



**REPORT OF THE SCIENTIFIC ADVISORY BOARD
AT ITS THIRTIETH SESSION
10 – 12 NOVEMBER 2020**

1. AGENDA ITEM ONE – Opening of the session

1.1 The Scientific Advisory Board (SAB) met virtually for its Thirtieth Session from 10 to 12 November 2020 via the Microsoft Teams platform. The session was chaired by Dr Christophe Curty, with Dr Zrinka Kovarik serving as Vice-Chairperson.

Executive summary

1.2 Due to the current coronavirus (COVID-19) pandemic, this SAB meeting was held and conducted entirely in a virtual format.

1.3 The SAB received ten presentations from seven invited external speakers, three OPCW staff members, and three current SAB members on topics that included new tools to strengthen verification capabilities, approaches to improving laboratory synthesis and industrial production of chemicals, and methods used to treat the victims of chemical weapons, as well as an update on and discussion of the activities of the SAB and the Advisory Board on Education and Outreach (ABEO).

1.4 Based on the deliberations at its Thirtieth Session, the Board recommends to the Director-General that:

- (a) the SAB hold a workshop in partnership with the Technical Secretariat (hereinafter “the Secretariat”) and the chemical industry to discuss several topics of mutual interest, such as the toxicities of chemicals, chemical decontamination and waste procedures, and chemical risk assessments and their utility in managing chemical inventories (see agenda item 11(a));
- (b) the Secretariat convene a workshop to discuss the most recent scientific and technological achievements countering the newly listed chemicals regarding detection, identification, decontamination, and medical countermeasures (see agenda item 8); and
- (c) the Secretariat evaluate the possible utility of a new technique that was described for detecting human chlorine exposure (see agenda item 8(a)).



2. AGENDA ITEM TWO – Adoption of the agenda

The SAB adopted the following agenda for its Thirtieth Session:¹

1. Opening of the session
2. Adoption of the agenda
3. *Tour de table*
4. Establishment of a drafting committee
5. Welcome address by the Director-General
6. Overview of developments at the OPCW since the last session of the Scientific Advisory Board
7. OPCW projects and presentations
 - (a) OPCW Laboratory 2020 updates
 - (b) Project 22: Creation of a dedicated chemical database
 - (c) Distributed ledger technology and its possible application to international trade in chemicals scheduled under the Chemical Weapons Convention
8. Effects of toxic chemicals on living organisms and the forensic applications thereof
 - (a) The potential of Raman and FT-IR spectroscopic methods for the detection of chlorine exposure in human nail samples
 - (b) Therapeutic options against acute carbamate poisoning
 - (c) Development of novel bioindicators for the detection of arsenic contaminants in aquatic environments: Insight from one of Canada's most contaminated sites
9. Advances and considerations in chemical industry
 - (a) Artificial intelligence for automated chemical synthesis
 - (b) Insight into actual pharmaceutical production requirements
10. Statement on behalf of the OPCW Advisory Board on Education and Outreach

¹ It should be noted that while presentations and agenda items are grouped in this report based on topic matter, they were not always presented sequentially as listed due to scheduling considerations of the presenters.

11. Current and future activities of the Scientific Advisory Board
 - (a) Industry focus: Brainstorming session
 - (b) Current and upcoming Scientific Advisory Board meetings and commitments
 - (c) Election of the Chairperson and Vice-Chairperson of the Scientific Advisory Board
12. Any other business
13. Adoption of the report
14. Closure of the session

3. AGENDA ITEM THREE – *Tour de table*

An opportunity was given for SAB members to take the floor should they wish, but an introduction by each member was deemed unnecessary given the recent Twenty-Ninth Session and the lack of change in SAB membership in the interim.

4. AGENDA ITEM FOUR – Establishment of a drafting committee

The SAB established a drafting committee to prepare the report of its Thirtieth Session.

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

- 5.1 The Director-General of the OPCW delivered a welcome address. He began by conveying his well wishes and appreciation to the Board for their efforts during the pandemic. He then highlighted the Secretariat's assistance to Germany in the case of Mr Alexei Navalny and its continued support to all States Parties in addressing the matter. He noted that the analysis of biomedical samples from Mr Navalny by designated labs indicated the presence of biomarkers of a cholinesterase inhibitor that, while similar in structure to recently scheduled chemicals, is not in the Annex of Chemicals to the Chemical Weapons Convention (hereinafter "the Convention"). The Director-General also updated the Board on the recent discussions by States Parties at the Ninety-Fifth Session of the Executive Council (hereinafter "the Council") on central nervous system-acting chemicals (CNS-acting chemicals). He then noted that the Open-Ended Working Group on Terrorism convened recently, and that the threat from non-State actors remains a matter of priority for the Secretariat. He reminded the Board that their recent scientific advice on the aforementioned topics has been valuable and that they may be called upon to provide further advice.

- 5.2 The Director-General then announced that he is establishing a new temporary working group (TWG) on the analysis of biotoxins, an area that requires further research and analysis in light of recent technological developments. He mentioned that he will work closely with the SAB Chairperson to develop the new TWG's terms of reference and select its members. He also remarked on the Secretariat's focus on determining its needs in terms of forensics, noting there will be an internal workshop on the matter in the near future.

5.3 The Director-General then took a few minutes to update the SAB on the progress of the project for the Centre for Chemistry and Technology (ChemTech Centre), highlighting some of the recent developments on its design and construction. He welcomed the SAB's ideas on future science and capacity-building projects at the Centre. He concluded by congratulating the SAB on their efforts and wishing them a productive session.

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

6.1 The Secretariat's Senior Science Policy Officer and Secretary to the SAB briefed the Board on developments at the OPCW since the SAB's Twenty-Ninth Session.

6.2 The SAB Secretary first highlighted news relevant to the SAB that had occurred in the period since its Twenty-Ninth Session, including the case of Mr Alexei Navalny and the recent discussion on CNS-acting chemicals that took place at the Ninety-Fifth Session of the Council. He also spoke of the ongoing work the Secretariat is conducting in relation to Syria. The Declaration Assessment Team (DAT), the Fact-Finding Mission (FFM), and the Investigation and Identification Team (IIT) are still conducting their work and publishing reports detailing their respective findings.²

6.3 The focus then shifted to recent events directly impacting Board members. The SAB Secretary congratulated a number of Board members on their recent appointments to various committees, their involvement in different OPCW capacity-building events, and the general success in scientific engagement that Board members have achieved throughout 2020.

6.4 Of particular importance, the SAB Secretary discussed a recent experience that one Board member had in relation to being asked to comment to the media on the Navalny case. The Board member duly contacted the OPCW to seek guidance. The guidance provided was that the individual was welcome to comment to the media about any matter in their own personal capacity or in the capacity of their employer, but should not speak as a member of the SAB. The Secretary reminded the Board of their obligations as members of the SAB,³ and advised that should they ever be contacted by the media on a matter concerning chemical weapons, the OPCW, or the SAB, they are welcome to contact the Secretariat for guidance.

² See: (a) "Note by the Technical Secretariat: Report of the OPCW Fact-Finding Mission in Syria Regarding the Incident of Alleged Use of Chemicals as a Weapon in Saraqib, Syrian Arab Republic, on 1 August 2016" (S/1901/2020, dated 1 October 2020); (b) "Note by the Technical Secretariat: Report of the OPCW Fact-Finding Mission in Syria Regarding the Incident in Aleppo, Syrian Arab Republic on 24 November 2018" (S/1902/2020, dated 1 October 2020); and (c) "Opening Statement by the Director-General to the Ninety-Fifth Session of the Executive Council" (EC-95/DG.29, dated 6 October 2020).

³ The SAB Terms of Reference can be found at: https://www.opcw.org/sites/default/files/documents/SAB/en/SAB_ToR_RoP.pdf.

7. AGENDA ITEM SEVEN – OPCW projects and presentations

- 7.1 It is important that the SAB periodically receives updates on internal scientific and technical projects and developments, not only to ensure that the SAB remains informed, but also for the benefit of having the SAB provide their input on or bring their attention to these projects. Accordingly, the Board received a presentation from the Head of the OPCW Laboratory on their recent and ongoing activities and was also briefed by Secretariat staff members on several internal projects of potential interest.

Subitem 7(a): OPCW Laboratory 2020 updates

- 7.2 Dr Hoe Chee Chua, Head of the OPCW Laboratory, apprised the Board of recent events of note. The OPCW Laboratory conducted the Forty-Seventh Proficiency Test from April to August 2020. The test was concluded successfully, and the OPCW now has a network of 21 laboratories from 18 Member States in the OPCW's designated laboratory (DL) network for environmental sample analysis. Twelve of these laboratories from 12 States Parties have signed technical agreements and are available to analyse authentic environmental samples. The OPCW is currently actively engaged with DLs to increase the number of laboratories with technical agreements. The Forty-Eighth Proficiency Test for the analysis of environmental samples is currently under way. The OPCW Laboratory faced shipment challenges due to the situation resulting from the COVID-19 pandemic, which caused delays of sample shipments up to two weeks for some participants.
- 7.3 The OPCW Laboratory conducted the Fifth Biomedical Proficiency Test from February to September 2020. The test was concluded successfully, and the OPCW now has a network of 18 DLs from 13 States Parties. Ten laboratories from ten States Parties have signed technical agreements and are able to conduct off-site analysis of authentic biomedical samples. The OPCW Laboratory has also conducted four biotoxin confidence-building exercises, each with approximately 25 participants. The OPCW biotoxin network has established robust reporting criteria from past exercises.
- 7.4 The OPCW Laboratory is currently developing the electronic laboratory management system to enhance laboratory tracking activities. This system will also overcome the knowledge transfer gaps that might occur when personnel leave the laboratory.
- 7.5 After the presentation, there was discussion on how to best incentivise, and perhaps even reward, DLs for their participation and efforts moving forward. The Head of the Laboratory noted that sometimes the technical agreement negotiation process between the OPCW and different DLs can be long and onerous, and stated that some of these issues should be brought up at the next DL working group meeting. The Board also asked whether the Laboratory is considering adapting the proficiency tests in light of the changing requirements and the Secretariat's needs for real sample analysis. The Head of the Laboratory noted that this is not so straightforward, but that they are looking to brainstorm with DLs to understand how progress could be made on this front. She concluded by saying that the OPCW Laboratory plans to hold a workshop with DLs to identify current gaps and propose ways forward to address them in the first quarter of 2021. Many of the Board's questions and suggestions will be incorporated into this workshop.

Subitem 7(b): Project 22: Creation of a dedicated chemical database

- 7.6 Mr Oliver Allard from the OPCW Inspectorate Division delivered a brief on Project 22, an ongoing OPCW project related to the chemistry of chemical warfare agents. It is designed to assist OPCW inspectors in Article VI (i.e., industry) inspections. The project is essentially the development of a tool containing two lists that are linked together. One list contains all the scheduled chemicals and relevant non-scheduled chemicals that are direct precursors of Schedule 1, 2, or 3 chemicals. Each chemical on this list is registered with around 30 aspects of data, if available (e.g., molecular weight, boiling point, MOL file, presence in other control lists such as at the Australia Group, HS code, etc.). The second list contains all the possible recipes and chemical pathways for the synthesis of Schedule 1, 2, and 3 chemicals from various open sources.
- 7.7 Inspectors will be able to use the tool when performing Article VI inspections to help them better understand the chemistry of chemical warfare agents and sourcing dual-use chemicals. Project 22 could also support first responder activities, and may be useful to States Parties, as it can potentially be used by their customs officials, for example.
- 7.8 Mr Allard noted that Project 22 takes into account several recommendations from previous SAB activities,⁴ and welcomes additional feedback and comments on the project. The Board asked whether the lists of chemical and synthetic pathways will be expanded to include other threat materials, such as explosives, for example. Mr Allard explained that while it would be both possible and interesting, it is outside the mandate of the project and the scope of the Convention. The Board also asked whether the tool will have any artificial intelligence (AI) aspect to it. For various reasons, Mr Allard explained, the tool will not be intelligent in nature—just a searchable database.

Subitem 7(c): Distributed ledger technology and its possible application to international trade in chemicals scheduled under the Chemical Weapons Convention

- 7.9 Mr Alejandro Hernandez, Head of Data Analytics, Reporting, and Quality Control within the Verification Division of the OPCW, gave a presentation to the Board on distributed ledger technology (DLT) and its possible application in relation to the international trade of scheduled chemicals. DLT-specific features such as hashing and distributed storage of information make this technology reliable, immutable, transparent, and trustworthy. A DLT-based application can be used to register individual international transfers of scheduled chemicals. Each transfer and its details can be confirmed by the recipient of the chemicals. This would allow early identification of discrepancies by trading entities and National Authorities. In addition, GPS tracking and timestamping would increase confidence that chemicals are not diverted for nefarious activities.
- 7.10 Mr Hernandez noted that the Secretariat is planning the execution of a proof of concept to confirm the aforementioned benefits of this technology. The proof of concept will require the voluntary participation of National Authorities and their chemical trading

⁴ “Report of the Scientific Advisory Board on Developments in Science and Technology for the Third Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention” (RC-3/DG.1, dated 29 October 2012).

entities. One Board member commended this approach to addressing transfer discrepancies and asked how the confidentiality of the data would be ensured in a DLT-based system. Mr Hernandez noted that there are access control options to ensure that only certain States Parties, or certain companies or entities, have access to the system, and further noted that the data within can be compartmentalised to protect privacy. The Board was very supportive of this initiative and looks forward to hearing about its progress.

8. AGENDA ITEM EIGHT – Effects of toxic chemicals on living organisms and the forensic applications thereof

- 8.1 Given the resurgence of the use of chemical weapons over the past ten years, the Secretariat has focused more on forensics and investigative science in order to be prepared to assist States Parties and conduct its own investigations into incidents of the alleged use of chemical weapons. The Secretariat is thus ensuring it stays up to date on new approaches and techniques in this area. The recent addition of some extremely toxic chemicals to Schedule 1 and the actual use of a chemical with similar structural characteristics as the toxic chemicals listed on schedules 1.A.14 and 1.A.15 raise new issues. The Secretariat and States Parties need practical information on the detection, identification, and decontamination of, as well as the medical countermeasures against, such chemicals. A workshop to compile and discuss best practices in these areas is recommended. In addition to assisting the Secretariat and States Parties, this will make it possible to update the OPCW’s “Practical Guide for Medical Management of Chemical Warfare Casualties”.⁵

Subitem 8(a): The potential of Raman and FT-IR spectroscopic methods for the detection of chlorine exposure in human nail samples

- 8.2 Dr Sadik Toprak of Istanbul University shared his research—partially funded by the OPCW—on using Raman and FT-IR spectroscopic methods to detect chlorine exposure in human nail samples.⁶ Explaining the rationale behind his research, he noted that it can often be extremely difficult to diagnose chlorine exposure, as chlorine is a reactive gas that dissipates quickly into the environment. There are instances when it is impossible for the authorities to reach a crime scene promptly, and more often than not, exposed corpses are discovered after long periods of time, leading to difficulties in the detection of chlorine content.
- 8.3 Raman and FT-IR spectroscopic methods can give inexpensive, fast results. Moreover, sample preparation is not necessary, and the analytical methods are non-destructive. Over the course of nine months, Dr Toprak’s research team conducted experiments on two nail samples taken from 55 male and 104 female volunteers. One sample from each participant was chlorinated, while the second sample was used as a control. His team then developed partial least squares regression-discriminant analysis techniques in order to differentiate between chlorinated and control-group nail samples with up to 95 – 97% total accuracy.

⁵ The Guide can be found at the following link: <https://www.opcw.org/resources/assistance-and-protection/practical-guide-medical-management-chemical-warfare-casualties>.

⁶ Toprak, S., Kahrıman, F., et al. “The Potential of Raman and FT-IR Spectroscopic Methods for the Detection of Chlorine in Human Nail Samples”, Forensic Science, Medicine, and Pathology, September 2020.

- 8.4 While the research is interesting in its potential applications, more work needs to be done. Dr Toprak explained that in addition to the fact that current methods are not able to differentiate by gender, the dose of chlorine used in the study was much higher than what would be encountered in real-life scenarios. That being said, now that the appropriate methods have been developed and substantiated, Dr Toprak's team are continuing their research using lower doses. These results should hopefully be published soon.
- 8.5 The Board was keen to discuss Dr Toprak's presentation with him, due to the numerous reported cases of chlorine used as a chemical weapon in recent years and the challenges encountered in investigating these allegations.⁷ In response to one of the questions raised concerning the length of time between chlorine exposure and analysis, Dr Toprak indicated that it was several weeks. Additionally, Board members were curious as to whether portable spectrometers could be used, to which the response was "yes", although of course the sensitivity and accuracy of the spectrometer would be important factors. Board members were also curious as to why hair samples were not taken and analysed in order to understand the possible observable markers of chlorine exposure. Dr Toprak explained that they started with nails in order to have a more focused study, and because nails do not require intensive sample preparation. Now that the initial results have been obtained, Dr Toprak's team are expanding their research and indeed looking at hair as well.

Subitem 8(b): Therapeutic options against acute carbamate poisoning

- 8.6 Dr Miloš Stojiljković, from the University of Banja Luka (Bosnia and Herzegovina), presented his team's work on the toxicology of carbamates to the SAB.⁸ Poisoning by carbamates, along with poisoning by organophosphates, present a treatment challenge. Based on data available in literature, atropine and other muscarinic receptor antagonists afford better protection against carbamates than against organophosphates when administered as a therapy. However, while most oximes are a beneficial addition to atropine in the case of organophosphates, this is not necessarily true when it comes to carbamates. In fact, clinical case reports and several experiments in rats have shown that the use of pralidoxime (2-PAM) actually increases the toxicity of carbaryl, a carbamate insecticide. However, some published clinical studies indicate that nicotinic receptor-mediated signs of poisoning also occur in victims of carbamate and organophosphate intoxications. Previous results published in literature led his team to look into anti-nicotinic drugs as an adjunct to atropine in carbamate poisoning.
- 8.7 Two carbamates—physostigmine and pyridostigmine—were chosen for this experimental study, both of which have been extensively investigated as potential prophylactic antidotes against poisonings with nerve agents such as tabun, sarin, soman, and VX. Physostigmine contains tertiary nitrogen and is therefore lipophilic,

⁷ Examples include: (a) "First Report by the OPCW Investigation and Identification Team pursuant to Paragraph 10 of Decision C-SS-4/DEC.3 'Addressing the Threat from Chemical Weapons Use', Ltamenah (Syrian Arab Republic) 24, 25, and 30 March 2017" (S/1867/2020, dated 8 April 2020); and (b) Markus K. Binder, Jillian M. Quigley, Herbert F. Tinsley "Islamic State Chemical Weapons: A Case Contained by its Context?" *CTC Sentinel*, Volume 11, Issue 3, March 2018.

⁸ Miloš P. Stojiljković, Ranko Škrbić, et al. "Efficacy of antidotes and their combinations in the treatment of acute carbamate poisoning in rats," *Toxicology*, volume 408, 2018, pages 113-124.

which enables it to penetrate the blood-brain barrier and enter the brain, while pyridostigmine contains a quaternary nitrogen and is therefore deprived of access to the central nervous system and limited to peripheral tissues only.

- 8.8 The concept of the study was to test three doses of each of the four antidotes—atropine, hexamethonium, d-tubocurarine, and HI-6—as therapies and in combinations (one of the components was always atropine, while the other component was alternated among the three remaining antidotes). Protective ratios were determined as a therapeutic value of each antidote or combination of antidotes.
- 8.9 All antidote monotherapies and their combinations were efficient in both physostigmine- and pyridostigmine-induced intoxications. Atropine and hexamethonium (which, in high doses, also enters the brain to some extent) were very effective in rats poisoned with physostigmine, while d-tubocurarine and HI-6—as compounds mostly limited to the peripheral tissues—afforded the best protection against pyridostigmine, an equally peripherally active carbamate. It was concluded that the success of various antidotes depends on the properties of the carbamate in question, such as its access (or lack thereof) to the brain, interactions with acetylcholinesterase (described as carbamylation and decarbamylation rates), and the dose and route of administration.
- 8.10 The Board asked Dr Stojiljković what type of treatment would be recommended if an individual were exposed to the class of carbamates recently added to Schedule 1 of the Annex on Chemicals to the Convention. Upon briefly examining the structure shown by the SAB Secretary, he suggested that these compounds are leaning towards being lipophobic, mainly due to the presence of the quaternary nitrogen moiety, and so they should not penetrate the blood-brain barrier as observed with pyridostigmine. Dr Stojiljković noted that what could be beneficial in this case is the use of oximes, and possibly neuromuscular blockers. The discussion that followed also focused on potential future areas of research; several members of the Board indicated that they would be interested in collaborating with Dr Stojiljković, and vice versa.

Subitem 8(c): Development of novel bioindicators for the detection of arsenic contaminants in aquatic environments: Insight from one of Canada’s most contaminated sites

- 8.11 Dr Jennifer Galloway, from Natural Resources Canada, and Dr Nawaf Nasser, from Carleton University, presented their team’s work on the potential for using bioindicators to detect arsenic contaminants.⁹ Environmental monitoring programmes often use direct geochemical measurements to track spatial and temporal changes in the concentration of contaminants in aquatic environments. While useful, this direct approach can only provide information on environmental conditions and contamination levels at the time of sample collection, and cannot account for any post-depositional mobility of redox sensitive elements such as arsenic, the behaviour of which can lead

⁹ See: (a) Nasser, Nawaf, Patterson, R. et al. (2016). “Lacustrine Arcellinina (Testate Amoebae) as Bioindicators of Arsenic Contamination”. *Microbial Ecology*, 72, (2016); and (b) Miller, Clare, Parsons, Michael et al. “Impact of Climate Warming on the Speciation and Long-Term Stability of Arsenic in Sub-Arctic Lakes: Implications for Environmental Monitoring of Mine Sites”, presented at Goldschmidt 2019, (2019)

to significant surface enrichment in the uppermost sediments. This type of approach also fails to evaluate factors influencing the mobility of elements in the natural environment.

- 8.12 Biological proxies (i.e., bioindicators) have the potential to be robust tools for monitoring contamination, as they can reflect the ecological impact of contamination and provide a time-averaged signal of environmental conditions. Arcellinida, a group of shelled protozoans that live in fresh and brackish aquatic habitats, have been successfully used as sensitive bioindicators of anthropogenically derived heavy metal contamination.
- 8.13 Foraminifera, a group of shelled microscopic protozoans, and the marine relatives of Arcellinida, have also been used for decades as environmental bioindicators of contamination (e.g., Murray, 2006). Their value as bioindicators is derived from their ubiquitous distribution and their decay-resistant shells, which allow them to preserve well in the sedimentary record and respond to environmental contamination spatially (the relative proximity to a point source) and temporally (Yanko et al. 1999). These organisms have been shown to exhibit sensitivity to arsenic contamination, which impacts their overall abundance and species diversity, shell chemistry, and shell morphology (e.g., Alve, 1995; Smith and Goldstein, 2019).
- 8.14 Materials collected from known chemical munition dump sites in the Baltic Sea and control locations by the MODUM, DAIMON, and CHEMSEA projects show that in the majority of sediment samples, the degradation products of arsenic-bearing chemical munitions are detectable. These samples present an opportunity to evaluate the role of organic matter in arsenic mobility and fate in this northern environment contaminated by chemical munitions, and to test the efficacy of foraminifera as a bioindicator of sedimentary arsenic in areas surrounding the dump sites.
- 8.15 The Board posed a number of questions to Drs Galloway and Nasser. Industrial arsenic contamination has a timeline similar to that of chemical weapons that were dumped or abandoned after WWII. Therefore, the methodologies that were presented may be considered a tool to track and localise arsenic contamination resulting from abandoned or dumped chemical ammunition containing arsenic compounds.

9. AGENDA ITEM NINE – Advances and considerations in chemical industry

- 9.1 Another main focus of the meeting was on industry and industrial processes. Recent advances and developments in AI, robotics, material processing, and analytical instrumentation have led to new ways to think about chemical synthesis.

Subitem 9(a): Artificial intelligence for automated chemical synthesis

- 9.2 Dr Connor Coley, from the Massachusetts Institute of Technology, shared his group's research on AI and its use in automated chemical synthesis.¹⁰ Developments in AI promise to accelerate and, one day, to automate the synthesis of new small molecules. In early stage drug discovery, during the preclinical stages of hit-to-lead and lead

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Sources: (a) Coley C. W., Eyke N. S., and Jensen K. F., Autonomous Discovery in the Chemical Sciences Part I: Progress. *Angew. Chem. Int. Ed.* (2019); and (b) Coley C. W., Eyke N. S., and Jensen K. F., Autonomous Discovery in the Chemical Sciences Part II: Outlook. *Angew. Chem. Int. Ed.* (2019).

optimisation, researchers proceed through iterative design-synthesis-test cycles. In one campaign, hundreds to thousands of molecules might be tested in total, and each cycle requires weeks or months to go from the idea (“design”) to physical synthesis and testing. This iterative process is somewhat inherent to discovery. One opportunity to accelerate this process involves facilitating the synthesis of new molecules through a combination of computer-aided synthesis planning and experimental automation. Artificial intelligence and machine learning can help us in this process by learning the complex input-output relationships related to the chemical reactivity of molecules. There are hundreds of thousands or millions of published chemical reactions to learn from; the goal of data-driven computer-aided synthesis planning is to generalise from this information and extrapolate it to new molecules.

- 9.3 On the hardware side, there has been interest from the pharmaceutical industry in exploring continuous-flow technologies due to the smaller footprint, process intensification, and potential for increased process safety. In a proof of concept, a robotic flow chemistry platform was used to execute the synthetic ‘recipes’ proposed by the AI programme; however, expert chemists were still needed to refine the AI recommendations and provide missing details, making this process only ‘semi-automated’. There are many platforms that can perform the physical steps of synthesis once the plan is reduced to a series of fluid transfer-mixing-heating steps. Since model predictions of process details will not be perfect or complete, techniques for automated reaction optimisation can be quite handy. If analytical results can be automatically read, an experimental platform can automatically change its settings (e.g., temperatures, concentrations) to try to optimise performance (e.g., yield). This paradigm has been used to identify optimal catalysts, solvents, etc., for one-step and multi-step processes. Optimised flow routes can then be scaled up for manufacturing.
- 9.4 As a very brief overview of AI for molecular design, the role of machine learning in quantitative structure-property relationship (QSPR) modelling is clear, as these are complex input/output relationships. An emerging class of algorithms for deep generative modelling have shown promise in proposing brand new molecular structures that have never been made, which can then be combined with the synthesis planning programme. Overall, these automated synthesis tools are very promising and are starting to make a difference in medicinal chemistry and drug discovery, but there is still a gap between what can be computationally planned and what it takes to fully specify an experiment. In time, as less and less expertise is required to operate these systems, dual-use concerns will grow.
- 9.5 When taking questions, Dr Coley indicated that while this approach to synthesis is useful, it is still very much biased towards the pharmaceutical industry. Additionally, he noted that he does not think it fully usurps the role of a trained chemist; chemists are far more creative than AI, and creativity is a critical component of drug development. The Board was particularly interested in potential dual-use concerns related to this research and technology. Dr Coley indicated that these concerns have been identified and discussed in the community, but with no clear indication of how they will be addressed. This area of research is developing fast, and the Board feels it is important and may require more attention.

Subitem 9(b): Insight into actual pharmaceutical production requirements

- 9.6 Dr Andreas Beyeler, from Roche, delivered an overview of basic requirements for pharmaceutical production in a highly regulated environment, guidelines given by health authorities and translated into more stringent internal rules, and chemicals ultimately manufactured according to cGMP (current good manufacturing processes). Future trends were briefly mentioned. He gave insight into the development activities required for a new active pharmaceutical ingredient, indicating that focus should be given to aspects of safety, security, health, and the environment. He also presented approaches implemented by Roche in the development of safe, efficient, robust, and scalable processes.
- 9.7 Given the interest in boosting the understanding of industry trends and developments, the Board had multiple questions. Dr Beyeler highlighted the trend of outsourcing actual pharmaceutical production to contract manufacturers, noting that his company had closed most of its own production sites. He stressed that pharmaceutical companies and the companies actually producing their products have long-term relationships built on a high level of trust and exchange of expertise, enabling high quality to be maintained.

10. AGENDA ITEM TEN – Statement on behalf of the OPCW Advisory Board on Education and Outreach

- 10.1 Dr Craig Cormick, member of the ABEO, briefed the SAB on ABEO developments over the past year. The key outcomes for 2020 included the drafting of a strategic plan, the establishment of a TWG on e-learning, the incorporation of relevant OPCW materials in the United Nations report on disarmament education, and the translation of the “Did You Know?” series of animations into the OPCW’s six official languages.
- 10.2 He also described some ongoing projects that are currently on hold due to the COVID-19 pandemic. These consist of the development of active learning training for OPCW staff and a draft education resource on the use of chemical weapons throughout history. In the coming year, the ABEO will look at options to enhance awareness of dual-use chemicals, use its strategic plan to better focus its work, continue to produce practical materials to support the work of the National Authorities, identify larger projects in consultation with the Director-General and OPCW, and continue the work of the TWG on e-learning.
- 10.3 The Board commended Dr Cormick and the rest of the ABEO on the work they have done and are currently doing. The SAB Chairperson noted that greater collaboration and visibility of the work of both the ABEO and SAB would be beneficial to everyone. On that note, the Board indicated it would like to have more of its members involved, even if only as observers, with ABEO efforts.

11. AGENDA ITEM ELEVEN – Current and future activities of the Scientific Advisory Board

- 11.1 As is customary, the SAB Secretary also reminded the Board of its near-term objectives and commitments. The SAB devoted time at its Thirtieth Session not only to taking inventory of forthcoming SAB commitments and its plans for meeting those commitments, but also to brainstorming for a potential workshop that would involve partnering with industry representatives.

Subitem 11(a): Industry focus: Brainstorming session

- 11.2 At its Twenty-Ninth Session, the Board discussed the importance of maintaining good coordination and collegiality with the chemical industry. Not only is the chemical industry a main partner of the OPCW, but its research and developments are areas that the SAB needs to monitor, considering the impact on the entire chemical sector, and thus on the Convention. SAB members Dr Syeda Sultana Razia, Dr Renate Becker-Arnold, and Dr Daan Noort led a brainstorming session to determine topics of interest and overall guidelines for a potential SAB-industry partnered workshop.
- 11.3 The SAB members highlighted the genesis of the idea for the workshop, potential topics that could be covered, and potential participants. Much discussion ensued, and the Board was very supportive of this idea. The SAB Chairperson noted that the information gained will be critical to the SAB's advice for the Fifth Review Conference.¹¹ The SAB Secretary noted that many good ideas were proposed by the Board on topics to include, and the challenge is to focus on specific topics in order to ensure useful outcomes. To that end, the Board recommends that the SAB hold a workshop that would allow the SAB and the chemical industry to discuss topics of mutual interest, such as decontamination and waste procedures associated with toxic chemicals, the determination and assignment of hazardous properties to chemicals, chemical risk assessments and their applicability within industry, and the general management of chemical inventories. Finally, it was noted that there have been several workshops in the last few years focusing on the chemical industry, and that this proposed workshop should build upon the knowledge gained from previous workshops.

Subitem 11(b): Current and upcoming Scientific Advisory Board meetings and commitments

- 11.4 The SAB Secretary discussed the SAB's future meetings and commitments, with a focus on 2021. Discussion centred on the Fifth Review Conference in 2023, the newly announced Biotoxin Analysis TWG, and the SAB meeting schedule for 2021.
- 11.5 As the SAB report for the Fourth Review Conference presented a complete review of topics of interest, it has been determined, for the purposes of the Fifth Review Conference, to focus instead on the areas of science and technology that have seen recent substantive change and growth. In addition, special attention will be paid to subject areas in which there have been pertinent changes at the OPCW or in the Convention (e.g., the newly scheduled chemicals) and those in which the Secretariat has a keen interest in moving forward (such as forensics). It was decided that the Board will establish working groups in order to systematically and completely investigate, gather information, and form advice on a variety of scientific and technical topic areas for the Fifth Review Conference. Given that the Board's advice is due six to nine months ahead of the Fifth Review Conference, work will be conducted with the initial goal of completing the review and formation of advice by summer 2022.

¹¹ The Fifth Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention.

- 11.6 The Board welcomed the Director-General's decision to establish a TWG on the analysis of biotoxins. The SAB Secretary reminded the Board members of the process for establishing a TWG and their roles and responsibilities for support. The SAB Secretary asked Board members to share contact information for experts in the general field of biotoxins so that an initial list can be created for consideration, either as TWG members or external guest speakers at meetings. The Board stands ready to support this important TWG, pending the drafting of its terms of reference and the selection of its chairperson and members.
- 11.7 The Board also discussed plans for its meetings in 2021, so that dates can be reserved and preparations may begin. Given the current challenges with travel and in-person meetings, as well as the uncertainty related to the pandemic, the Board deemed it best to schedule one or two virtual meetings in the first half of 2021, with the hope that an in-person meeting in The Hague can be conducted in the autumn of 2021. The Board also noted that while not optimal in some ways, virtual meetings do offer some advantages over traditional in-person meetings: Lengthy travel can be avoided and certain external speakers who otherwise may not be interested or able to travel or attend an in-person meeting in The Hague are more available to share their research with the Board. The SAB is therefore considering incorporating regular virtual sessions into its meeting strategy moving forward, not only as a contingency but as a complement to in-person sessions.

Subitem 11(c): Election of the Chairperson and Vice-Chairperson of the Scientific Advisory Board

- 11.8 As this was the last scheduled SAB meeting for the calendar year, the Board held its election of the Chairperson and Vice-Chairperson for 2021. Dr Christophe Curty was re-elected as Chairperson. Dr Zrinka Kovarik stepped down as Vice-Chairperson, and Dr Andrea Leisewitz Velasco was elected as the new Vice-Chairperson for 2021.
- 11.9 It was noted that the process for filling the positions of chairperson and vice-chairperson could be optimised, especially given the potential for virtual elections in the future. As such, the Board will consider options to make the Chairperson election process smoother and more transparent.

12. AGENDA ITEM TWELVE – Any other business

The SAB expressed its appreciation to the Director-General and Deputy Director-General, as well as to Mr Gorjan Damjanovic of the Information Services Branch, Ms Virginie Poujade and Mr Vasily Titushkin of the Secretariat for the Policy-Making Organs, and Ms Ernesa Ademagic of the Office of Strategy and Policy, for their support of and contributions to the SAB's Thirtieth Session and its preparations. A special thanks went to the interpretation teams, who made the meeting possible by allowing everyone to participate. The SAB is grateful for the voluntary contributions to support its work received from Australia and Saudi Arabia, as well as the European Union for its April 2019 Council decision, which provides funding for TWGs.

13. AGENDA ITEM THIRTEEN – Adoption of report

The SAB considered and agreed upon a process for the preparation of the report for its Thirtieth Session, with a view to adopting it via correspondence after the session.

14. AGENDA ITEM FOURTEEN – Closure of the session

The Chairperson made concluding remarks on the session, and the SAB Secretary closed the virtual session at 16:13 CET on 12 November 2020.

Annex: List of Participants in the Thirtieth Session of the Scientific Advisory Board

Annex

**LIST OF PARTICIPANTS IN THE THIRTIETH SESSION
OF THE SCIENTIFIC ADVISORY BOARD**

	Participant	Institution
1.	Prof Isel Pascual Alonso	University of Havana, Cuba
2.	Dr Khaldoun Bachari	Algerian Public Scientific and Technical Research Centre in the Physico-Chemical-CRAPC, Algeria
3.	Dr Renate Becker-Arnold	BASF, Germany
4.	Dr Elma Biscotti	Scientific and Technical Research Institute for Defense, Argentina
5.	Dr Anne Bossée	DGA CBRN Défense, France
6.	Dr Christophe Curty (Chairperson of the SAB)	Spiez Laboratory, Switzerland
7.	Prof Vladimir Dimitrov	Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, Bulgaria
8.	Prof Mostafa Ghanei, MD	Baqiyatallah University of Medical Sciences, the Islamic Republic of Iran
9.	Dr Norman Govan	Defence Science and Technology Laboratory, the United Kingdom of Great Britain and Northern Ireland
10.	Mr Wilford Zungkat Jwalshik	Institute of Chartered Chemists of Nigeria, Nigeria
11.	Prof Victor Kholstov	Ministry of Industry and Trade, "GosNIIOKhT", the Russian Federation
12.	Dr Zrinka Kovarik (Vice-Chairperson of the SAB)	Institute for Medical Research and Occupational Health, Croatia
13.	Dr Andrea Leisewitz	Pontificia Universidad Católica de Chile, Chile
14.	Prof Imee Su Martinez	University of the Philippines-Diliman, the Philippines
15.	Dr Robert Mikulak	United States Department of State, the United States of America
16.	Dr Daan Noort	TNO, Rijswijk, the Netherlands
17.	Prof Ponnadurai Ramasami	University of Mauritius, Mauritius
18.	Mr Günter Povoden	EU CBRN Centres of Excellence Initiative, Ministry of Defence, Austria
19.	Prof Syeda Sultana Razia	Bangladesh University of Engineering and Technology (BUET), Dhaka, Bangladesh
20.	Prof Ahmed E. M. Saeed	Sudan University of Science and Technology, Sudan
21.	Dr Yasuo Seto	RIKEN SPring-8 Center, Japan
22.	Dr Maciej Sliwakowski	Lukasiewicz Research Network – Institute of Industrial Organic Chemistry, Poland
23.	Prof Fengxia Sun	Hebei University of Science and Technology, China
24.	Dr Nomandla Magnificent Vela	Protechnik Laboratories, South Africa
25.	Ms Farhat Waqar	Pakistan Atomic Energy Commission, Islamabad, Pakistan

	Participant	Institution
26.	Mr Olivier Allard	Organisation for the Prohibition of Chemical Weapons, The Hague, the Netherlands
27.	Dr Andreas Beyeler	Roche Chemical, Switzerland
28.	Dr Hoe Chee Chua	Organisation for the Prohibition of Chemical Weapons, The Hague, the Netherlands
29.	Dr Connor Coley	Massachusetts Institute of Technology, United States of America
30.	Dr Craig Cormick (Member of the ABEO)	Independent Consultant, Australia
31.	Dr Jennifer Galloway	Natural Resources Canada, Canada
32.	Mr Alejandro Hernandez	Organisation for the Prohibition of Chemical Weapons, The Hague, the Netherlands
33.	Dr Nawaf Nasser	Carleton University, Canada
34.	Dr Miloš Stojiljković	University of Banja Luka, Bosnia and Herzegovina
35.	Dr Sadik Toprak	Istanbul University, Turkey
36.	Dr Peter Hotchkiss (Secretary to the Scientific Advisory Board)	Organisation for the Prohibition of Chemical Weapons, The Hague, the Netherlands