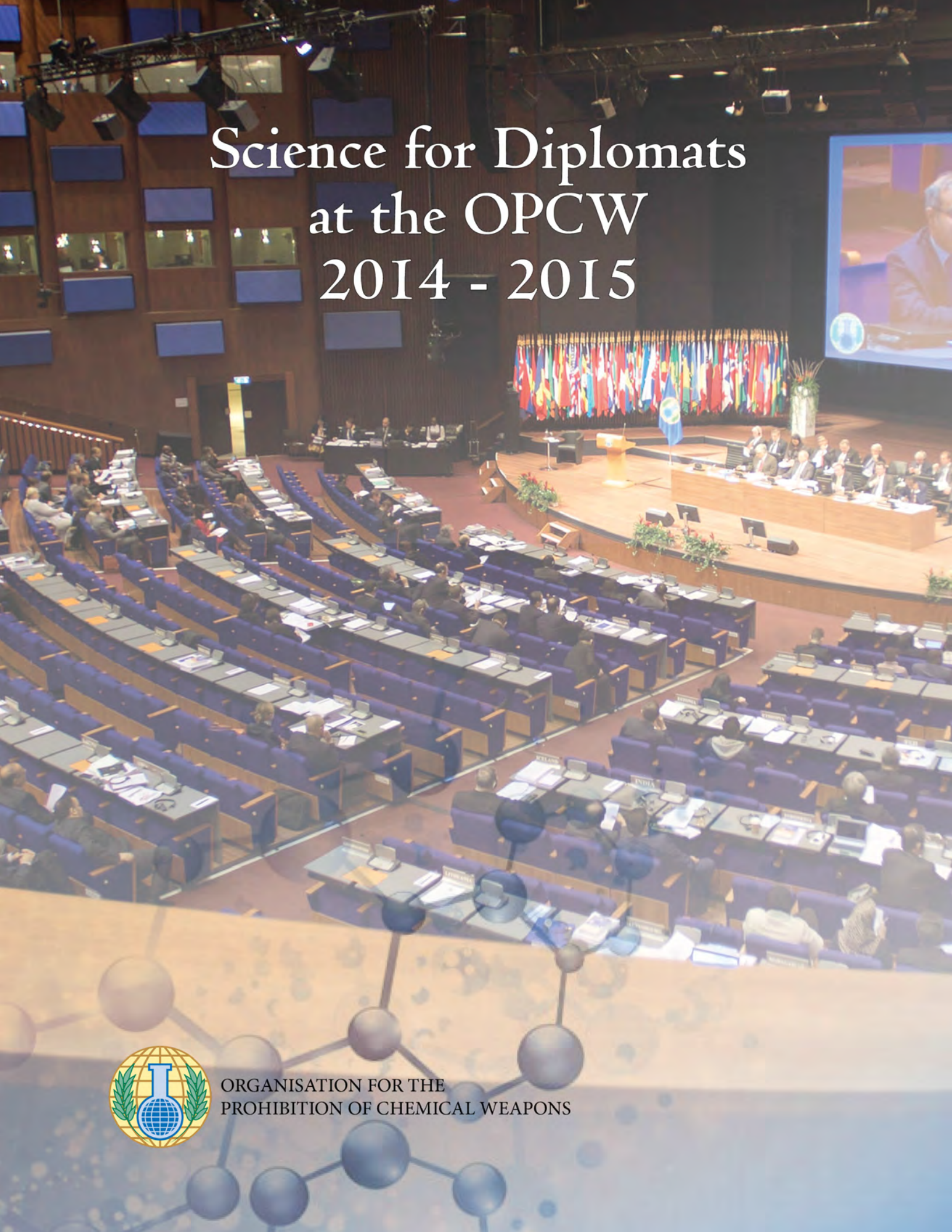

Science for Diplomats at the OPCW 2014 - 2015

ORGANISATION FOR THE
PROHIBITION OF CHEMICAL WEAPONS

Science for Diplomats at the OPCW
2014 - 2015

A compilation of materials presented in and as part of the OPCW Office of Strategy and Policy Science for Diplomats initiative. Original materials can be downloaded from the OPCW website: www.opcw.org/special-sections/science-technology/science-for-diplomats/

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Editors: Jonathan E. Forman (Science Policy Adviser), Wesam Alwan

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Foreword

Science and technology play a critical role in international disarmament policy and diplomacy; technical considerations inform negotiation of international agreements and underpin the key provisions that define the mechanisms of treaty implementation. To be effective, disarmament treaties require a sound science and policymaker partnership, a partnership that must overcome challenges to communication and trust (much like the partnerships between States Parties to international treaties). To make such a parternship work, clear science communication and engagement between the two perspectives is needed, where scientists provide analytical thinking and technical assessments to policy makers, who in turn provide global perspectives on the role and need for science in their work. As the dynamism of science can both improve and potentially undermine our ability to maintain an effective disarmament regime, this partnership has never been more important! For this reason, we must look at science and technology as a priority in our work, actively engage with scientific experts and ensure that policymakers use scientific insights in their decision making.

To stimulate more effective, science engagement with policy makers, the OPCW initiated a series of "Science for Diplomats" briefings in 2014. As the Science for Diplomats initiative moves into its third year in 2016, we present here a compilation of the briefings held in 2014 and 2015. Individual presentations and further materials relevant to science communication and science engagement between scientists and policy-makers can be obtained on the OPCW website at:

www.opcw.org/special-sections/science-technology/science-for-diplomats/

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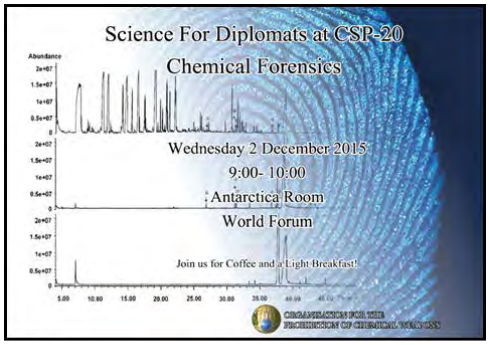

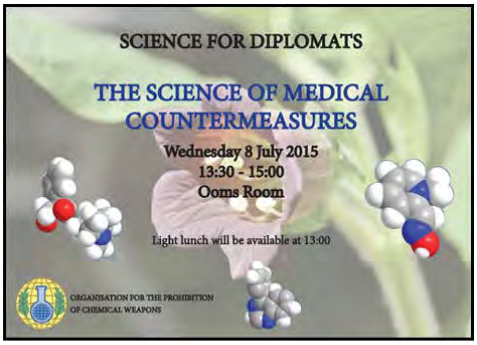

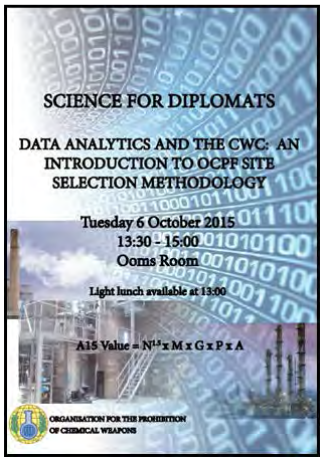

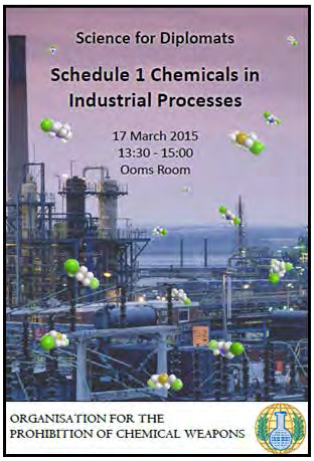

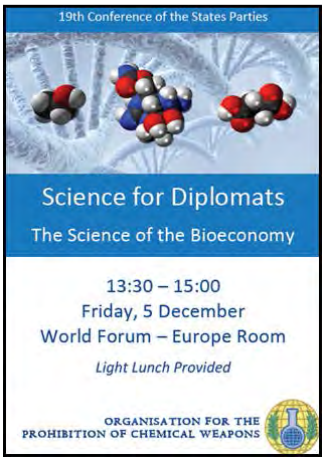

Science for diplomats (Introduction)

Scientific discovery and technology development: trends and topics for the CWC policy-maker

Brought to you by the Office of Strategy and Policy

26 June 2014
OPCW Headquarters
The Hague, The Netherlands

Jonathan E. Forman
Science Policy Adviser
Office of Strategy and Policy
Organisation for the Prohibition of Chemical Weapons

ORGANISATION FOR THE
PROHIBITION OF CHEMICAL WEAPONS

Working together for a world free of chemical weapons

From The Convention

- **The Conference of States Parties Shall:**
  - **"Review scientific and technological developments that could affect the operation of this Convention** and, in this context, direct the Director General to establish a Scientific Advisory Board to enable him, in the performance of his functions, to render specialized advice in areas of science and technology relevant to this Convention, to the Conference, the Executive Council or States Parties."
  - *CWC Article VIII, Section B, paragraph 21(h)*

The Third Review Conference

- **"Conviction** that the provisions of the Convention are mutually reinforcing and that the full, effective, and non-discriminatory implementation of all of its provisions, taking into account relevant developments in science, technology and industry, is of critical importance;"

  RC-3/3 paragraph 9.4*

- **"Recognition** that new challenges related to the Convention continue to arise and that its implementation may need to be improved to continue to achieve the object and purpose of the Convention and to stay abreast of developments in science and technology;"

  RC-3/3, paragraph 9.9*

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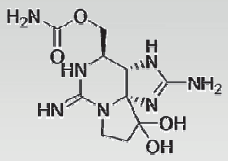
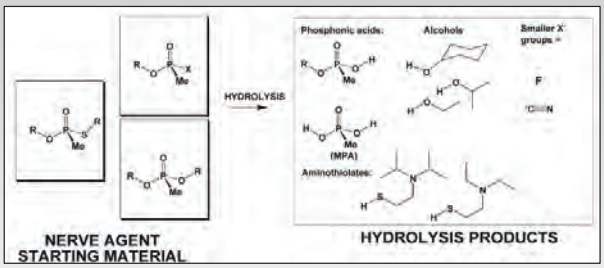
Science and Technology Underpin the CWC



Article II

Article III

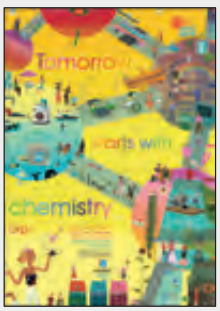


Articles IV and V

Article VI

Article VIII

Articles IX and X



Article XI

Article VII

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SAB Report of the Developments in S&T to The Third review Conference

(RC-3/DG.1, Dated 29 October 2012)

Director General's Recommendations

(RC-3/DG.2, Dated 31 January 2013)

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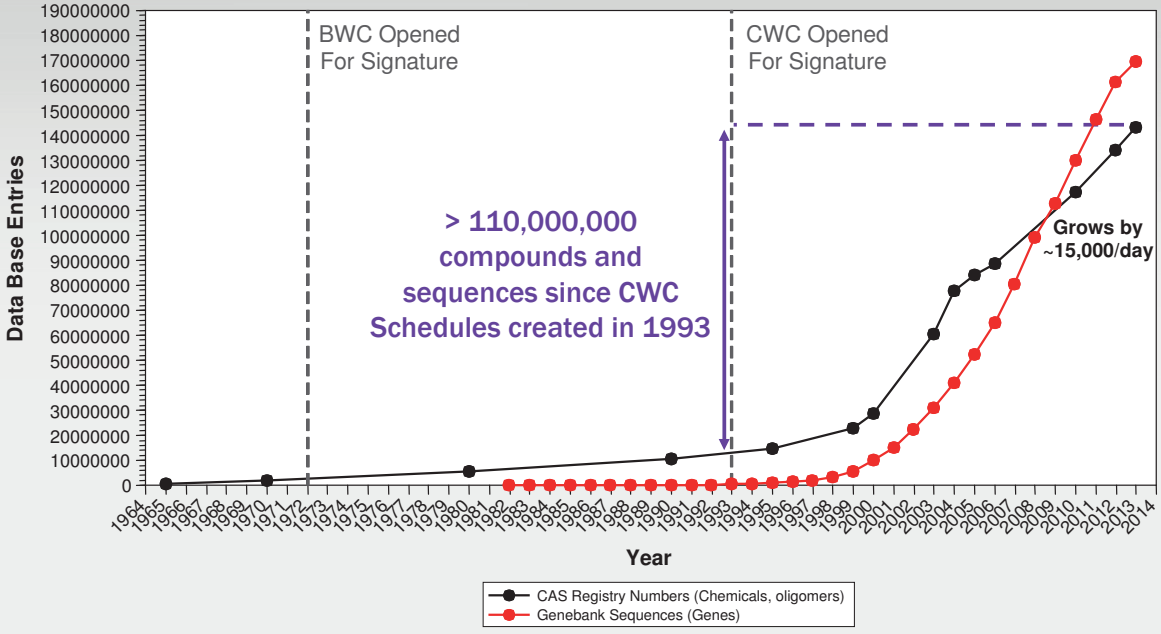
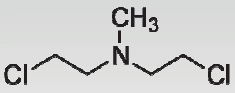
Monitoring Science

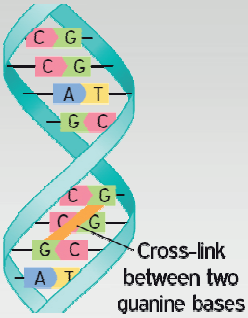


www.opcw.org

Chemicals Have Multiple Uses



Nitrogen Mustard
Schedule 1A



and Anti-Cancer Drug
(as a salt)

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Research On Toxic Substances

THE BACTERIAL TOXIN TOOLKIT

Giampietro Schiavo and F. Gisou van der Goot‡*

Pathogenic bacteria and higher eukaryotes have spent a long time together, leading to a precise understanding of one another's way of functioning. Through rapid evolution, bacteria have engineered increasingly sophisticated weapons to hit exactly where it hurts, interfering with fundamental host functions. However, toxins are not only useful to the bacteria — they have also become an essential asset for life scientists, who can now use them as toolkits to explore cellular processes.

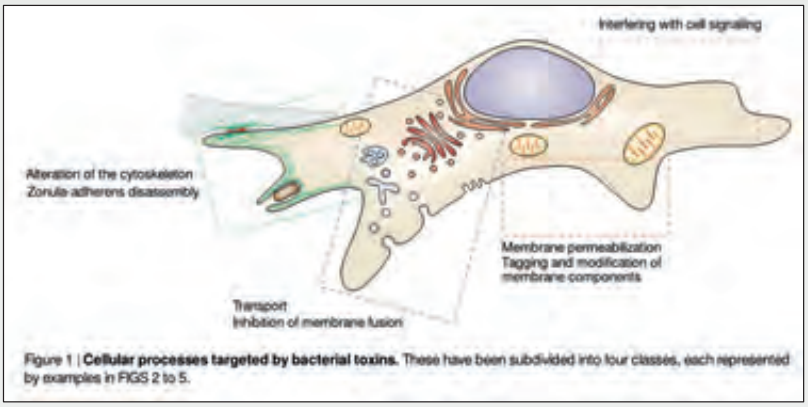

Figure 1 | **Cellular processes targeted by bacterial toxins.** These have been subdivided into four classes, each represented by examples in FIGS 2 to 5.

From: Nature Reviews, Molecular cell Biology, 2001, 531-537

Can This Be Easily Discussed?

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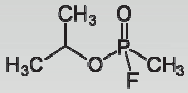
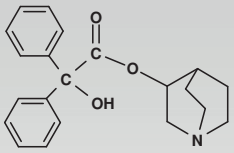
What Defines a Chemical?

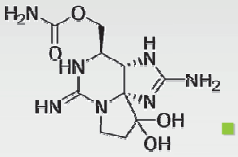
Understanding Chemicals

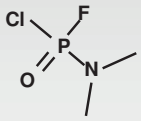




- **> 140 Million CAS Numbers!**
- **How Many Possible Scheduled Chemicals?**

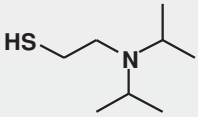
Infinite number of possibilities!
(generic structures in Schedule 1 and Schedule 2)

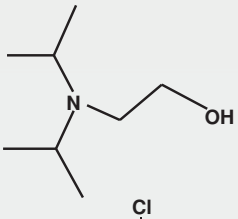




- **How Many Actual Scheduled Chemicals**

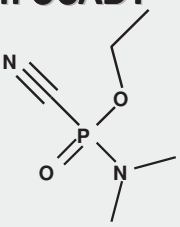
~35,000 CAS Numbers Reported

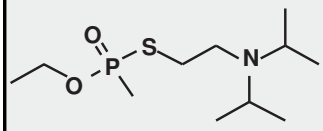


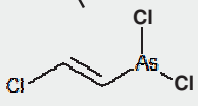


- **How Many Mass Spectra in OCAD?**

~5,000







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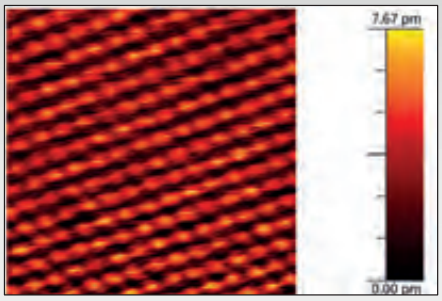
Organic chemicals: A broad class of substances containing carbon

PSF = Phosphorous, Sulfur, Fluorine

From Atoms to Compounds

- **Atoms are the building blocks**

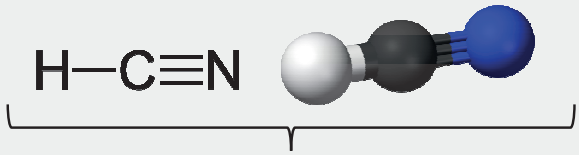
Silver (Ag) atoms in a crystal



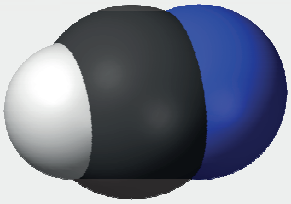
$$1\ \text{pm} = \frac{1\ \text{meter}}{1{,}000{,}000{,}000{,}000}$$

- **Atoms combine to form molecules**

HCN
Hydrogen (H)
Carbon (C)
Nitrogen (N)



Depiction of how atoms are bonded to one another



3D Representation showing relative sizes of atoms

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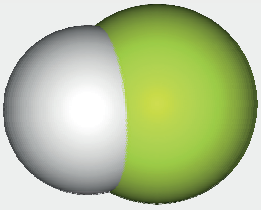
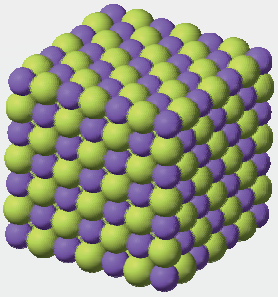
Some Definitions

- **Elements can be described as atoms or molecules**
  - Fluorine atom (F)
  - Fluorine molecule (F_2)

- **Compounds are composed of multiple elements**
  - Hydrogen Fluoride (HF)
  - Sodium Fluoride (NaF)

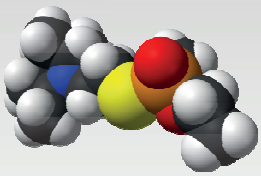




Scheduled Chemicals Span a Broad Range of Properties

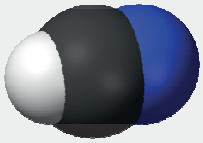
<u>*O*-ethyl-*S*-[2(diisopropylamino)ethyl] methylphosphonothiolate (VX)</u>

43 atoms ($C_{11}H_{26}NO_2PS$)
Schedule 1
liquid
Molecular mass = 267



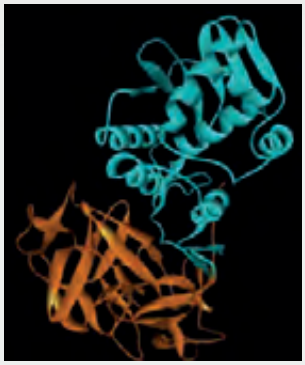
<u>Hydrogen Cyanide (HCN)</u>

3 atoms
Schedule 3
Gas
Molecular mass = 27



<u>Ricin</u>

A sequence of
> 520 amino acids
Schedule 1
Solid
Molecular mass ~62,000
(~260X larger than VX)



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The Convergence of Chemistry and Biology

Chemistry Underpins Biology

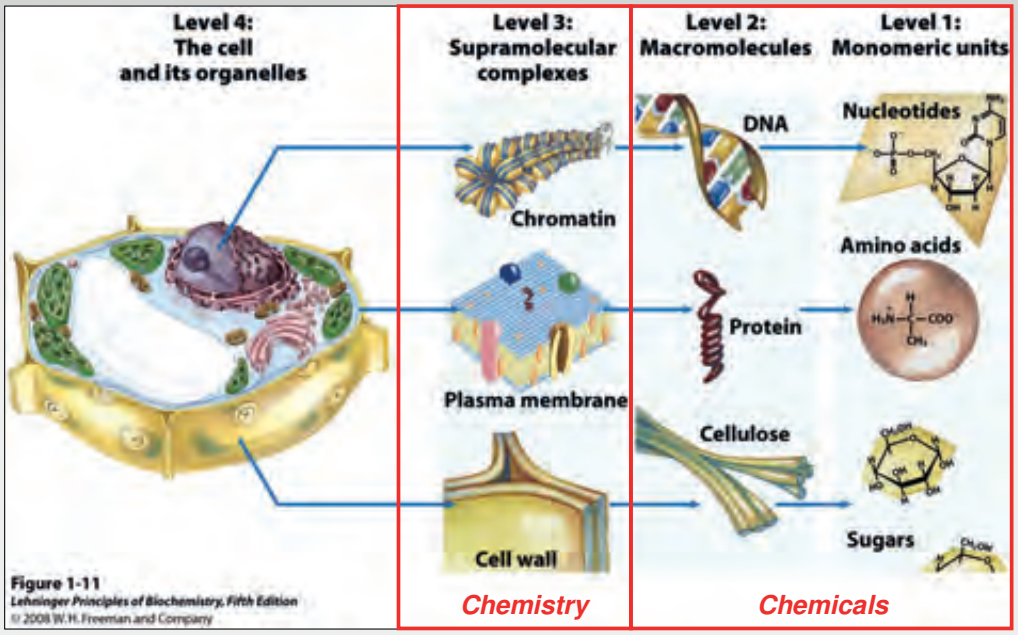

Figure 1-11
Lehninger Principles of Biochemistry, Fifth Edition
© 2008 W. H. Freeman and Company

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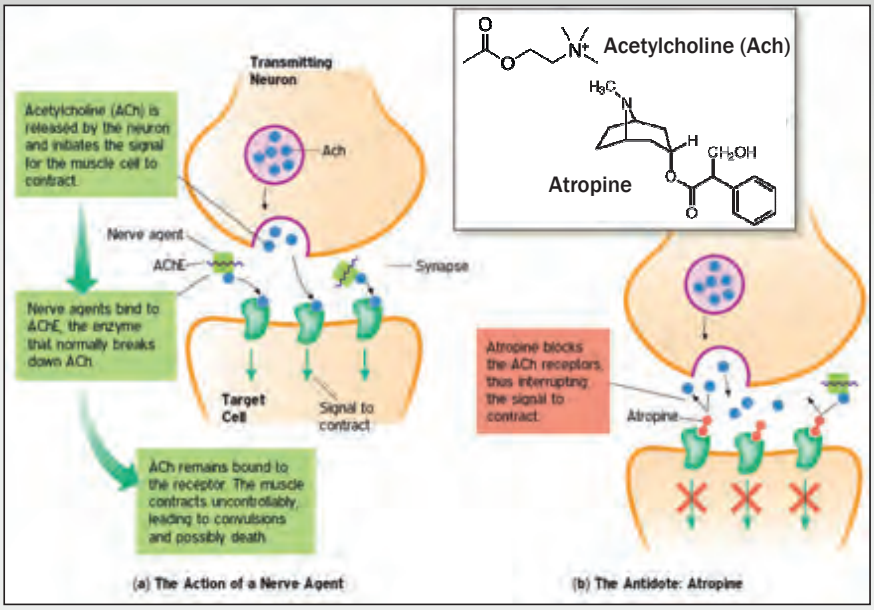
Chemicals Influence Biology



Chemical Production

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Chemistry is a Science of Change

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Technology is the Integration of functional components into Multifunctional Tools

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Production Technology: Production by Synthesis?

Raw Material ***(Bulk Chemical)***

Pre-Process

Chemical Formation (Synthesis?)

Separate (Purify)

Product ***(Bulk Chemical)***

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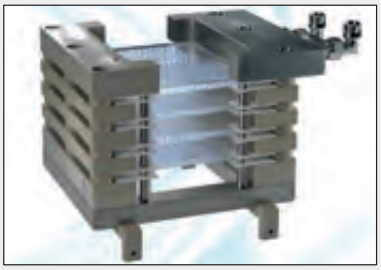
Continuous Flow Technologies

Microreactor
1 metric tonne ~700,000 days

Larger "Microreactor"
1 metric tonne ~1,070 days
"number up" to increase throughput



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Production Scale Continuous Flow System

Scientific and Technological Development

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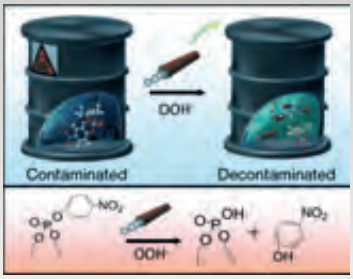
Basic Research vs. Fieldable Applications

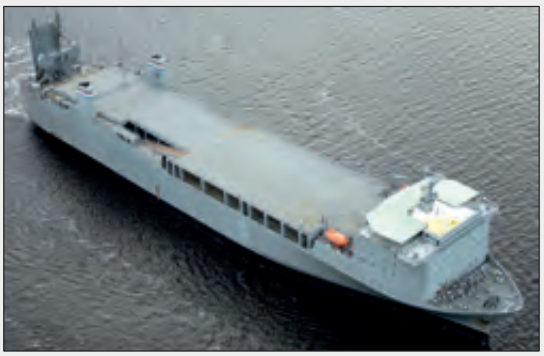


Clever ideas – but are they practical and effective?

~150,000/ml ~ 200 rpm mechanical stirring in 15 ml volume using H_2O_2 as both fuel for stirrers and neutralization agent

Angewandte Chemie International Edition, 2013, 50, p13276

Portable systems adopted for use in 2013



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How Do Ideas and Research Results Become Realities?

?

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Converging Science is the Norm, Not the Exception!

Chemistry – Biology – Physics – Engineering – Informatics and More...

Deciphering Technical Reports

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What Does It Mean and How Applicable Is it?

Scrutinizing Technical Reports

- Differences and chance cause variation
- No measurement is exact
- Bias is rife
- Bigger is usually better for sample size
- Correlation does not imply causation
- Regression to the mean can mislead
- Extrapolating beyond the data is risky
- Beware the base-rate fallacy
- Controls are important
- Randomization avoids bias
- Seek replication, not pseudoreplication
- Scientists are human
- Significance is significant
- Separate no effect from non-significance
- Effect size matters
- Study relevance limits generalizations
- Feelings influence risk perception
- Dependencies change the risks
- Data can be dredged or cherry picked
- Extreme measurements may mislead

From: "Twenty tips for interpreting scientific claims", *Nature*, 2013, 503,p337

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Summary and Future Discussion

From The Director General's Recommendations to RC-3

(RC-3/DG.2, Dated 31 January 2013)

- Monitoring S&T Developments (paras 7, 8, 29, 37)
- Verification (paras 12, 13, 14, 17, 18, 20, 21, 22)
  - Includes recommendations on Transfer Notifications (para 11) and
  - Incapacitating Agents (paras 15, 16)
- Laboratory Capabilities and Analysis (paras 24, 25, 26, 30, 32)
- Expertise, Training and Knowledge (paras 34, 36, 37)
- Assistance and Protection (para 35)
- Education and Outreach (para 28)

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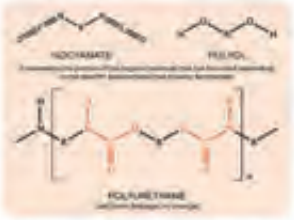
S & T For Diplomats: A Series of Discussions

- 9 July (On the margins of EC-76)
  - **S&T for Diplomats (1): Chemical analysis in verification**
    - SAB Laboratory recommendations
    - Sampling and analysis
- October (On the margins of EC-77, To be confirmed)
  - **S&T for Diplomats (2): Biological processes and chemical production**
    - SAB convergence related recommendations
    - Production by synthesis
- **Other topics to be scheduled**

THE CHEMISTRY OF THE WORLD CUP BALL

POLYURETHANE COVERING

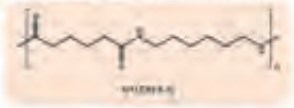
The surface covering of a football is composed of synthetic leather; in professional footballs, this is made from polyurethane polymers. The World Cup ball is made from six polyurethane panels, which are thermally bonded together. This covering protects the ball and minimises water absorption. In cheaper footballs, the coating can be made from PVC.



Polyurethane is a polymer - a very large molecule built up from many smaller units bonded together. The basic synthesis of polyurethanes involves the addition reaction of isocyanate and polyol molecules to form urethane groups.

NYLON LINING

Several layers of lining are used between the covering of the football and the bladder to improve the bounce and strength of the ball. This lining is made of nylon, another class of polymers also known as polyamides. Polyesters can also be used for this purpose.



BUTYL BLADDER

The bladder is the part of the ball in which the air is contained. Butyl rubber is often used because it retains the air better than the other option, latex. However, latex bladders can provide better surface tension.

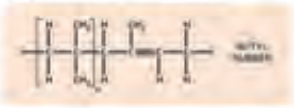


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PHOTO BY -RENATOGIZZI (FLICKR.COM/PHOTOS/27) - SHARED UNDER A CREATIVE COMMONS BY SA LICENCE

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Science for diplomats (1)

Chemical Analysis in Verification

9 July 2014
OPCW Headquarters
The Hague, The Netherlands

Jonathan E. Forman, Ph.D.
Science Policy Adviser, Office of Strategy and Policy

Hugh Gregg, Ph.D.
Head Laboratory
Organisation for the Prohibition of Chemical Weapons

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SAB Report of the Developments in S&T to The Third review Conference

(RC-3/DG.1, Dated 29 October 2012)

Director General's Recommendations

(RC-3/DG.2, Dated 31 January 2013)

Laboratory Capabilities and Analysis	
"The Secretariat will continue to monitor developments relating to **unscheduled and novel toxic chemicals** and will explore ways in which to augment its **technical capabilities** in this area." "…notes the SAB's views on the **OPCW Central Analytical Database** and…the Secretariat needs to have analytical data on relevant unscheduled chemicals." (paragraphs 9 and 32 of RC-3/DG.2)	• The OPCW Laboratory (LAB) is monitoring developments, has noted the SAB's advice on RCAs and is working with the Validation Group to obtain analytical data on relevant unscheduled chemicals • LAB is establishing a training laboratory • LAB participates in various activities and programmes (e.g. EQuATox). • OCAD continues to be regularly updated, it currently contains validated data for > 5000 scheduled chemicals
"..note the importance of continuing to **improve on-site and off-site analysis**" "…future such exercises will progress towards the more difficult analysis of longer-lived biomarkers of exposure, such as protein adducts" "…resources be made available to enable **regular exercises of the entire off-site analysis process** to be conducted in conjunction with OPCW field exercises." (paragraphs 24, 25, and 30 of RC-3/DG.2)	• Effective capability was demonstrated in the investigation of alleged use in 2013. • LAB and OPCW Designated Laboratories are continually working on refining methodologies. • LAB is continuing to improve its capabilities for conducting biomedical sampling and analysis.
"…a **review of the proficiency-testing programme** be undertaken" (paragraph 26 RC-3/DG.2)	• Dr. Robin Black, former SAB member, is chairing a group to review the proficiency testing programme

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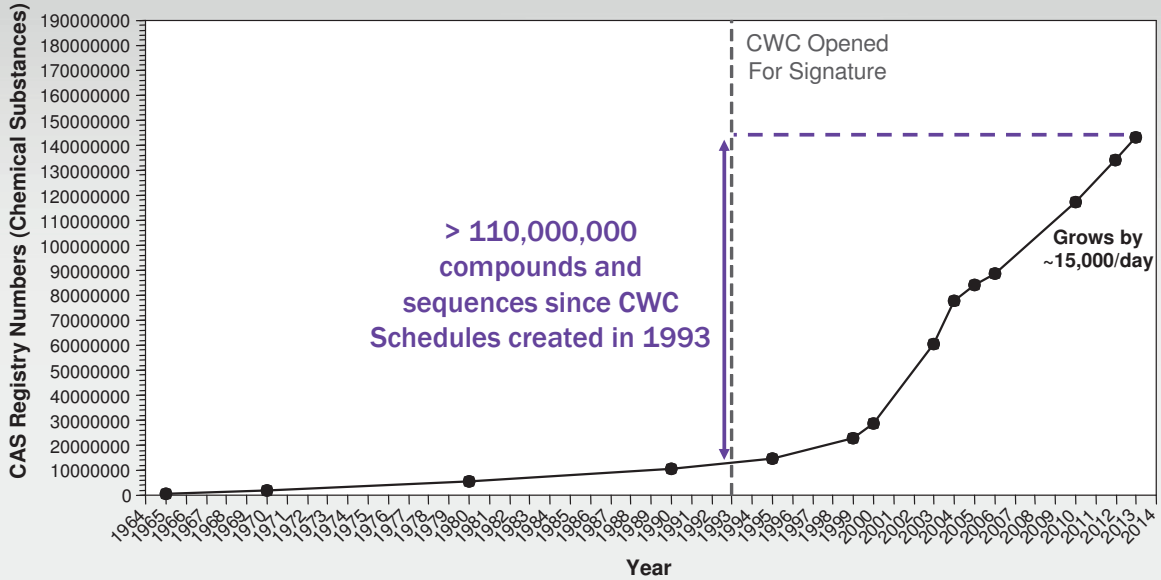
Reported Chemical Substances 1965-2013



www.opcw.org

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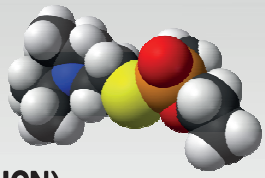
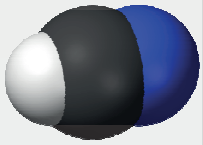
Scheduled Chemicals Span a Broad Range of Properties

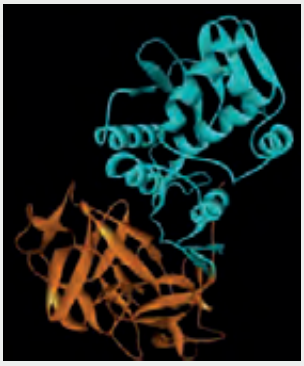
VX (*O*-ethyl-*S*-[2(diisopropylamino)ethyl] methylphosphonothiolate



Hydrogen Cyanide (HCN)



Ricin



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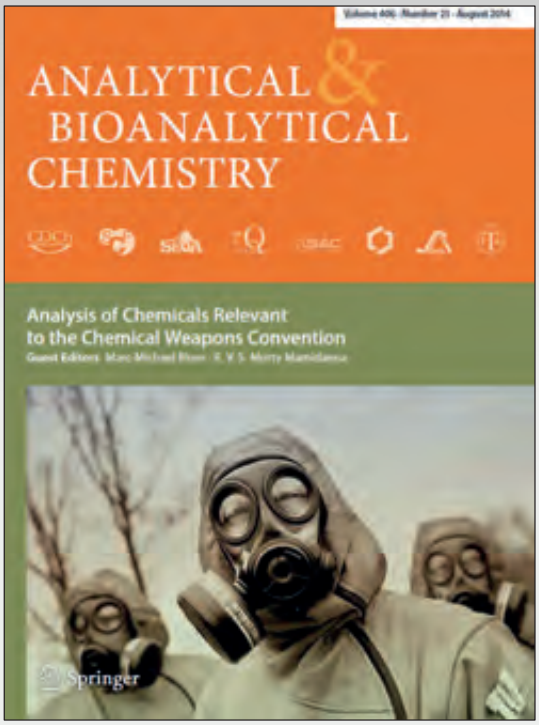
The Most Appropriate Analytical Method?



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Presentation by Hugh Gregg

Chemical Analysis in the Verification of the Chemical Weapons Convention

Presentation given in the series
Science for Diplomats
9 July 2014

Hugh Gregg, Ph.D.
Head, OPCW Laboratory

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Outline

- Basis for Sampling and Analysis
- Sampling & types of samples
  - Industry inspections
  - Challenge Inspection or Investigation of Alleged Use
    - Environmental
    - Biomedical
- Analysis
  - On-site
    - Primary tool: GC/MS
    - Other tools: FTIR, Raman
    - Test kits (Saxitoxin, Ricin)
  - Off-site
  - S&A in support of the UN mission to Syria in 2013

Verification Annex of the CWC: S&A

VER annex	Text
Part VII, §27 Ind., S2	Sampling and analysis shall be undertaken to check for the absence of undeclared scheduled chemicals. 68 S2 S&A missions to date
Part VIII, §22 Ind., S3	Sampling and on-site analysis may be undertaken to check for the absence of undeclared scheduled chemicals. …
Part IX, §19 Ind., OCPF	Sampling and on-site analysis may be undertaken to check for the absence of undeclared scheduled chemicals. …
Part X, §36 Challenge Inspection	In conducting the perimeter activities, the inspection team shall have the right to: … (b) Take wipes, air, soil or effluent samples; …
Part XI, §16-17 Investigation of Alleged Use	The inspection team shall have the right to collect samples of types, and in quantities it considers necessary. … Samples of importance in the investigation of alleged use include toxic chemicals, munitions and devices, remnants of munitions and devices, environmental samples (air, soil, vegetation, water, snow, etc.) and biomedical samples from human or animal sources (blood, urine, excreta, tissue etc.).

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Sampling at Industry Inspections

- Samples collected by plant personnel, following plant protocols and their health and safety policies
- Samples can be any of the following:
  - Bulk (pure) final product
  - Bulk starting materials
  - Intermediate chemicals
  - Waste materials
  - Wipes of reactors, piping, etc.
- Goal: check for the absence of undeclared scheduled chemicals

Sampling at Challenge Inspections or Investigations of Alleged Use

- Samples collected by OPCW Inspectors
- Samples can be any of the following:
  - Bulk (pure) chemicals
  - Waste materials
  - Wipes of reactors, piping, etc.
  - Soil/vegetation samples
  - For IAU: Blood, urine, tissue
- Goal: Determine if the Challenge was correct or not, or determine if toxic chemicals were used

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Sample types and assumed concentrations

- "Environmental" samples may include
  - "Neat" agent from a reactor or bomb
  - Residue from a reaction or waste container
  - Contaminated clothing, hair, soil, water, etc.
  - Concentrations usually expected >1 µg/g (ppm)
  - Survey analysis is possible
- "Biomedical" samples may include
  - Urine, blood, plasma, tissue, etc.
  - Intact analyte likely not present (degradation/reaction product or metabolite)
  - Concentration levels quite low, < 5 ng/g (ppb)
  - Survey analysis not possible; must use targeted analysis

How much is one part per million (ppm)?

Four drops of ink in one 55-gallon (200 liter) barrel of water (mixed thoroughly) would produce an ink concentration of 1 ppm.

- This concentration is easily identified using GC/MS
- Survey mode is possible (i.e. you don't need to know what you are looking for)

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How much is one part per billion (ppb)?

One ppb is like one sheet in a roll of toilet paper stretching from New York to London

- This concentration is difficult to identify using simple GC/MS
- Survey mode is NOT possible
- Must use targeted analysis and/or other techniques (e.g. MS/MS)

Star Trek's Tricorder: the ideal analytical tool

- Instant answers!
- Small, portable!
- Easy to operate!
- No false positives!
- No sampling required, just point and get the answer!

- Cons:
  - Not available for purchase (yet)

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Transportable Agilent GC/MS

- Research grade
- Very low detection limits
- Analysis of wide range of chemicals
- Flexible instrument
- Restricted mode of operation possible
- Cons:
  - Bulky equipment
  - Lengthy setup time
  - Sample prep time

How does a GC/MS work?

Autosampler:
Injects a small amount (1 µL) of sample into the Gas Chromatograph

Gas Chromatograph:
Separates chemical species, in time, to create a **chromatogram** of all the species in the sample.

Mass Spectrometer:
Creates a **spectrum** or "fingerprint" of each compound as it elutes from the GC

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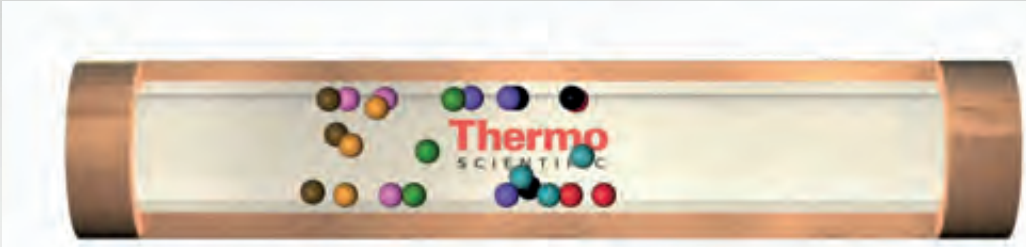
Animation of how a GC works (courtesy of Thermo)

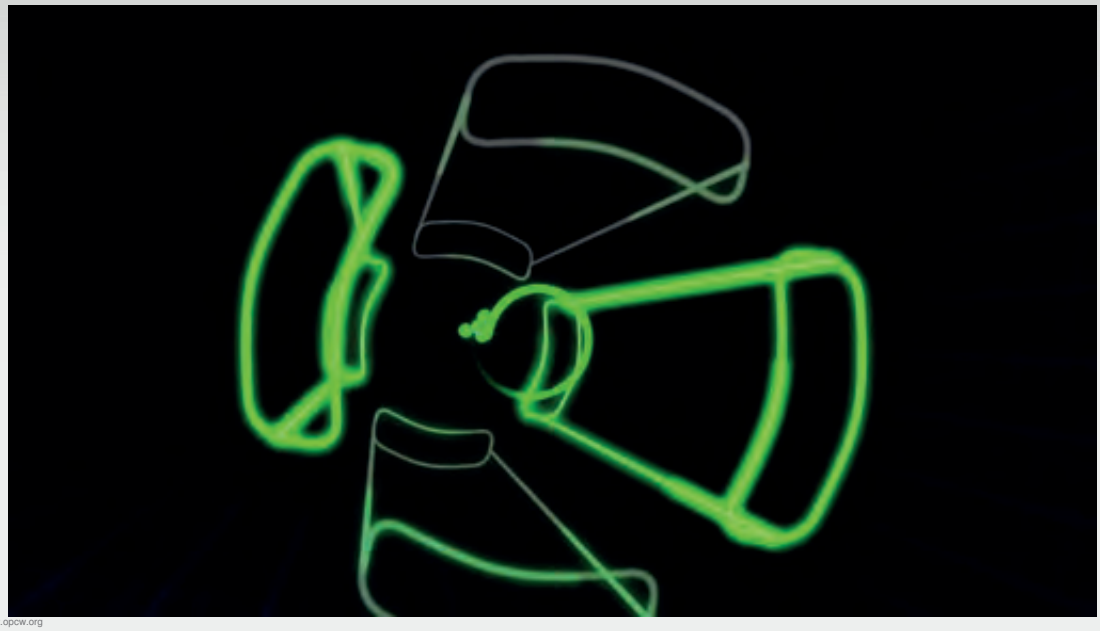


Compound Separation:

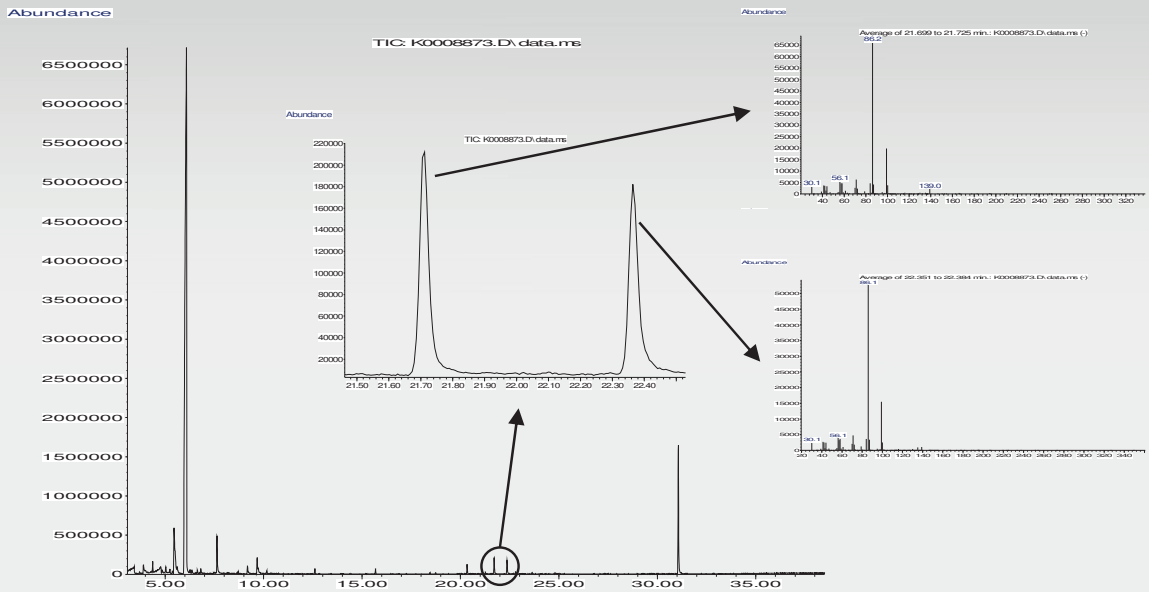
- Compounds separate according to volatility and polarity
- As compounds elute they are quantified by the detector

Retention Time	Compound
04:48 min	Methprylon
04:48 min	Butalbital
04:48 min	Amobarbital
04:48 min	Meprobamate
04:48 min	Gluthethimide
04:48 min	Phenolbarbital
04:48 min	Methaqualone
04:48 min	Primidone

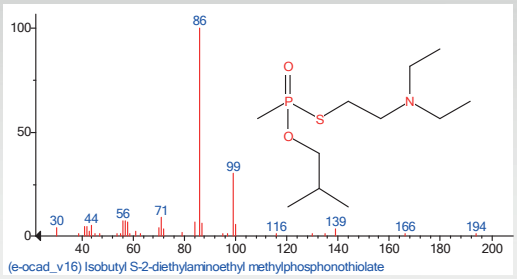
Animation of how a MS works (courtesy of NASA)

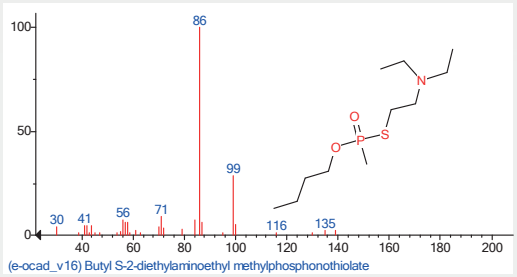


GC/MS data: Chromatograms and Spectra



GC/MS results: Spectra match to library





- Note the major ions in both spectra are identical
- Small differences in mass spectra indicate different structures
- The first chromatographic peak matches the top spectra with a match factor of 97 of 100
- Likewise, the second peak and spectrum match at 97
- Both are V-agents

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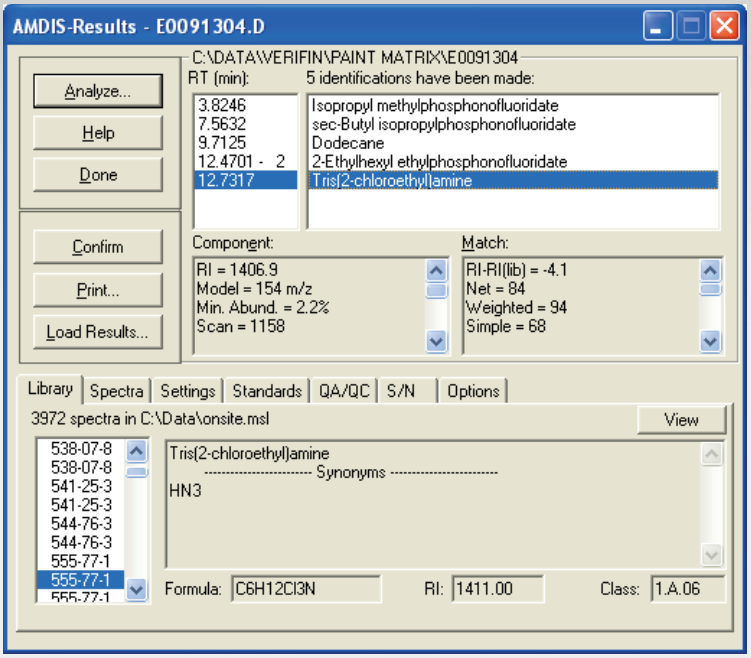
Confidentiality during analysis:
no disclosure of proprietary business information

- AMDIS: Automatic Mass spectral Deconvolution and Identification Software
  - Developed at NIST (USA) for the OPCW
  - Identify low concentrations of *target* compounds in complex matrices
  - Low levels of false positive identifications
  - Ability to restrict access to non-treaty related data
- Only searches for compounds that are in the analytical reference database, i.e. those compounds that are relevant to the inspection

AMDIS shows only the chemicals identified using OCAD



Chemicals Identified

Analysis Information

Chemical Identification Information

Any tools other than GC/MS?

- Yes, there are other analytical tools that can assist with sampling and analysis
- Different tools have different pros and cons
- Analytical tools in use by the OPCW include:
  - Infrared spectroscopy
  - Raman spectroscopy
  - Test kits
  - Various hand-held (non-specific) detecors (CAM, RAID, AP2C, LCD 3.3, etc.)

Bruker mobile FT-IR

- Attenuated total reflectance fourier transform infrared spectroscopy (ATR FT-IR)
- No sample prep
- Fast analysis
- Portable
- Easy use
- Cons:
  - Not as sensitive as GC/MS
  - Works best with pure chemicals
  - Not set to work in restricted mode

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Thermo hand-held FT-IR

- Attenuated total reflectance fourier transform infrared spectroscopy (ATR FT-IR)
- No sample prep
- Fast analysis
- Portable
- Easy use
- Cons:
  - Not as sensitive as GC/MS
  - Works best with pure chemicals
  - Not set to work in restricted mode

Thermo hand-held Raman

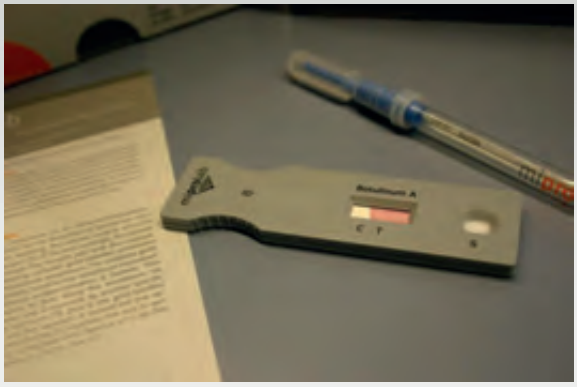
- Laser driven Raman Spectroscopy
- Analysis through glass!
- No sample prep
- Fast analysis
- Portable
- Easy use
- Cons:
  - Not as sensitive as GC/MS
  - Works best with pure chemicals
  - Not set to work in restricted mode

Hapsite mobile GC/MS

- Minimal sample prep
- Relatively fast analysis
- Portable
- Easy use
- Cons:
  - Not as “full-range” as research grade GC/MS
  - Not set to work in restricted mode
  - Battery change every 3 hours

Test kits for "problematic" scheduled chemicals

- Ricin is a protein that cannot be analyzed by GC/MS
- Saxitoxin, due to its chemical nature, cannot be analyzed by GC/MS
- Test kits similar to pregnancy test kits
- Relatively fast analysis (20 min)
- Portable, easy use



- Cons:
  - Need different kit for Ricin and Saxitoxin
  - Single use kits
  - Kits expire in 2 years

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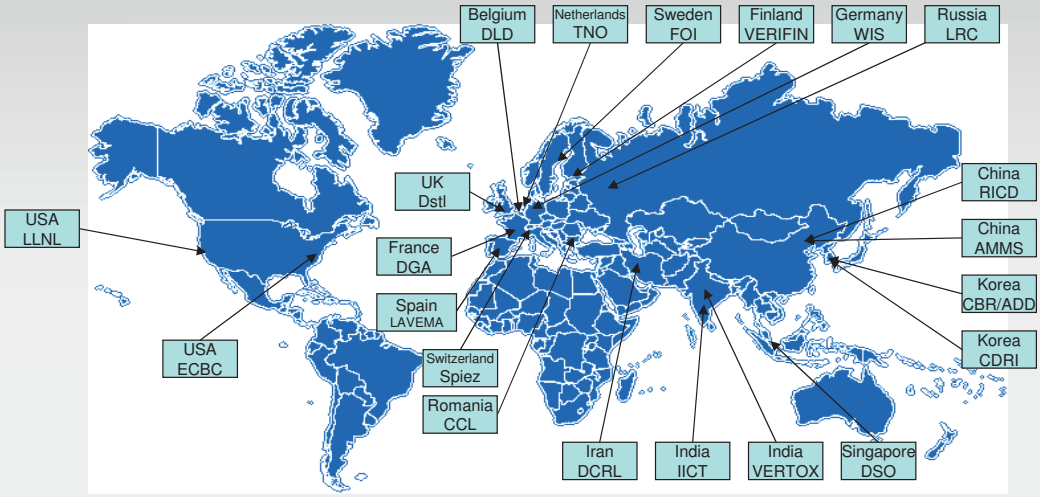
OPCW Designated Laboratories



21 Designated Laboratories in 17 countries

as of May 2014

Designated Laboratories: equipment

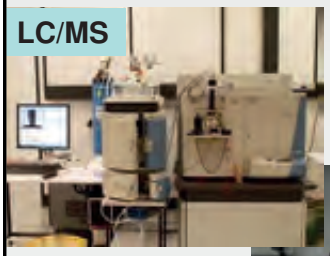
GC/MS

GC/FTIR

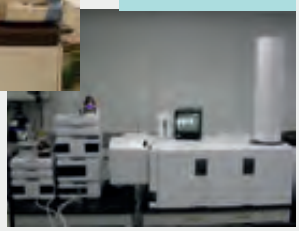
GC/FPD

GC/AED

LC/MS



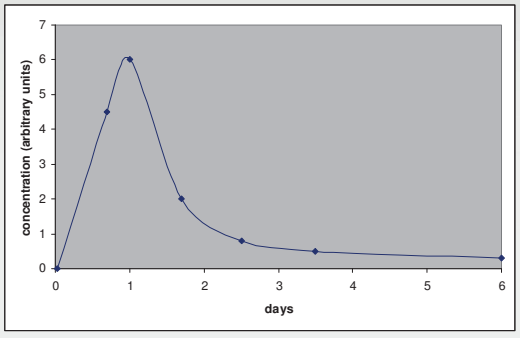
LC/HRMS

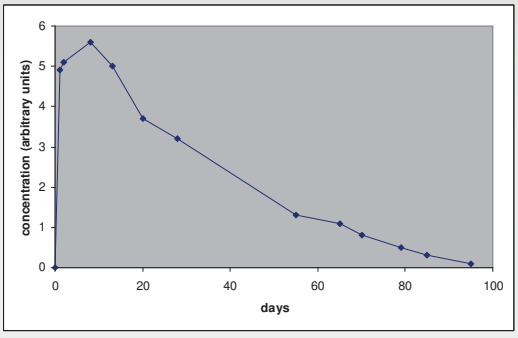


NMR

Biomarkers of exposure

- Intact agent
- Metabolites
- Adducts with DNA
- Adducts with proteins





Typical excretion profile: Urine metabolites*

Typical concentration profile: Protein adducts*

*Data extracted from a report by TNO, Netherlands

Syria: Environmental sampling & analysis

- Sample collection
  - Used standard OPCW sample collection techniques
- Sample splitting
  - Not done in country
  - Samples split and/or extracted at the OPCW Laboratory
- Sample analysis
  - On-site – not performed
  - Off-site – samples sent to two Designated Laboratories

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Syria: Biomedical sampling & analysis

- Sample collection
  - OPCW and WHO staff interviewed victims and collected samples
- Sample splitting
  - Blood samples were centrifuged, plasma separated and refrigerated on-site
  - No splitting on-site – done at OPCW Laboratory
- Sample analysis
  - On-site – not possible
  - Off-site – samples sent to two Designated Laboratories

Timeline and conclusion

- 21 August: the attack
- 26, 28, 29 August: Samples collected
- 30 August (late): Samples received at OPCW Laboratory
- 2 & 4 September: Samples dispatch to Designated Laboratories
- 8-10 September: Preliminary summary analysis reports from the 4 labs were received by the UN team
- 13 September: The UN team report was transmitted to the Secretary-General of the United Nations
- Conclusion: Sarin was used in the attack
- These results would not be possible without our partner laboratories excellent work – Thank you!

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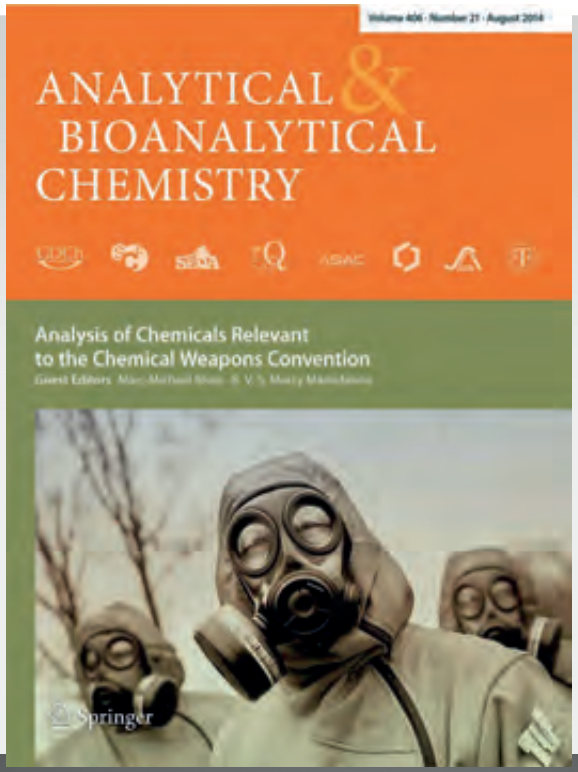
ABC Special Issue

- High impact scientific journal - agreed to the special issue in June 2013
- Guest editors: two Senior Analytical Chemists from the OPCW Laboratory
- 17 peer-reviewed articles plus feature article by the Director-General
- To be published mid/late July
- Articles freely available for 24 weeks
- Notice will be placed in OPCW social media



S & T For Diplomats: A Series of Discussions

- October (On the margins of EC-77, to be confirmed)
  - **S&T for Diplomats (2): Biomedical Samples**
    - SAB Laboratory recommendations
    - Sampling and analysis
- December (On the margins of CSP-19, To be confirmed)
  - **S&T for Diplomats (3): The meaning of production by synthesis and biomediated chemical production**
    - SAB convergence related recommendations
    - Production by synthesis
- **Other topics to be scheduled**

Science for Diplomats (2)

Biomedical Sample Analysis

10 October 2014
OPCW Headquarters
The Hague, The Netherlands

Jonathan E. Forman, Ph.D.
Science Policy Adviser
Office of Strategy and Policy

Marc-Michael Blum, Ph.D.
Senior Analytical Chemist
Organisation for the Prohibition of Chemical Weapons

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SAB Report of the Developments in S&T to The Third review Conference
(RC-3/DG.1, Dated 29 October 2012)

Director General's Recommendations
(RC-3/DG.2, Dated 31 January 2013)

Status of the Follow-Up to the Recommendations on S&T to the Third Review Conference
(EC-77/DG.11, Dated 5 September 2014)

Laboratory Capabilities and Analysis	
"The Secretariat will continue to monitor developments relating to **unscheduled and novel toxic chemicals** and will explore ways in which to augment its **technical capabilities** in this area." "…notes the SAB's views on the **OPCW Central Analytical Database** and…the Secretariat needs to have analytical data on relevant unscheduled chemicals." (paragraphs 9 and 32 of RC-3/DG.2]	• The OPCW Laboratory (LAB) is monitoring developments, has noted the SAB's advice on RCAs, and is working with the Validation Group to obtain analytical data on relevant unscheduled chemicals • LAB is establishing a training laboratory • LAB participates in various activities and programmes (e.g. EQuATox). • OCAD continues to be regularly updated, it currently contains validated data for > 5000 scheduled chemicals
"..note the importance of continuing to **improve on-site and off-site analysis**" "…future such exercises will progress towards the more difficult analysis of longer-lived biomarkers of exposure, such as protein adducts" (paragraphs 24 and 25 of RC-3/DG.2)	• Effective capability was demonstrated in the investigation of alleged use in 2013. • LAB and OPCW Designated Laboratories are continually working on refining methodologies. • Workshops are routinely held with the Designated Laboratories and for review of proficiency testing • LAB is continuing to improve its capabilities for conducting biomedical sampling and analysis. • Chemical analysis was the topic for the first workshop (on 9 July) of the "Science for diplomats" series
"…a **review of the proficiency-testing programme** be undertaken" "…resources be made available to enable **regular exercises of the entire off-site analysis process** to be conducted in conjunction with OPCW field exercises." (paragraphs 26 and 30 of RC-3/DG.2)	• In July 2014, LAB held discussions with Designated Laboratories. • Dr. Robin Black, former SAB member, is chairing a group to review the proficiency testing programme • TS intends to seek funding through the annual programme and budget; not yet done due to the financial situation.

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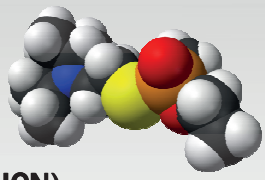
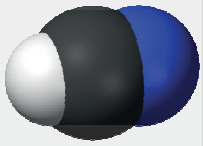
Scheduled Chemicals Span a Broad Range of Properties

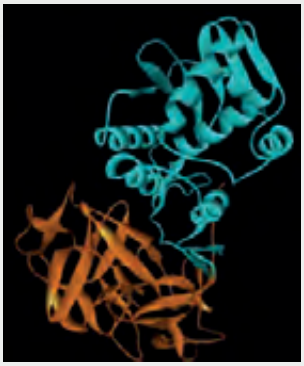
VX (*O*-ethyl-*S*-[2(diisopropylamino)ethyl] methylphosphonothiolate



Hydrogen Cyanide (HCN)



Ricin



Chemistry Underpins Biology

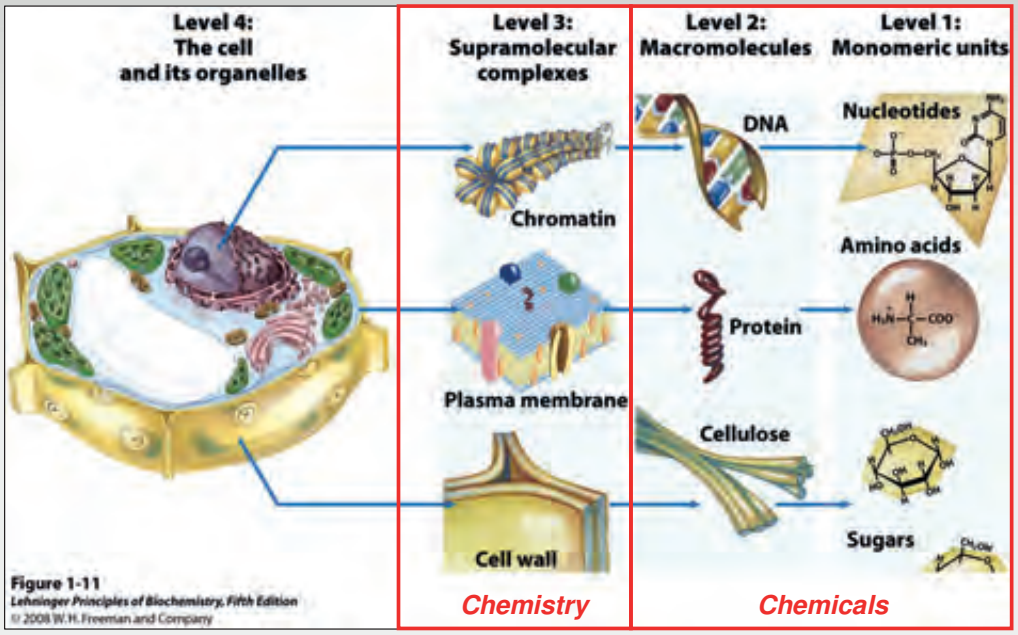


Figure 1-11
Lehninger Principles of Biochemistry, Fifth Edition
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Biomedical Sample Analysis

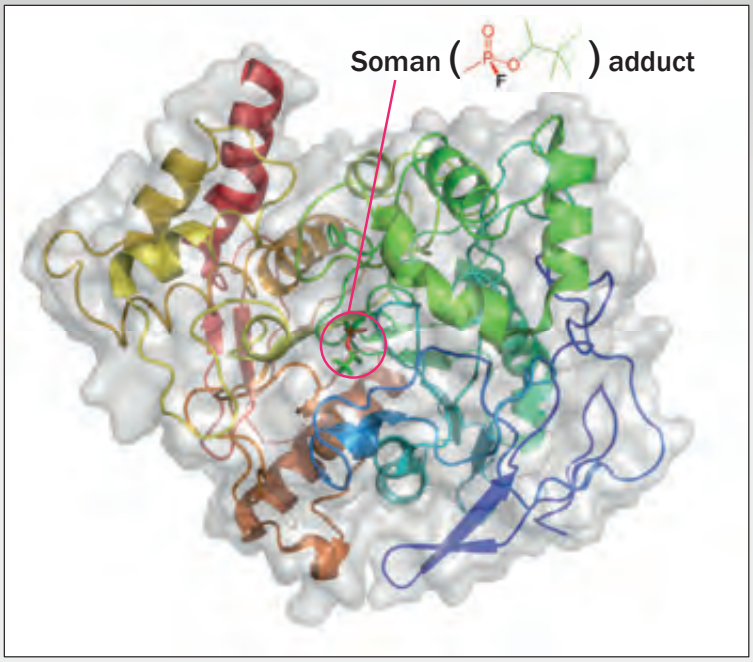
Table 4.2 Summary table of laboratory results for biomedical samples taken from one deceased individual

SN	Sample	Laboratory 1 Sarin and its metabolites	Laboratory 2 Sarin and its metabolites
1	Hair	Positive	Positive
2	Kidney	Positive	Positive
3	Skin	Positive	Positive
4	Blood	Positive	Positive
5	Liver	Positive	Positive
6	Breast fat	Positive	
7	Muscle	Positive	
8	Bronchus	Positive	Positive
9	Lung	Positive	Positive
10	Eye	Positive	
11	Brain	Positive	Positive
12	Heart	Positive	

Note: Identification is positive when either the Sarin metabolite isopropyl methylphosphonic acid (IMPA) or the fluoride reactivation product of IMPA (Sarin) is detected.

From: Final Report of United Nations Mission to Investigate Allegations of the Use of Chemical Weapons in the Syrian Arab Republic (13 December 2013)

Chemical Signatures in a Biological System



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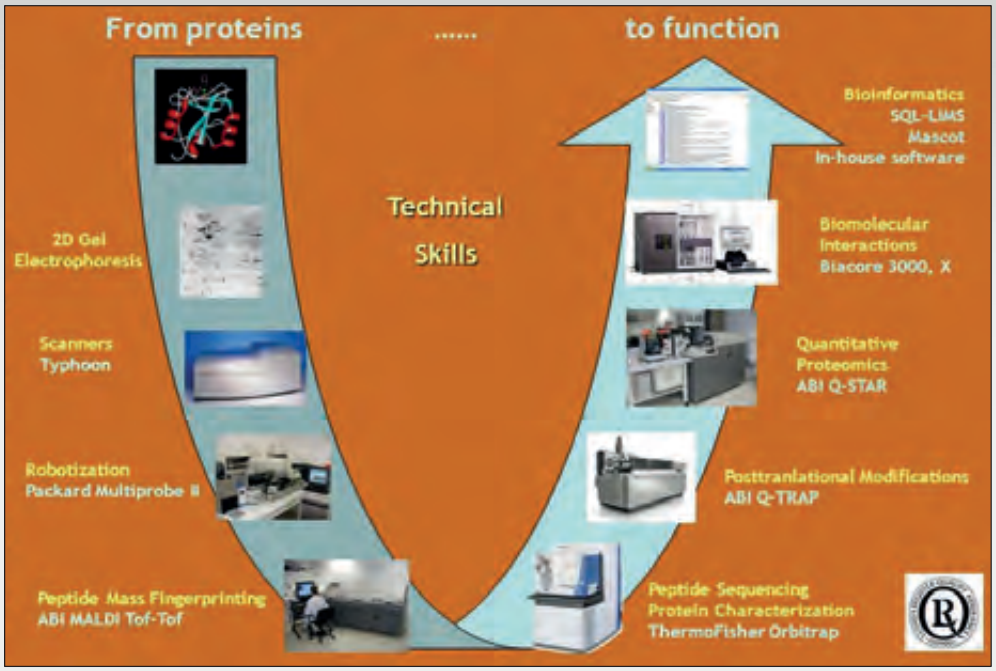
Tools for Protein Analysis



Presentation by Marc-Michael Blum

CONDUCTING ANALYSIS OF BIOMEDICAL SAMPLES TO ASSESS EXPOSURE TO ORGANOPHOSPHORUS NERVE AGENTS

Marc-Michael Blum, Murty Mamidanna, Hugh Gregg
OPCW Laboratory, Rijswijk, The Netherlands

ORGANISATION FOR THE PROHIBITION OF CHEMICAL WEAPONS

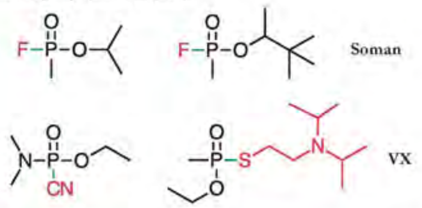
1. INTRODUCTION

Highly toxic **nerve agents** such as **Tabun, Sarin, Soman** and **VX** are banned under the Chemical Weapons Convention (CWC) and formed major parts of **large stockpiles** of chemical weapons during the **Cold War**. **Terrorist attacks** carried out by the cult Aum Shinrikyo in **Japan** in 1994/95 employed **Sarin**. The OPCW supported UN mission that investigated the August 2013 chemical attacks in **Ghouta/Syria** determined that the chemical agent used was also **Sarin**. **Sampling and analysis** of **environmental samples** can reveal the presence of absence of these agents (and/or their degradation products) but in order to assess if a **potential victim** was exposed, the analysis of **biomedical samples** is required. **Blood** and **urine** samples are preferred as they are easily collected but the analysis of body **tissues** is also possible. Tissue samples are especially relevant in case of deceased individuals.

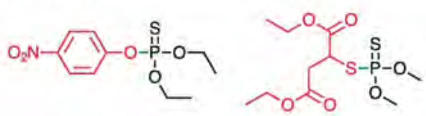
2. NERVE AGENTS - CHEMISTRY AND STRUCTURE

Nerve agents are **organophosphorus** compounds and are liquid at room temperature. For understanding their reactions in the human body it is helpful to introduce the concept that the molecules are made up by **two different parts**: A. The **phosphorus containing part** (shown in black) in which a phosphoryl group (P=O) is bonded to an O-alkyl (-O-R) group and a short alkyl group (R) or a small dialkylamino group ($-NR_2$) in case of Tabun. The other part of the molecule is the so-called **"leaving group"** (shown in red). In case of Sarin and Soman this is a fluorine atom (-F), in case of Tabun a cyano group (-CN) and in case of VX a larger group containing nitrogen and sulphur. Most relevant reactions of the agents involve the chemical bond connecting these two groups (shown in green).

Sarin, Soman, Tabun, VX



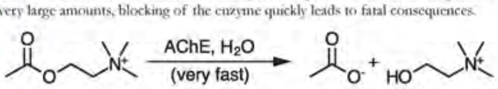
Organophosphorus **pesticides** are **similar** in structure (nerve agents were found while looking for new effective pesticides) and mode of action. Parathion and Malathion are shown as examples below. The substitution of oxygen in the phosphoryl group with sulphur lowers toxicity for humans.



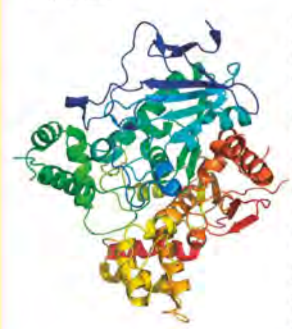
Parathion Malathion

3. ACETYLCHOLINESTERASE - THE TARGET

The primary **toxicity** of nerve agents is due to their ability to **inhibit** the action of an **enzyme** (protein with catalytic activity) crucial in the process of **conducting nerve signals**. **Acetylcholinesterase** (**AChE**) is responsible to break down the **neurotransmitter acetylcholine** at neuronal junctions by hydrolysis (reaction with water, see figure below). In a simplified view this switches a nerve signal from on to off. If the enzyme is **blocked**, acetylcholine will **accumulate** and signal transmission cannot be terminated. This leads to **cholinergic crisis** and typical symptoms including **sweating, salivation, miosis (pinpoint pupils), paralysis, respiratory failure** and eventually **death**. Because **AChE** is a very **fast and efficient enzyme** (one enzyme molecule can break down 25000 molecules of acetylcholine per second) and is not present in very large amounts, blocking of the enzyme quickly leads to fatal consequences.



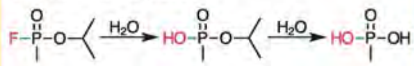
Acetylcholine Acetate Choline



Human AChE consists of **640 amino acids**. In the human body most of the AChE is found as units of two (**dimer**) or four (**tetramer**) AChE molecules that are **anchored** to a **membrane**. The figure to the left shows the complicated folding of the protein leading to its three dimensional **structure**. Helical substructures and so called beta-sheets (thick arrows) can be identified. The catalytic active site is buried deep inside the enzyme. It contains three amino acids crucial for catalytic activity: Serine 200, Histidine 440 and Glutamate 327. The nerve agents attach to Serine 200 to block the enzyme.

4. ANALYSIS OF METABOLITES

Nerve agents that are not interacting with AChE or other proteins in the human body (see below) normally **hydrolyze** quite rapidly. This is especially the case of **hydrophilic** agents such as Sarin while **lipophilic** agents such as VX can form **depots** of intact agent **in fatty tissues**. In case of Sarin the **primary hydrolysis product** (which is unable to block AChE) is **isopropyl methylphosphonic acid (IMPA)** that can further degrade to **methylphosphonic acid (MPA)**. Other indicators for the presence of the agent are **typical sideproducts** formed during Sarin synthesis such as **diisopropyl methylphosphonate (DIMP)**.

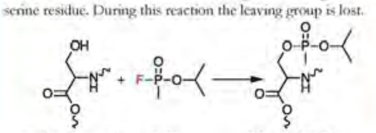


Sarin IMPA MPA

These compounds can be detected in **urine** and **blood** samples using **liquid** or **gas chromatography**. Due to the **low concentrations** in body fluids (in the **parts per billion** range) **GC-MS/MS** or **LC-MS/MS** methods employing **single ion monitoring (SIM)** or **multiple reaction monitoring (MRM)** modes are commonly used. This requires **targeted analysis**, meaning that one has to specifically analyize for a specific compound such as IMPA.

5. PROTEIN ADDUCTS AND THEIR FATE

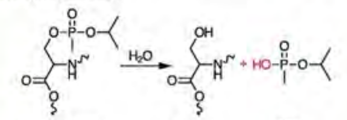
Nerve agents do not only react with AChE but also with other proteins. One highly similar to AChE is **Butyrylcholinesterase (BChE)**. In contrast to the membrane anchored AChE, BChE is found in **blood serum** and can be used for analysis more easily. The active site of BChE also contains a **catalytic triad** of serine, histidine and glutamate and the **molecular mechanism of inhibition** is **identical** with AChE with the agent attaching itself to the serine residue. During this reaction the leaving group is lost.



Serine in protein Sarin inhibited Serine

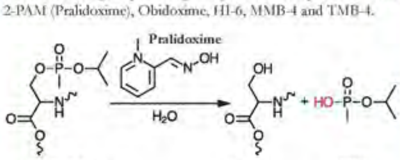
After the attachment of the agent to the serine residue, the enzyme is **blocked** and cannot perform its normal activity. This primary protein adduct can react further in a number of ways:

Spontaneous reactivation:
The inhibited Serine might react with water to **produce the original and functional serine residue** plus the hydrolysis product of the agent (IMPA in case of Sarin). While this process plays a role for certain pesticides, it is **too slow** to be of relevance in case of nerve agent poisoning.



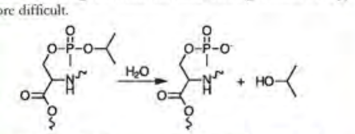
inhibited Serine Serine IMPA

Reactivation with a nucleophile
Nucleophilic compounds such as **oximes** can be used for induced **reactivation**. Such oximes are commonly used as **therapeutics** in case of nerve agent poisoning. They include compounds such as 2-PAM (Pralidoxime), Obidoxime, HI-6, MMB-4 and TMB-4.



inhibited Serine Serine IMPA

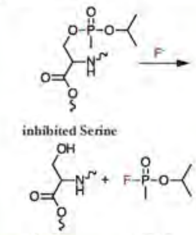
Ageing
The inhibited serine can **loose an additional group** from the phosphorus atom leading to a structure with a negative charge at an oxygen connected to the phosphorus (a process called ageing). This structure **cannot be reactivated** using oximes. While some agents age relatively slow ly (over hours and days) others are much faster. **Soman ages within minutes**, making medical therapy even more difficult.



inhibited Serine aged form Isopropanol

6. FLUORIDE REACTIVATION

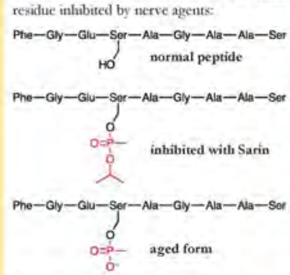
One advantage of analysing protein adducts over free metabolites in blood is that they persist for much longer times. While **free metabolites** are cleared from blood in a **couple of days, protein adducts** may persist for **several weeks**. One approach for analysis that does not require a look at large protein molecules or fragments is **fluoride regeneration**. Sodium fluoride solution is added to the blood or plasma sample and the **fluoride ions** react with the protein adducts to **release the agent** again. In case of Sarin, Soman and Cyclosarin the original agent is regenerated. In case of Tabun, Fluorotabun is produced and in case of VX the product of fluoride regeneration is Ethylsarin. The one problem that exists with this procedure is that **aged protein does not react with fluoride** and **these molecules escape detection**.



Serine Sarin
(to be analyzed)

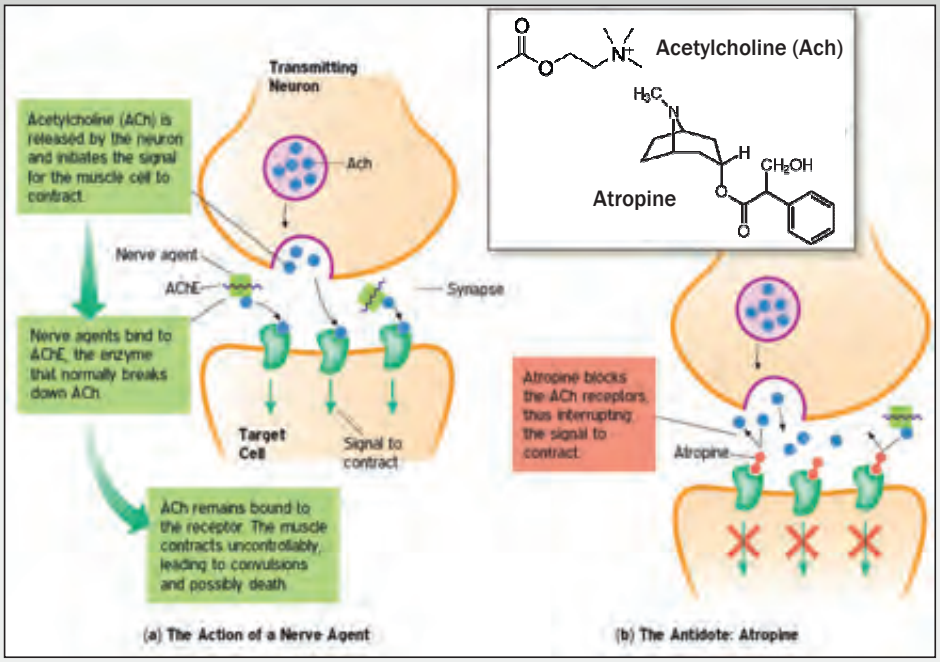
7. DIRECT ANALYSIS OF ADDUCTS

When a nerve agent binds to AChE or BChE there is a **characteristic mass change in the protein** that can be used to identify the agent. The established procedure is relying on BChE in human blood plasma. Instead of using the intact protein (consisting of 574 amino acids) the **protein is cut into smaller pieces** (so called peptides) by using the **digestive enzyme Pepsin**. The fragment of interest is a **peptide of nine amino acids** that contains the serine residue inhibited by nerve agents:



The different peptides generated by the Pepsin digest are **separated** using **liquid chromatography (LC)** and analysed using **tandem mass spectrometry (MS/MS)**. As the **leaving group** of the agent is **lost** when binding to AChE or BChE, this analysis **can not reveal the absolute identity** of the used agent (the same is true for fluoride regeneration and any other analysis that does not identify the intact agent). For example, an adduct that is identical to the one produced upon exposure to Sarin might actually come from an agent that featured a leaving group similar to that of VX. Aged adducts caontain less information, but these peptides contain **more information** than just finding free MPA, as MPA is also a degradation product of some legitimate chemicals such as the flame retardant dimethyl methylphosphonate (DMMP). The **aged adduct is clear proof** that the body was **exposed** to a **toxic methyl-phosphonic chemical** that is **able to bind to and block AChE and BChE**. DMMP, for example, is unable to do this.
An alternative source for protein adducts is **serum albumin**. After digestion with **Pronase** adducts with the amino acid **Tyrosine** can be detected.

The Chemistry of Countermeasures



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S & T For Diplomats: A Series of Discussions

- December 2014 (On the margins of CSP-19, to be confirmed)
  - **S&T for Diplomats (3): The meaning of production by synthesis and biomediated chemical production**
    - SAB Convergence Related Recommendations
    - Production by Synthesis
- March 2015 (On the margins of EC-78, To be confirmed)
  - **S&T for Diplomats (4): The Chemistry of Countermeasures**
    - Assistance and Protection Related Recommendations
    - Immediate response and longer term considerations
- **Other topics to be scheduled**

19th Conference of the States Parties

Science for Diplomats

The Science of the Bioeconomy

13:30 – 15:00

Friday, 5 December

World Forum – Europe Room

Light Lunch Provided

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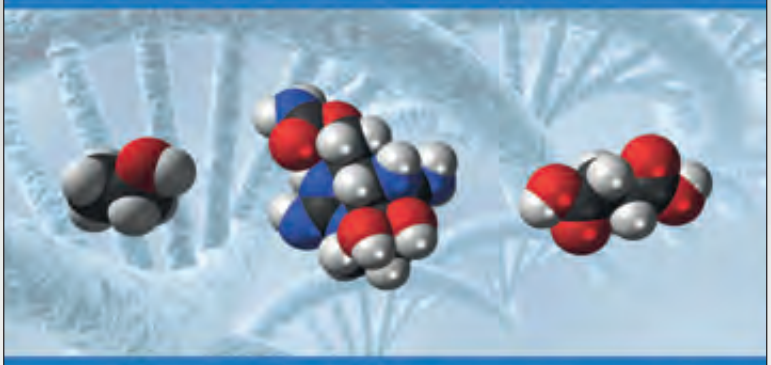
ORGANISATION FOR THE
PROHIBITION OF CHEMICAL WEAPONS

Working together for a world free of chemical weapons

19th Conference of the States Parties



Science for Diplomats

The Science of the Bioeconomy

Jonathan E. Forman, Ph.D.
Science Policy Adviser
Office of Strategy and Policy
OPCW

Dr. Henrike Gebhardt
Senior Project Manager Bioeconomy
Corporate Innovation Strategy & Management
Evonik Industries AG

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SAB Report of the Developments in S&T to The Third review Conference
(RC-3/DG.1, Dated 29 October 2012)

Director General's Recommendations
(RC-3/DG.2, Dated 31 January 2013)

Response to the Report of the Twenty-First Session of the Scientific Advisory Board
(EC-77/DG.10, Dated 5 September 2014)

Status of the Follow-Up to the Recommendations on S&T to the Third Review Conference
(EC-77/DG.11, Dated 5 September 2014)

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The Temporary Working Group on Convergence

www.opcw.org/index.php?eID=dam_frontend_push&docID=17438

(see EC-77/DG.10, Dated 5 September 2014 for Director-General response to recommendations)

ORGANISATION FOR THE PROHIBITION OF CHEMICAL WEAPONS

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Recommendations from the TWG on Convergence

- 19 Recommendations presented in report; **Status in EC-77/DG.10**
- Continue to **monitor** advances and trends in **production technologies** and assess the relevance of these processes to verification under the CWC.
- **Monitor** advances in **systems and synthetic biology**, particularly in terms of enhancing the capability and capacity to synthesise more complex chemicals.
- **Monitor** advances in **nanotechnology**, particularly as they apply to improved defensive countermeasures against CW.
- Consider **development of outreach materials** to assist States Parties in understanding possible implications for the CWC.
- Establish a structured approach to **maintain contact with the BWC community**.
- Consider re-activating the TWG on Convergence periodically, in order to assess recent advances

Chemistry Underpins Biology

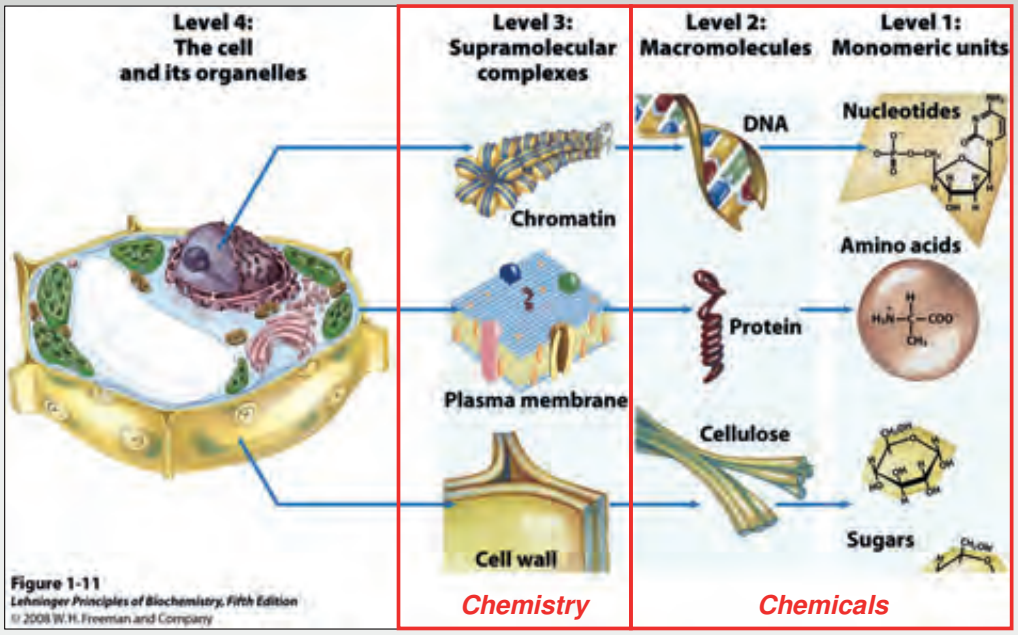

Figure 1-11
Lehninger Principles of Biochemistry, Fifth Edition
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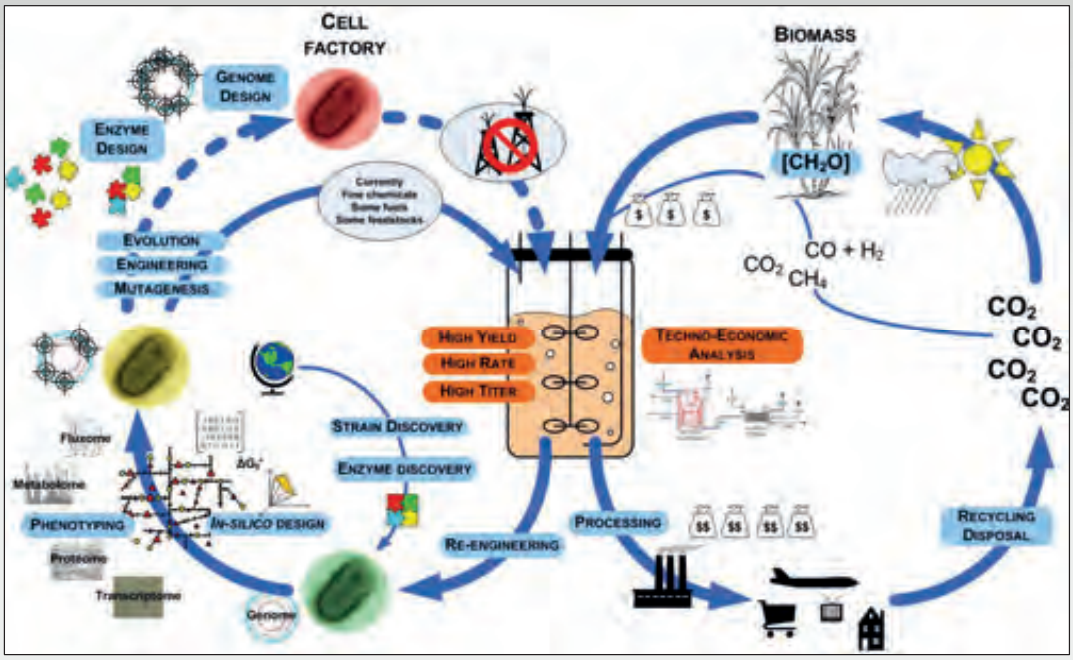
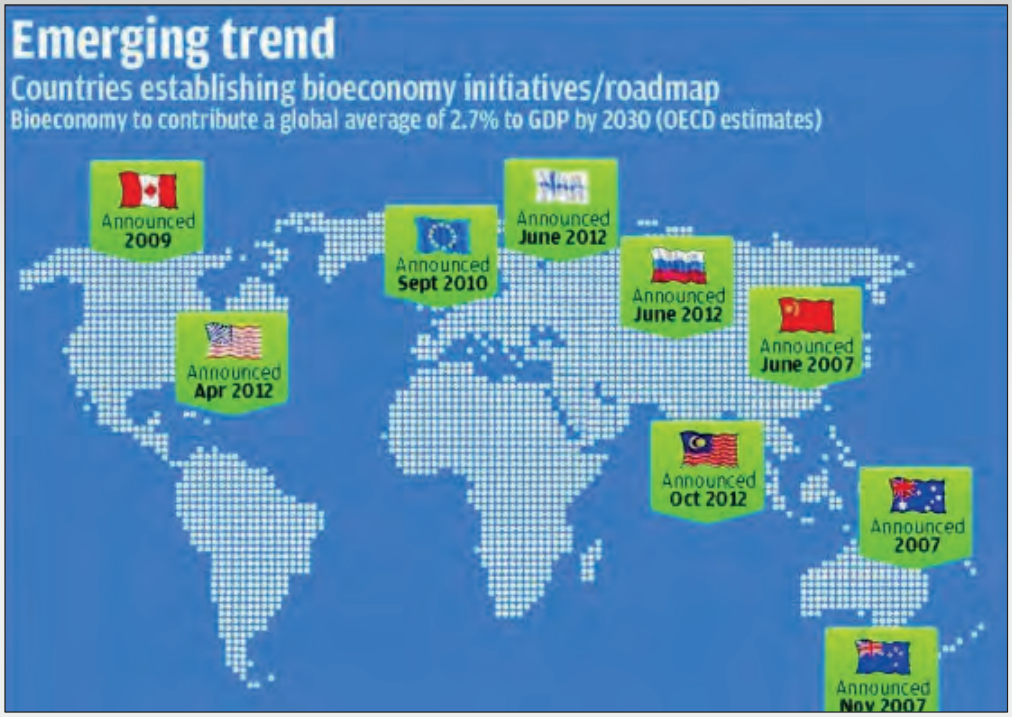
Bio-Mediated Chemical Production





ORGANISATION FOR THE
PROHIBITION OF CHEMICAL WEAPONS

Working together for a world free of chemical weapons

Presentation by Dr Henrike Gebhardt

The science of the Bioeconomy

Dr. Henrike Gebhardt

05 December 2014

EVONIK INDUSTRIES

Our positioning

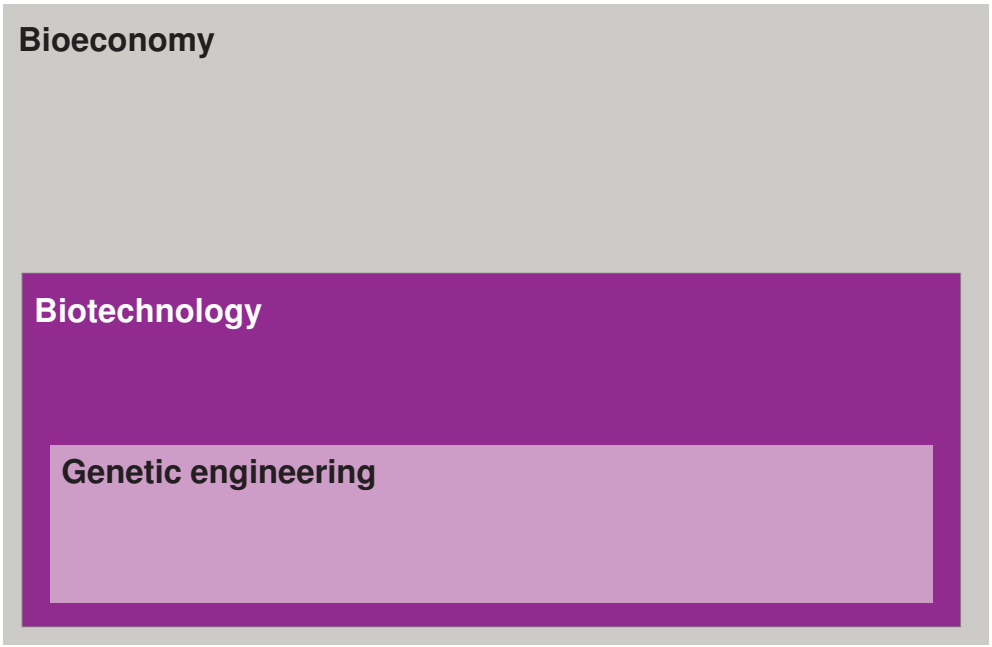
Evonik is the creative industrial group from Germany and one of the world's leading specialty chemicals companies.

Our credo

The Bioeconomy is one driver to promote a more resource-efficient and sustainable economy.

Industrial biotechnology is a key technology for realising the bioeconomy.

Overview



Definitions

Bioeconomy

Production of renewable biological resources and the conversion of these resources and waste streams into value added products, such as food, feed, and other industrial products and energy. COM(2012) 60, EU Commission, mod.

Bio-based products

Products wholly or partly derived from biomass. EN 16575

Bio-based products offered by Evonik

bio-based

Polyamids

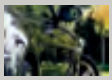
VESTAMID®*Terra*

Polyesters

DYNACOLL®*Terra*

DYNAPOL®*Terra*

VISIOMER®*Terra*



Additives

BioMTBE

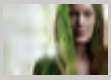
Amino acids

Feed additives

Health – purified

Cosmetics

TEGOSOFT®MM



Additives

VISCOPLEX® Series 10

Cleaning

Esterquats

Health

RESOMER®

bio-degradable

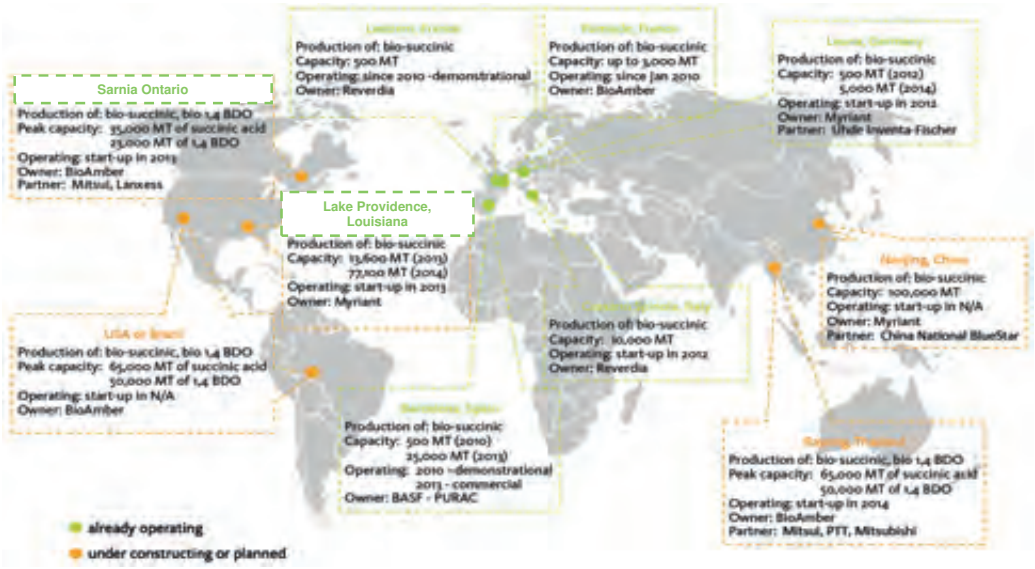
Evonik invests in high-growth chemical megatrends

Lighthouse investment projects

Bioeconomy Press releases

Company Date of Issue	Raw Material	Intermediate Volume	Product Commissioning
DSM/POET (USA) Jan 2012	Cellulosics from corn cobs	Ethanol 90 kta	Biofuels H1.2014
Purac/BASF (ES) Mar 2014	Cellulosics	Succinic acid 10 kt	e. g. Biopolymers 03.2014
Solvay/NBE (US) Mar 2014	Sawmill residues	Torrefied biomass 250 kt	Substitute coal Q4.2014
LanzaTech (USA) Aug 2010	Wood residues (syngas)	Ethanol 15 kt	Biofuels 2014
Butamax (USA) Oct 2013	Corn mash	Butanol ~180 kt	Biofuels 2015

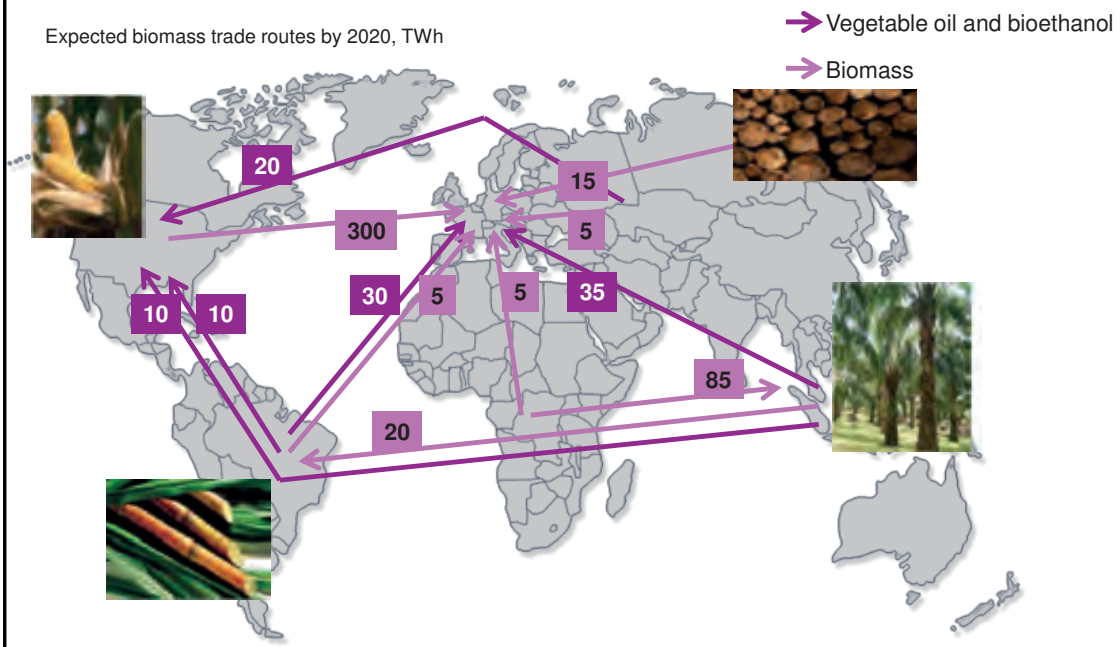
Commercializing bio-based succinic acid technology – first operating plants in Europe, expansion in Asia/Americas



Source: Determination of market potential for selected platform chemicals, weastra, 2012

Europe will depend on import of renewable carbon sources

Expected biomass trade routes by 2020, TWh



Source: World economic forum 2010; the future of industrial biorefineries

Overview

Bioeconomy

Bio-based products

Products wholly or partly derived from biomass. EN 16575

Biotechnology

Genetic engineering

Technologies

Bioeconomy

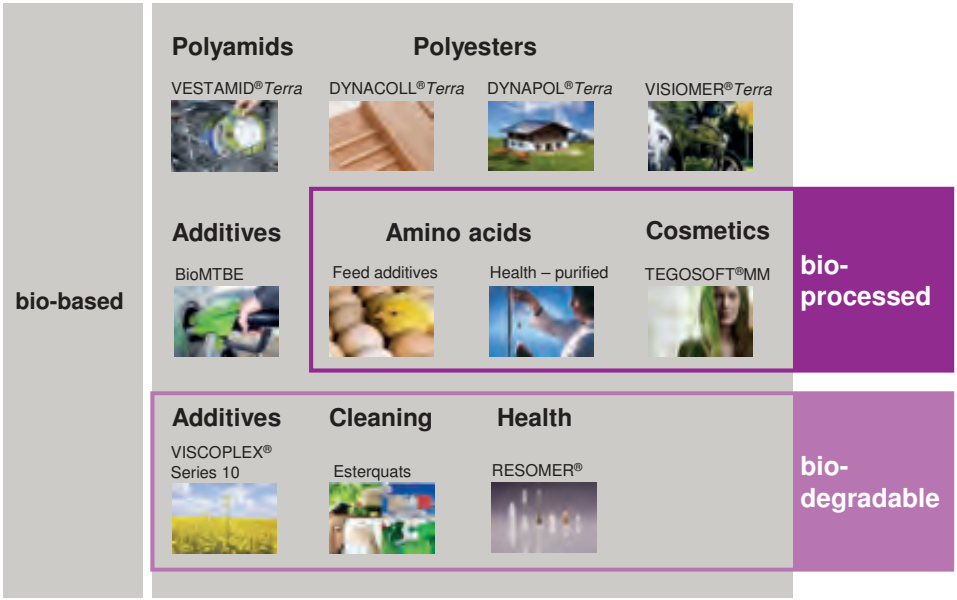
Bio-based products
can be produced by conventional chemical processes or by biotechnology

Biotechnology

The use of living organisms or their components to make products.

Genetic engineering

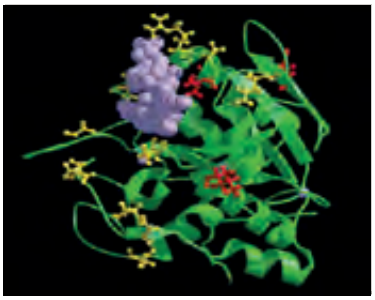
Bio-based products offered by Evonik



Biotechnological processes

Bio-catalysis:

use of natural catalysts such as isolated enzymes or whole-cells to perform chemical transformations



Fermentation:

use the metabolism of a whole living cell to produce substances e.g. chemicals

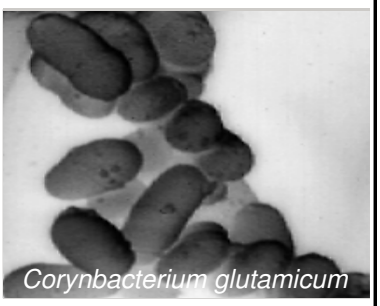
Performed in bio-reactor or fermenter

Bio-reactor - Production

Living Cells

Micro-organisms

- Bacteria e. g. *Corynbacterium glutamicum*
  Product: sodium-glutamate, flavour enhancing compound, umami taste of food
- Yeast e. g. *Saccharomyces cerevisiae*
  Product: bread, beer



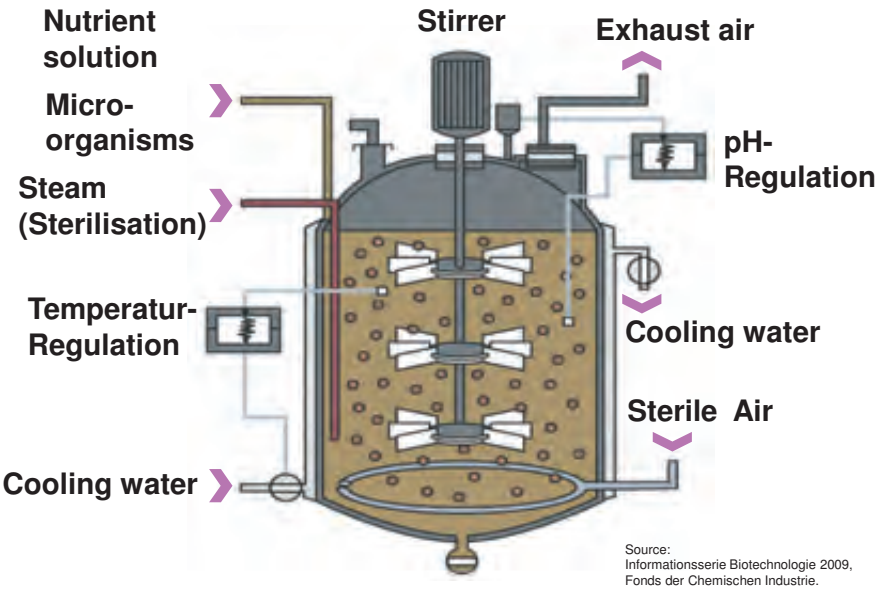
Corynbacterium glutamicum

Higher Organisms

Cells of mammals, humans, insects, plants

Saccharomyces cerevisiae

Bio-reactor - Principle



Source:
Informationsserie Biotechnologie 2009,
Fonds der Chemischen Industrie.

Example: Fermentation to produce amino acids

Sugar → Fermentation → **Amino acid L-lysine** → Feed additive

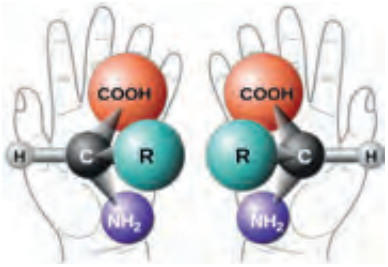
Advantages of biotechnology compared to chemical synthesis

Specificity and selectivity

Final product derived directly, not via intermediate

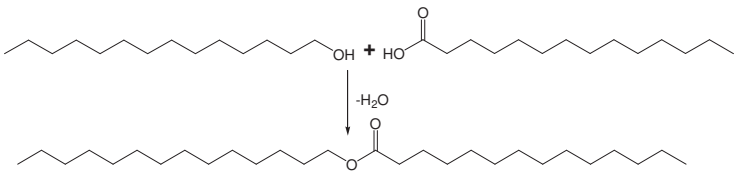
Stereoselective synthesis of chirale compounds
e. g. only L-amino acid, no D-amino acid

- no racemates (mixture of D/L)
- no complex separation process
- no impurities in final product

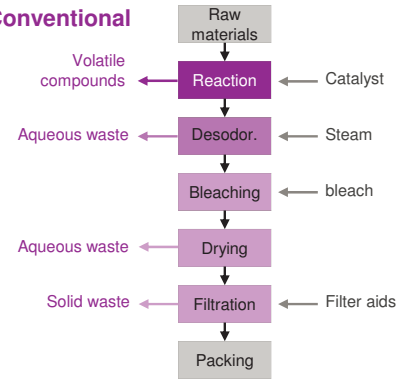


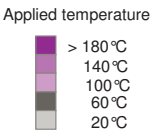
Source: Wikimedia Commons

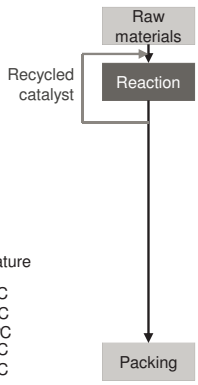
Sustainability that goes under the skin: Myristyl myristate for cosmetics



Conventional







Enzymatic - Biocatalysis

- **Less steps**
- **Lower temperatures**
- **Less energy**
- **Less waste**
- **More resource efficiency**

Advantages of biotechnology compared to chemical synthesis

Specificity and selectivity

Final product derived directly, not via intermediate

Stereoselective synthesis of chiral compounds
e. g. only L-amino acid, no D-amino acid

- no racemates (mixture of D/L)
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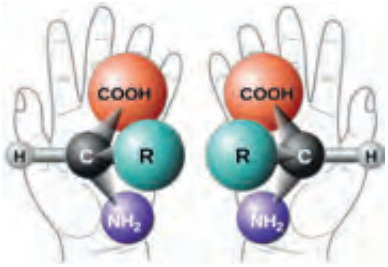


Source: Wikimedia Commons

Efficiency and environmental sustainability

- Economic / safe feedstocks: water, sugar, air, salts
- Mild / safe process conditions: room temperature, atmospheric pressure, medium pH
- Less energy needed, less waste produced

Technologies

Bioeconomy

Bio-based products can be produced by conventional chemical processes or by biotechnology

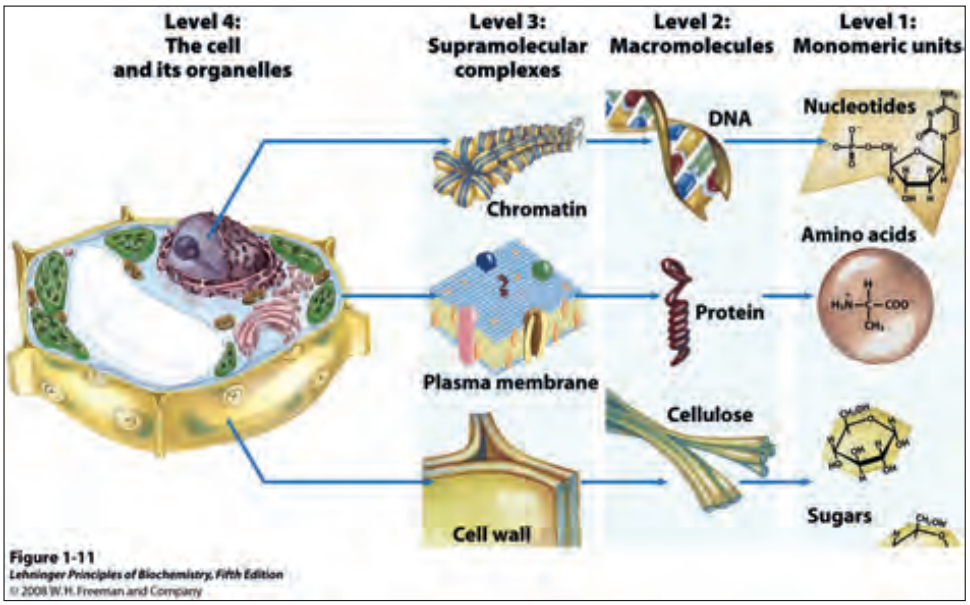
Biotechnology

The use of living organisms or their components to make products.

Genetic engineering

Any of various applications of biological science used in the manipulation of the genome of an organism

The Genome



Genetic engineering methods to generate producing strain

Mutagenesis

Chemicals
or radiation

Exchange of nucleotide

Recombination

Availability of 10^{11} genes
(biodiversity)
Recombination in vector

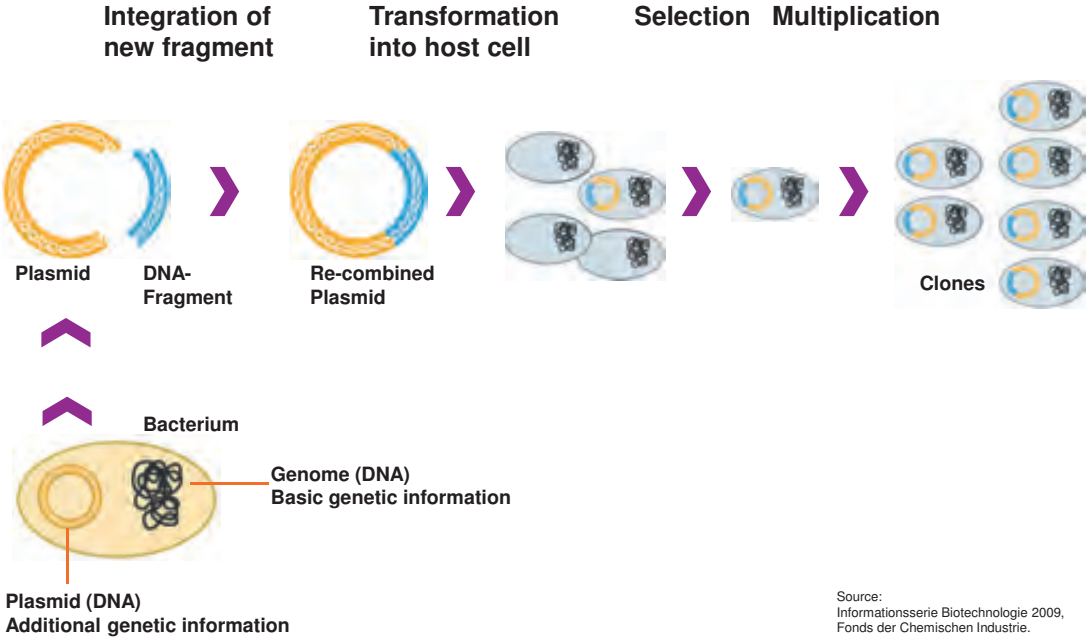
Additonal gene

Selection of desired property

Producing strain

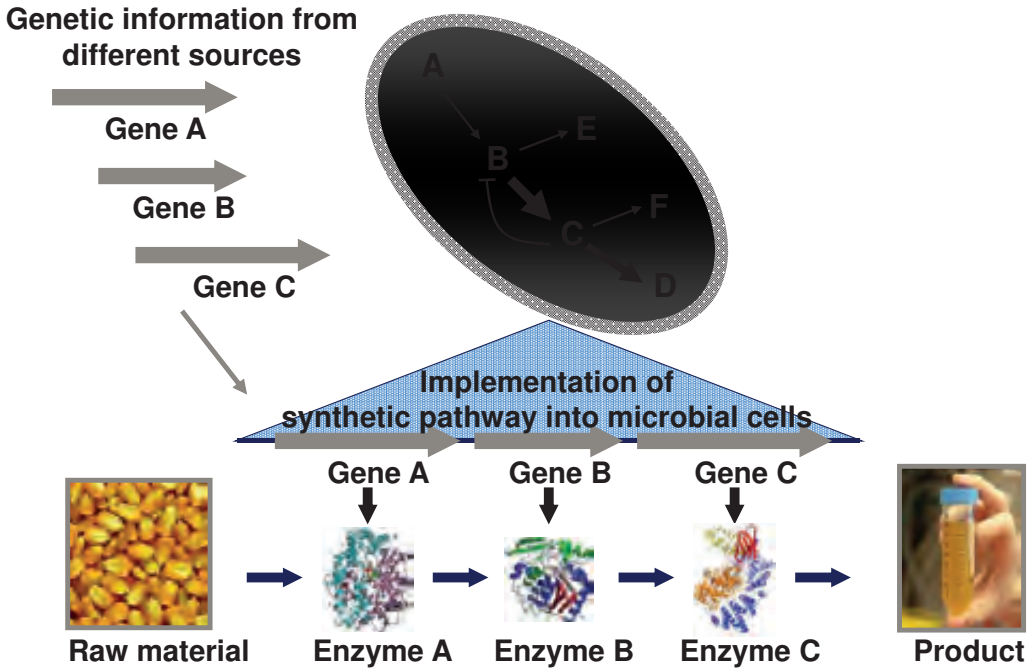
Source:
Informationsserie Biotechnologie 2009,
Fonds der Chemischen Industrie.

Recombination of DNA and transformation into bacterial cell



Source:
Informationsserie Biotechnologie 2009,
Fonds der Chemischen Industrie.

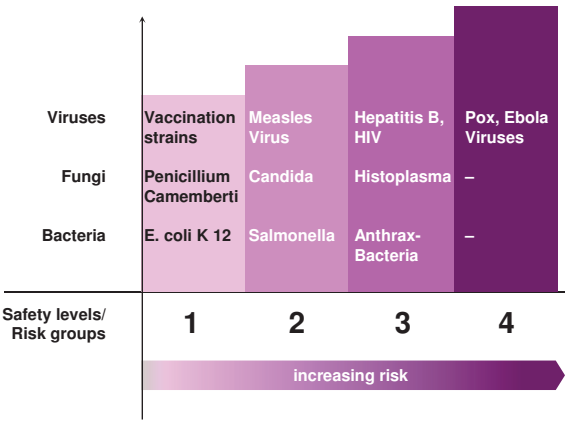
Cell factories to provide customized precursors



Is genetic engineering dangerous?

Risk Groups and Biosafety Level Definitions

Risk Groups (World Health Organization)



Biosafety Levels

Safety Level	Description
S1	no or low individual and community risk
S2	moderate individual risk, low community risk
S3	high individual risk, low community risk
S4	high individual and community risk

Source: Informationsserie Biotechnologie 2009, Fonds der Chemischen Industrie.

Potential chemical weapons from living organisms: Toxins

- Use of toxins is covered by
  1925 Geneva Protocol
  Biological and Toxin Weapons Convention of 1972
  Chemical Weapons Convention
- Toxins are poisons produced by living organisms e.g. bacteria, fungi, algae and plants
- Toxins are peptides, proteins or low-molecular organic compounds
- Toxins are less suitable for dispersal on a large scale. Nonetheless, they could be used for sabotage or in especially designed inputs, e.g. against key persons.
- Most toxins are unstable in alkaline water solutions and are thus easily destroyed by means of normal decontamination methods.

Source: A FOA Briefing Book on Chemical Weapons.

Examples
Bacterial Toxins

Botulinum toxin

produced by *Clostridium botulinum,* causes a severe form of food-poisoning (botulism),
used in treating squinting and other muscular disorders.

Staphylococcus enterotoxin type B

produced by *Staphylococcus aureus,*
causes food-poisoning symptoms

Saxitoxin

produced by blue-green algae (*cyanobacteria*) which are food for mussels,
attacks the nervous system and has a paralyzing effect,
included in Schedule 1 of the CWC

Source: A FOA Briefing Book on Chemical Weapons.

Examples
Plant Toxin and Bioregulators

Plant Toxin

Ricin extracted from seeds of the castor oil plant or produced by *E. coli*,
blocks the body's synthesis of proteins, death frequently occurs through heart failure,
included in Schedule 1 of the CWC

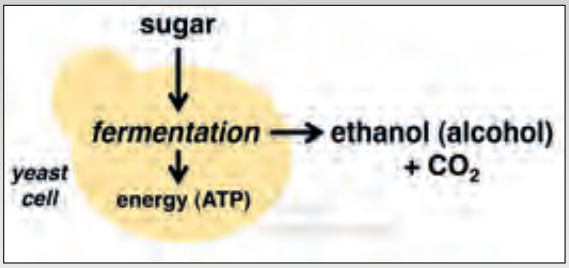
Bioregulators

No toxins, but possible use is similar

Example: Substance P, a polypeptide,
causes a rapid loss of blood pressure which may cause unconsciousness

Source: A FOA Briefing Book on Chemical Weapons.

Bio-Mediated Chemical Production: The Basics



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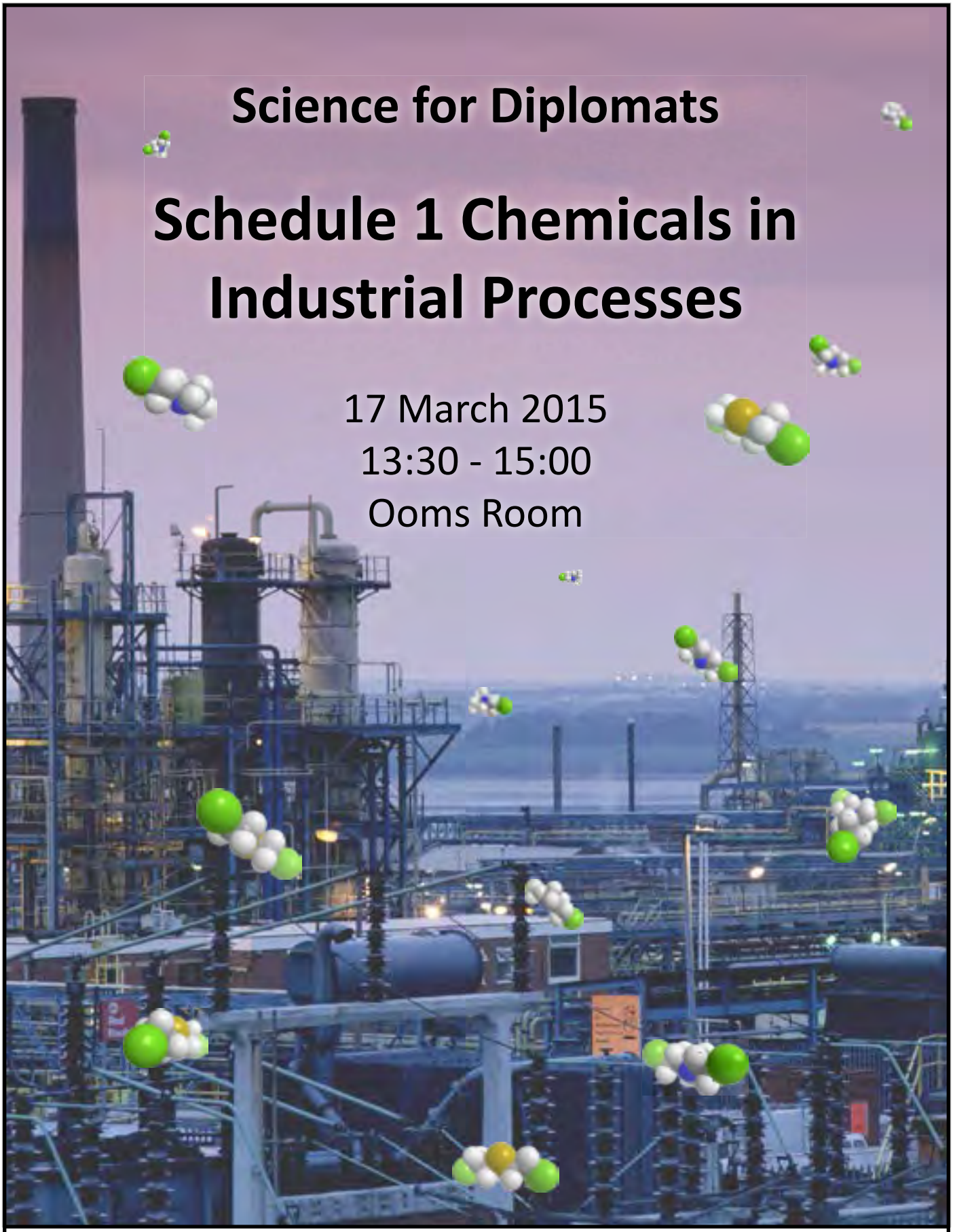
S & T For Diplomats: A Series of Discussions

- March 2015 (On the margins of EC-78, To be confirmed)
  - **S&T for Diplomats (4): Schedule 1 Chemicals**
    - Verification related SAB recommendations
    - Low concentration limits and captive use
- June (SAB-22) or July 2015 (EC-79); To be confirmed
  - **S&T for Diplomats (5): The Chemistry of Countermeasures**
    - Assistance and protection related SAB recommendations
    - Immediate response and longer term considerations
- **Other topics to be scheduled**



Science for Diplomats

Schedule 1 Chemicals in Industrial Processes

17 March 2015
13:30 - 15:00
Ooms Room

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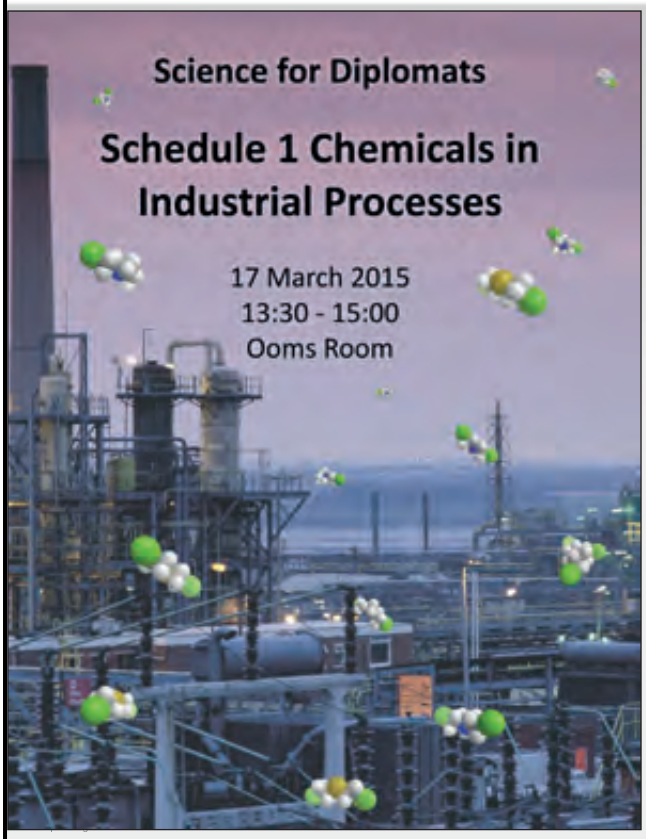

Dr Christopher M. Timperley
Vice Chair, OPCW Scientific Advisory Board
Defence Science and Technology Laboratory (Dstl),
United Kingdom of Great Britain and Northern Ireland

Jonathan E. Forman, Ph.D.
Science Policy Adviser
Office of Strategy and Policy
OPCW

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SAB Report of the Developments in S&T to The Third review Conference

(RC-3/DG.1, Dated 29 October 2012)

Director General's Recommendations

(RC-3/DG.2, Dated 31 January 2013)

Status of the Follow-Up to the Recommendations on S&T to the Third Review Conference

(EC-77/DG.11, Dated 5 September 2014)

Recommendations Concerning Schedule 1 Chemicals

(from EC-77/DG.11, Dated 5 September 2014)

Recommendation	Status of Implementation
"…establishment of a **low-concentration limit for Schedule 1 chemicals** …which could be achieved through various mechanisms." "...encourage States Parties to further discuss this regulatory aspect" (paragraphs 21 and 22 of RC-3/DG.2]	• The TS intends to issue a Note on its procedure for handling cases of unavoidable Schedule 1 by-products • Schedule 1 issues will be a topic for one of the "Science for Diplomats" workshops.
"…**captive use of Schedule 1 chemicals**…an important issue about which the chemical industry needs to be informed through the National Authorities" "...request States Parties to share the relevant information with their chemical industry and to report other examples of captive use of Schedule 1 chemicals to the Secretariat" "...encourage States Parties to assess if some Schedule 1 chemicals could occur in certain types of their industries." (paragraphs 17, 18 and 20 of RC-3/DG.2)	• Schedule 1 issues will be a topic for one of the "Science for Diplomats" workshops. • The DG is reminding States Parties of these recommendations.

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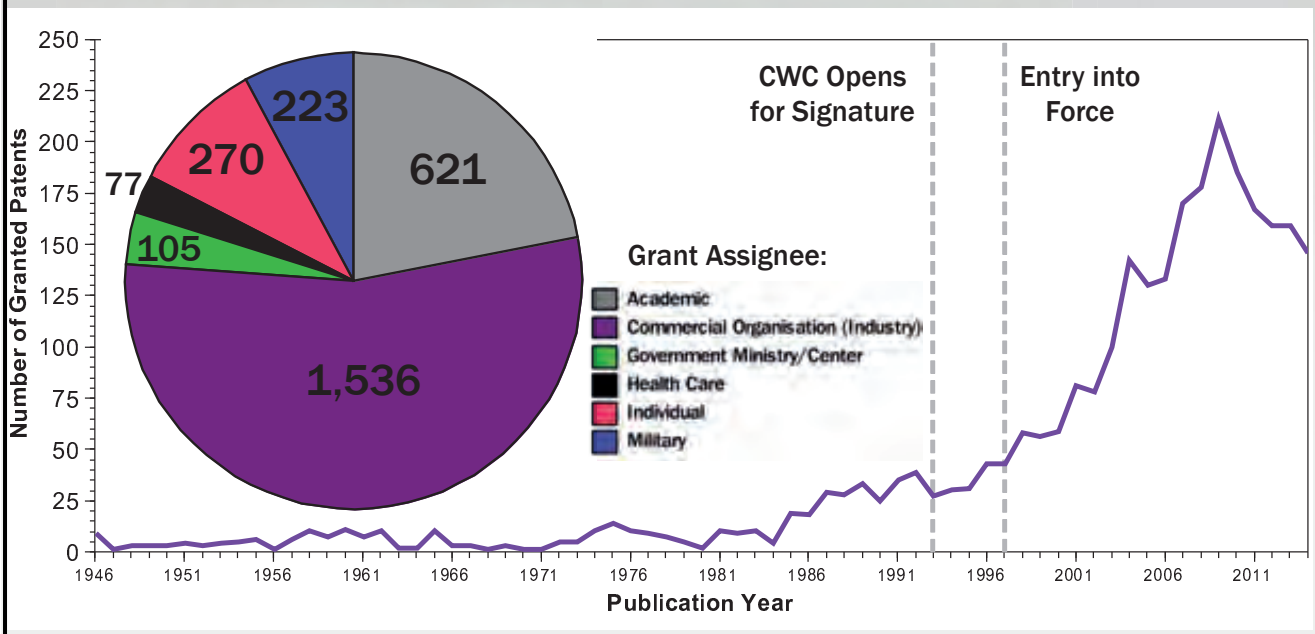
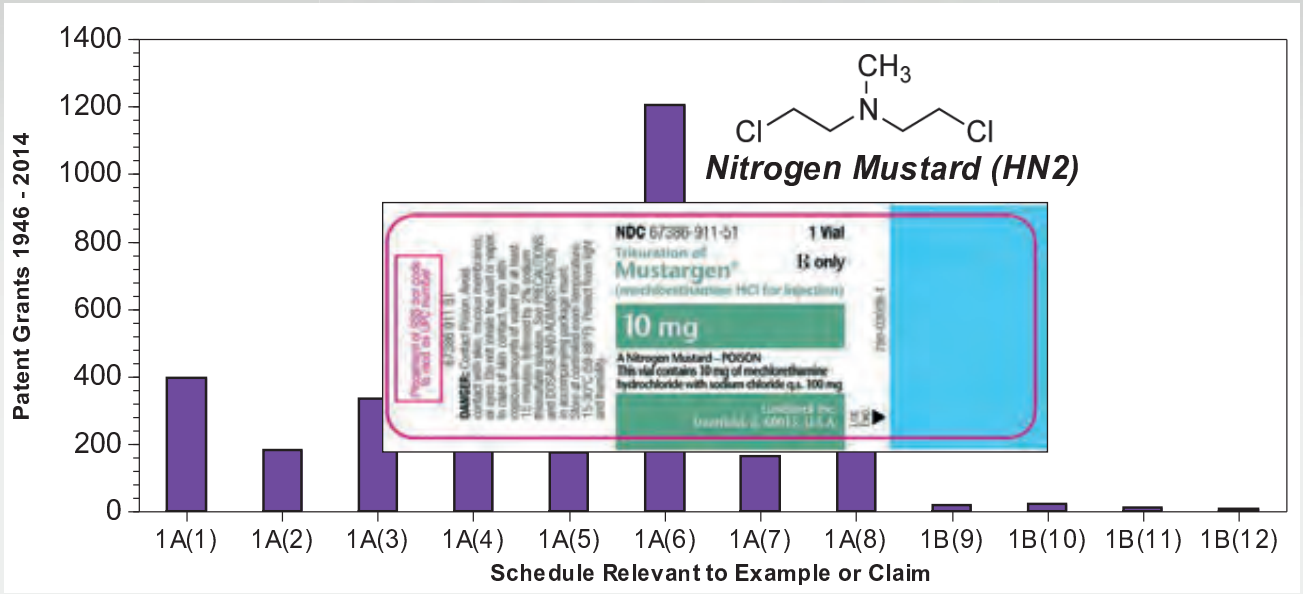
Schedule 1 Chemicals in Patent Grants 1946 - 2014



Schedules Represented



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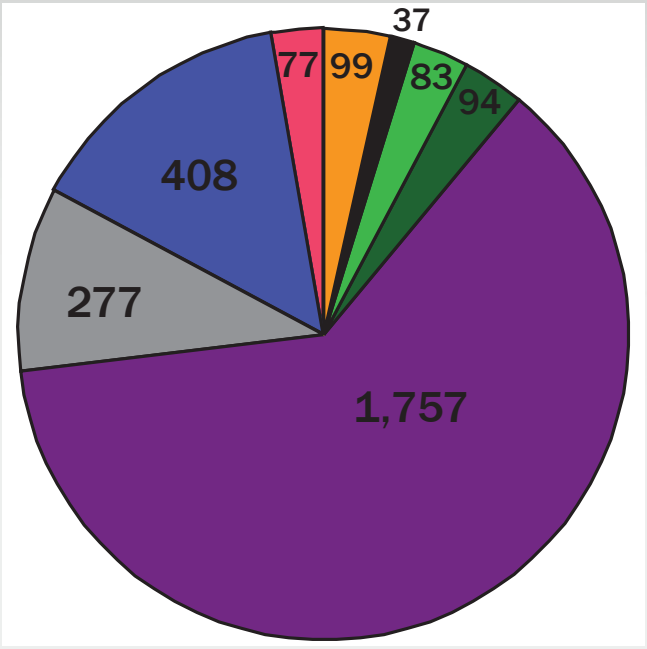
What Are All These Patents About?



Application:

- Analytical Chemistry
- Cosmetics
- Food Chemistry
- Polymers
- Biomedical (Drugs, Treatments, Research)
- Pollution (Clean Up/Monitoring)
- Chemical Synthesis/Production
- Other

What Are All These Patents About?

Abstracts for 146 Patent Grants References to Schedule 1 Chemicals From 2014

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Patents: Examples vs. Claims

System and method for detecting liquid and aerosol forms of chemical analytes
WO 2014113106 A2

ABSTRACT

A detection system capable of detecting liquid, liquid droplet and aerosol forms of chemical analytes. The system includes a detection element that it is able to function reliably in challenging environmental conditions over extended periods of time without degrading in performance. The element may also be part of a larger detection system which contains transduction mechanisms capable of transforming the detection element response into an electronic signal(s) for data transmission and remote signaling of detection events. The detection element may be a substrate that is composed of paper, plastic, polymer material, glass, metal, metal oxide, ceramic, or combinations thereof. The substrate may contain impregnated materials such as dyes, reactive chemicals, chemosorptive chemicals, physisorptive chemicals, and/or electronically or optically reactive media. A related method of the invention includes deployment of the detection system in an environment for the purpose of detecting chemical analytes of interest and reporting such detection.

Publication number	WO2014113106 A2
Publication type	Application
Application number	PCT/US2013/068826
Publication date	24 Jul 2014
Filing date	17 Oct 2013
Priority date	17 Oct 2012
Inventors	Carl TRIPP, Luke Doucette, Dean Smith, Eric Roy, Tyler Martin, Changfeng CHEN
Applicant	Orono Spectral Solutions, Inc.
Export Citation	BiBTeX, EndNote, RefMan
Classifications (2), Legal Events (1)	
External Links: Patentscope, Espacenet	

Example:
Patent describes live agent testing of invention

Method of treatment of wrinkles using topical chemodenervating agents
WO 2013142755 A1

ABSTRACT

Methods for reducing the appearance of wrinkles in a subject are provided herein. The methods of the present invention comprise identifying a wrinkle distribution on a subject and applying a topical composition comprising at least one chemodenervating agent onto and along the wrinkle distribution. The methods disclosed herein provide alternative methods for delivery of chemodenervating agents to the skin for the treatment of wrinkles.

Publication number	WO2013142755 A1
Publication type	Application
Application number	PCT/US2013/033417
Publication date	Sep 26, 2013
Filing date	Mar 22, 2013
Priority date	Mar 22, 2012
Also published as	US20130251770
Inventors	Jacob Waugh, L. Daniel Browne
Applicant	Revance Therapeutics, Inc.
Export Citation	BiBTeX, EndNote, RefMan
Patent Citations (3), Non-Patent Citations (1), Classifications (7), Legal Events (1)	
External Links: Patentscope, Espacenet	

Example:
Patent describes topical treatment for wrinkles

Claim: ...at least one chemodenervating agent is selected from the group consisting of botulinum toxin, **saxitoxin**, tetanus toxin, tetrodotoxin and combinations thereof.

Presentation by
Dr Christopher M. Timperley

Science for Diplomats

Schedule 1 and 2 chemicals as captive intermediates and unintended by-products

Dr. Christopher M. Timperley

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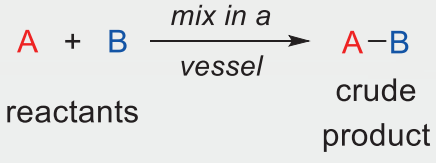
Chemical production

The deliberate encouragement of chemical reactions to obtain one or more products by physical manipulations

What is a chemical reaction?



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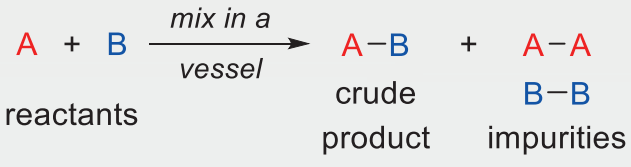

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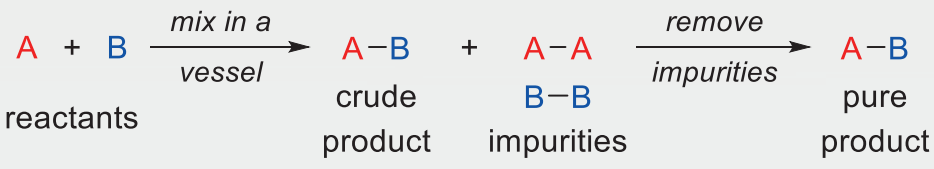

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Science for Diplomats, 17 March 2015

Chemical production

The deliberate encouragement of chemical reactions in a stepwise sequence to obtain one or more target products

An example of two step reaction sequence :

$$2\,A + 2\,B \xrightarrow{\text{step 1}} 2\;A{-}B \xrightarrow{\text{step 2}} A{-}A + B{-}B$$

reactants products

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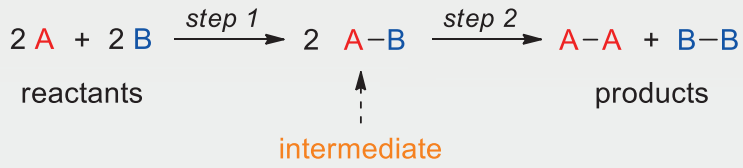

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Chemical production

The deliberate encouragement of chemical reactions in a stepwise sequence to obtain one or more target products

An example of two step reaction sequence :

2 A + 2 B → (step 1) → 2 A–B → (step 2) → A–A + B–B

reactants — intermediate — products

Some intermediates can be made biologically

Schedules of Chemicals

Schedule 1
- Developed, produced, stockpiled or used as a chemical weapon
- Pose otherwise a high risk to the object and purpose of the CWC
- Have little or no use for purposes not prohibited under the CWC

Schedule 2
- Possesses lethal or incapacitating toxicity and other properties that could enable them to be used as chemical weapons or to obtain Sch. 1
- Not produced in large commercial quantities in chemical industry

Schedule 3
- Have been produced, used or stockpiled as a chemical weapon
- Possess lethal or incapacitating toxicity and other properties that could enable them to be used as a chemical weapon or to obtain Sch. 1 or 2
- Produced in large commercial quantities in the chemical industry

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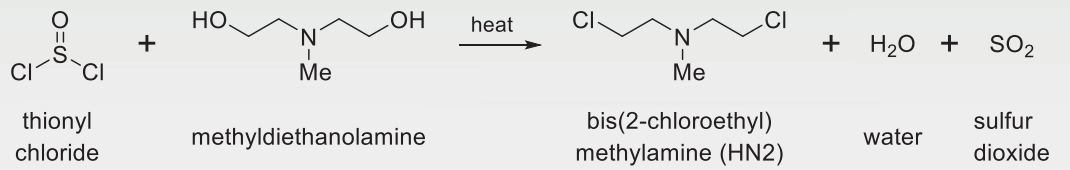
Nitrogen mustard HN2

Moving through the Schedules to make a chemical warfare agent :

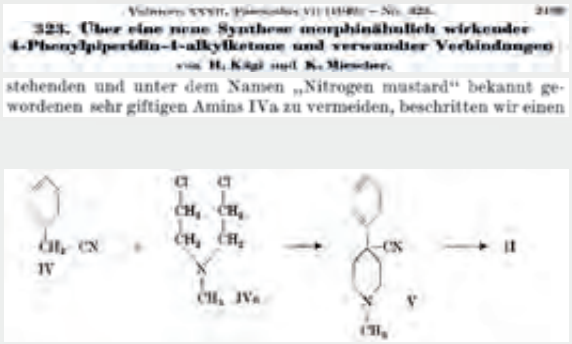


thionyl chloride | methyldiethanolamine | bis(2-chloroethyl) methylamine (HN2) | water | sulfur dioxide

Schedule 3B14 | Schedule 3B16 | Schedule 1A6 | Not scheduled

Schedule 1 captive intermediate in production of a pharmaceutical

HN2 can be used to make the anti-cancer drug ketobemidone, a pain-killer for children with cancer that are allergic to morphine



323. Über eine neue Synthese morphinähnlich wirkender 4-Phenylpiperidin-4-alkylketone und verwandter Verbindungen

von H. Kägi und K. Miescher.

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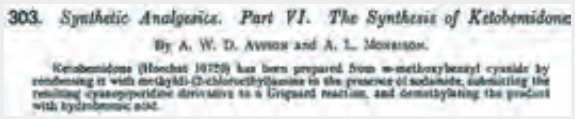
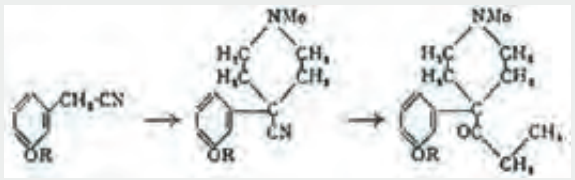
Helv. Chim. Acta 1949, 32, 2489



303. *Synthetic Analgesics. Part VI. The Synthesis of Ketobemidone*

By A. W. D. Avison and A. L. Morrison.

Ketobemidone (Hoechst 10758) has been prepared from *m*-methoxybenzyl cyanide by condensing it with methyldi-(2-chloroethyl)amine in the presence of sodamide, submitting the resulting cyanopyridine derivative to a Grignard reaction, and demethylating the product with hydrobromic acid.



J. Chem. Soc. 1950, 1469-1471

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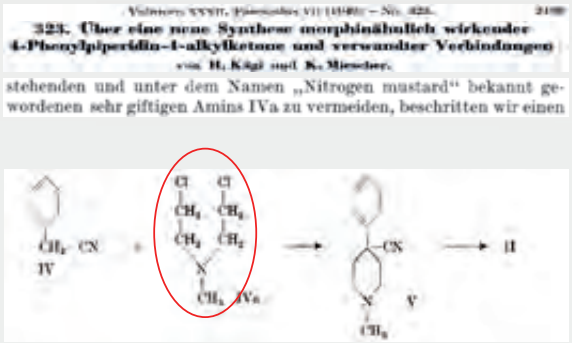

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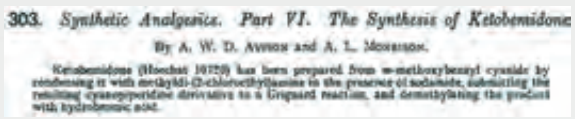

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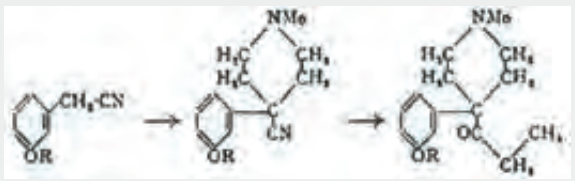

J. Chem. Soc. 1950, 1469-1471

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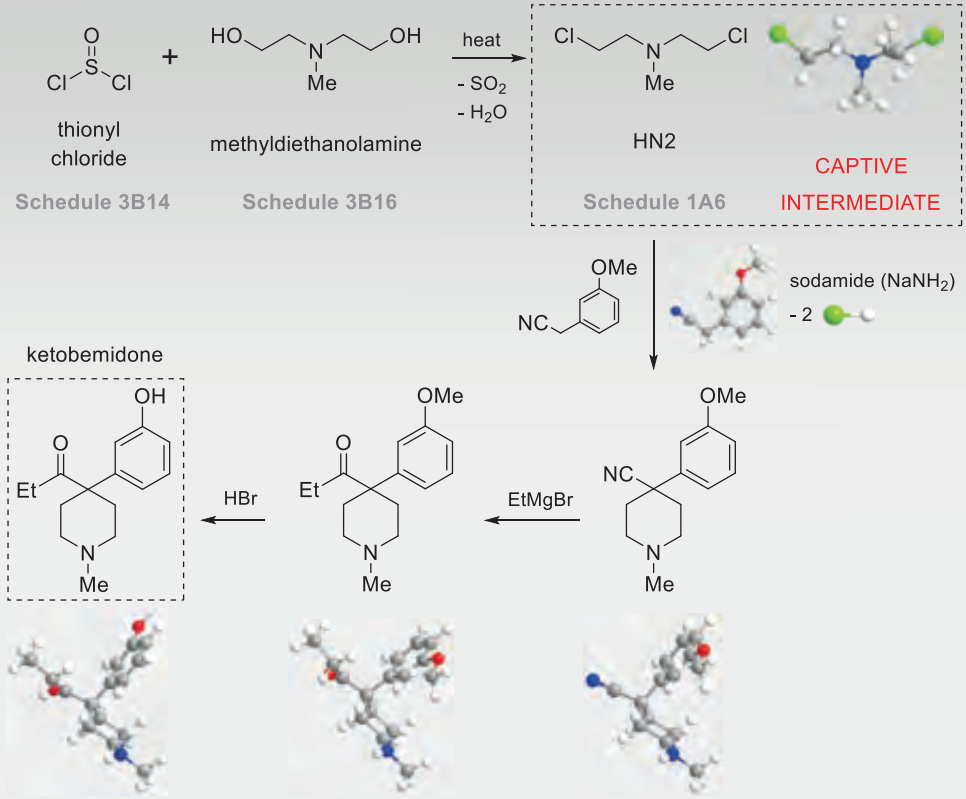

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Production of Schedule 1 chemical

'is understood for declaration purposes to include intermediates, by-products, or waste products that are *produced and consumed* within a defined chemical manufacturing sequence, where such products are chemically stable and therefore exist for a *sufficient time* to make isolation from the manufacturing stream possible, but where, under normal design or operating conditions, isolation does not occur'

Decision of OPCW CSP (C-10/DEC.12 dated 10 November 2005)

www.opcw.org

Science for Diplomats, 17 March 2015

Production of Schedule 1 chemical

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Decision of OPCW CSP (C-10/DEC.12 dated 10 November 2005)

Expectation to declare a facility consuming a Schedule 1 chemical as an intermediate in production of, for example, a pharmaceutical

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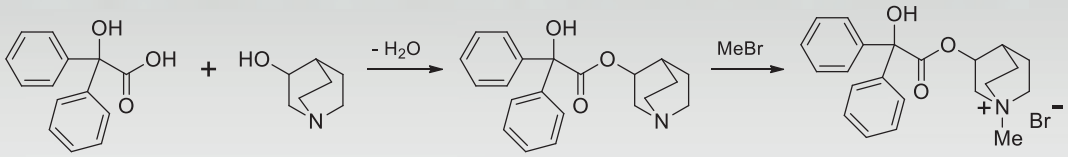
BZ as a captive intermediate

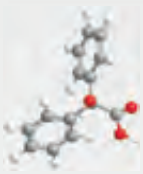


2,2-Diphenyl-2-hydroxyacetic acid

Quinuclidin-3-ol

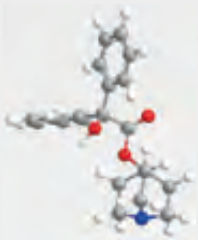
3-Quinuclidinyl benzilate (BZ)

Clinidium bromide (pharmaceutical)

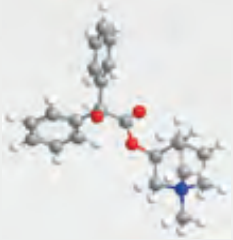


Schedule 2B8

Schedule 2B9



Schedule 2A3



Not scheduled

Clinidium bromide (Librax®) is used to treat irritable bowel syndrome

Unintended by-products

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Unintended by-products

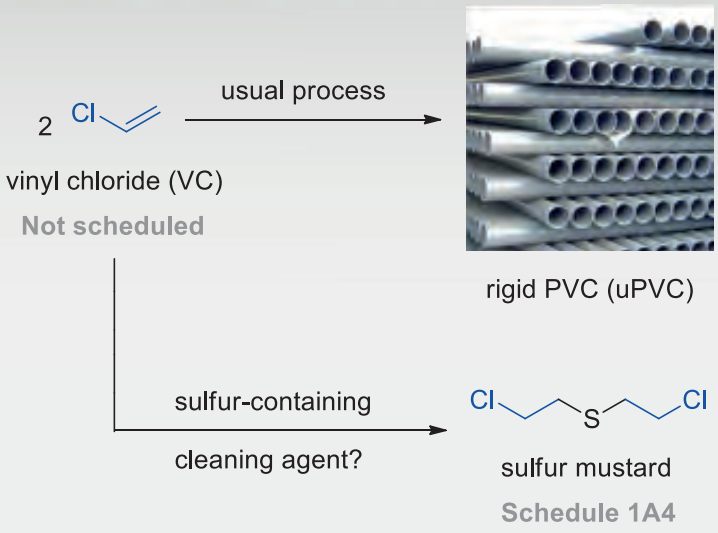
An unintended by-product is a Schedule 1 or 2 chemical formed unintentionally during a sequence of planned chemical reactions

Processes most likely to involve the formation of a blister agent

An accident involving the formation of the Schedule 1 chemical agent sulfur mustard occurred 6 years ago during cleaning of an industrial plant that manufactured polyvinylchloride (PVC) pipes

C Curty, J Ducry, S Mogl. Schedule 1 chemicals as captive intermediates or unavoidable by-products in chemical production: technical feasibility assessment based on literature review, LN 2013-01-CC, Spiez Laboratory, Switzerland, 2013.

Unintended Schedule 1 production



Employees experienced skin blistering, burns and respiratory problems

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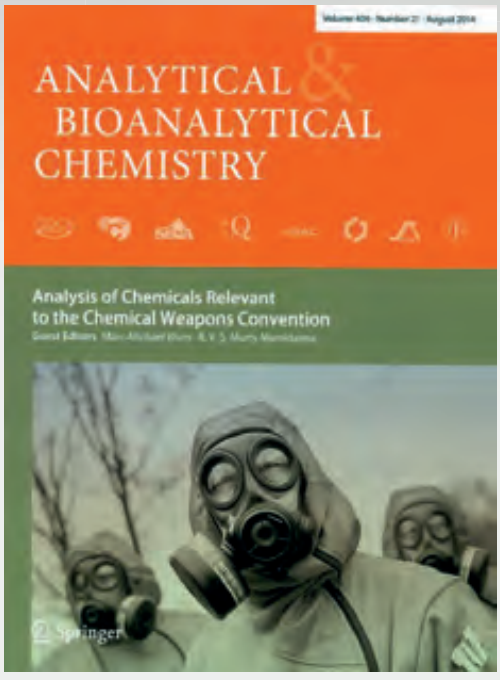
Improved analytical capabilities



Over the last decade the power of analytical chemistry techniques has increased hugely

Analysis using mass spectrometers allows detection of minute amounts of chemicals

Practical aspects of isolating Schedule 1 captive intermediates and by-products

Infrastructure of chemical plants that employ a process that involves captive use of a Schedule 1 chemical - or that yields a Schedule 1 chemical as a by-product - would generally be suitable for producing nitrogen or sulfur mustard

Schedule 1 by-products are likely to be present in reaction mixtures as impurities in low concentrations and therefore not suitable for activities prohibited by CWC (i.e. to be used as a toxic agent)

In theory, it is possible to extract a Schedule 1 chemical by-product using an extra purification step or to concentrate it in the reaction mixture, but the cost to isolate a low concentration of pure material would be unreasonably high (versus the ease of deliberate synthesis)

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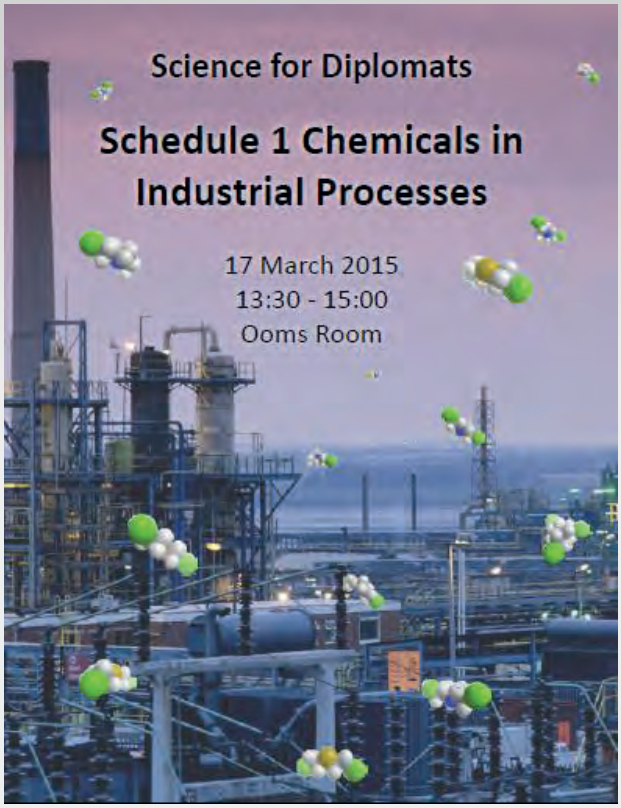
Conclusions

Very few examples of captive use or production as a by-product of Schedule 1 chemicals have been officially reported up to this day

Alternative synthetic methods can be found to avoid this problem

Discussion on the topic of this presentation initiated through the OPCW SAB in 2012: up to the policy making organs and Technical Secretariat to find solutions in cooperation with chemical industry


Science for Diplomats
Schedule 1 Chemicals in Industrial Processes
17 March 2015
13:30 - 15:00
Ooms Room

Questions?

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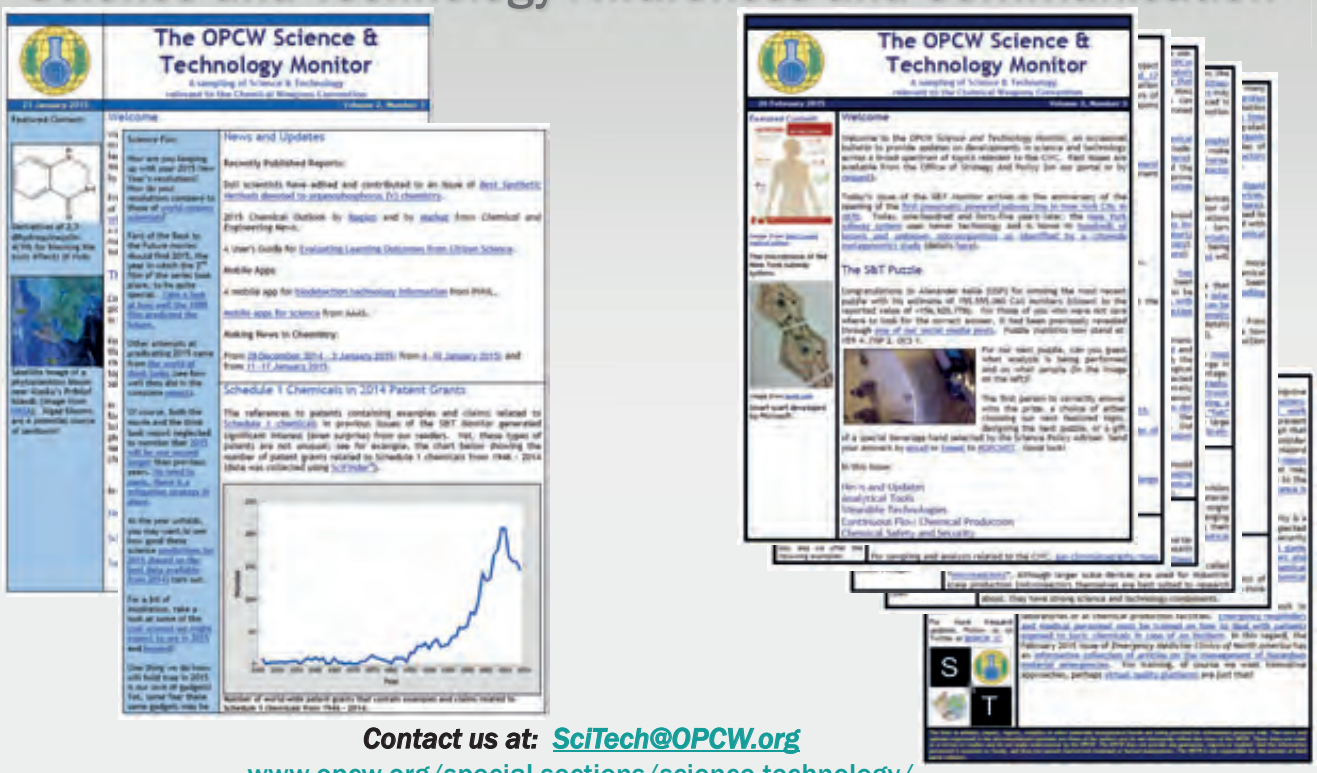
Science and Technology Awareness and Communication



Contact us at: *SciTech@OPCW.org*

www.opcw.org/special-sections/science-technology/

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S & T For Diplomats: A Series of Discussions

- July 2015 (On the margins of EC-79, To be confirmed)
  - **S&T for Diplomats (5): The Chemistry of Countermeasures**
    - Assistance and protection related SAB recommendations
    - Immediate response and longer term considerations
- October 2015 (On the margins of EC-80, To be confirmed)
  - **S&T for Diplomats (6): Chemical Forensics**
    - Introduction and overview of developments in the field
- **For more information on S&T from OPCW**

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www.opcw.org/special-sections/science-technology/

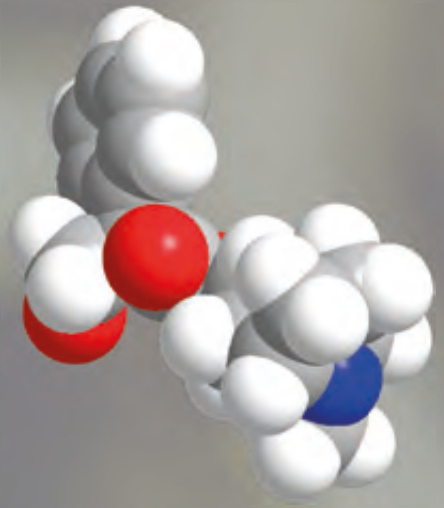
www.opcw.org

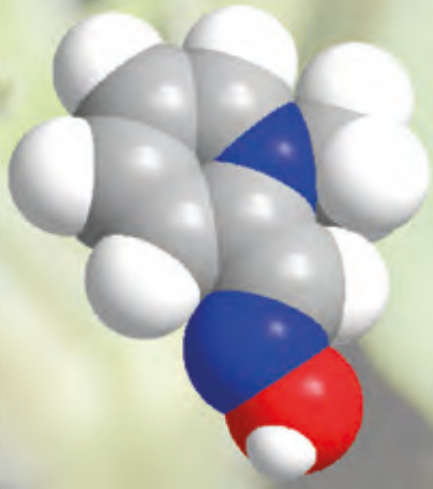
SCIENCE FOR DIPLOMATS

THE SCIENCE OF MEDICAL COUNTERMEASURES

Wednesday 8 July 2015
13:30 - 15:00
Ooms Room

Light lunch will be available at 13:00





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OF CHEMICAL WEAPONS

SCIENCE FOR DIPLOMATS

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Professor Slavica Vučinić
National Poison Control Centre
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Jonathan E. Forman, Ph.D.
Science Policy Adviser
jonathan.forman@opcw.org

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Advice on Assistance and Protection

OPCW — **Scientific Advisory Board**

Twenty-First Session
23 – 27 June 2014

SAB-21/WP.7
29 April 2014
ENGLISH only

RESPONSE TO THE DIRECTOR-GENERAL'S REQUEST TO THE SCIENTIFIC ADVISORY BOARD TO PROVIDE FURTHER ADVICE ON ASSISTANCE AND PROTECTION

DIRECTOR-GENERAL'S REQUEST TO THE SCIENTIFIC ADVISORY BOARD

1. Article X establishes the obligations and rights of a State Party concerning the assistance and protection against chemical weapons, and accords each State Party the right to request and to receive assistance and protection against the use or threat of use of chemical weapons. It is anticipated that, in most cases, the main assistance needed from the OPCW would be provision of medical countermeasures and treatment for chemical weapons casualties.

2. At its Sixteenth Session (in 2012) the Conference of States Parties to the Chemical Weapons Convention established the international support network for the victims of chemical weapons. This decision requires the establishment of a webpage and a databank to include information on offers by Member States relevant to the victims of chemical weapons and information on needs of the victims of chemical weapons. In order to be in a position to fully meet the expectations of the Convention States Parties with regard to the victims' network, it is necessary for the Technical Secretariat to compile information on relevant scientific advances with respect to new medical countermeasures and treatments of victims of nerve and blister agents.

3. In its report on developments in science and technology to the Third Review Conference (cf. paragraphs 120-123 in RC-3/DG.1, dated 29 October 2012), the Scientific Advisory Board informed the Technical Secretariat on the status of currently available countermeasures and treatments. As a follow up to this information, the Director-General requests the Scientific Advisory Board to:

   (a) recommend to the Technical Secretariat pre-treatments, vaccines, emergency care, and long term treatments that are currently available for blister and nerve agents; and

   (b) To inform the Technical Secretariat of the most relevant information sources that can be monitored to keep abreast of new developments in these areas.

OPCW — **Scientific Advisory Board**

Twenty-Second Session
8 – 12 June 2015

SAB-22/WP.2/Rev.1
10 June 2015
ENGLISH only

RESPONSE TO THE DIRECTOR-GENERAL'S REQUEST TO THE SCIENTIFIC ADVISORY BOARD TO PROVIDE FURTHER ADVICE ON ASSISTANCE AND PROTECTION

1. DIRECTOR-GENERAL'S REQUEST

1.1 At the Twentieth Session of the OPCW Scientific Advisory Board (SAB), the Director-General requested that the SAB provide further advice on assistance and protection against chemical weapons (see Annex 6 of the SAB-20/1, dated 14 June 2013). The SAB completed its work and provided the Director-General with the report of their findings (see SAB-21/WP.7, dated 29 April 2014).

1.2 In light of recent events and victims of chemical weapons currently undergoing medical care, there is a compelling need to have a better understanding of what can be done to mitigate the longer term effects of chemical agent exposure. Such information would be a valuable addition to the International Support Network for Victims of Chemical Weapons (C-16/ DEC.13, dated 2 December 2011).

1.3 At the Twenty-First Session of the SAB (Paragraph 9.20 of SAB-21/1, 27 June 2014) the Director-General requested the SAB to provide further advice, namely:

   (a) identify best practices for preventing and treating the health effects that arise from acute, prolonged, and repeated organophosphorus nerve agent exposure; and

   (b) identify any emerging medical countermeasures, intended for use at the point of exposure, that can reduce or eliminate longer term health effects arising from acute, prolonged, and repeated organophosphorus nerve agent exposure.

1.4 This report addresses these questions and reviews current and promising developments in nerve agent medical countermeasures.

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Treaty Implementation

The Chemical Weapons Convention

- Disarmament (Destruction and Verification)
- Non-proliferation (Verification)
- Assistance and Protection against CWs
- International Cooperation

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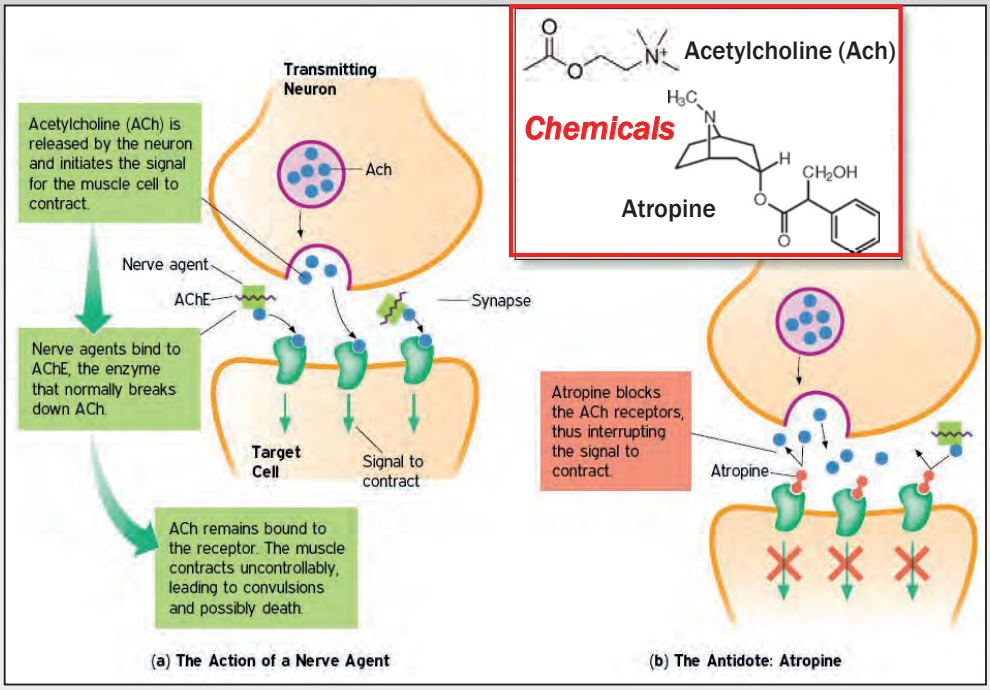
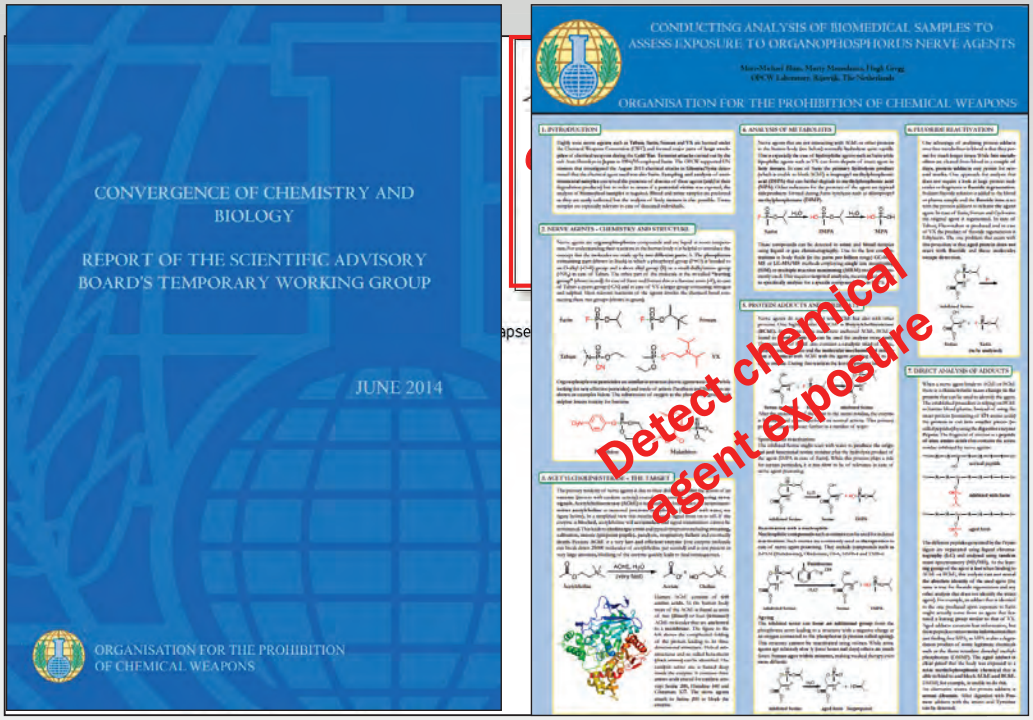
Medical Countermeasures: Cross-Cutting S&T



Medical Countermeasures: Cross-Cutting S&T

www.opcw.org/fileadmin/OPCW/Science_Technology/Diplomats_Programme/S_T_Biomed_Analysis_Poster.pdf



www.opcw.org/fileadmin/OPCW/SAB/en/TWG_Scientific_Advsiory_Group_Final_Report.pdf

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Presentation by Professor Slavica Vučinić

Response to the DG's request to the SAB to provide further advice on assistance and protection

The Science of Medical Countermeasures

Slavica Vucinic
Member of the SAB
The Hague, 8 July 2015

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Overview

1. Executive summary
2. Nerve agents
3. Adjunct agents and new trends in the treatment of NA poisoning
4. Acknowledgement

Executive summary

The Director-General requests the SAB to:

- identify best practices for preventing and treating the health effects that arise from acute, prolonged, and repeated organophosphorus (OP) nerve agent (NA) exposure; and
- identify any emerging medical countermeasures, intended for use at the point of exposure, that can reduce or eliminate longer term health effects arising from acute, prolonged, and repeated OP NA exposure.

This report addresses these questions and reviews current and promising developments in NA medical countermeasures.

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Nerve agents

- Organophosphorus (OP) nerve agents (NAs) are stable OP compounds. They are easily dispersed and highly toxic when inhaled or absorbed through skin. They are classified into G and V agents, but some are hybrid in structure, and are called GV agents.

Nerve agents

G agents		
GA	Tabun	*O-ethyl N,N-dimethylphosphoramidocyanidate*
GB	Sarin	*O-isopropyl methylphosphonofluoridate*
GD	Soman	*O-pinacolyl methylphosphonofluoridate*
GF	Cyclosarin	*O-cyclohexyl methylphosphonofluoridate*
V agents		
VE		*O-ethyl S-2-(diethylamino)ethyl ethylphosphonothiolate*
VM		*O-ethyl S-2-(diethylamino)ethyl methylphosphonothiolate*
VG	Amiton	*O-O-diethyl S-2-(diethylamino)ethylphosphorothiolate*
VR		*O-isobutyl S-2-(diethylamino)ethyl methylphosphonothiolate*
VX		*O-ethyl S-(diisopropylamino)ethyl methylphosphonothiolate*
GV agents		
GV		*2-(dimethylamino)ethyl N,N-dimethylphosphoramidofluoridate*

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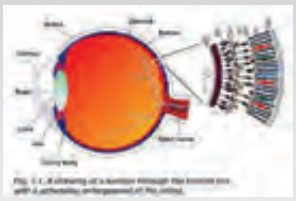
Psychological reactions always have an organic background.

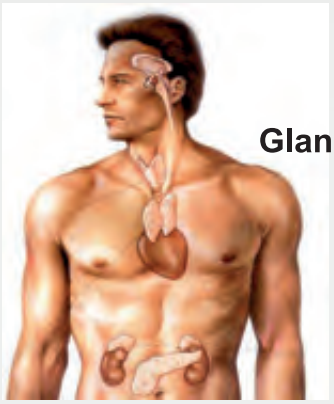
senses



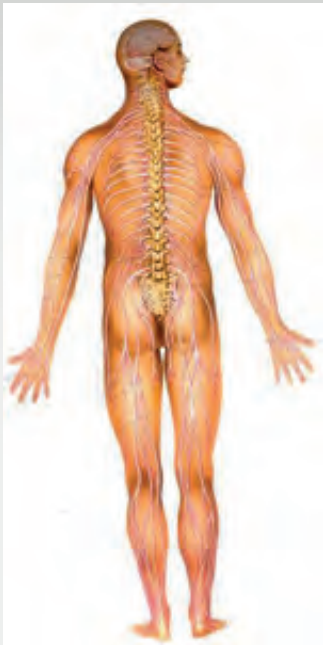
Nervous system is the organic base for psychological life. Every man has a couple of billions of neurons.

Senses, muscles and glands are important.

muscles

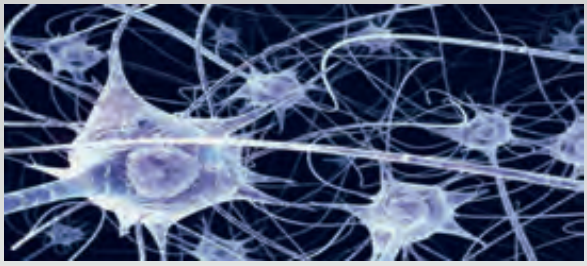


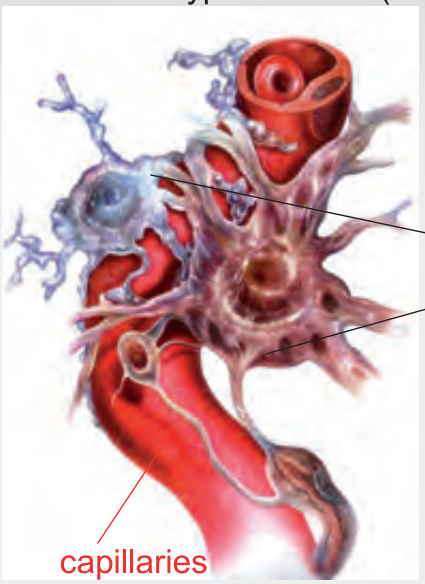
Glands

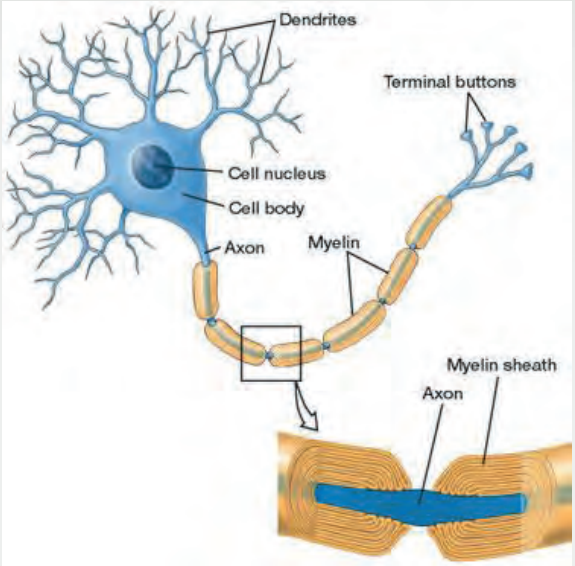


Nervous system

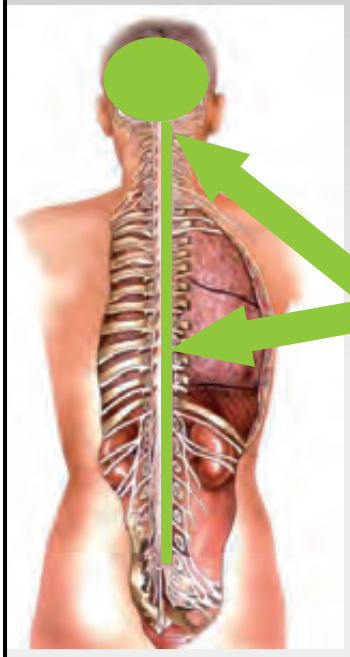
Neuron possesses a cell body (soma), dendrites and an axon. Generates and transmits the impulses between neurons and other types of cells (muscles, glands).





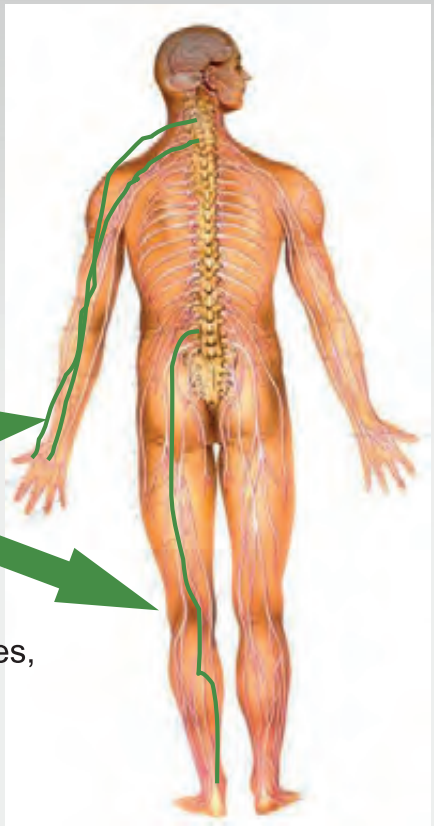


1. Central nervous system
Brain and spinal cord



CNS

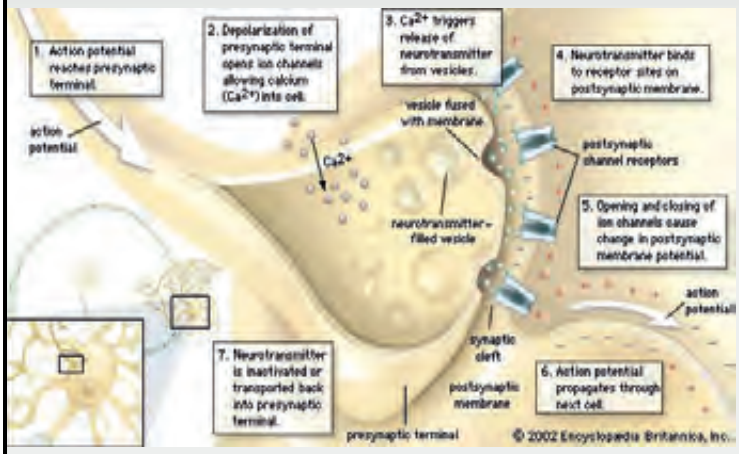
PNS



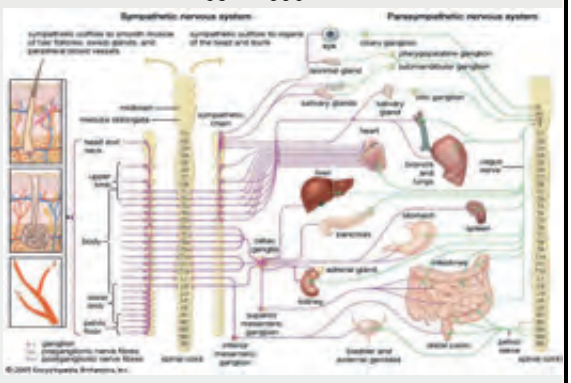
2. Perif. nervous system
Neurons outside the CNS, muscles, senses, organs

ACh, AChE, Mechanism of OP NA

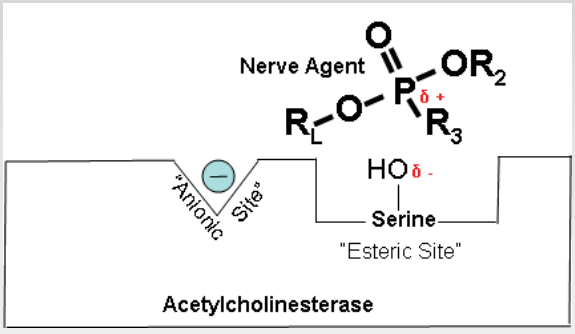
ACh functions in the PNS (activates muscles) and
CNS (forms a cholinergic system with other neurons- inhibitory actions).
Major NT in ANS.

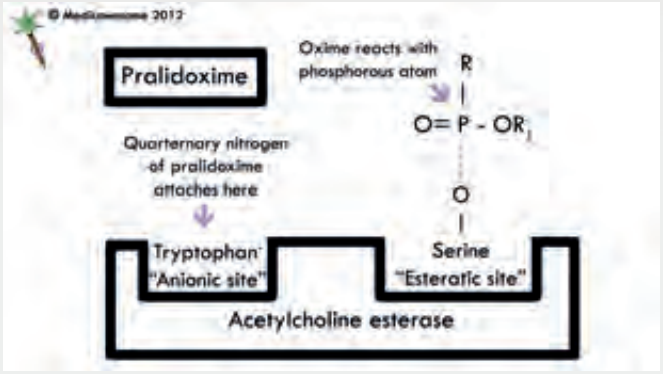


Henry Hallett Dale,1914, Otto Loewi 1936



Nerve agent, acetylcholinesterase and oxime





SIGNS AND SYMPTOMS AFTER ACUTE INHALATION EXPOSURE TO NA	SIGNS AND SYMPTOMS AFTER ACUTE DERMAL EXPOSURE TO NA
Low-dose with mild effects	***Low-dose with mild effects***
Runny nose	Localized sweating at exposure site
Miosis (blurred vision)	Fine muscle fasciculations at exposure site
Conjuctival inflammation	Miosis not an early sign and may be absent
Bronchoconstriction (chest tightness)	
Mild bronchosecretion	
Medium-dose with moderate effects	***Medium-dose with moderate effects***
Shortness of breath	Nausea and vomiting
Coughing	Severe headache
Wheezing	Generalized fasciculation
Nausea and vomiting	Feelings of weakness
Fasciculation	BEWARE: No respiratory signs present yet
Generalized feelings of weakness	
High-dose with severe effects	***High-dose with severe effects***
Loss of consciousness	Sudden loss of consciousness
Seizures	Seizures
Flaccid paralysis	Flaccid paralysis
Apnea	Apnea
Death usually within minutes	Death

From Crit. Care Med. 30 (2002)

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Medical treatment of NA exposure

- Pretreatment and prophylaxis
- Post-exposure therapy

Pretreatment

- Pretreatment - before poisoning, to increase the efficacy of treatment post-exposure. Carbamates, e.g. pyridostigmine, have the ability to carbamoylate AChE, preventing the OP inhibitor from binding.

- Pyridostigmine (30 mg/8 h) provides good protection against lethality within 2 h of the 1st dose, but is not optimal until the 3rd dose. To be stopped upon observation of NA poisoning symptoms and post exposure therapy started.

- Pretreatment for poisoning (tablets, sublingual or transcutaneous patch).

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Prophylaxis

- Administration of drugs before poisoning, designed to prevent poisoning.

- In the last decades, several topical skin protectants (TSP) have been produced (SERPACWA, AG7, IB1) but they have not always been fielded. They will increase the protection afforded by other protective equipment.

- Its purpose is to reduce or delay the absorption of CWA through the skin. However, effectiveness can only be expected when the TSP is applied prior to exposure.

Post - exposure treatment

A therapeutic scheme for NA poisoning includes early decontamination, supportive measures and specific pharmacological treatment to achieve:

- muscarinic cholinergic blockade (atropine),
- enzyme reactivation (oximes),
- and anticonvulsant effect (benzodiazepines associated with other drugs in case of refractory seizures).

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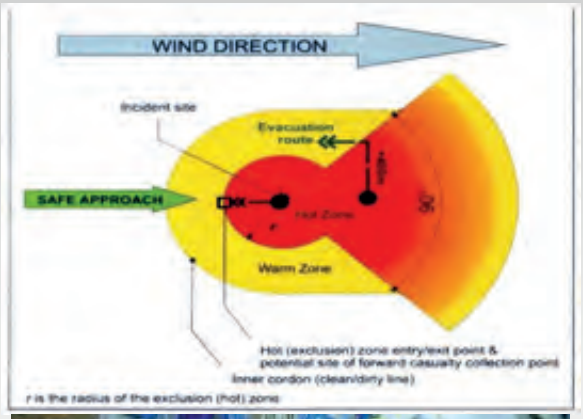
Emergency field therapy

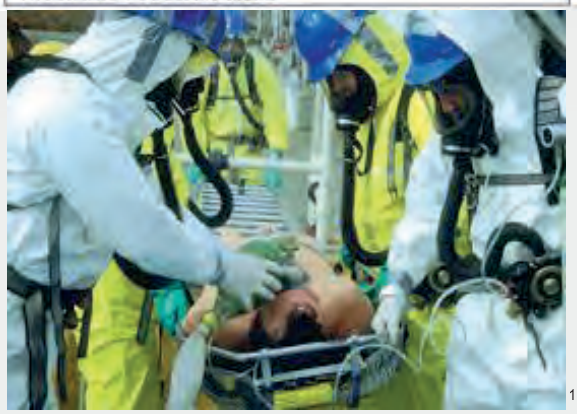
- Pralidoxime chloride (600 mg) and atropine (2 mg)
- Pralidoxime methylsulfate (350 mg), atropine (2 mg) and avizafone chlorhydrate (20 mg)
- Obidoxime chloride (220 mg) and atropine (2 mg)
- TMB-4 (80 mg) and atropine (2 mg)
- HI-6 dimethanesulfonate (750 mg), atropine (2 mg) and diazepam (10 mg)

Strategies using these autoinjectors depend on the country in which they are used.

Hot Zone

- Responders should have received training and wear protective clothing before entering a Hot Zone.
- If PPE is unavailable, or rescuers have not been trained, a call for assistance should be made according to local Emergency Operational Guides (EOG).





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First aid recommendations under field conditions

Treatment should be commenced immediately and the casualty given an antidote by self or buddy aid via autoinjectors:

- **MARK I kit:** Atropine (2 mg, 0.7 ml) and 2-PAM (600 mg)
- **AIBC Ineurope®:** Pralidoxime methylsulfate (350 mg), atropine (2 mg) and avizafone chlorhydrate (20 mg)
- **ATOX II:** Atropine (2 mg, 0.7 ml) and obidoxime (220 mg)
- **ATNAA:** Atropine (2 mg/0.7 ml) and 2-PAM (600 mg/2 ml); 1 needle injects both drugs
- **ATROPEN:** Atropine (2 mg, 0.7 ml). Each soldier must have 3 kits and 1 auto-injector with diazepam (10 mg) (if warned of NA attacks).
- Based on the severity of poisoning, I-III autoinjectors are applied.

Emergency medical treatment of NA poisoning

Symptoms and signs	Mark-1 Kit	Repeat dosing
Severe difficulties with breathing, apnea, cyanosis, muscle fasciculation or twitching, seizure, loss of consciousness	ABC (Maintain patent airway; assist breathing as needed, give oxygen, provide suction, restore normal cardiac rhythm) Administer Mark I Kit (3 times at 10-15 min intervals)	Diazepam autoinjector may be repeated 3 times every 10-15 min
Severe respiratory distress	Administer Mark I Kit (2 doses)	
Sweating, miosis, rhinorrhea, nausea, vomiting, anxiety	Administer Mark I Kit (1 dose)	
NOTE:	Monitor for symptoms every 10 min. Repeat atropine if needed	

Civilian population

- Important differences between relatively well protected armed forces and civilians.
- Do not have PPE, and are not pretreated by PB. At least 30 min delay for administration of specific therapy.

Atropine dosage after transfer to hospital

- Lower atropine doses needed.
- No established atropine dosage protocol.
- Individual titration of atropine dose.
- High concentration (100 mg/ml) or large volume ampules (10 or 20 mL) of 2 mg/mL atropine solutions are recommended for stockpiling.
- After initial hyper-atropinisation, 10-20% of a loading dose of atropine should be used in 5% glucose solution as a continuous infusion.

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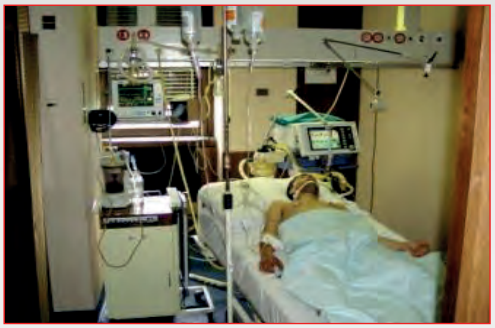
Oxime treatment after transfer from the first line to hospitals

- Pralidoxime (30 mg/kg in 5% glucose solution i.v, followed by 8 mg/kg/h continuously, until clinical recovery, or 12 h after the last dose of atropine was given.
- Obidoxime is a more potent reactivator in the case of VX, sarin. Dosage: 8 mg/kg i.v initially, followed by 3 mg/kg/h (500 mg loading dose, followed by 750-1000 mg in a continuous infusion).



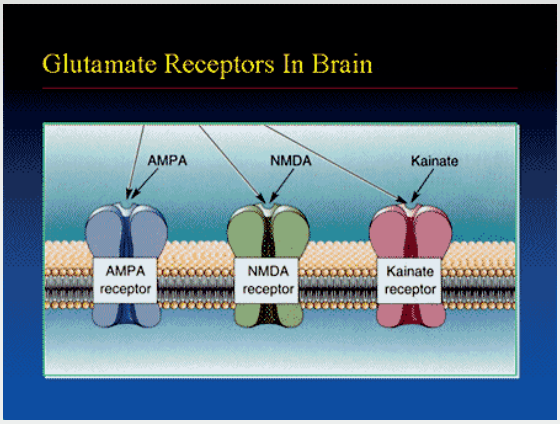
Anticonvulsants

- Anticonvulsants (e.g. diazepam, lorazepam or midazolam) having a neuroprotective effect, should be administered as necessary.
- Diazepam should be injected i.m starting with a 10 mg dose (adjusting the frequency of later injections).
- Midazolam should replace diazepam in cases requiring urgent treatment.

Adjunct agents and new trends

Gacyclidine

- A non-competitive NMDA receptor antagonist with neuroprotective properties.
- Prevents glutamate - induced neuronal death, enhances the neuroprotective activity of antidotes in soman poisoning (inhibits neuropathologic changes occuring 3 weeks after a soman challenge), and prevents convulsions.
- Unfortunately not anymore available – could be replaced by ketamine.



Adjunct agents and new trends

Tezampanel

- A competitive antagonist of the AMPA and kainate sub-type receptor. It reduces the length of status epilepticus and neuropathy induced by soman (exp). The best results - 1 h after exposure.

Ketamine

- Anaesthetic, a non-competitive antagonist of NMDA receptors. Experimentally confirmed to stop seizures and reduced related brain damage (1 h after exposure).
- Large clinical use world wide, should be considered for the treatment of NA - induced refractory status epilepticus.

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Adjunct agents and new trends

Huperzine A

- NMDA receptor antagonist (prevents status epilepticus, reduces the severity of seizures), inhibits AChE reversibly, similar to donepizil, rivastigmine or galantamine. It is used to treat Alzheimer's disease and myasthenia gravis.

Caramiphen

- Antimuscarinic drug with antiglutamergic and gaba-ergic properties. Therapeutic efficacy against OP-poisoning as a prophylactic and post-exposure (confirmed experimentally).

Adjunct agents and new trends

Galantamine

- Galantamine (GAL) inhibits AChE and potentiates ACh-induced currents in brain neurons, potentiates the activity of NMDA receptor.
- In contrast to pyridostigmine that inhibits BuChE also, it should help preserve the scavenger capacity of plasma BuChE for OPs.
- Experimentally confirmed (VX challenge) to reduce lethality, impairment of muscle tension, EEG changes.

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Adjunct agents and new trends

Scopolamine

- Anticholinergic. No randomized controlled studies.

Penehyclidine hydrochloride

- The anticholinergic agent used clinically for treating poisoning by OPs. Crosses the blood-brain barrier and antagonizes muscarinic and nicotinic receptors in the brain.
- Pauses ongoing seizures and has a better neuroprotective effect if administered soon after seizure onset in soman poisoning (experimentally). However compared to other drugs the body of evidence is smaller.

Adjunct agents and new trends

Sodium hydrogencarbonate and blood alkalinization

- To increase the hydrolysis of OP molecules *in vivo*, the effects of higher doses of $NaHCO_3$ (5 mEq/kg in 1 h, followed by 5 mEq/kg/day) were assessed.
- Increasing one unit of pH (accompanied by a 10-fold increase in OP hydrolysis, and alkalinization products of NAs).
- **Better control of cardiotoxicity, increased bio-availability of oximes, increased atropine activity, and/or a direct effect of $NaHCO_3$ on neuromuscular function. Not a standardized procedure so far.**

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Adjunct agents and new trends

Magnesium sulfate

- The mechanism - inhibition of ACh release through blocking Ca^{2+} channels in the CNS and at peripheral sympathetic and parasympathetic synapses.
- In acute OP poisoning - decreased mortality and reduced overstimulation of the CNS due to NMDA receptor activation.
- No side effects with doses of 4-16 g.
- **Insufficient evidence to recommend routine use in NA casualties.**

Adjunct agents and new trends

Antioxidants

- Possible additional mechanism for NA: induction of oxidative stress and generation of free oxygen radicals.
- Chronic toxicity studies have revealed an increased level of oxidative stress biomarkers as well as increased DNA damage.
- A beneficial effect of **vitamin E and *N*-acetyl-cysteine** has been shown (exp. studies).
- **Insufficient evidence to recommend routine use in NA casualties.**

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Adjunct agents and new trends

Protective bioscavengers

- New medical treatment of NA exposure should provide reduced lethality, reverse toxicity following exposure, and help eliminate the need for further treatment.
- The need to start treatment within 1 min after exposure has prompted the development of pretreatment therapy, such as bioscavengers of different profile.

Adjunct agents and new trends

Bioscavengers - enzymes or antibodies that sequester and neutralize toxic OP compounds before they reach their biological targets.

Conditions:

- a) broad spectrum vs different NAs and a rapid activity;
- b) suitable retention time in circulation (ideally 11-15 days);
- c) be available in sufficient concentration to be effective;
- d) have no adverse immunogenic properties.
- e) be available at a reasonable cost

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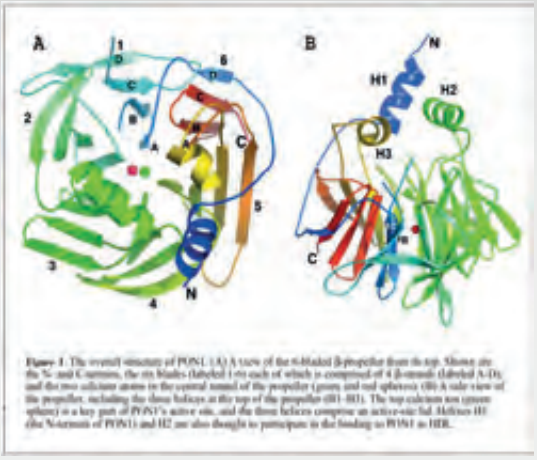
Adjunct agents and new trends

Bioscavengers:

- a) **Stoichiometric bioscavengers** - (ChEs), especially BChE, and carboxylesterases (CaEs) react stoichiometrically with OP compounds (1 mole of enzyme neutralizes 1 mole of OP, inactivating it).

- b) **"Pseudo catalytic bioscavengers"** that combine AChE (that has scavenging properties and binds NA) and oxime (that acts as a pseudocatalytic bioscavenger reactivating ChE) and thus restore AChE function;

- c) **Catalytic bioscavengers** (OP hydrolase, OP anhydrase, and paraoxonase (PON) that trap and degrade neurotoxic OP compounds rendering them non-toxic.



Adjunct agents and new trends

- **pHuBChE** has scavenging properties against different NAs (soman, sarin, VX).
- Advantages for human use: rapid reaction with a broad spectrum of OPs, a good retention time in circulation, and no immunogenic activity.
- Methods for mass production of pHuBChE: **purification of the enzyme from human plasma,** recombinant HuBChE (rHuBChE) **produced in the milk of transgenic goats** ('Protexia') developed by Nexia.
- Possible sources of **rHuBChE** are transgenic plants, transgenic animals, adenovirus or algae, and it can be derived in cell-lines.

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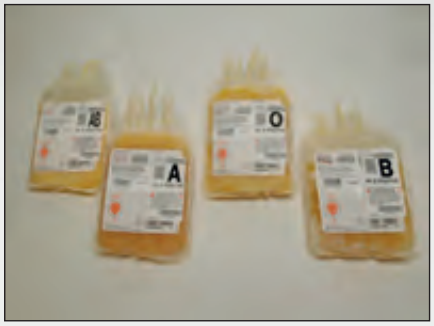
Adjunct agents and new trends

- **Fresh frozen plasma (FFP)** is a blood fraction prepared by removing the cellular components by apheresis.
- It contains clotting factors, proteins, and enzymes.
- It is hypothesised that in OP poisoning BuChE from FFP will sequester the poison present in blood and remove it from circulation.
- **No general agreement about the routine use for the treatment of exposure to OP compounds.**



Methods for decontamination

Methods of decontamination of CW agents: (i) mechanical, (ii) physical, and (iii) chemical. They were presented last year by SAB members (*OPCW Today*, Vol. 3, No. 1, Aug 2014).

Oxidiser gels

- To detoxify NA, a formulation with a adsorbent (e.g. silica, alumina or alumino-silicate clays) and oxidising agent (aqueous sodium hypochlorite) can be prepared and applied at the site of decontamination. **Suitable for field implementation.**

Bacterial phosphotriesterase

- Phosphotriesterase (PTE) is an enzyme isolated from the bacterium *Pseudomonas diminuta*. Modified by biotechnological processes, engineered PTE enzymes are useful for detoxification of NA ***in vivo*.**

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Methods for decontamination

Nanosized metal oxides as CWA decontaminants

- Nanosized metal oxide aerogels (MgO, Al_2O_3 and CaO) (with a high surface area, potent adsorbent properties and reactivity towards NAs) are promising sorbent materials for removing NAs from **contaminated surfaces** and degrading them *in situ*, leading to non-toxic products.

Future trends

- Formulations have to be user and eco-friendly,
- Without corrosive properties,
- Stable active ingredients.
- Nanoporous materials,
- Nanosized metal oxide aerogels

Methods for decontamination

- TSP (RSDL)
- Intended to remove or neutralize CWAs (GA; GB; GD; GF; VX; HD), T-2 toxin and many pesticides.
- Originally developed by Canadian Department of National Defense, adopted by several military services around the world.
- FDA has approved use thereof in 21 and 42 mL packets.
- EXTERNAL USE ONLY, CONTACT WITH EYES AND MUCOUS MEMBRANES SHOULD BE AVOIDED!

Identify best practices for preventing and treating the health effects that arise from acute, prolonged and repeated NA exposure

- In the case of NA exposure, it is necessary to administer the adequate antidotal treatment:

  - the reactivator of NA - inhibited AChE,

  - the anticholinergic drug to counteract the overstimulation of peripheral and central cholinergic muscarinic receptors, and

  - the anticonvulsive drug to prevent centrally mediated seizures and subsequent tonic - clonic convulsions.

- Treatment must continue as long as NA - induced clinical and laboratory signs and symptoms are visible.

Identify best practices for preventing and treating the health effects that arise from acute, prolonged and repeated NA exposure

- In the case of repeated NA exposure, each exposure must be treated in the same way as the first exposure using adequate antidotes and supportive symptomatic drugs.
- Humans can be more sensitive to acute toxicity of NAs in the case of repeated exposure (lower activity of AChE due to previous NA exposures).
- The prognosis of repeated exposure to NA is more severe and the antidotal and supportive treatment must be as intensive as possible.

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Identify any emerging medical countermeasures, intended for use at the point of exposure that can reduce or eliminate longer term health effects arising from acute, prolonged and repeated NA exposure

- To reduce or eliminate longer term health effects - treat correctly acute cholinergic crisis.
- Delayed and prolonged effects of NA are mostly caused by damage to the CNS through centrally - mediated seizures.
- To prevent seizures, it is necessary to prevent prolonged stimulation of muscarinic receptors by a centrally - acting anticholinergic drug and an anticonvulsive drug.
- If longer term health effects (especially neurological, including symptoms such as increased excitability and a deficit of cognitive function) emerge symptomatic and supportive treatment should be recommended in this situation.

The role of prophylactic antidotes against NAs

- Prophylactic antidotes should increase the:
- **Resistance of the organism against acute toxicity of NAs**
- **Efficacy of post-exposure antidotal treatment of NA poisoning**
- Prophylactic antidotes to NAs should be administered in response to the threat of exposure to NAs. Generally, the combination of pre-treatment and post - exposure adequate antidote treatment increases the probability of avoiding the delayed and prolonged effects of NAs.

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The role of prophylactic antidotes against NA

- **Pyridostigmine** drawbacks: limited dosage (due to adverse effects), it cannot penetrate the blood-brain barrier.
- A combined oral prophylaxis called **PANPAL** was developed in the Czech Republic. It consists of **pyridostigmine** and two centrally-acting anticholinergic drugs (**benactyzine and trihexyphenidyl**).
- Higher efficacy than pyridostigmine alone to avoid or diminish the acute toxicity and to prevent delayed and long-lasting health effects from acute, prolonged and repeated exposure to NA.
- **Clinical approval from the FDA and EMA would be necessary prior a general recommendation.**

The role of prophylactic antidotes against NA

- Another approach is to administer reactivators of NA - inhibited AChE in advance.
- A special prophylactic antidote called TRANSANT (involving the **oxime HI-6**) was developed and introduced into the Czech Army.
- The combination of both prophylactic antidotal means (PANPAL and TRANSANT) represents an effective prevention, increases the resistance of humans and prevents centrally - mediated seizures as well as subsequent delayed and prolonged health effects from acute, prolonged and repeated exposure to NA.
- **Clinical approval of the FDA and EMA would be necessary prior a general recommendation.**

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The role of prophylactic antidotes against NA

- Recent alternative approach to the development of prophylaxis - **bioscavengers** able to bind or hydrolyse NA before they reach the biological target.
- Valuable, but until now has not been prepared for clinical use.
- However, it represents a promising approach to preventing the longer term health effects arising from acute, prolonged and repeated NA exposure.

Acknowledgements

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Augustin Baulig PhD,
Prof. Roberto Martinez PhD,
Cheng Tang

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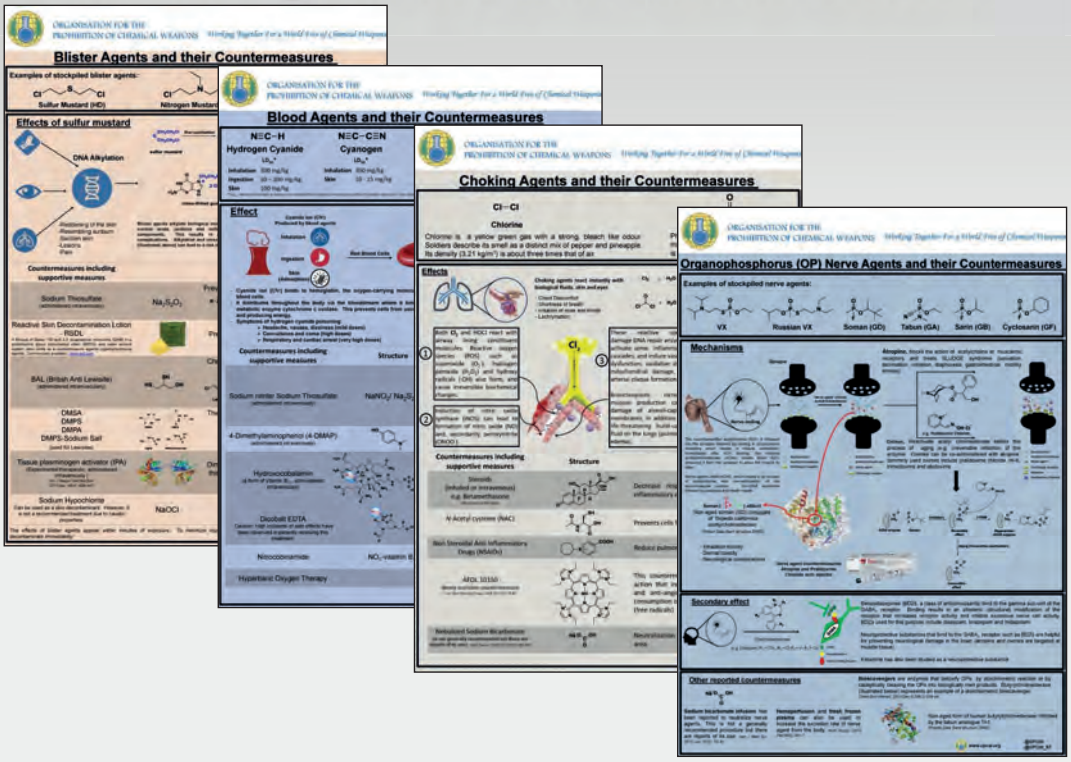
Chemical Agents and Their Countermeasures



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Science and Technology Awareness and Communication

VOLUME 2 NUMBER 1

The OPCW Science & Technology Monitor

A sampling of Science & Technology Relevant to the Chemical Weapons Convention

1 June 2015

In This Issue

Medical Countermeasures

Chemical Forensics

OPCW Research Projects Support Programme

Featured content

Image from DuoDote®
Medical countermeasures at work in a synapse

Fingerprinting chemicals

Image from PLoS One. 2013 Nov 8;8(11)
Drug discovery research in OPCW Supported Research Projects

Welcome

Welcome to the *OPCW Science and Technology Monitor*, an occasional bulletin to provide updates on developments in science and technology across a broad spectrum of topics relevant to the CWC. Past issues are available from the Science and Technology section of the OPCW website.

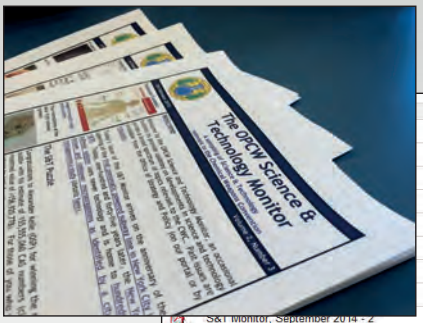
Thanks to all of you who have taken our survey. For those who have not yet responded, the survey is still open (click here). There are only six questions, all easier than the puzzle (we promise) and all responses are anonymous. Your feedback is highly appreciated!

Today marks the 25th anniversary of the signing of the 1990 Chemical Weapons Accord by the United States of America and the Soviet Union. This agreement, which pre-dated the CWC, marks one of many steps taken in the journey toward a world free of chemical weapons. Steps taken in chemical disarmament have been supported by the science of chemistry itself: a scientific field that provides opportunities for international collaborations and brings forth new developments with peaceful economic and technological benefits. As we move into the future, we look forward to a wealth of new discoveries from this evolving scientific field.

The S&T Puzzle

We once again congratulate our colleagues at the CTBTO, whose entry correctly recognized four of the top five spoken words of the Director-General in the eight statements delivered from 22 January to 29 April 2015 (in case you were wondering, they missed "States"). The prize for best visualisation of the words of the Director-General, however, goes unclaimed as no submissions (except our own, below) were received. Puzzle statistics now stand at: VER 4, OSP 2, OCS 1, INS 1 and CTBTO 3.

For this edition of the puzzle, we look at the multiple uses of a cup of coffee. Can you tell us the identity and LD_{50} (that's right, the median lethal dose) of the most abundant chemical in the cup; the molarity (M) of caffeine (molecule above); and the LD_{50} of coffee itself? To keep this simple, assume this coffee is made with Arabica beans and brewed by a certified procedure (for



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S&T Monitor, September 2014 - 2	12/09/2014
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S & T For Diplomats: A Series of Discussions

- 6 October 2015 (On the margins of EC-80)
  - **S&T for Diplomats (6): Data Analytics and The CWC: An Introduction to OCPF Site Selection Methodology**
    - The "nuts and bolts" of OCPF site selection methodology
- December 2015 (On the margins of CSP-20, To be confirmed)
  - **S&T for Diplomats (7): Topic To Be Determined**
    - *S&T topic considered in the TWG on Verification Report*
- **For more information on S&T from OPCW**

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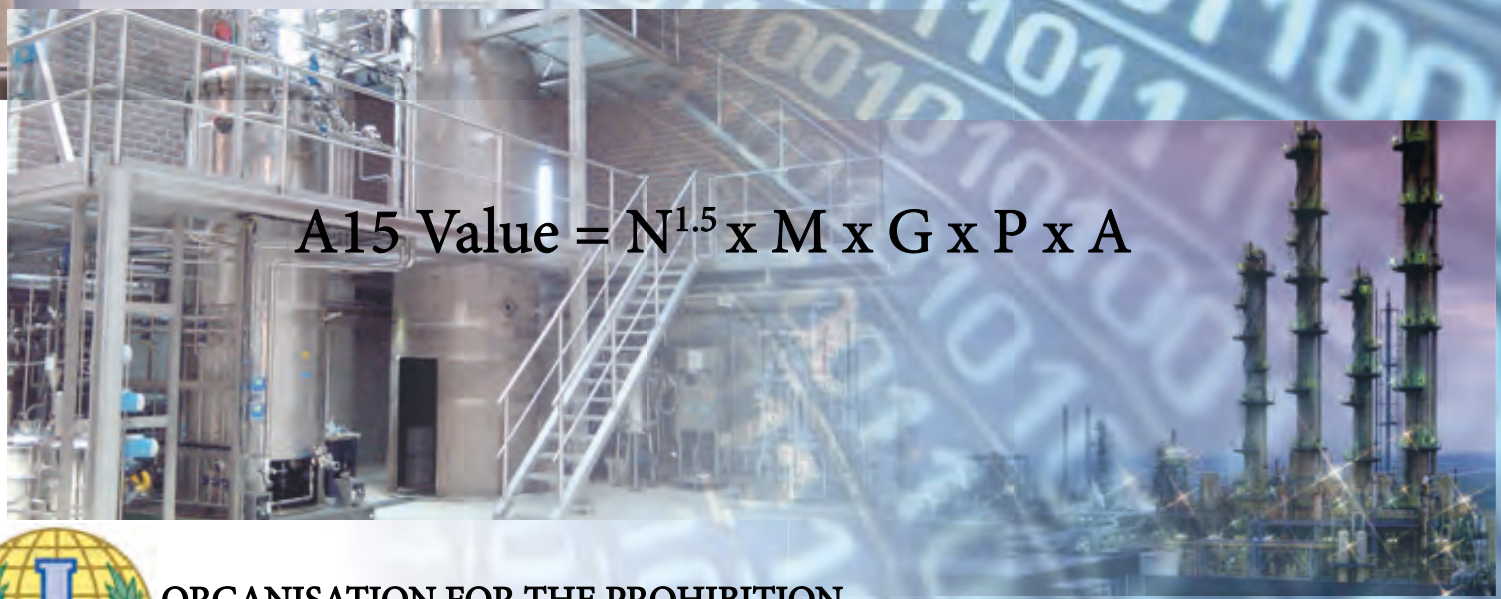
SCIENCE FOR DIPLOMATS

DATA ANALYTICS AND THE CWC: AN INTRODUCTION TO OCPF SITE SELECTION METHODOLOGY

Tuesday 6 October 2015
13:30 - 15:00
Ooms Room

Light lunch available at 13:00



$$A15\ Value = N^{1.5} \times M \times G \times P \times A$$

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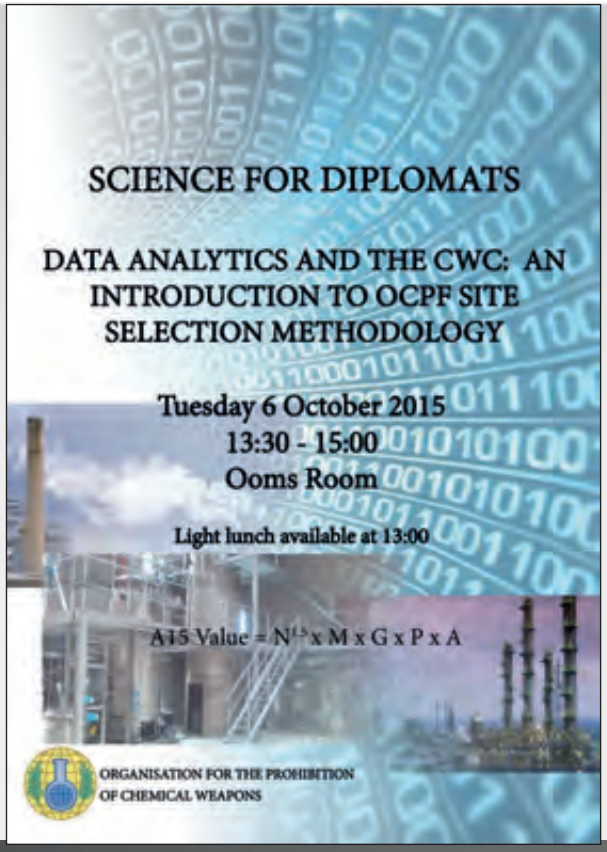

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Treaty Implementation

The Chemical Weapons Convention

- Disarmament (Destruction and Verification)
- Non-proliferation (Verification)
- Assistance and Protection against CWs
- International Cooperation

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Treaty Implem

Disarmament (Destruction and Verification)

International Cooperation

Non-p (Ve

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The Many Faces of Chemical Production

EC-80/DG.7 (28 August 2015)

Action to implement the recommendations made by the SAB in its report on Verification

https://www.opcw.org/fileadmin/OPCW/SAB/en/ec80dg07_e_.pdf

Recommendation from the SAB	Implementation	Expected outcomes/results
Recommendation 9 Not all facilities that fall under Part IX of the Verification Annex should be considered of the same relevance to the object and purpose of the Convention. The TWG recommends a practical approach for enhancing the utilisation of verification resources for OCPF declaration and on-site inspection processes.	• See (a), (b) and (c) below.	• More effective verification. • Continued strong support from the global chemical industry for sound and proportionate implementation of the CWC. • Adaptation of the verification regime in line with developments in the chemical industry.
Recommendation 9a The OPCW policy-making organs should exempt certain OCPFs from declaration requirements.	• Industry cluster: Discussion based on Secretariat proposal. • Executive Council: Decision.	
Recommendation 9b The Secretariat should reassess which product group codes are highly relevant to the Convention. Facilities declared with these product group codes should be subject to a higher probability to be selected for inspection.	• Secretariat: Review the performance of the site-selection methodology. • Industry cluster: Potential discussion depending on Secretariat review.	
Recommendation 9c For facilities in product group codes that are considered less relevant, the Secretariat should identify appropriate mechanisms to augment the declared information with validated and credible sources to allow for an assessment regarding the need for on-site inspection.	• Secretariat: The review and potential discussion on implementation of recommendation 9(b) will inform Secretariat guidance to States Parties and Secretariat action. • Action to implement recommendations 1, 2 and 3 will also be relevant.	

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Presentation by Murat Gulay

Data Analytics and the CWC: An Introduction to OCPF Site Selection Methodology

Science for Diplomats
6 October 2015

Murat Gülay
Verification Division

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Background

Activities not Prohibited in the CWC

- CWC Article VI, paragraph 2
  - Each State Party ..... shall subject .....to verification measures as provided in the Verification Annex.

- Verification Annex
  - Part VI. (Schedule 1 chemicals and facilities)
  - Part VII. (Schedule 2 chemicals and facilities)
  - Part VIII. (Schedule 3 chemicals and facilities)
  - **Part IX. (Other Chemical Production facilities)**

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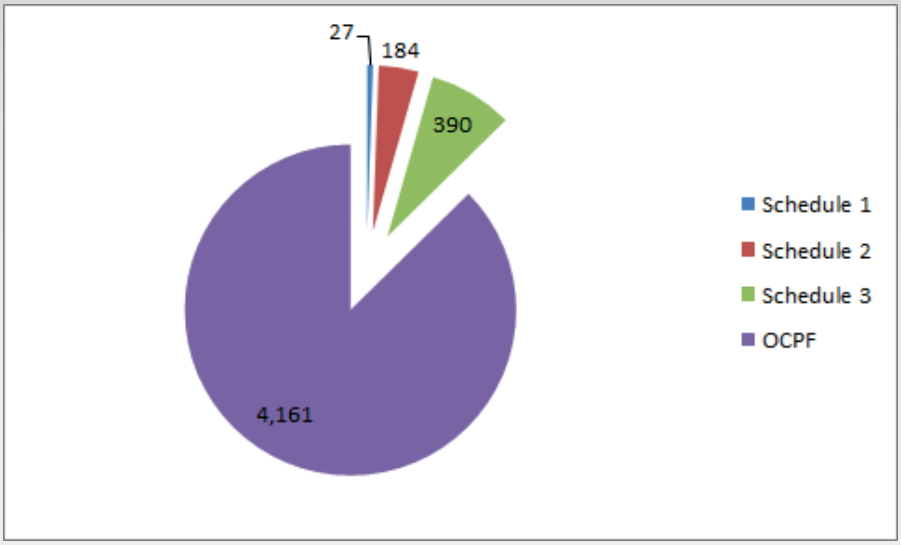
Summary of Article VI Inspection Process

- Submission of declarations by the States Parties as per relevant part of the Verification Annex
- Selection of facilities for inspection (those above the verification threshold)
- Annual budget approved by the CSP with number of Article VI inspections
- Planning of the actual inspections for the selected sites
- Conduct of the budgeted number of inspections

Inspectable Facilities/Plant Sites (as at 30 September 2015)



Annual Budget

- Annual budget approved by CSP specifies:
  - Overall number of Article VI inspections
  - Breakdown (for 2015)

SCHEDULE 1	11
SCHEDULE 2	42
SCHEDULE 3	19
OCPF	169
TOTAL	241

Policy guidelines on Number of Article VI inspections
(EC-66/Dec.10, 7 October 2011)

- Inspectable scheduled and unscheduled Article VI facilities which have not received yet inspections, should be given priority.
- Length of time between two Article VI inspections in any SP should not exceed approximately 8 years.
- At least 50%, and if possible 60%, of SPs that have declared inspectable Article VI facilities should receive at least one Article VI inspection each in any one year.

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Mixed plant sites selection

- Objective is to reduce probability of re-inspection at Schedule 3 and OCPF mixed plant sites already inspected under another Article VI regime
- A Schedule 3 or OCPF mixed plant site already inspected under another Article VI regime but not yet inspected under Part VIII or IX of VA will be considered as inspected for the purpose of the random selection
- All OCPF and Schedule 3 plant sites with activities above verification threshold continue to be eligible to receive inspections

OCPF Site Selection Methodology

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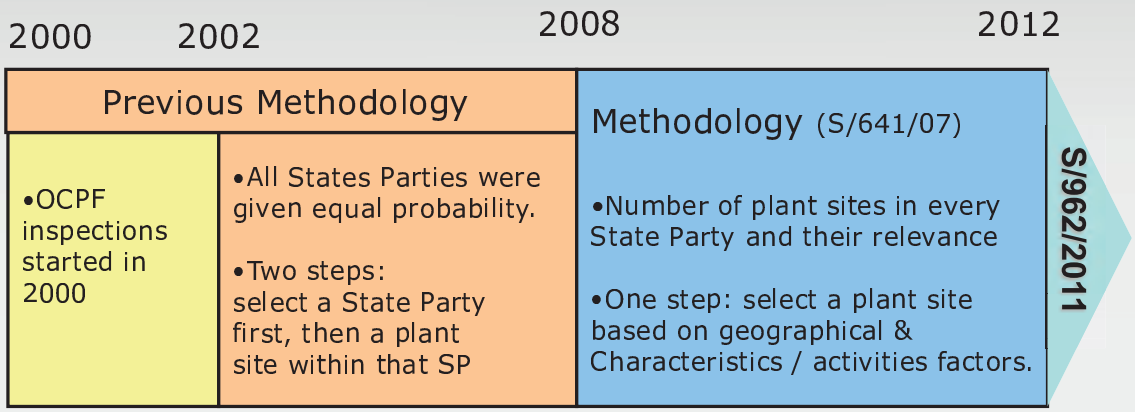
Current Selection Methodology

- Selection of OCPF plant sites for inspection
  - S/641 methodology between 2008-2011
  - S/962 methodology from 2012 onwards
- Objective of improvements to the interim site-selection methodology (S/962) to achieve better "targeting" of OCPF inspections
- Secretariat to report annually on the performance of the interim site-selection methodology
  - Latest report: S/1240/2015, dated 6 February 2015

Evolution of the Selection Methodology



Current Selection Methodology

- Combined contributions from equitable geographical distribution and information available to the TS.
- Use of multiple selection pools:
  - three pools for never inspected plant sites for each State Party (Pool A, B & C)
  - the respective pools for each State Party combined into three overall pools (Pool A, B & C)
  - one additional pool for previously inspected plant sites (Pool D)
- Random selection of 20% of the total number of budgeted OCPF inspections for subsequent inspections in 2015.
- Of the remaining OCPF inspections, random selection of 85% OCPF plant sites from pool A, 10% from pool B and 5% from pool C.

Current Selection Methodology

- The A15 Algorithm

$$A15 = N^{1.5} \times M \times G \times P \times A$$

- N: number of DOC plants (including PSF plants)
- M: production range
- G: Main activities (product group codes)
- P: PSF plant or not
- A: Occurrence of the previous inspection

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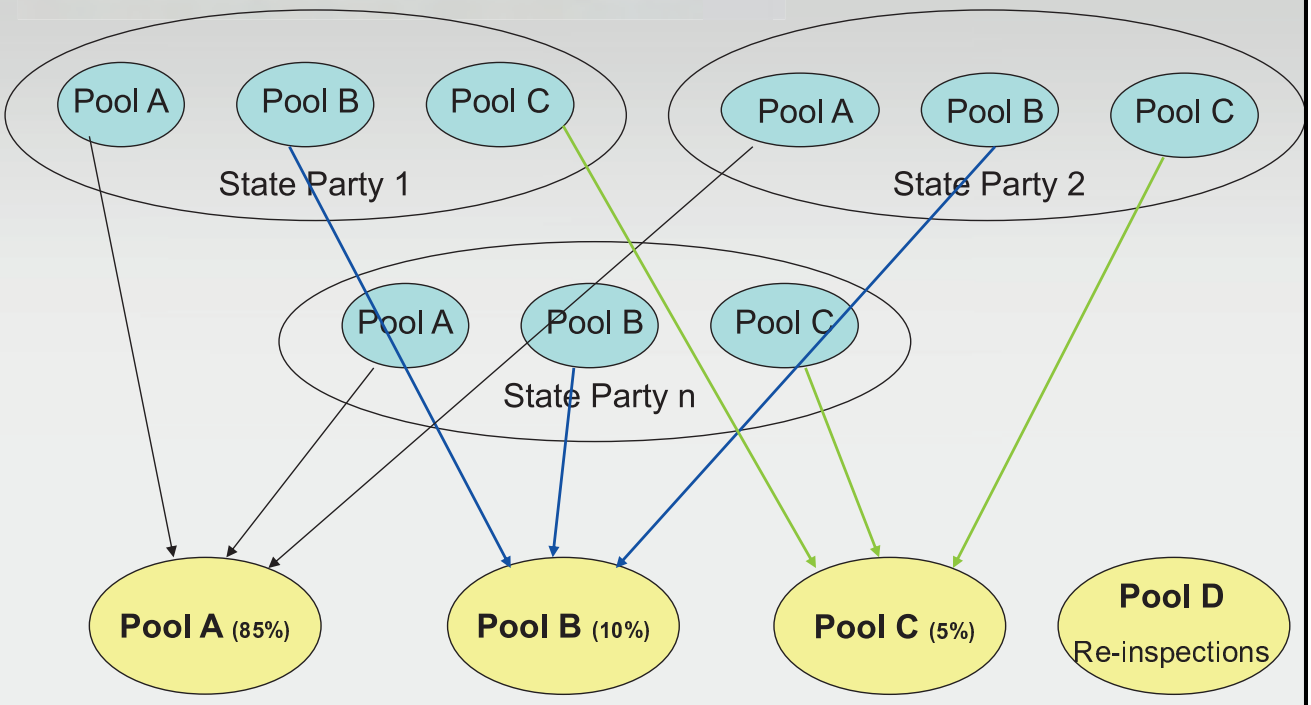
Current Selection Methodology



Selection Process

Data Quality

- Routine data quality checks
- Quality of declaration data
  - Complete, accurate, timely declarations
  - Updates of information (e.g. amendments) regarding OCPFs
  - Follow-ups and clarification regarding declared data
- Quality of inspection data
  - Update of inspection data in the Verification Information System (VIS)
  - Analysis for mixed plant sites

Simulations and Official Selection

- Several rounds of simulations for the selection
- Analysis of the results
  - Pool distribution
  - Geographical distribution
- Further clarifications with the respective VER units
- Correction of data, if necessary
- Freeze of data and updates to the system
- Execution of the computer program which implements the current selection methodology by the DG
- Hand over of the official selection report to the Industry Verification Branch

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Results

Selection of OCPF Sites for 2015 inspections

- Number of inspectable sites: **4278**
- Approved number of inspections for 2015: **169**
  - 135 Initial Inspections
  - 34 subsequent inspections @ **20 %**

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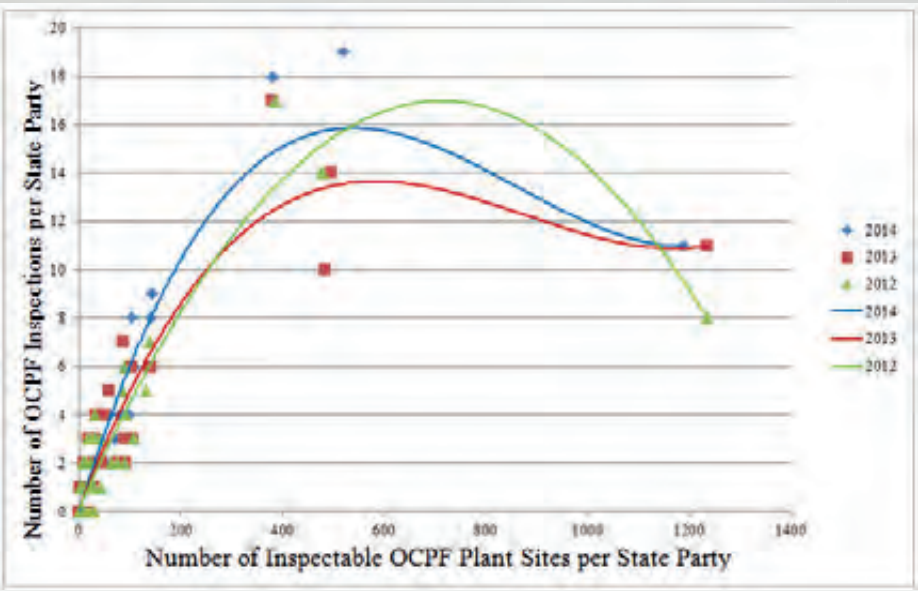
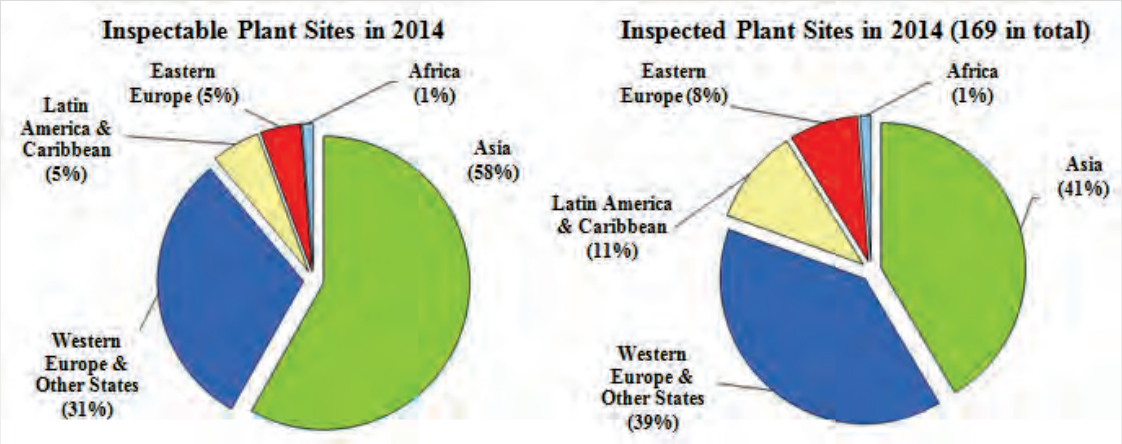
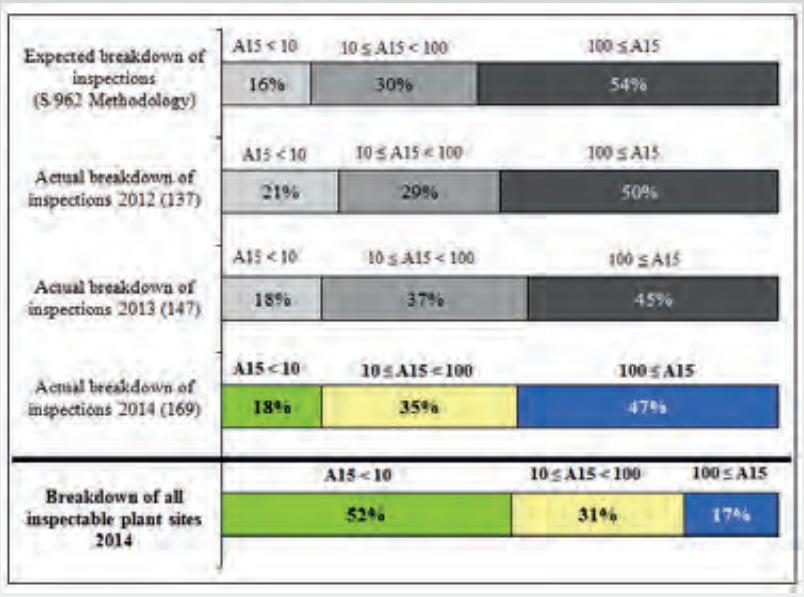
- Number of OCPF inspections per State Party against the total number of inspectable OCPF plant sites (2012 - 2014)



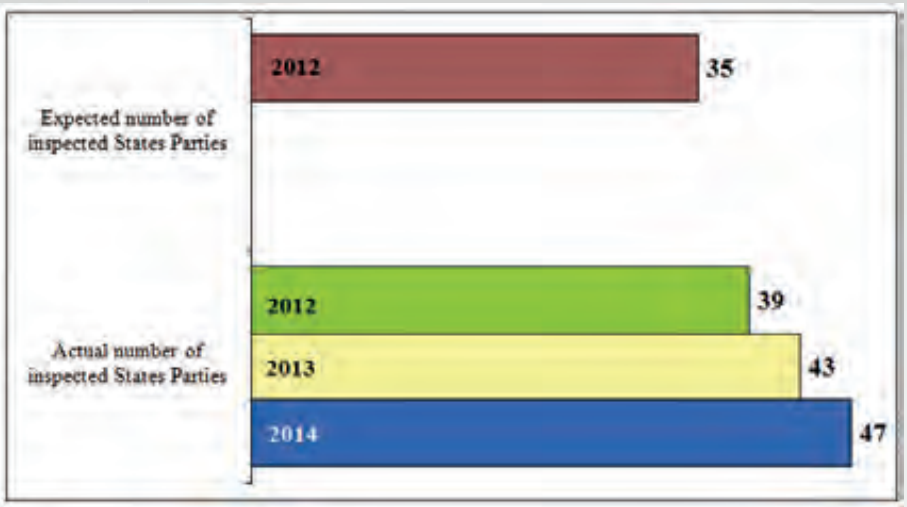
- Comparison of the regional distribution of plant sites and inspections (as at 6 November 2014)



- Relative share of inspections according to the relevance of OCPF plant sites



- Coverage of the States Parties selected to receive OCPF inspections



Key Results

- The methodology takes into account both the number and the relevance of plant sites declared
- The number of inspections conducted in each SP is positively correlated with the number of declared OCPF plant sites in that SP
- The methodology continues to result in more inspections in highly relevant sites
- There is a continued increase in the number of State Parties receiving inspections

- **Conclusion:** The selection process using the S/962 methodology continues to achieve the goals set forth to better target OCPF inspections

Reference Documents

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Reference Documents

- Initiative by the DG on a methodology for the OCPF for inspection (S/962/2011, dated 8 September 2011)
- Initiative by the DG on a Methodology for the OCPF for Inspection (S/641/2007, dated 25 May 2007 and Corr.1, dated 4 June 2007)
- Report on the performance of the revised methodology for the selection of OCPF for inspection (S/1240/2015, dated 6 February 2015)
- Alternative approach to verification at mixed plant sites (S/1202/2014, 23 July 2014)
- Report of the co-facilitators for the consultation on the site-selection methodology for OCPF (EC-65/WP.1 , dated 10 June 2011)
- Report on the results of the implementation of policy guidelines for determining the number of Article VI inspections (EC-79/DG.4, dated 7 April 2015)

Thank you for your attention.
Questions ?

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Science and Technology: Awareness and Communication

Contact us at: ***SciTech@OPCW.org***

www.opcw.org/special-sections/science-technology/

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Science and Technology For Diplomats
Upcoming Events

- 2 December 2015 (On the margins of CSP-20, To be confirmed)
  - **S&T for Diplomats (7): Chemical Forensics**
    - An introduction to the field and its applications
- March 2016 (On the margins of EC-81, To be confirmed)
  - **S&T for Diplomats (8): Topic To Be Determined**
- **For more information on S&T from OPCW**

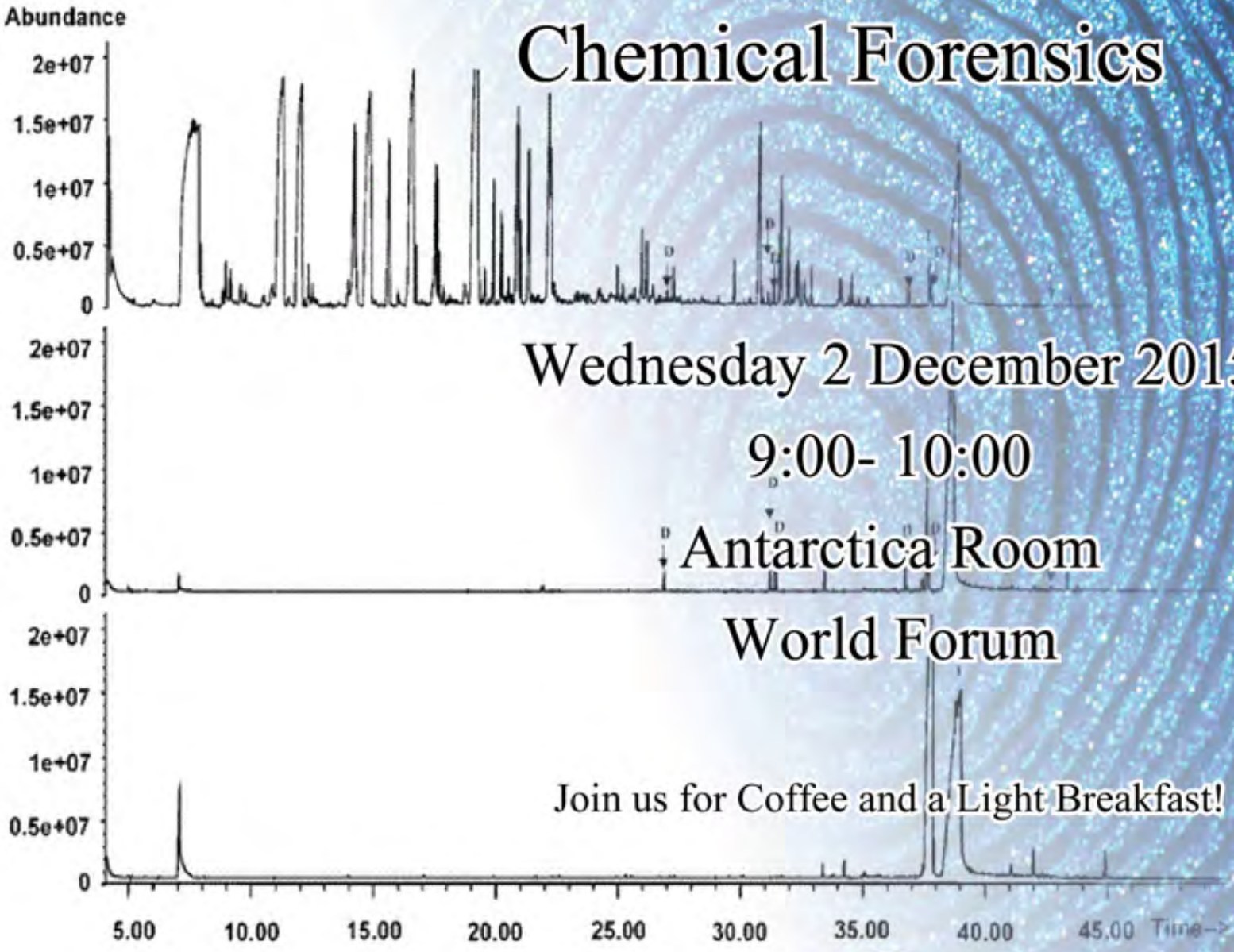
SciTech@OPCW.org (*email*)

@OPCW_ST (Twitter)

www.opcw.org/special-sections/science-technology/

Science For Diplomats at CSP-20

Chemical Forensics



Wednesday 2 December 2015

9:00- 10:00

Antarctica Room

World Forum

Join us for Coffee and a Light Breakfast!

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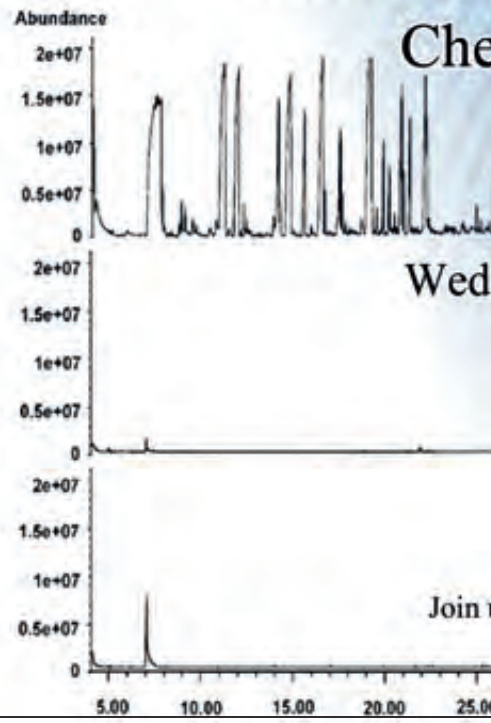
Science For Diplomats at CSP-20

Chemical Forensics



Wednesday 2 December 2015

9:00- 10:00

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World Forum

Join us for Coffee and a Light Breakfast!

Professor Paula Vanninen
Director Verifin

Jonathan E. Forman, Ph.D.
OPCW Science Policy Adviser
jonathan.forman@opcw.org

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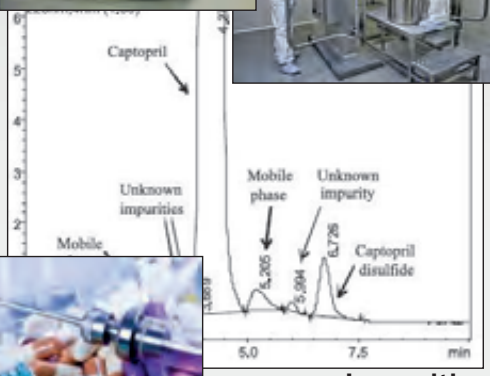
Chemical Fingerprinting

Stable isotopes: geographic origins, age



Impurities:
manufacturing processes
process/handling conditions
precursor batches

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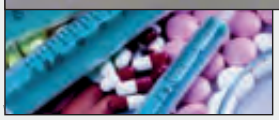
Chemical Fingerprinting



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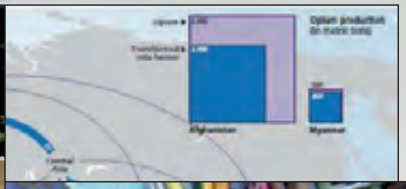
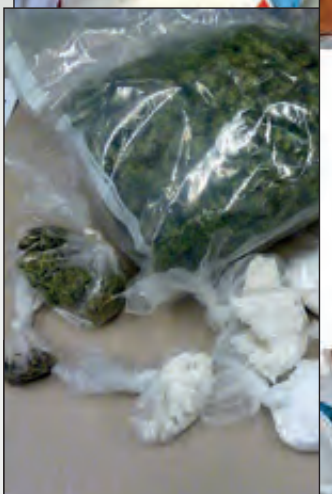
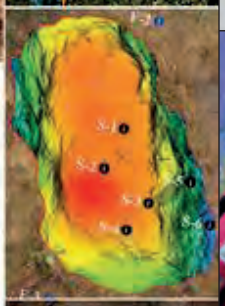
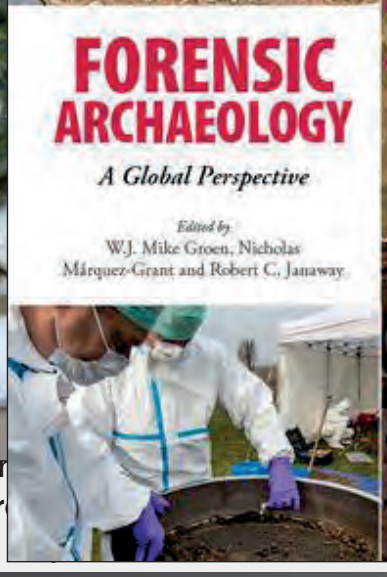
Chemical Fingerprinting









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Treaty Implementation

The Chemical Weapons Convention

- **Disarmament (Destruction and Verification)**
- **Non-proliferation (Verification)**
- **Assistance and Protection against CWs**
- **International Cooperation**

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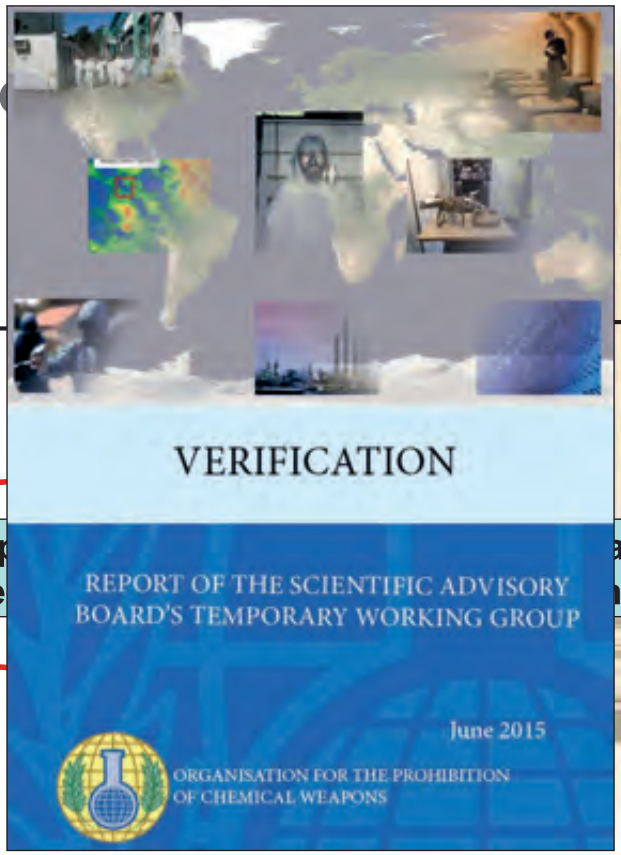
Treaty Implem



- **Disarmament (Destruction and Verification)**
- **Non-p (Ve**
- **and st CWs**
- **International Cooperation**

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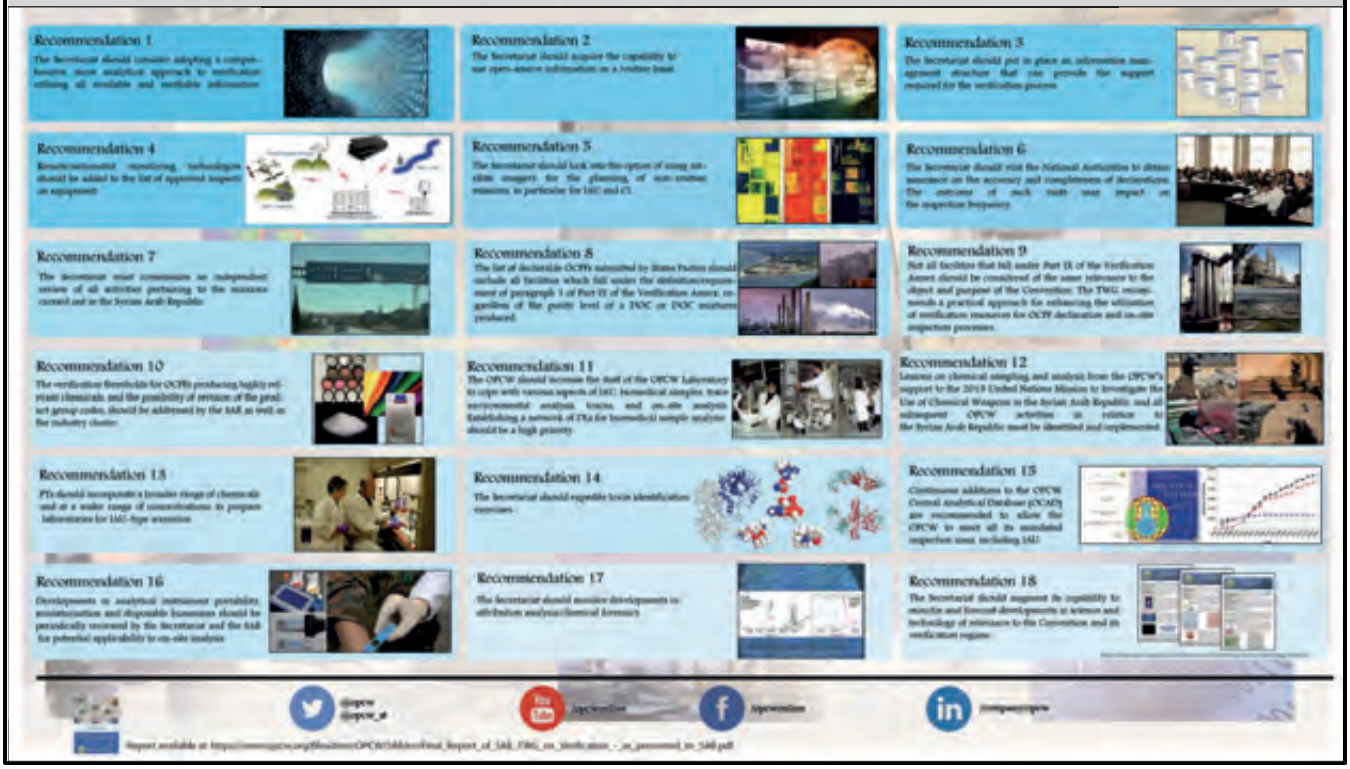
Recommendations from the OPCW Scientific Advisory Board Temporary Working Group on Verification



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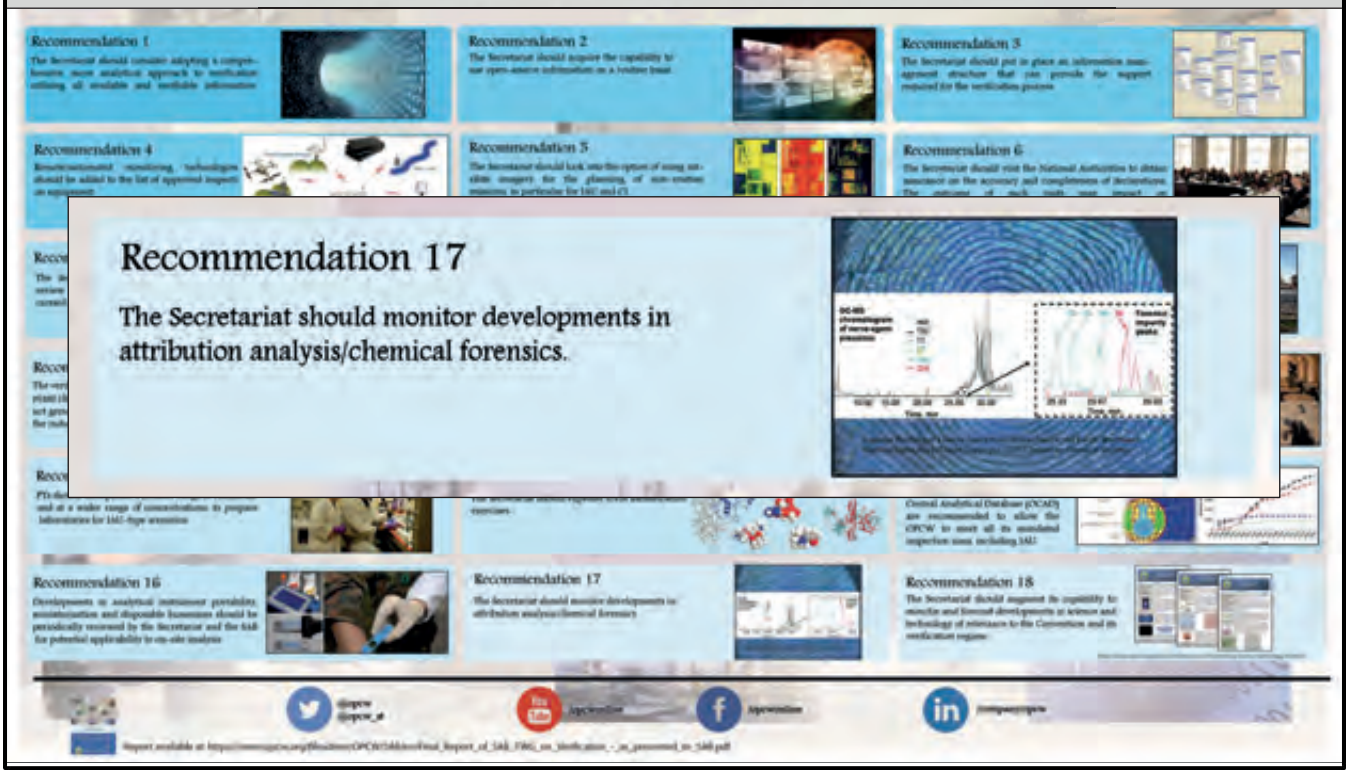

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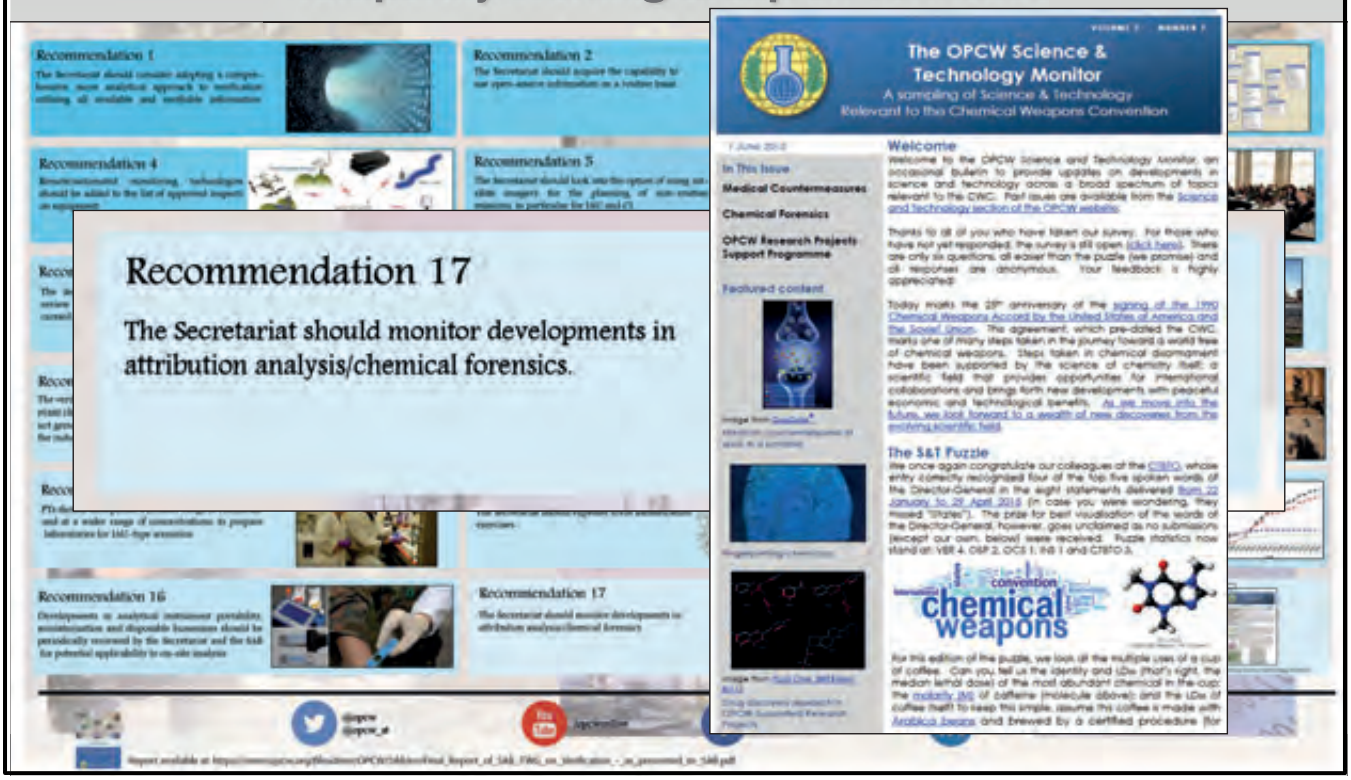

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EC-80/DG.7 (28 August 2015)

Action to implement the recommendations made by the SAB in its report on Verification
https://www.opcw.org/fileadmin/OPCW/SAB/en/ec80dg07_e_.pdf

Recommendation from the SAB	Implementation	Expected outcomes/results
Recommendation 17 The Secretariat should monitor developments in chemical forensics.	• Secretariat: Continue to monitor developments in chemical forensics, together with Designated Laboratories. Explore collaboration with the industry and States Parties to develop methodology tailored to the needs of the OPCW. Develop the capability of the OPCW Laboratory for chemical forensics. • Scientific Advisory Board: Assess development in an expert workshop in 2016 and in the Board's report to the Fourth Review Conference.	• Effective investigations of alleged use and other non-routine situations. • Adaptation of the verification regime in line with scientific and technological developments.

- SAB Workshop planned for June 2016 at Verifin

Presentation by Professor Paula Vanninen

Science for Diplomats
Chemical Forensics

Paula Vanninen

VERIFIN, Finnish Institute for Verification of
the Chemical Weapons Convention
Department of Chemistry
University of Helsinki

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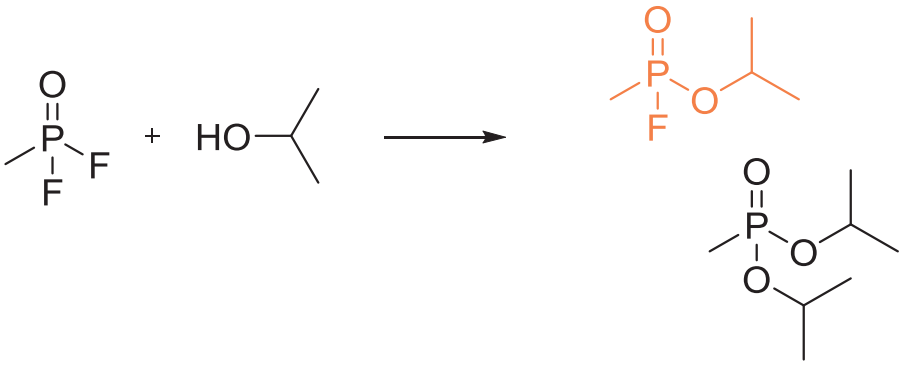
TOKYO
3HR
FIRST REPONSE

5

Synthesis route

- Starting materials
- Impurities



SYRIAN ARAB REPUBLIC 2013

INTERVIEWS AND BIOMEDICAL SAMPLING


ENVIRONMENTAL
SAMPLING


CHAIN OF
CUSTODY!

OPCW Fact Finding Missions

- Number of FFM?
- Collection of evidence
  - Sampling
  - Interviews
  - Photos, video
- On-site detectors, on-site analysis
- OPCW designated laboratory network
  - Chain-of custody
  - Environmental samples
  - Biomedical samples

Workshop: Chemical Forensics

Capabilities across the field and potential applications in the CWC Implementation

- Chemical weapons
  - An OPCW perspective
- Law enforcement
  - illegal drug attribution analysis
- Biomedical samples
  - post-mortem analysis
- Route of synthesis and other attribution analysis
- Chemical forensics in other fields: Art, Archeology
- Discussions
- Report

Workshop: Chemical Forensics

Capabilities across the field and potential applications in the CWC Implementation

- Questions
  - How can chemical forensics be combined with investigative chemical analysis?
  - Limitations and required reference materials?
  - Methodologies with potential for use in CW applications?
  - Normal vs. highly toxic samples?

Workshop: Chemical Forensics: Capabilities across the field and potential applications in the CWC Implementation

- SAB and experts
- Helsinki, Finland
- June 2016 (Dates TBC)
- Preparation for the SAB report for the Review Congress in 2017

Next
2016?
2017?

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Science and Technology For Diplomats Upcoming Events

- March 2016 (On the margins of EC-81, to be confirmed)
  - **S&T for Diplomats (8): Sensors and Biosensors**
- July 2016 (On the margins of EC-82, to be confirmed)
  - **S&T for Diplomats (9): Briefing on SAB Chemical Forensics Workshop**
- **For more information on S&T from OPCW**

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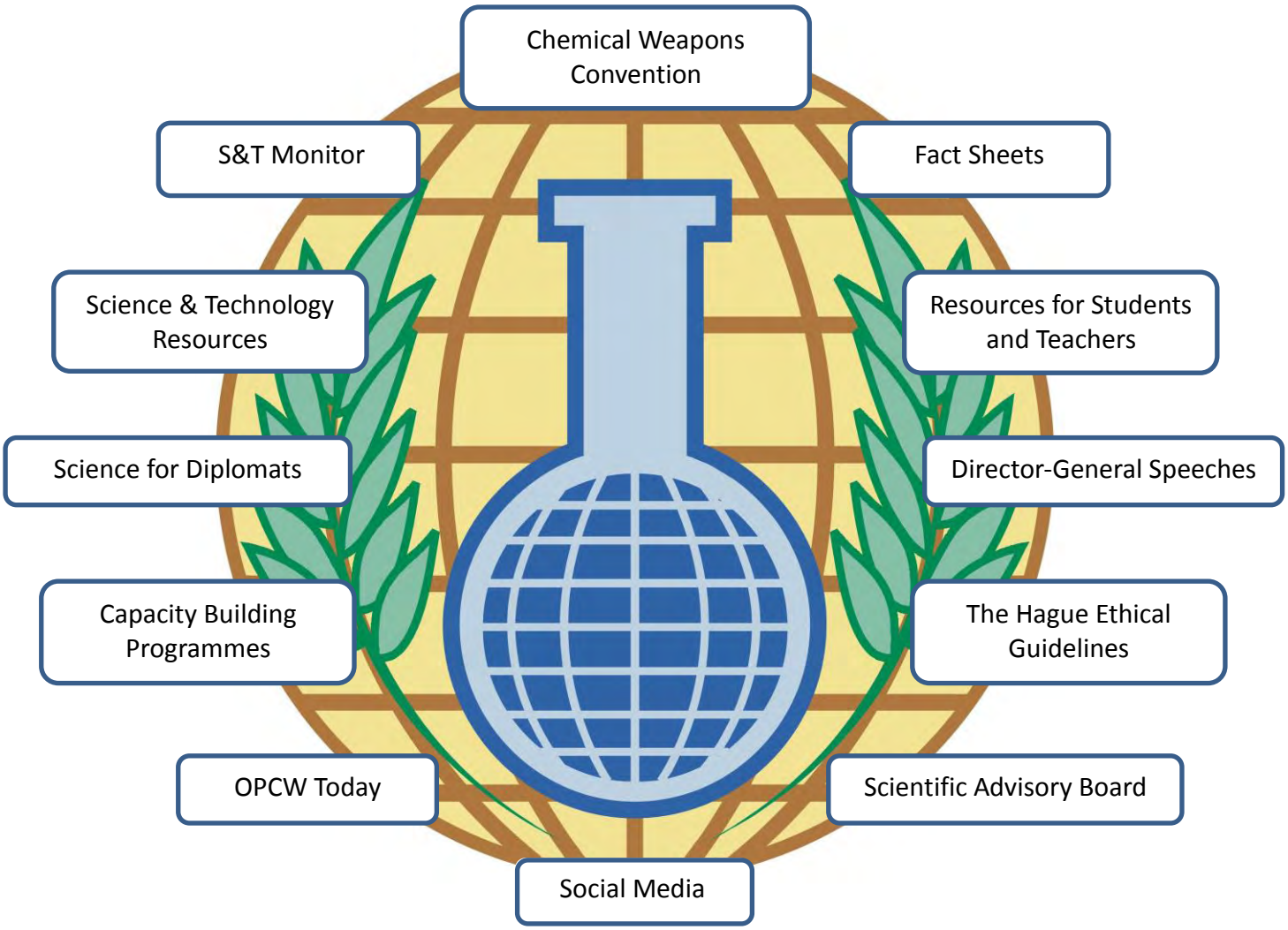
An Interactive Guide to OPCW Science & Technology Resources and More



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