International Workshop on Trends in Chemical Production

Presented to
Side event for Conference of States Parties 21
28 November 2017

Cheng Tang
Vice Chairperson, the Scientific Advisory Board

Plan

- **Summary of the Workshop on Trends in Chemical Production** ***(Cheng Tang)***
  - Experiments of making ice creams *(Chris, Jonathan, Siqing and Amy)*
    - ✓ Science ABC relevant to the experiment
  - Outcomes of the workshop
- **Conclusions and the future plan** ***(Jonathan Forman)***
  - Additional ice cream test & observations
  - Road map towards the Fourth Review Conference

International Workshop on Trends in Chemical Production

3-5 October 2017, Zagreb, Croatia

Institut za medicinska istraživanja i medicinu rada | Institute for Medical Research and Occupational Health

Funded by

Under the auspices of the Croatia President Kolinda Grabar-Kitarović

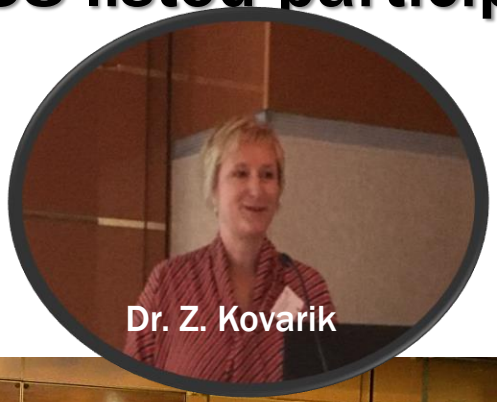
REPUBLIC OF CROATIA
MINISTRY OF ECONOMY, ENTREPRENEURSHIP AND CRAFTS

City of Zagreb

The fourth and final workshop of a series intended to inform the SAB report for the 4th RevCon

with 38 listed participants


Dr. C. Timperley


Dr. Z. Kovarik


Dr. J. Forman

Mr Mario Antonić

State Secretary
Ministry of Economy, Entrepreneurship and Crafts of Croatia

“achievements in the field of chemistry should be exclusively used to the benefit of humans in a manner not forbidden by the Convention, by means of promoting free trade in chemical”

Overview
workshop sessions and discussions

Trends in chemical production

Examined trends in all sectors of the chemical industry

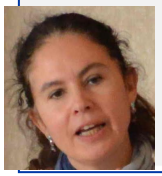
- *Chemical economy*
- *Commodity chemicals*
- *Pharmaceuticals*
- *Fine/speciality chemicals*
- *Custom automated synthesis*
- *Proteins and nucleic acids*
- *Agricultural chemicals*
- *Regulatory issues*

The workshop discussed in 10 different sessions:

Chemical Industry and the Chemical Weapons Convention

Mr Cheng Tang (OPCW SAB Vice-Chairperson), Moderator

Trends in the European and global chemical industry
(Dr *René van Sloten, cefic*)



Industry inspections and Chemical Weapons Convention policy: looking toward the future
(Dr Stephanie Dare-Doyen, OPCW Office of Strategy and Policy)

Commodity and Platform Chemicals

Professor Ferruccio Trifiró (OPCW SAB), Moderator

Future directions of the modern chemical industry
(*Professor Fabrizio Cavani, University of Bologna*)

Sustainability in Chemistry
(*Dr Detlef Maennig, Evonik Industries AG*)

Chemical production by conversion of carbon to products through gas fermentation
(*Dr Sean Simpson, LanzaTech*)

Bio-based Production

Professor Isel Alonso (OPCW SAB), Moderator

Manufacturing: current status and future of biologicals in therapy
(Dr Florian M. Wurm, ExcellGene SA)

European bio based industries sector
(Mr Andrea Božić, Saponia)

Specialty and Fine Chemicals, and Small Scale Production

Dr Koji Takeuchi (OPCW SAB), Moderator

Fine chemicals – current trends and challenges in industry
(*Dr Olaf Burkhardt, Evonik Industries AG*)

Custom synthesis in chemical production
(Dr Tony Bastock, Contract Chemicals UK)

Trends in bioproduction and bioreactor design in relation to specialty chemical production (*Dr i.r. Nico M.G. Oosterhuis, Director of Technology, Celltainer Biotech BV*)

Pharmaceuticals

Dr Renate Becker-Arnold (OPCW SAB), Moderator

Highly active pharmaceutical ingredients
(Dr Andreas Beyeler, F. Hoffmann-La Roche AG)

Safety and quality by design: minimizing risk and environmental impact in pharmaceutical production
(Dr Ernest Meštrović, Teva Group)

Agricultural Chemicals

Ms Barbara Hedler (OPCW Industry Verification Branch), Moderator

Pesticides (*Dr Syed Raza, OPCW SAB*)

Synthesis Tools

Dr Christophe Curty (OPCW SAB), Moderator

Dial-a-Molecule *(Professor Richard Whitby, University of Southampton)*

Continuous flow reactor technology
(Dr Kerry Gimore, Max Planck Institute of Colloids and Interfaces)

Nucleic Acids

Dr Pål Aas (OPCW SAB), Moderator

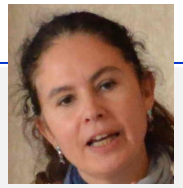
Next-generation DNA synthesis: a biological tool driving innovation in metabolic engineering *(Dr Devin Leake, Ginko Bioworks)*

Chemical Analysis and Informatics

Professor Roberto Martínez-Álvarez (OPCW SAB), Moderator

Transferable learnings from a decade of mutagenic impurity analysis (*Dr Dave Elder, CMC Consultant*)

Machine learning in chemical synthesis
(*Dr Marwin Segler, Westfälische-Wilhelms Universität Münster*)



Regulatory Frameworks

Dr Stephanie Dare-Doyen (OPCW Office of Strategy and Policy), Moderator

Regulation in the chemical industry (*Dr Renate Becker-Arnold, OPCW SAB*)

Biomediated processes and industry verification under the Chemical Weapons Convention *(Ms Barbara Hedler, OPCW Industry Verification Branch)*

Highlights of the trends in chemical production and the implementation of CWC

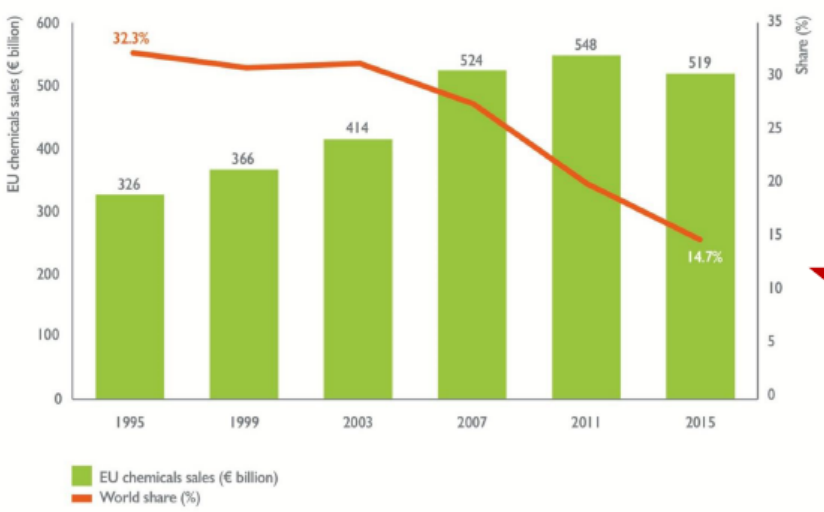
Trends in the European and global chemical industry

- **Dr René van Sloten from Cefic (Europe Chemical Industry Council) discussed the evolution of chemical production after entry into force of the Convention.**
  - 1997 as “tripolar”, with the European Union (EU), the United States of America (USA), and Japan as the top three chemical producing regions;
  - The world has since witnessed the emergence of multiple new production platforms in Brazil, India, the Middle East, South East Asia, and Korea. Roughly 40% of world chemical production now occurs in China.

Trends in the European and global chemical industry

EU chemicals sales increase by nearly 60% in 20 years, while its world market share halves

EU share of global chemicals market



We see also a worrying decline in domestic EU market share over the past ten years

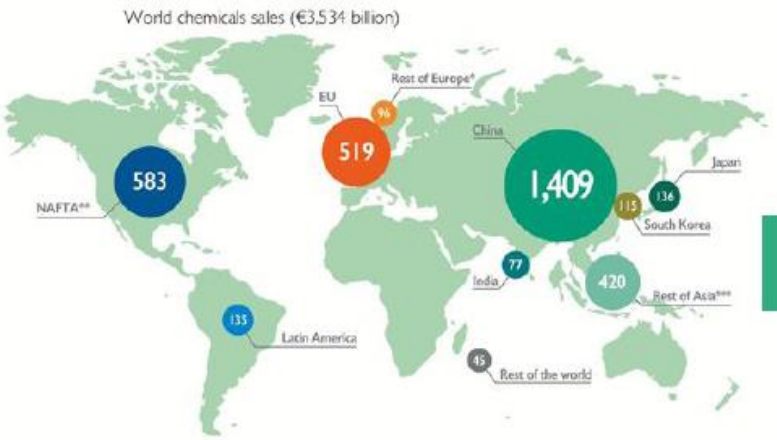
Source: Cefic Chemdata International

Page 3

Trends in the European and global chemical industry

Asia chemicals production outpaces other regions

World chemicals sales: geographic breakdown

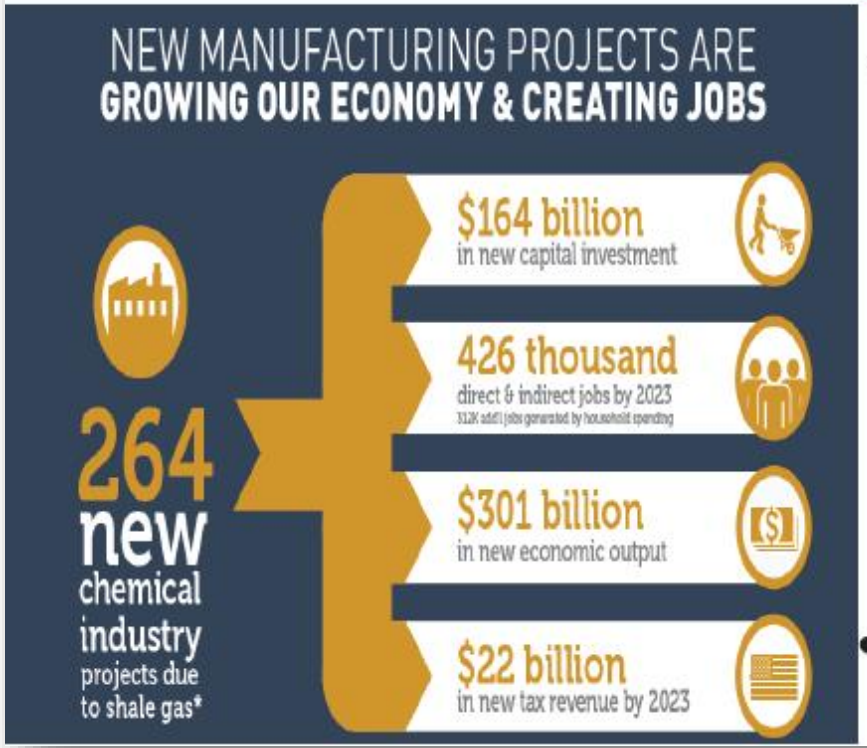


China dominates chemicals world

Source: Cefic Chemdata International
* Rest of Europe covers Switzerland, Norway, Turkey, Russia and Ukraine
** North American Free Trade Agreement
*** Asia excluding China, India, Japan and South Korea

Page 2

World landscape of the chemical industry is changing rapidly



"13th Five-Year Plan"

- From "following the lead" to "taking the lead" and from a big country of petroleum and chemical industry to a "great power"
- Leading on technology innovation and trade
- Prevailing in international markets

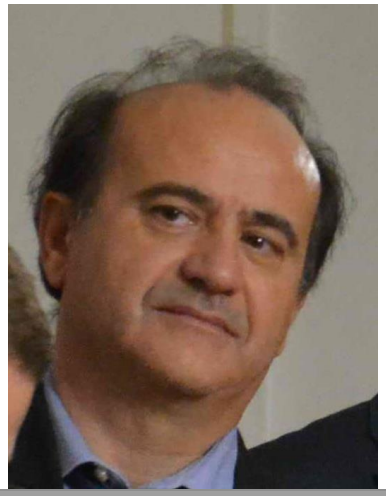
- A shale gas boom has revived the chemical industry in the USA;
- EU chemical industry are seeking to move up the innovation ladder by developing products that provide solutions to global challenges that include climate change, energy, water, health, and food.

Several significant developments in the global chemical industry observed over the past 20 years were not recognized until they actually took shape (e.g. they were unanticipated in the years just before they happened).

Future directions of the modern chemical industry

Fabrizio Cavani

Dipartimento di Chimica Industriale “Toso Montanari”,
ALAM MATER STUDIORUM Università di Bologna



Future directions of the modern chemical industry

- chemicals represent one of the largest and most research and development (R&D) intensive manufacturing sectors in all of the advanced economies, whose patterns of innovation can profoundly impact economic growth;
- highlighted some areas of significant change occurring in the European chemical industry with the aim of lowering environmental impact, while maintaining competitiveness

The new Sustainability Paradigma: Replacement of fossil-derived building blocks with **renewable raw** materials

existing carbohydrate feedstocks

existing C6 carbohydrates

emergent lignocellulosic feedstocks

future lignocellosic carbohydrates

Chemo-catalytic or bio-catalytic transformation

Conclusions

The chemical industry is facing important challenges, and is now committed at maintaining the **competitiveness** but also at improving its **environmental performance**

One of the most important target is the replacement of fossil-based raw materials with **renewable-based building blocks** (bioplatform molecules). The main issue here is the **economic sustainability**. The **co-location** model may help in achieving substantial savings of investments.

However, also the **environmental sustainability** has to be carefully evaluated, since a truly better performance can be achieved only under specific conditions.

Sustainability in Chemical Industry

Dr. Detlef Maennig

OPCW Workshop on Trends in Chemical Production

Zagreb, Croatia, October 3 – 5, 2017

Responsible Care®

Sustainability is not a fashion or a marketing gimmick, let alone a cost driver. It is a driver for innovation, profitability and social progress.

Why is that so?

Responsible Care®

Sustainability-driven companies are more successful

Responsible Care®

Sustainability as a value driver

Compliance	Risk mitigation	Opportunities
▪ Legal and regulatory requirements ▪ Acceptance and trustworthiness	▪ Plant and work safety, environmental protection ▪ Transparent value chains ▪ Reputation and brand integrity	▪ Innovation driver ▪ Process efficiency and continuous improvement ▪ Differentiation from competitors ▪ Entering new markets
License to operate	**Operative excellence**	**Profitable growth**

Responsible Care®

Flagship programs to drive sustainability in chemical industry are

Responsible Care®

and

Global Product Strategy

OPCW

Organisation for the Prohibition of Chemical Weapons

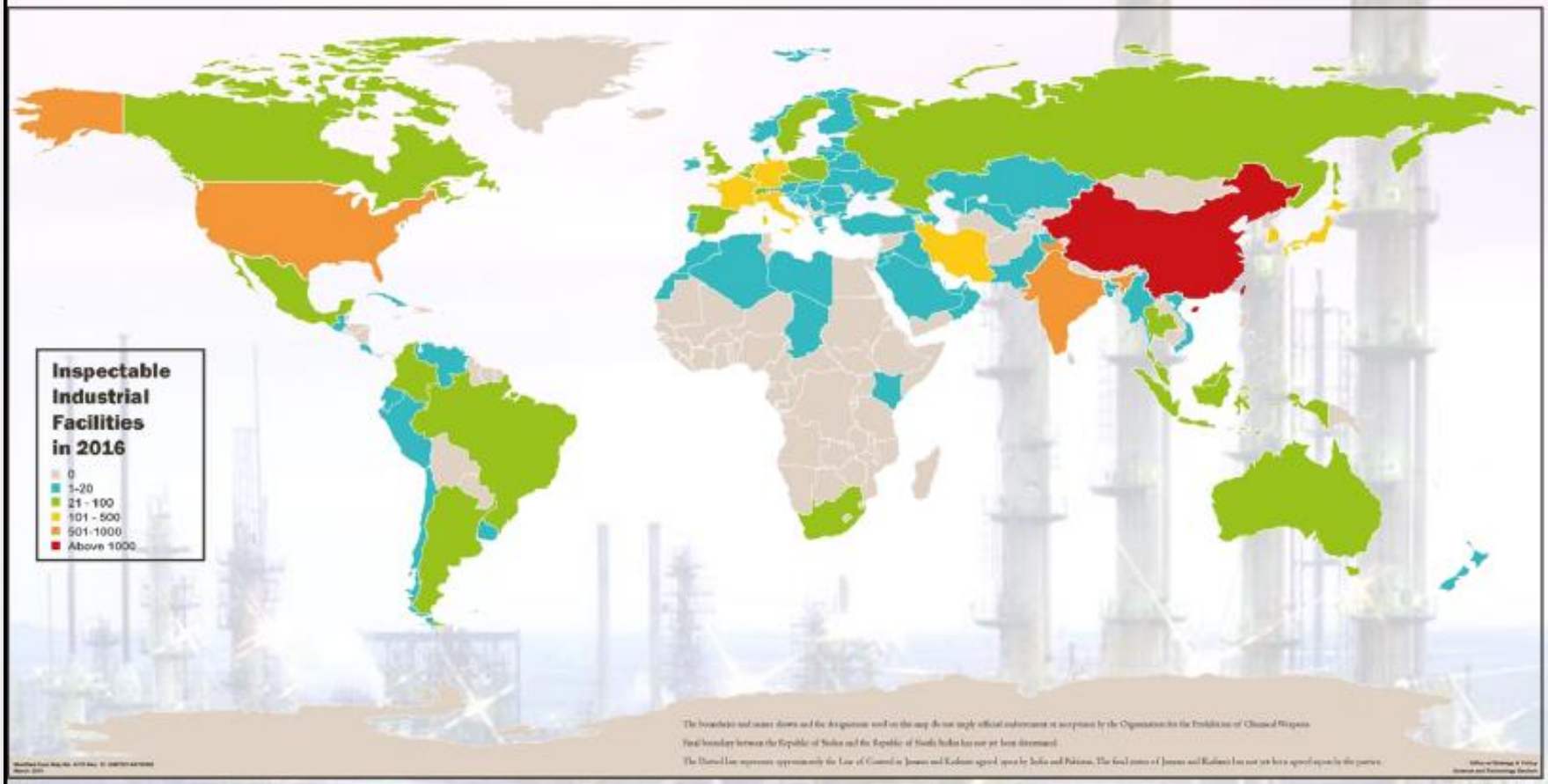
1997–2017 OPCW 20 YEARS

Industry inspections and Chemical Weapons Convention Policy: looking toward the future

Dr Stephanie Daré Doyen
OPCW Office of Strategy and Policy

Inspectable Industrial Facilities

(data from 2015 OPCW Annual Report)



3,023 "Inspector Days" for Industry Inspections in 2015

Article VI Inspections – Overview (up to 31 August 2017)

Facilities/Sites By Type	SPs with Declared Facilities	Declared Facilities/Sites	Inspectable Facilities/ Sites	Inspections Conducted since EIF	Inspection days since EIF
Schedule 1	23	26	26	288	4,955
Schedule 2	36	492	201	810	18,893
Schedule 3	35	402	362	468	7,169
OCPF	80	4,299	4,128	1,932	24,120
Total		5,219	4,717	3,498	55,137

A total of 3,498 industry inspections was conducted until 31 August 2017 and over 55,100 days spent on-site by our inspectors.

Adapting to changing realities

Advances in Sciences & Technologies

Emerging questions

2. Each State Party shall ...ensure that toxic chemicals and their precursors are only developed, produced, ...or used ... for purposes not prohibited under this Convention. To this end, and in order to verify that activities are in accordance with obligations under this Convention, each State Party shall subject S1, S2, S3....other facilities ... to verification measures as provided in the Verification Annex.

- In light of new threats, having in mind the provisions of Article VI, what should be the focus of the inspections?
  - Only declared activities / scheduled chemicals?
  - Or all toxic chemicals in the plant site?

THE ROLE OF CUSTOM SYNTHESIS IN THE CHEMICAL INDUSTRY

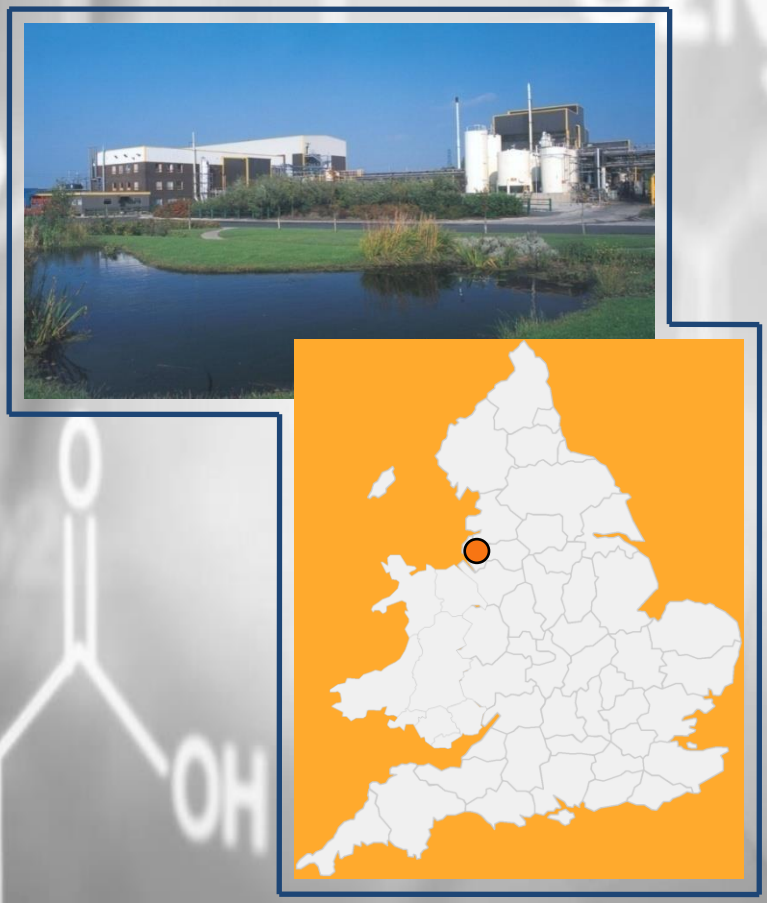
Dr Tony Bastock

Chairman Contract Chemicals Ltd

Vice President Cefic

Contract Chemicals Company Profile

- established in1977
- privately owned
- turnover ca. €30m per annum
- sales in over 40 countries
- employ around 100 people
- based in Knowsley, UK



CMO's - Custom, Toll, Contract Manufacture

- **CMO: Custom/Contract Manufacturing Organisation**
- **Custom manufacturing:**

  the process of making products or product lines to a customer's unique specifications.

- **Toll Manufacturing:**

  the process of a company providing its raw materials or semi-finished goods to a third-party CMO who often has specialized equipment or chemistry, to carry manufacturing processes on its behalf using those materials or goods for a fee or toll.

- **Contract Manufacturing:**

  either of the above, with a term/conditions contract in place

CMO's - Custom, Toll, Contract Manufacture

- **CMO: Custom/Contract Manufacturing**
- **Custom manufacturing:**

  the process of making p… product lines to a custo… specifications.

- **Toll Manufacturing:**

  the process… its raw materials or semi-fini… …ty CMO who often has … …emistry, to carry … …s behalf using those … or toll.

- **Cont…**

  …ve, with a te… …ns contract in place

Contract Manufacturing Market for Pharma API's €11.8 billion

The Need for Contract Manufacture

The customer company:-

- fills its capacity, but needs more product
- develops a new product and wants to test the market before investing in a new plant
- does not have the equipment and/or chemistry to produce a new product
- wants to outsource early stages, but produce the final compound in-house
- wants local production for local markets
- needs building blocks (intermediates) for its products or formulations manufactured to bespoke specifications

Choosing a CMO

- Every chemical company is a CMO!
- Almost every toll manufacturing process is carried out under a non-disclosure agreement

  -These can be onerous and restrictive

- Choose a company whose equipment, chemistry and regulatory position fits the process/product

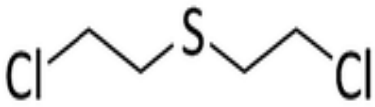
  -Large amounts of information available through Web, trade shows, trade press and company literature

- Be prepared to invest

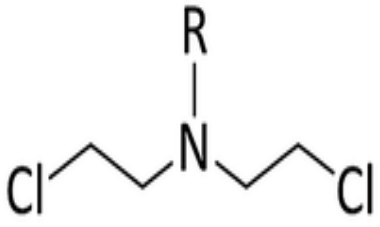
£ € $!!

£ € $!!

Chemical Weapons Manufacture

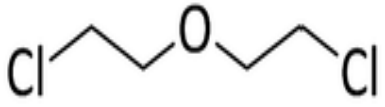


Sulfur mustard

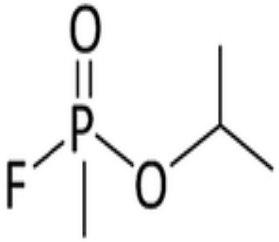


Nitrogen mustard

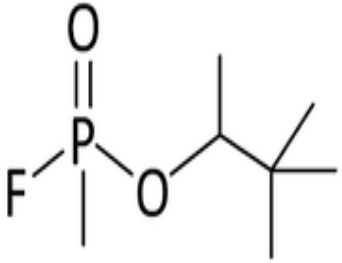
NH1 R = CH_2CH_3
HN2 R = CH_3
NH3 R = CH_2CH_2Cl



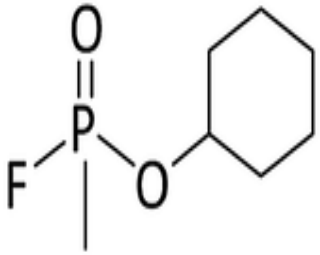
Bis(2-chloroethyl)ether



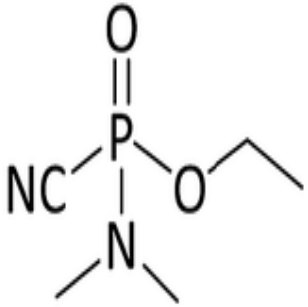
Sarin



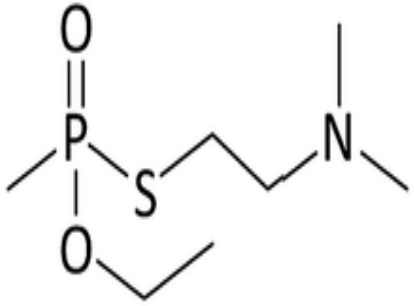
Soman



Cyclosarin

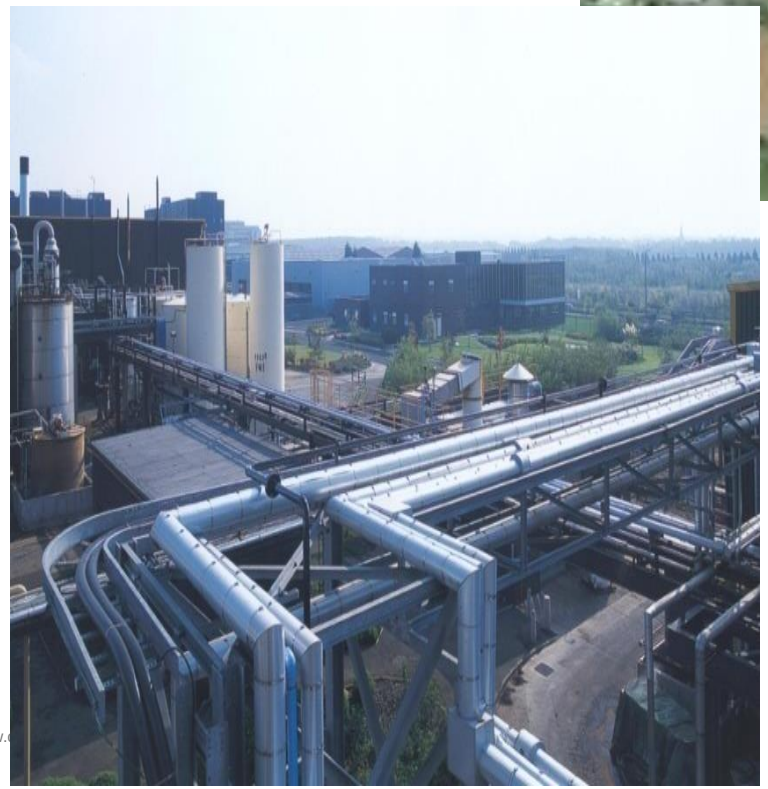


Tabun



Vx

Chemical Weapons Manufacture



Thematic Discussions: four topics considered

Interactive Discussions

Topic 1:

Advances in chemical production technologies and the synthesis of chemicals scheduled under the Chemical Weapons Convention

Facilitated by Jonathan Forman

- *What has changed and what impact might it have on recognizing a relevant process?*
- *If the answer changes when considering different production scales?*

Topic 2:
Advances in biological production technologies and the synthesis of bioregulators and/or biological toxins

Facilitated by Cheng Tang

- *What is the current status of the chemical synthesis of bioregulators and/or biological toxins?*
- *Is there an impact to the Chemical Weapons Convention given the capabilities available for production of bioregulators and/or toxins?*

Topic 3:
New synthesis tools and technologies for enhancing the capabilities of the OPCW Designated Laboratories

Facilitated by Chris Timperley

- *What synthetic tools and methods are available for enhancing the capabilities of OPCW Designated Labs?*
- *And which synthetic technologies being adopted in academia and/or industry could benefit the Designated Labs?*

Topic 4:

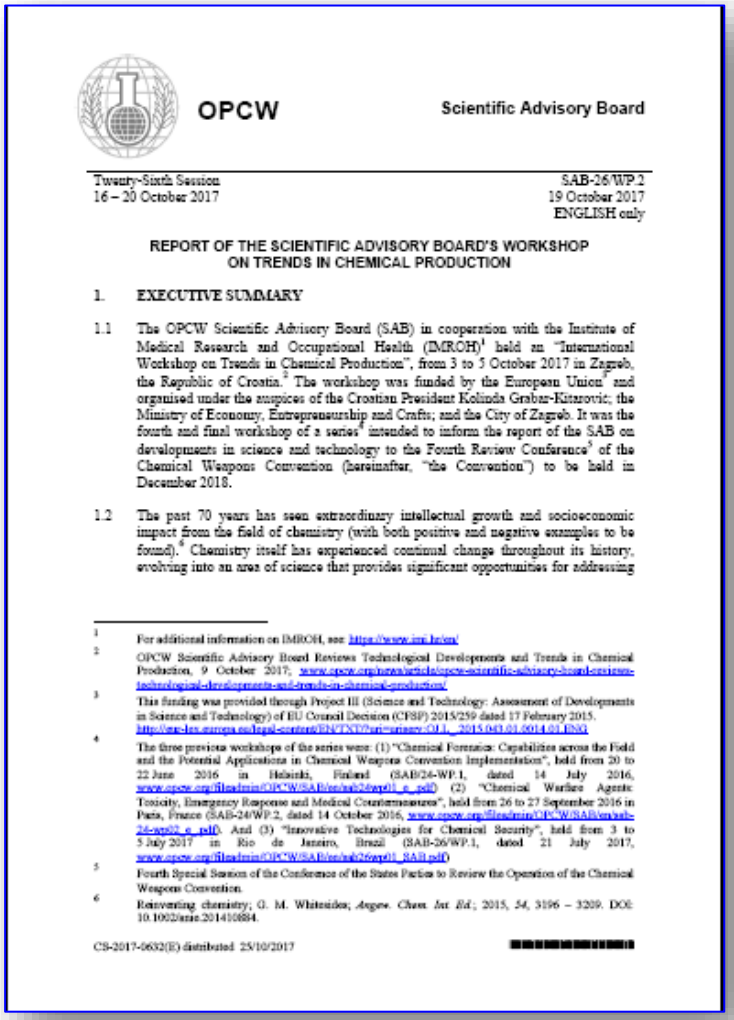
The impact of current trends and future directions in chemical production on the Chemical Weapons Convention verification regime

Facilitated by Stephanie Dare-Doyen

- *Which current trends and potential future directions in chemical production would be of concern for the Convention?*
- *In light of advances in science and technology, and a changing security environment, are revisions to the verification approach necessary?*

The Final Report (SAB-26/WP.2)

(REPORT OF THE SCIENTIFIC ADVISORY BOARD'S WORKSHOP ON TRENDS IN CHEMICAL PRODUCTION)



OPCW Scientific Advisory Board

Twenty-Sixth Session
16 – 20 October 2017

SAB-26/WP.2
19 October 2017
ENGLISH only

REPORT OF THE SCIENTIFIC ADVISORY BOARD'S WORKSHOP ON TRENDS IN CHEMICAL PRODUCTION

1. EXECUTIVE SUMMARY

1.1 The OPCW Scientific Advisory Board (SAB) in cooperation with the Institute of Medical Research and Occupational Health (IMROH)[1] held an "International Workshop on Trends in Chemical Production", from 3 to 5 October 2017 in Zagreb, the Republic of Croatia.[2] The workshop was funded by the European Union[3] and organised under the auspices of the Croatian President Kolinda Grabar-Kitarović; the Ministry of Economy, Entrepreneurship and Crafts; and the City of Zagreb. It was the fourth and final workshop of a series[4] intended to inform the report of the SAB on developments in science and technology to the Fourth Review Conference[5] of the Chemical Weapons Convention (hereinafter, "the Convention") to be held in December 2018.

1.2 The past 70 years has seen extraordinary intellectual growth and socioeconomic impact from the field of chemistry (with both positive and negative examples to be found).[6] Chemistry itself has experienced continual change throughout its history, evolving into an area of science that provides significant opportunities for addressing

1 For additional information on IMROH, see: https://www.imi.hr/en/

2 OPCW Scientific Advisory Board Reviews Technological Developments and Trends in Chemical Production, 9 October 2017; www.opcw.org/news/article/opcw-scientific-advisory-board-reviews-technological-developments-and-trends-in-chemical-production/

3 This funding was provided through Project III (Science and Technology: Assessment of Developments in Science and Technology) of EU Council Decision (CFSP) 2015/259 dated 17 February 2015. http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2015.043.01.0014.01.ENG

4 The three previous workshops of the series were: (1) "Chemical Forensics: Capabilities across the Field and the Potential Applications in Chemical Weapons Convention Implementation", held from 20 to 22 June 2016 in Helsinki, Finland (SAB/24-WP.1, dated 14 July 2016, www.opcw.org/fileadmin/OPCW/SAB/en/sab24wp01_e_.pdf) (2) "Chemical Warfare Agents: Toxicity, Emergency Response and Medical Countermeasures", held from 26 to 27 September 2016 in Paris, France (SAB-24/WP.2, dated 14 October 2016, www.opcw.org/fileadmin/OPCW/SAB/en/sab-24-wp02_e_.pdf). And (3) "Innovative Technologies for Chemical Security", held from 3 to 5 July 2017 in Rio de Janeiro, Brazil (SAB-26/WP.1, dated 21 July 2017, www.opcw.org/fileadmin/OPCW/SAB/en/sab26wp01_SAB.pdf)

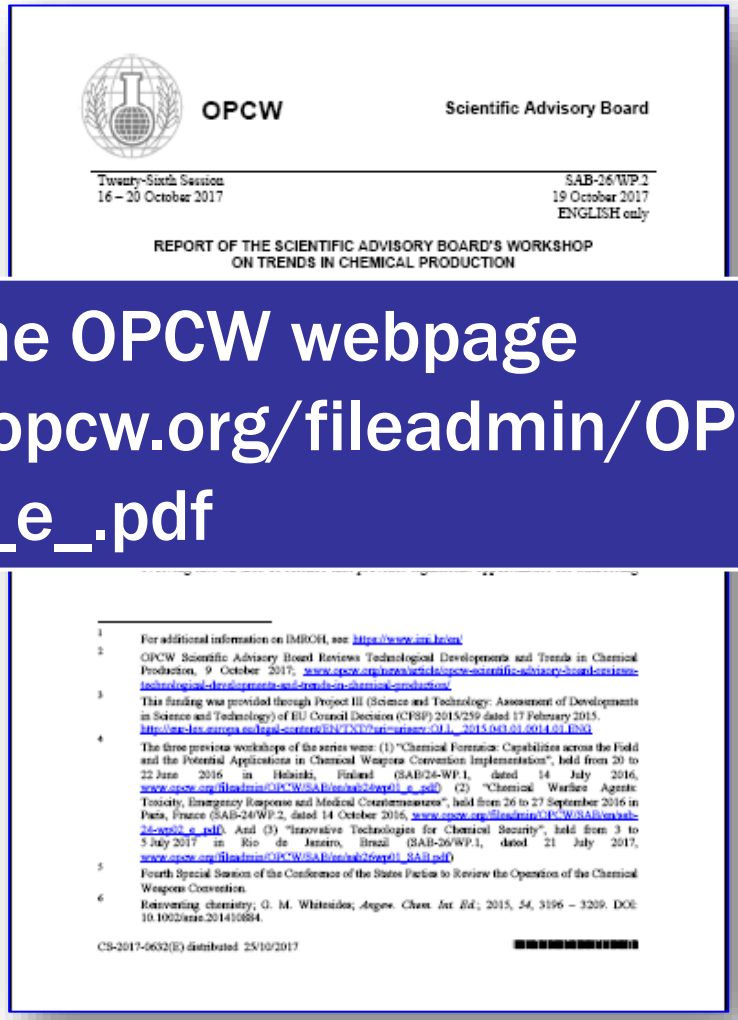
5 Fourth Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention.

6 Reinventing chemistry; G. M. Whitesides; *Angew. Chem. Int. Ed.*; 2015, *54*, 3196 – 3209. DOI: 10.1002/anie.201410084.

CS-2017-0632(E) distributed: 25/10/2017

The Final Report (SAB-26/WP.2)

(REPORT OF THE SCIENTIFIC ADVISORY BOARD'S WORKSHOP ON TRENDS IN CHEMICAL PRODUCTION)



OPCW

Scientific Advisory Board

Twenty-Sixth Session
16 – 20 October 2017

SAB-26/WP.2
19 October 2017
ENGLISH only

REPORT OF THE SCIENTIFIC ADVISORY BOARD'S WORKSHOP ON TRENDS IN CHEMICAL PRODUCTION

1 For additional information on IMROH, see: https://www.imroh.ir/en/

2 OPCW Scientific Advisory Board Reviews Technological Developments and Trends in Chemical Production, 9 October 2017, www.opcw.org/news/article/opcw-scientific-advisory-board-reviews-technological-developments-and-trends-in-chemical-production/

3 This funding was provided through Project III (Science and Technology: Assessment of Developments in Science and Technology) of EU Council Decision (CFSP) 2015/259 dated 17 February 2015. http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2015.043.01.0014.01.ENG

4 The three previous workshops of the series were: (1) "Chemical Forensics: Capabilities across the Field and the Potential Applications in Chemical Weapons Convention Implementation", held from 20 to 22 June 2016 in Helsinki, Finland (SAB/24-WP.1, dated 14 July 2016, www.opcw.org/fileadmin/OPCW/SAB/en/sab24wp01_e_.pdf) (2) "Chemical Warfare Agents: Toxicity, Emergency Response and Medical Countermeasures", held from 26 to 27 September 2016 in Paris, France (SAB-24/WP.2, dated 14 October 2016, www.opcw.org/fileadmin/OPCW/SAB/en/sab-24-wp02_e_.pdf). And (3) "Innovative Technologies for Chemical Security", held from 3 to 5 July 2017 in Rio de Janeiro, Brazil (SAB-26/WP.1, dated 21 July 2017, www.opcw.org/fileadmin/OPCW/SAB/en/sab26wp01_SAB.pdf)

5 Fourth Special Session of the Conference of the States Parties to Review the Operation of the Chemical Weapons Convention.

6 Reinventing chemistry; G. M. Whitesides; *Angew. Chem. Int. Ed.*; 2015, *54*, 3196 – 3209. DOI: 10.1002/anie.201410084.

CS-2017-0632(E) distributed: 25/10/2017

[redacted]

Available in the OPCW webpage https://www.opcw.org/fileadmin/OPCW/SAB/en/sab-26-wp02_e_.pdf

Outcomes of the workshop

a) A fit-for-purpose verification regime should maintain up to date operational knowledge of chemical (and biological) production methods (including aspects of synthesis and analysis).

b) Drew attention to previous advice from the SAB's temporary working group (TWG) on Verification that considered risk-benefit approaches as a means to focus verification, including consideration of relevant chemicals not on the current schedules.

c) Recognized a number of areas with potentially transferable learnings from industrial practices. These include approaches to trace analysis and tools for chemical risk assessment.

Outcomes of the workshop *(continue)*

d) Several significant developments in the global chemical industry observed over the past 20 years were not recognized until they actually took shape (e.g. they were unanticipated in the years just before they happened).

e) Synthesis tools being developed for chemical discovery purposes (complemented with machine learning approaches for predicting chemistry) can potentially enable capabilities for laboratories to quickly generate large sets of analytical data, screen for reactivity and toxicity properties, and elucidate degradation pathways of a broad range of chemical classes.

Outcomes of the workshop *(continue)*

f) The technical presentations and content of the workshop served as a reminder of the highly trans-disciplinary (convergent) nature of 21st century technology development, with scientific disciplinary convergence going well beyond the fields of chemistry and biology. Sharing of experience on science advice with other relevant disarmament communities (especially the Biological Weapons Convention stakeholders) should be encouraged.

g) In the discussion of changing realities and the relevance of current verification practices, it was acknowledged that greater levels of science and technology engagement, and knowledge sharing amongst States Parties could also support

Outcomes of the workshop *(continue)*

f) The technical presentations and content of the workshop served as a reminder of the highly trans-disciplinary (convergent) nature of 21st century technology dev nt, with scientific disciplinary convergence goin the fields of chemistry and biology. Sh science advice with other rele communities (especiall tion stakeholders) sh

g) In the di the relevance of s acknowledged that technology engagement, and mongst States Parties could also

The SAB 26 endorsed the report and these proposals

The next steps

- **The SAB will prepare a report to the Forth Review Conference based on the series of four workshops conducted :**
  - *Chemical Forensic (Helsinki, June 2016)*
  - *Medical Countermeasures (Paris, October, 2016)*
  - *Innovative Technologies for Chemical Security (Rio De Janeiro, July 2017)*
  - *Trends in Chemical Industry (Zagreb, October 2017)*
- **Jonathan will explain more…**