leanings used to mitigate political differences among nations, particularly in strained relations or non-existent diplomatic ties. Merit, openness, and sharing, which are common values among scientists, are expected to improve international exchanges through scientific diplomacy. However, there is also a need to examine the effectiveness of scientific diplomacy, and to develop a framework for evaluating its usefulness in improving international relations.

Social media and scientific advice

255. Given its popularity among the younger populations, social media may be leveraged as a tool for scientific literacy. It is therefore important that scientists both learn and teach how to use social media accurately and effectively for scientific communication. Easy access and use make these forms of media an important tool for communicating scientific advice. However, it is also an avenue for the possible spread of misinformation or disinformation (i.e., “fake news”). Sharing unvetted information and even direct distortion of the truth can be damaging. Misinformation could also potentially pose serious harm to society, as seen during the recent COVID-19 pandemic.

256. Microtargeted and biased information is an increasing risk dominating social media, especially when (pseudo)scientific contents are arbitrarily selected and prioritised algorithmically according to audience demographics, an abundance of digital trace data, or other consumer information.

Ethics and peer review

257. Ethical conduct in science should not be overlooked. Morality and ethics should be an integral part of education in science from elementary school to college level education. This will serve as a good foundation for the scientific policy interface, which requires an informed decision-making process.

258. The scientific review process is a means to ensure that scientific outputs meet standards of rigour, reproducibility, and integrity. Peer-reviewed publications are essential in policy decision making to ensure that relevant and accurate information is provided when crafting policy or addressing societal issues. It is important to communicate the limitations of research and results, including opposing views. These limitations should be clear and well presented to the public and/or policymakers, to ensure the most acceptable solution for an issue.

259. The peer review process has some drawbacks, such as the timeframe required for review and possible bias of the editors or reviewers. Use of the electronic peer review process has reduced the duration of review processes, but has also led to an explosion of electronic journals, which may not have stringent peer review processes or adhere to adequate scientific standards. In some fields, a double-blind review is considered a more ethical approach to the review process itself. At present, peer review is moving towards open review, where the reader can comment on an article post publication.

260. The continuous expansion of poor-quality, for-profit journals (so-called "predatory journals") poses further risk to the international scientific community, especially among inexperienced or opportunistic scientists who see these publishers as a shortcut to rapid and easy publications. The presence of such unreliable scientific literature may pose a problem for non-expert stakeholders and decision makers, who are often not able to judge the trustworthiness of published scientific evidence. They may base their decision on false, fabricated, or unethical data.

261. A recent trend is the rapid growth of the use of preprints as a first step in the circulation of scientific results. Preprints allow researchers to make their findings publicly available when they consider them ready for dissemination, without a formal peer-review process. The utility of such an approach has been highlighted during the recent pandemic for rapidly sharing data and research results on COVID-19. However, this led to an immediate and often acritical acceptance of such results as a source of trustworthy scientific evidence. There are, however, doubts about the value of preprints, especially in the biomedical sciences.

262. There is still a crucial need to have better mechanisms for solid science published in journals to be summarised and translated to the general public, media, policymakers, and others who frame public and policy debates. Without such work, good science can be overwhelmed by more media-friendly and social-media friendly anti-science and pseudoscience.

Science education and outreach

263. Science education and outreach (SEO) is defined as "informal science education", which occurs outside of the formal university or school curriculum setting. It overlaps with science communication, which describes various methods used to effectively transmit scientific knowledge, methods, and research in a manner that is accessible, understandable, useful, and even interesting to a non-expert audience. The goal is not only to inform, but to elicit a response to influence beliefs, behaviours, and most importantly, policies. It can inspire students to pursue a career in science, and the public to take interest about a scientific topic of concern. There are a number of SEO models being successfully applied.

264. Several studies have shown that SEO aimed at the very young can lead to important milestones in scientific education. These include an improved attitude towards science, an increase in the number of students taking science majors in college or choosing science as a career path, an improvement in scientific metacognition, and enhanced scientific literacy needed in policy and decision making. Effective platforms involve hands-on activities, gamification, and visually appealing presentations.

265. The COVID-19 pandemic emphasised the importance of online and remote learning and education. The development of learning management systems, e-learning materials, and assessment platforms became essential to continue learning in a time of crisis. Use of these modalities will clearly continue in the "new normal", assuming that the digital divide is addressed, and that the need for young people to socialise is considered.

266. Virtual learning tools save time, decrease necessary travel, provide ease of access, and are generally considered environmentally friendly. New technology such as hardware for hyflex learning (for example, owl labs) will enable blended or flexible learning modes. The use of AR, VR, and simulation software in learning (e.g., Labster) will be helpful in classes that require hands-on experience. These are also considered more sustainable and economically viable, as they remove the need for chemical reagents, living samples, and other materials and equipment. Nevertheless, a balanced approach to virtual learning should be followed, as it might find limited or ineffective application in teaching and training activities where highly practical skills and technical know-how have to be transferred.

267. The current activities of the OPCW include e-learning modules, websites with interactive resources, and videos and documentaries pertaining to the Convention. There are also training courses on disarmament and non-proliferation, and yearly activities involving films, history lessons, and art sessions.

ACKNOWLEDGEMENTS

268. The SAB thanks the States Parties for their sustained support throughout the science and technology review process and for their attendance at Science for Diplomats sessions. It also thanks the SAB Chairperson and Vice-Chairperson for their briefings over the last five years. The SAB wishes to thank the Director-General, Ambassador Fernando Arias, for his continued support, encouragement, and promotion of the Board's scientific work.

Annex 2

ABBREVIATIONS

TABLE 1: GENERAL ABBREVIATIONS

ABBREVIATION	DEFINITION
ABEO	Advisory Board on Education and Outreach
AI	Artificial intelligence
AM	Additive manufacturing
AR	Augmented reality
CBRN	Chemical, biological, radiological, and nuclear
ChemTech Centre	Centre for Chemistry and Technology
CFPS	Cell-free protein synthesis
CNS	Central nervous system
CWA	Chemical warfare agent
DBS	Dried blood spot
DL	Designated laboratory
ELISA	Enzyme-linked immunosorbent assay
EU	European Union
GC	Gas chromatography
GC-HRMS	Gas chromatography-high resolution mass spectrometry
GC-MS	Gas chromatography-mass spectrometry
GC-MS/MS	Gas chromatography-tandem mass spectrometry
HAS	Human serum albumin
HPLC	High performance liquid chromatography
HRMS	High resolution mass spectrometry
IC	Ionic chromatography
IMER	Immobilised enzyme reactor
IMS	Ion mobility spectrometry
INTERPOL	International Criminal Police Organization
IRMS	Isotope-ratio mass spectrometry
IUPAC	International Union of Pure and Applied Chemistry
LC-ESI-MS/MS	Liquid chromatography electrospray ionisation tandem mass spectrometry
LC-HRMS	Liquid chromatography-high resolution mass spectrometry
LC-MS	Liquid chromatography-mass spectrometry
LC-MS/HRMS	Liquid chromatography with tandem mass spectrometry experiments performed by low resolution isolation of ions of interest followed by high resolution analysis of those ions
LC-MS/MS	Liquid chromatography-tandem mass spectrometry
LC-Q-Orbitrap	Liquid chromatography hyphenated with quadrupole-Orbitrap mass spectrometry

ABBREVIATION	DEFINITION
LC-QTOF	Liquid chromatography hyphenated with quadrupole-time of flight mass spectrometry
MALDI-TOF	Matrix-assisted laser desorption/ionisation-time of flight
MOF	Metal-organic framework
MS	Mass spectrometry
MS/HRMS	Mass spectrometry/high resolution mass spectrometry
MS/MS	Tandem mass spectrometry at low resolution
MS-IMS	Mass spectrometry-ion mobility spectrometry
MTCR	Missile Technology Control Regime
NMR	Nuclear magnetic resonance
NSC	Newly scheduled chemical
OCAD	OPCW Central Analytical Database
OEL	Occupational exposure limits
OPCW	Organisation for the Prohibition of Chemical Weapons
OR	Olfactory receptor
PAGE	Polyacrylamide gel electrophoresis
PCR	Polymerase chain reaction
PPE	Personal protective equipment
PSIA-NMR	Position specific isotope analysis-nuclear magnetic resonance
PS-MS	Paper spray-mass spectrometry
RCA	Riot control agent
RFID	Radio-frequency identification
R/SOP	Recommended standard operating procedures
SAB	Scientific Advisory Board
SEO	Science education and outreach
TIC	Toxic industrial chemical
TWG	Temporary working group
UAV	Unmanned aerial vehicle
UGV	Unmanned ground vehicle
UNSGM	United Nations Secretary-General's Mechanism (for Investigation of Alleged Use of Chemical and Biological Weapons)
vHTS	Virtual high-throughput screening
VR	Virtual reality

TABLE 2: CHEMICALS

ABBREVIATION	DEFINITION
A230	Open-source publications indicate this is the abbreviated name given to the Schedule 1.A.13 chemical methyl-(1-(diethylamino)ethylidene)phosphonamidofluoridate
A234	Open-source publications indicate this is the abbreviated name given to the Schedule 1.A.14 chemical ethyl (1-(diethylamino)ethylidene)phosphoramidofluoridate
AChE	Acetylcholinesterase
AMP	Alkyl methylphosphonate
BChE	Butyrylcholinesterase
BChE-OP	Butyrylcholinesterase-organophosphate
ChE	Cholinesterase
Cl_2	Chlorine
CO	Carbon monoxide
CO_2	Carbon dioxide
DC	Methylphosphonic dichloride
DMMP	Dimethyl methylphosphonate
DNA	Deoxyribonucleic acid
GB	Sarin
GF	Cyclosarin
H_2O_2	Hydrogen peroxide
H_2S	Hydrogen sulfide
HF	Hydrogen fluoride
HN1	Nitrogen mustard 1
HN2	Nitrogen mustard 2
HN3	Nitrogen mustard 3
KF	Potassium fluoride
MPA	Methylphosphonic acid
NH_3	Ammonia
NO	Nitric oxide
NO_2	Nitrogen dioxide
O_2	Oxygen
OH	Hydroxyl group
OP	Organophosphate
POM	Polyoxometalate
RNA	Ribonucleic acid
SO_2	Sulfur dioxide
TCP	Trichlorophenol
TeCP	Tetrachlorophenol
VX	A V-series nerve agent

TABLE 3: UNITS OF MEASURE

ABBREVIATION	DEFINITION
Da	Dalton
kg	Kilogram
L	Litre
μg/mL	Microgram per millilitre
μL	Microlitre
μm	Micrometre
mm	Millimetre
ng/mL	Nanogram per millilitre
pg/mL	Picogram per millilitre
pH	A measure of the acidity or alkalinity of a substance

- - - o - - -