



**OPCW**

**Scientific Advisory Board**

---

Twenty-First Session  
24 – 27 June 2014

SAB-21/WP.2  
25 November 2013  
ENGLISH only

**REPORT OF THE FOURTH MEETING OF THE SCIENTIFIC ADVISORY BOARD  
TEMPORARY WORKING GROUP ON THE CONVERGENCE  
OF CHEMISTRY AND BIOLOGY**

1. The Report of the Fourth Meeting of the Scientific Advisory Board (SAB) Temporary Working Group on the Convergence of Chemistry and Biology is hereby circulated to States Parties. The meeting was held in The Hague from 5 to 7 November 2013.
2. The Chairman of the SAB and the Director-General have agreed that this report can be circulated to States Parties in advance of the Twenty-First Session of the SAB.
3. In accordance with the Rules of Procedure of the SAB, this report will be reviewed in detail by the SAB at its Twenty-First Session.

Annex: Report of the Fourth Meeting of the SAB Temporary Working Group on the Convergence of Chemistry and Biology



## **Annex**

### **REPORT OF THE FOURTH MEETING OF THE SAB TEMPORARY WORKING GROUP ON THE CONVERGENCE OF CHEMISTRY AND BIOLOGY**

#### **1. AGENDA ITEM ONE – Opening of the meeting and adoption of the agenda**

1.1 The Scientific Advisory Board Temporary Working Group (TWG) on the Convergence of Chemistry and Biology held its fourth meeting from 5 to 7 November 2013 at OPCW Headquarters in The Hague. As per the terms of reference, this was the final meeting of the TWG.

1.2 The meeting was chaired by William Kane on behalf of the SAB.

1.3 The list of TWG members attending this meeting is given in Appendix 1.

1.4 The following agenda was adopted:

- (a) Opening of the meeting and adoption of the agenda;
- (b) Biologically mediated synthesis of chemicals;
- (c) Chemical synthesis of agents of biological origin (e.g. toxins, bioregulators) and of replicating systems;
- (d) Whether any biotechnological processes exist, other than biologically mediated synthesis, that are of relevance to the implementation of the CWC;
- (e) The meaning of “produced by synthesis”;
- (f) Whether there are other scientific disciplines, apart from biology, that are converging in a significant way with chemistry;
- (g) The potential benefits to the CWC of the convergence of chemistry and biology;
- (h) Any other business;
- (i) End of Mandate Report;
- (j) Recommendations and adoption of the TWG report from this meeting; and
- (k) Closure of the meeting.

#### **2. AGENDA ITEM TWO – Biologically mediated synthesis of chemicals**

**The processes that are used in the biologically mediated synthesis of chemicals**

- 2.1 William Provine provided a summary and a reference article on the use of enzymes for decontamination of chemical agents.<sup>1</sup> Bacterial enzymes (phosphotriesterase and organophosphorus acid anhydrolase) have been isolated that catalyse the hydrolysis of organophosphate nerve agents with high rate enhancements and broad substrate specificity. Mutant forms of these enzymes have been constructed through rational redesign of the active site binding pockets and random mutagenesis to create protein variants that are optimised for the detoxification of agricultural insecticides and chemical warfare agents.
- 2.2 Dr Provine noted that enzymatic approaches to decontamination of toxic substances are being developed to respond to chemical and biological exposure, as they lend logistical and environmental advantages over chemical and physical approaches. Enzymes which are highly specific to G-type nerve agents such as sarin, soman, and other organophosphate materials, and which are highly specific to VX, Russian Vx, and pesticides such as parathion, have been developed in prototype form but are not commercially available. Both products contained an industrial-grade enzyme and a buffering mixture in one small, convenient package and are non-toxic and non-corrosive, easy to use, and water soluble. Both products can also be formulated with other solutions. The overall benefit of adopting universal enzymatic decontaminants is a quantum reduction of logistical burden along with remarkable improvements in the effectiveness of field decontamination operations.
- 2.3 Piers Millet briefed the TWG on the use of engineered DNA scaffolds to improve catalytic efficiency. After opening with a video from a recent iGEM competition ([www.youtube.com/watch?feature=player\\_embedded&v=jVA6qS8YPgg](http://www.youtube.com/watch?feature=player_embedded&v=jVA6qS8YPgg)), Dr Millet provided an overview of the use of scaffolds in improving yields and efficacy of chemicals produced using synthetic metabolic pathways. Research from 2006 to 2008 was used to illustrate the importance of the spatial arrangement of components in a metabolic pathway, that co-locating enzymes from the same metabolic pathway can increase yield, and the advent of several approaches to replicate known spatial arrangements. A second line of research was used to provide an overview of the use of protein scaffolds, including their use to arrange enzymes to increase yield, as well as to control dose-response, accelerate and delay response time, as well as enable tunable adaptation in metabolic pathways. Details of a review of the comparative strengths of protein and DNA-based scaffolds was included which suggests there could be many advantages from developing DNA scaffolds. A series of research papers was then highlighted: firstly, illustrating evolving capabilities to design and build single-stranded DNA shapes; secondly, the ability to build shapes from double-stranded DNA; thirdly, that DNA can be used as a scaffold for the spatial organisation of enzymes in a metabolic pathway, and finally describing their use in a system to synthesise a complex chemical. Additional research was described to illustrate that spatial organisation, including the use of scaffolds, was also important and feasible in yeast-based systems, more commonly used in industrial production.

### **The extent of use of biologically mediated synthesis in commercial chemical production**

---

<sup>1</sup>

F. M. Raushel, *Current Opinion in Microbiology*, 2002, 5, 288-295.

2.4 Piers Millet provided an overview of the survey published in July 2012 by the Synthetic Biology Project of the Woodrow Wilson International Center for Scholars. He noted that the survey results suggested that the production of chemicals was then the largest application of synthetic biology, and that half of the products detailed were already available, demonstrated, seeking a market, have had a pilot plant built, in clinical trials or had already prompted joint ventures between companies. The survey identified 68 products, across seven sectors, from companies in 10 countries. Two sectors were of particular note. Chemical applications were being found to produce 18 products, including both bulk and fine chemicals, ranging from lactic acid to anti-fungal agents. In medicine, 13 products were identified, ranging from modified insects to heavy metal sensors. More information on the synthetic biology survey can be found at: [www.synbioproject.org/library/inventories/applications\\_inventory/](http://www.synbioproject.org/library/inventories/applications_inventory/)

2.5 In discussion, the following point was raised: Production of chemicals is the largest area of application. Half of products surveyed are in (or beyond) the pilot plant phase and are expected to come to market in the near to mid-term.

#### **The utility of biologically mediated techniques for the synthesis of toxic chemicals**

2.6 This topic was discussed in the context of the End of Mandate report.

#### **The application of biologically mediated processes for the synthesis/production of toxins and bioregulators, and future trends**

2.7 Hua Li updated the TWG on recent research on the toxin ricin. She noted that through the end of October 2013, about 60 relevant articles on ricin research had been published, which mainly focused on toxicological effects and mechanism studies, detection and countermeasures against the toxin. There was no significant progress observed on the development of biologically mediated processes for ricin synthesis.

2.8 Dr Li noted that, as one of the research highlights in the field of genetics, a systematic mammalian genetic interaction map for revealing pathways underlying ricin susceptibility had been published recently.<sup>2</sup> An integrated platform was developed, based on pooled short hairpin RNA (shRNA) strategies, to functionally dissect complex biological processes in mammalian cells. Using a high density genetic interaction map, some unexpected insights were obtained to identify the protection or sensitisation roles of some components after ricin exposure. The study provides a potentially transformative tool for defining gene functions and designing combination therapies based on synergistic pairs.

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

This topic was discussed in the context of the End of Mandate report.

---

<sup>2</sup> M. C. Bassik, et al; *Cell*, 2013, **152**, 909-922.

**4. AGENDA ITEM FOUR – Whether any biotechnological processes exist, other than biologically mediated syntheses that are of relevance to the implementation of the CWC**

This topic was discussed in context of the End of Mandate report.

**5. AGENDA ITEM FIVE – The meaning of “produced by synthesis”**

5.1 Robin Black and Stefan Mogl summarised the outcome of the Second Meeting of the TWG on Verification where relevant aspects of this issue are currently being considered (see TWG report SAB-21/WP.1, dated 25 September 2013).

5.2 In discussion, the following point was raised: The technical issues that arise from discussion of the “produced by synthesis” recommendation underscore the importance of engaging experts from the biotech industry in the activities of the SAB and its TWGs.

**6. AGENDA ITEM SIX – Whether there are other scientific disciplines, apart from biology, that are converging in a significant way with chemistry**

6.1 Djafer Benachour briefed the TWG on the latest developments of nanotechnology that have many applications, most notably in medicine for drug delivery. In medical studies, nanoparticle-based formulations are being widely explored for enhanced or ‘smart’ drug delivery. Examples are controlled drug release, enhanced penetration of the blood-brain barrier (e.g. for therapeutic peptides), and targeting specific organs or cells (e.g. cancer cells). Nanoparticles most commonly used in drug formulations include imprinted polymers, dendrimers, vesicles, nanospheres, nanocapsules, micelles, carbon nanotubes, liposomes, and nano-emulsions. Additional bio-based nanocarriers are being researched including DNA-based systems<sup>3</sup> and viral-based systems.<sup>4</sup> These drug nanocarriers can be comprised of a variety of materials (e.g. organic, mineral, and composite) and architectures (e.g. spheres, rods, and tubes). Allied to these advances in therapeutics, nanotechnology is contributing to major developments in diagnostics.

6.2 Professor Benachour explained how nanocarrier delivery systems present several advantages over the classic ones: hindering solubility problems, protecting the drug from the external environment (temperature, UV radiations, pH) and reducing dose dumping by controlling the release profile. Nanocarrier-based delivery systems permit a more precise and controlled targeting at the site of action, while reducing the time of exposure at non-targeted tissues. This results in an increase of the treatment efficacy, and a reduction of toxicity and side effects, for the benefit of the patient. Improved efficiency of cancer treatment illustrates the effectiveness of the use of nanocarriers (e.g. tumour-targeted delivery of Taxol is in clinical trials).

6.3 Piers Millett provided an overview of past efforts under the Biological Weapons Convention (BWC) to review developments in science and technology. He provided

---

<sup>3</sup> J. Li, C. Fan, H. Pei, J. Shi, Q. Huang; *Adv Materials*, 2013, **32**, 4386-4396.

<sup>4</sup> Y. Ma, R. J. M. Nolte, J. J. L. M. Cornelissen; *Advanced Drug Delivery Reviews*, 2012, **64**, 811-825.

a snapshot of areas included in the last such review, including aspects of both general trends and specific enabling advances. Additional information was also provided on the review conducted prior to the last review conference by the IAP - Global Network of Science Societies. Dr Millett then introduced the standing agenda item on reviewing relevant developments included in the current annual work programme. He provided details of enabling advances including in background material covering: characterising biological systems and networks, such as advances in genomics, proteomics, transcriptomics, metabolomics, fluxomics, epigenomics, and integrating data from different “-omics”, manipulating biological systems and networks, such as gene silencing, zinc finger nucleases, TALENs, and CRISPR; engineering biological systems and networks, such as synthetic biology; gathering and manipulating biological information, such as programming languages, data mining, dealing with large data sets, modeling and simulation, as well as online tools and software; and converting biological information into digital data and back, such as gene sequencing and synthesis technologies.

- 6.4 Scott Mohr (guest speaker by teleconference) provided an overview on bioinformatics and how it is used in the biological sciences, including the amount of data generated, the logistics of handling large data sets, and current experts in the field and the large laboratory operations that are required for them to do their work. The presentation included how microbiomes can be used as targets for biological manipulation that could lead to harmful use of biotechnologies. The presentation concluded with suggestions for how to anticipate and prevent such activities.

**7. AGENDA ITEM SEVEN – The potential benefits to the CWC of the convergence of chemistry and biology**

- 7.1 Robin Black briefed the TWG on advances in biosensors. Further applications of research on miniaturised biosensors for chemical defence were reviewed. These incorporate elements of chemistry, biology, nanotechnology and electronics. Biosensors for detecting organophosphorus pesticides or nerve agents remain the most active area of research. These fall into two types: biosensors that detect an agent, most using immobilised acetylcholinesterase (AChE) or butyrylcholinesterase (BuChE) as the biological sensing element, and biosensors for diagnosing exposure to organophosphorus agents. The majority of the latter measure active cholinesterase levels, in some cases before and after reactivation with oxime or fluoride to overcome the problem of variable baseline levels of enzyme. These biosensors usually include selective capture of ChE from blood, e.g. with phosphoserine antibodies or zirconia or titanium oxide nanoparticles. At least one of these devices has been commercialised. Alternative approaches are biosensors based on antibody recognition of phosphorylated cholinesterase, or phosphorylated tyrosine residues on albumin. The former suffers from a lack of suitable antibodies, because the active sites of AChE and BuChE are located within a deep gorge. Very recently, two papers have described mono- and polyclonal antibodies to nerve agent phosphorylated albumin, which may find application in biosensors. Phosphorylated tyrosine on albumin is a less sensitive biomarker than phosphorylated ChE, but has the advantage that it does not age. A biosensor for sulfur mustard, and for diagnosing skin exposure to mustard based on alkylation of DNA, has recently been commercialised. Biosensors for ricin and saxitoxin have been reported.

- 7.2 Philip Coleman gave a presentation on recent developments in the area of portable field detectors and identification. The desired features of the ideal field detector for detection and/or identification of hazardous chemicals were summarised. Classical laboratory analytical techniques have recently been adapted for use in the field to improve the capacity to identify a wide range of hazardous chemicals. Many of the problems which made it difficult to use these technologies outside of a laboratory environment have been overcome. Portable GC-MS and infrared spectrometer systems have been developed. The presentation highlighted the features of a new man-portable GC-MS which weighs only 14 Kg and can identify a wide range of chemicals. This has been made possible by the use of a toroidal mass spectrometer with a direct GC-MS interface.
- 7.3 Dr Coleman noted that the development of a diamond ATR interface for infrared spectrometers with an integrated pressure device for solid materials has enabled compact man-portable infrared spectrometers to be produced. This enables a wide range of solid and liquid chemicals to be identified in sample mixtures.
- 7.4 Hua Li updated the TWG on developments introduced at the 11th International Symposium on the Protection against Chemical and Biological Warfare Agents held in Stockholm in June 2013. Personal protective equipment with enhanced protection capability for CBRN hazards and reduced physiological burden was observed in the Exhibition of CBW Defence Equipment. Optimisation of carbon cloth or fibres and multiple-layer material significantly improved the protection performance against toxic vapour, droplet and even aerosol. Physicochemical principles based chemical agent detectors are still the mainstream of the equipment displayed in the Exhibition. The smaller size and improved performance were observed for the new generation of the portable chemical weapons agent detection devices that allow rapid and easy operation. Portable devices with technologies of FTIR, GC-MS or Raman spectrometry offer enhanced capability and better choices for field and emergency detection. An immuno-chromatographic test strip based on specific antibody binding is available for field detection of small molecular chemical weapons agents, for instance sulfur mustard.

## **8. AGENDA ITEM EIGHT – Any other business**

The OPCW has been invited to participate in the BWC meeting of States Parties in Geneva being held from 9 to 13 December. Stefan Mogl will present on the outcome of the TWG on Convergence in the plenary session. A Technical Secretariat staff member will also participate, and a side event will be organised.

## **9. AGENDA ITEM NINE – End of Mandate report**

The draft of the End of Mandate report was accepted and a drafting committee formed to finalise the text.

## **10. AGENDA ITEM TEN – Recommendations and adoption of the TWG report from this meeting**

Recommendations for review by the SAB will be provided through the End of Mandate report.

**11. AGENDA ITEM ELEVEN – Closure of the meeting**

The Chairperson closed the meeting at 13:00 on 7 November 2013.

Appendix: List of Participants in the Fourth Meeting of the SAB Temporary Working Group on the Convergence of Chemistry and Biology



## Appendix

### LIST OF PARTICIPANTS IN THE FOURTH MEETING OF THE SAB TEMPORARY WORKING GROUP ON THE CONVERGENCE OF CHEMISTRY AND BIOLOGY<sup>5</sup> 5 – 7 NOVEMBER 2013

Participant	Institution
Professor Mahdi Balali-Mood	Medical Toxicology Centre, Imam Reza Hospital, University of Medical Sciences, Mashhad
Professor Djafer Benachour*	Ferhat Abbas University, Ministry of Higher Education and Scientific Research, Setif
Robin Black	Defence Science and Technology Laboratory (DSTL), Porton Down
Dr Philip Coleman	ECM Technology (Pty) Ltd, Pretoria
Mr William Kane <sup>6*</sup>	Consultant of Monsanto Company
Dr Hua Li	Chinese Academy of Military Medical Sciences
Dr Robert Mathews	Defence Science and Technology Organisation, Melbourne
Dr Piers Millett	United Nations, Switzerland
Mr Stefan Mogl	SPIEZ Laboratory, Spiez
Dr William Provine	DuPont Central Research & Development
Professor Igor Vladimirovich Rybalchenko	Military Science Centre of the Ministry of Defence, Moscow
Dr Muhammad Zafar-Uz Zaman*	National Engineering and Scientific Commission (NESCOM), Islamabad
Professor Scott Mohr (guest speaker)	Bioinformatics Graduate Program and the Department of Chemistry, Boston University

\*Member of the Scientific Advisory Board.

---

<sup>5</sup> Professor Roderick Flower (William Harvey Research Institute at Barts London School of Medicine and Dentistry) and Professor Alejandra Graciela Suárez (Universidad Nacional de Rosario. Consejo Nacional de Investigaciones Científicas y Técnicas), could not attend the fourth meeting of the TWG. Dr Robert Mathews, Dr Bill Provine, and Professor Scott Mohr participated by teleconference.

<sup>6</sup> Chairperson of the TWG on the Convergence of Chemistry and Biology.