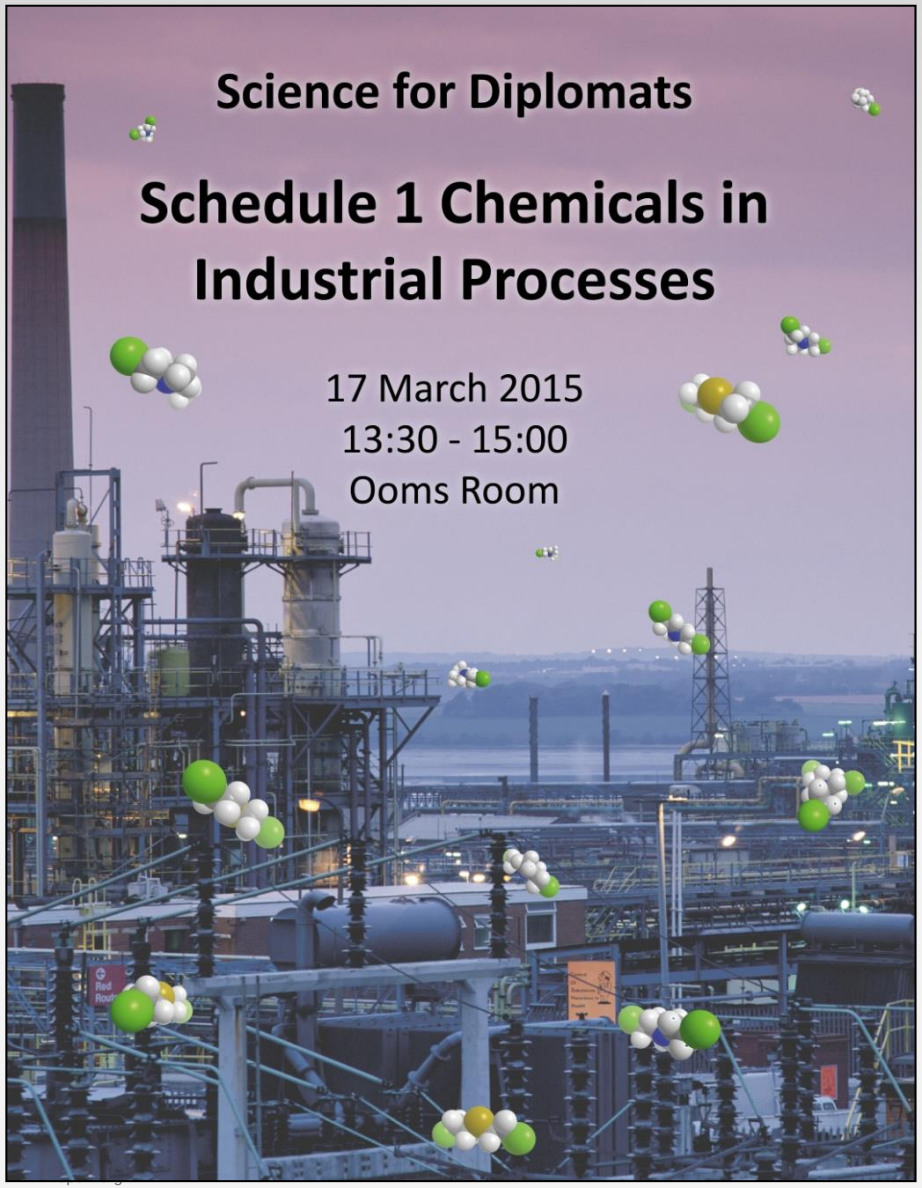


Dr Christopher M. Timperley
Vice Chair, OPCW Scientific Advisory Board
Defence Science and Technology Laboratory (Dstl),
United Kingdom of Great Britain and Northern Ireland

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

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)

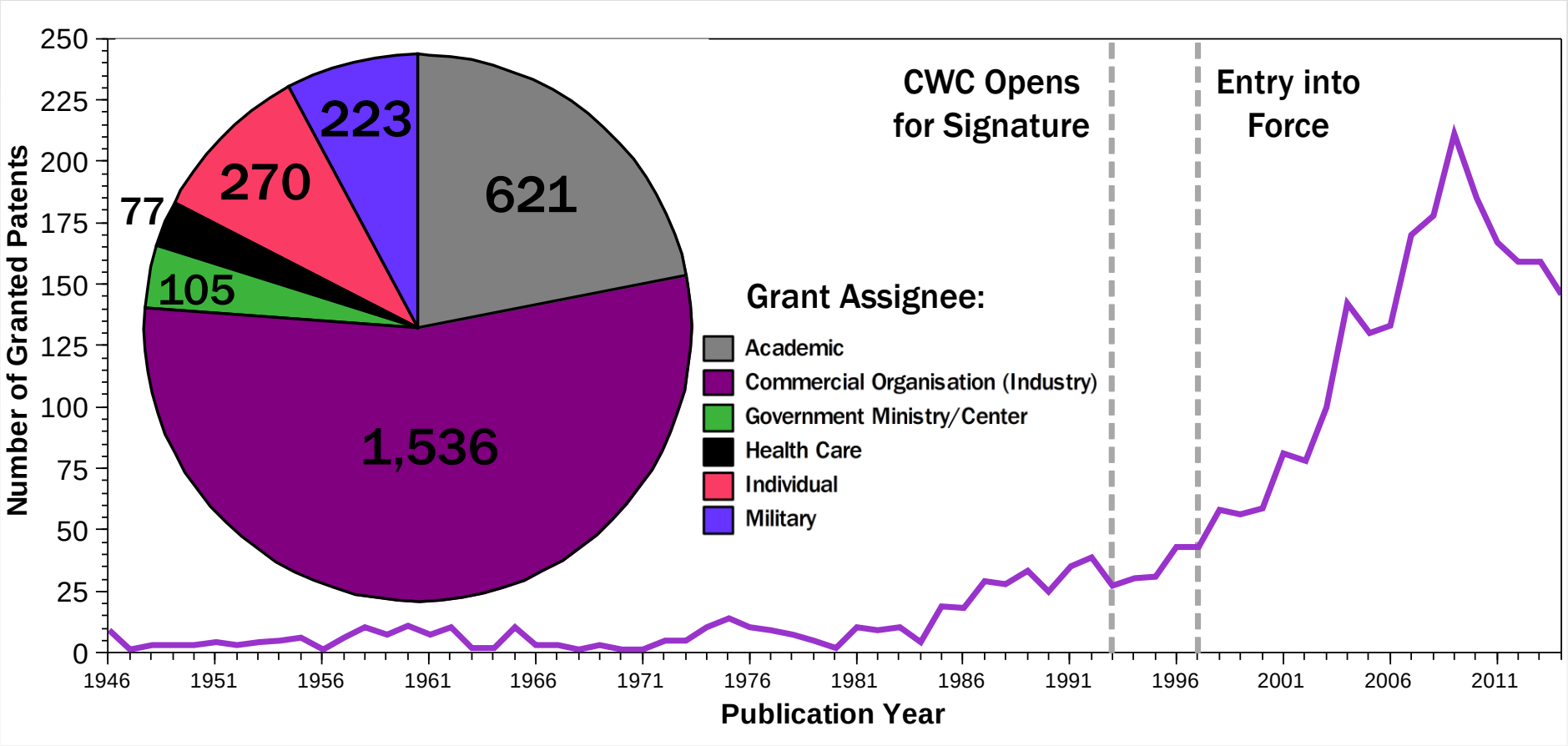
Status of the Follow-Up to the Recommendations on S&T to the Third Review Conference

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

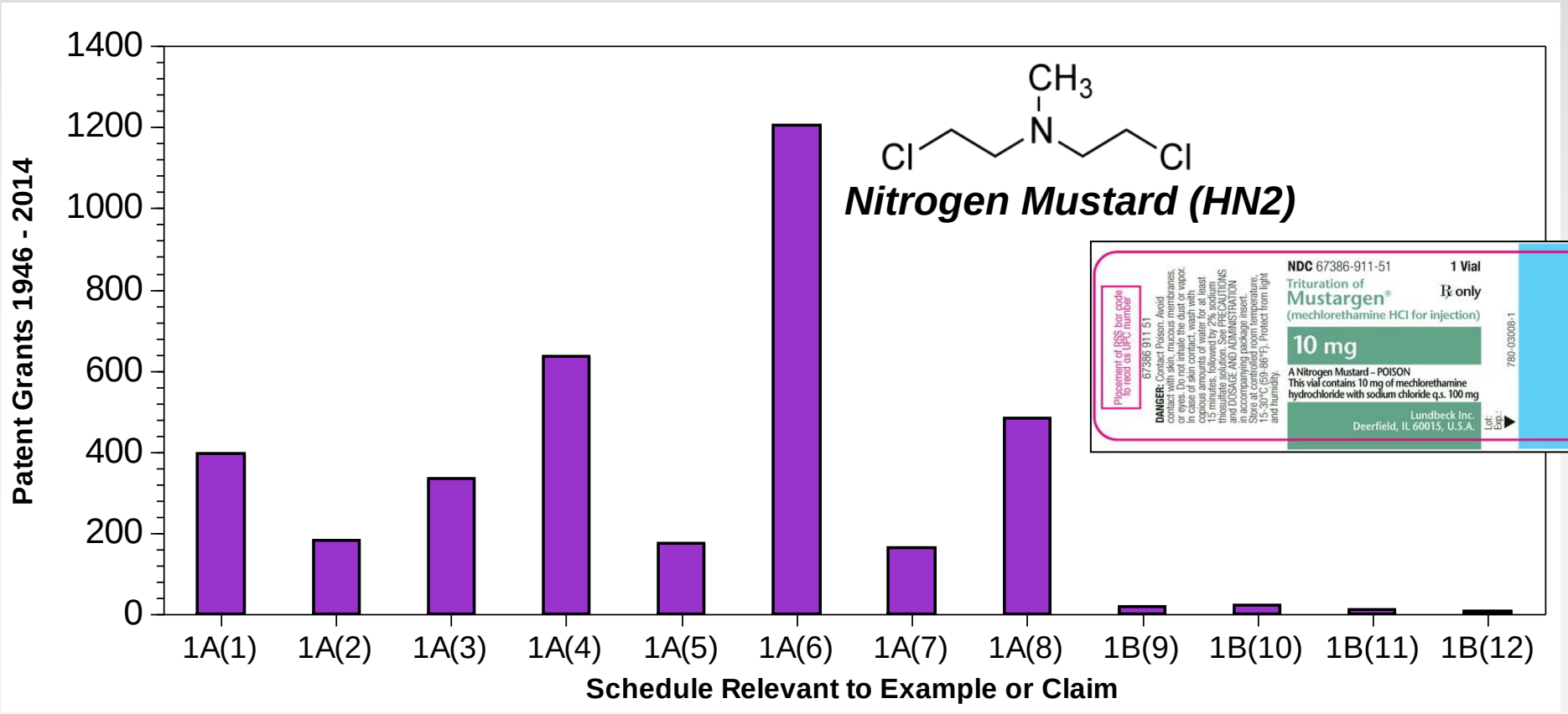
Recommendations Concerning Schedule 1 Chemicals
(from EC-77/DG.11, Dated 5 September 2014)

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.

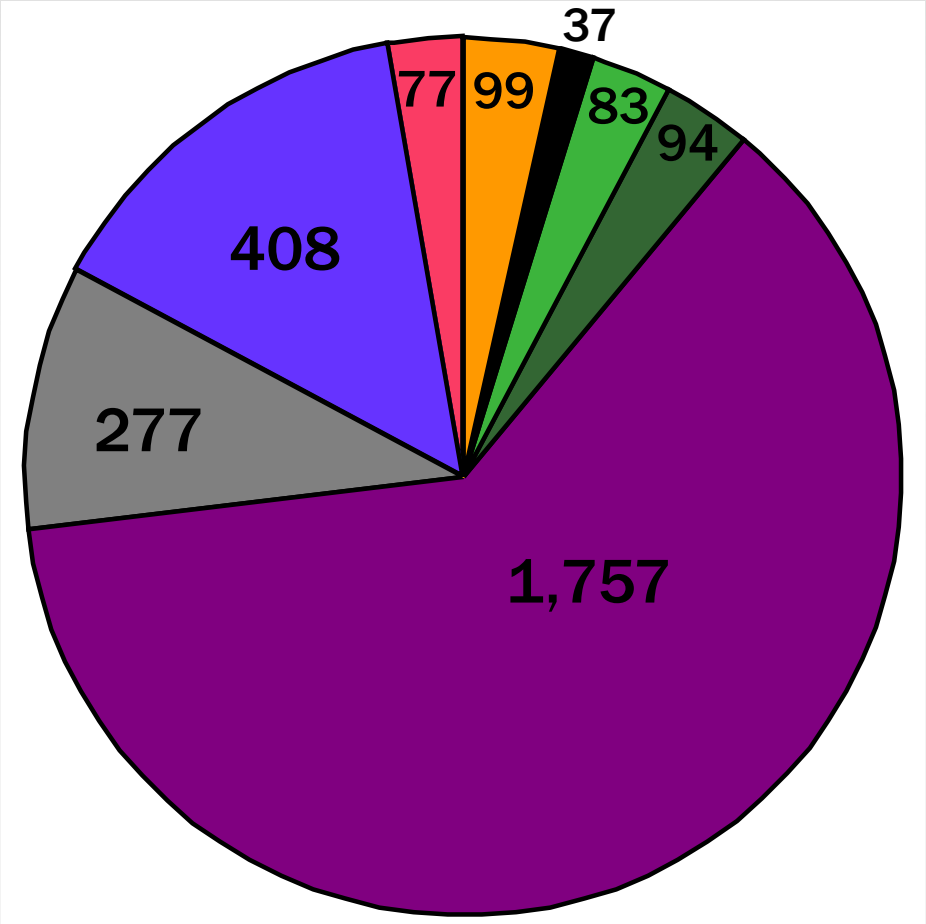
Schedule 1 Chemicals in Patent Grants 1946 - 2014



Schedules Represented

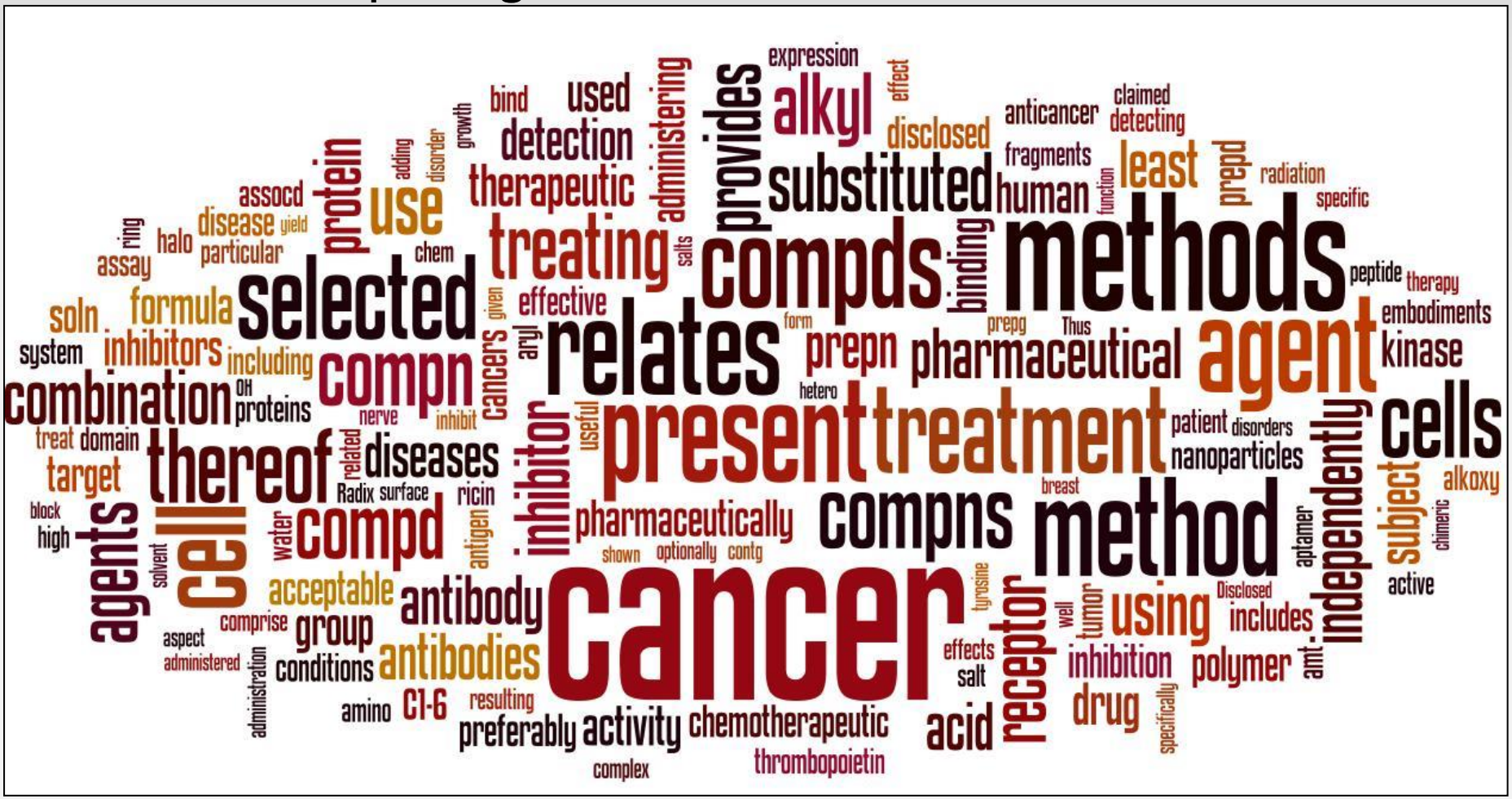


What are all these patents about?



What are all these patents about?

Abstracts for 146 patent grants references to Schedule 1 chemicals from 2014



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, chemisorptive 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/US2013/065526
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.

Science for Diplomats

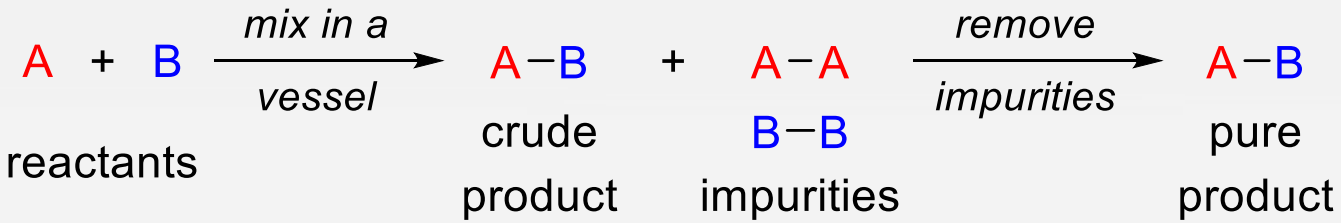
Schedule 1 and 2 chemicals as captive intermediates and unintended by-products

Dr. Christopher M. Timperley

Chemical production

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

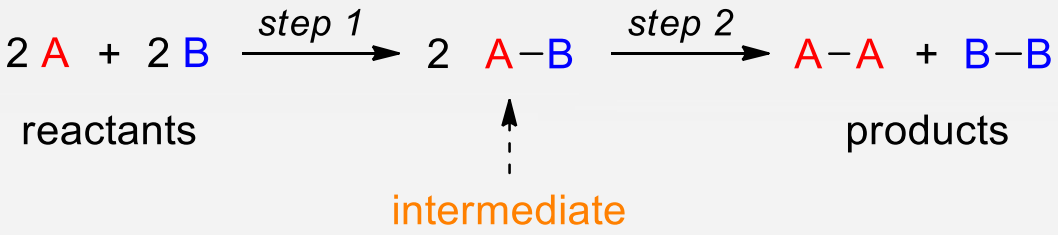
What is a chemical reaction?



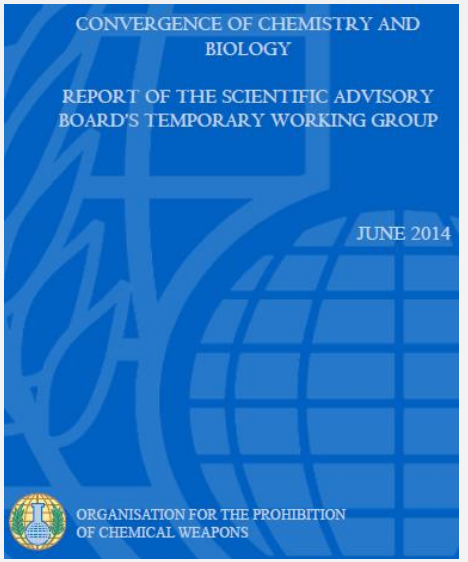
Chemical production

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

An example of two step reaction sequence :



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

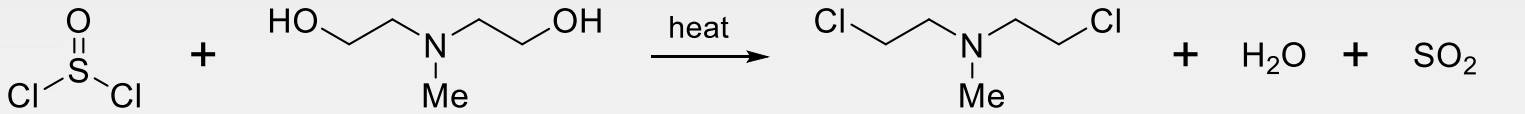
- Possesses lethal or incapacitating toxicity and other properties that could enable them to be used as chemical weapons or to obtain Sch. 1
- Not produced in large commercial quantities in chemical industry

Schedule 3

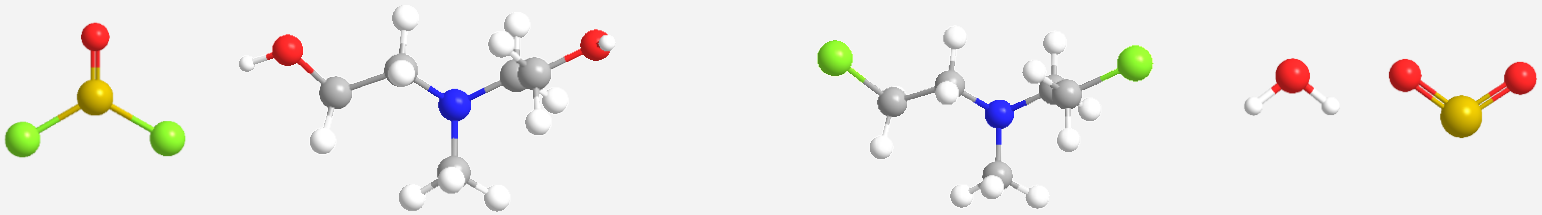
- Have been produced, used or stockpiled as a chemical weapon
- Possess lethal or incapacitating toxicity and other properties that could enable them to be used as a chemical weapon or to obtain Sch. 1 or 2
- Produced in large commercial quantities in the chemical industry

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

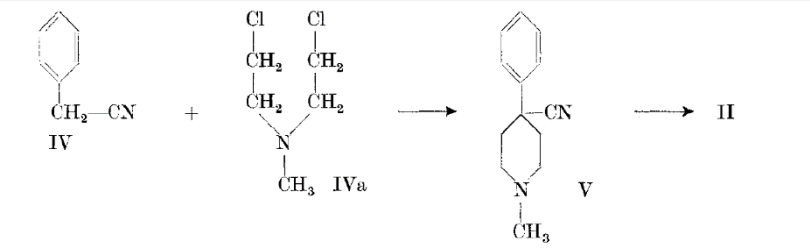
HN2 can be used to make the anti-cancer drug ketobemidone, a pain-killer for children with cancer that are allergic to morphine

Volumen XXXII, Fasciculus VII (1949) – No. 323. 2489

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

von H. Kägi und K. Miescher.

stehenden und unter dem Namen „Nitrogen mustard" bekannt gewordenen sehr giftigen Amins IVa zu vermeiden, beschritten wir einen

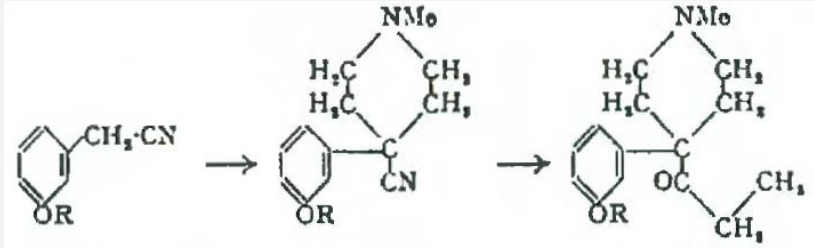


Helv. Chim. Acta 1949, 32, 2489

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

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

Ketobemidone (Hoechst 10720) has been prepared from *m*-methoxybenzyl cyanide by condensing it with methyldi-(2-chloroethyl)amine in the presence of sodamide, submitting the resulting cyanopiperidine derivative to a Grignard reaction, and demethylating the product with hydrobromic acid.



J. Chem. Soc. 1950, 1469-1471

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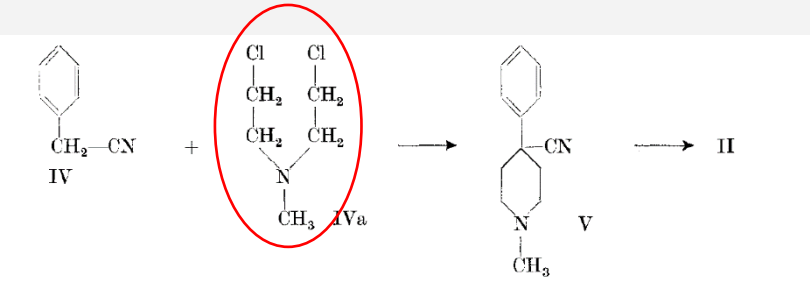

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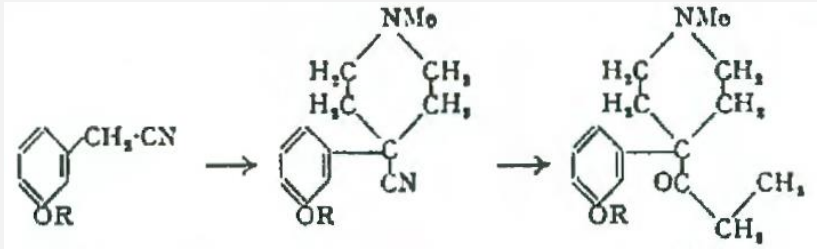
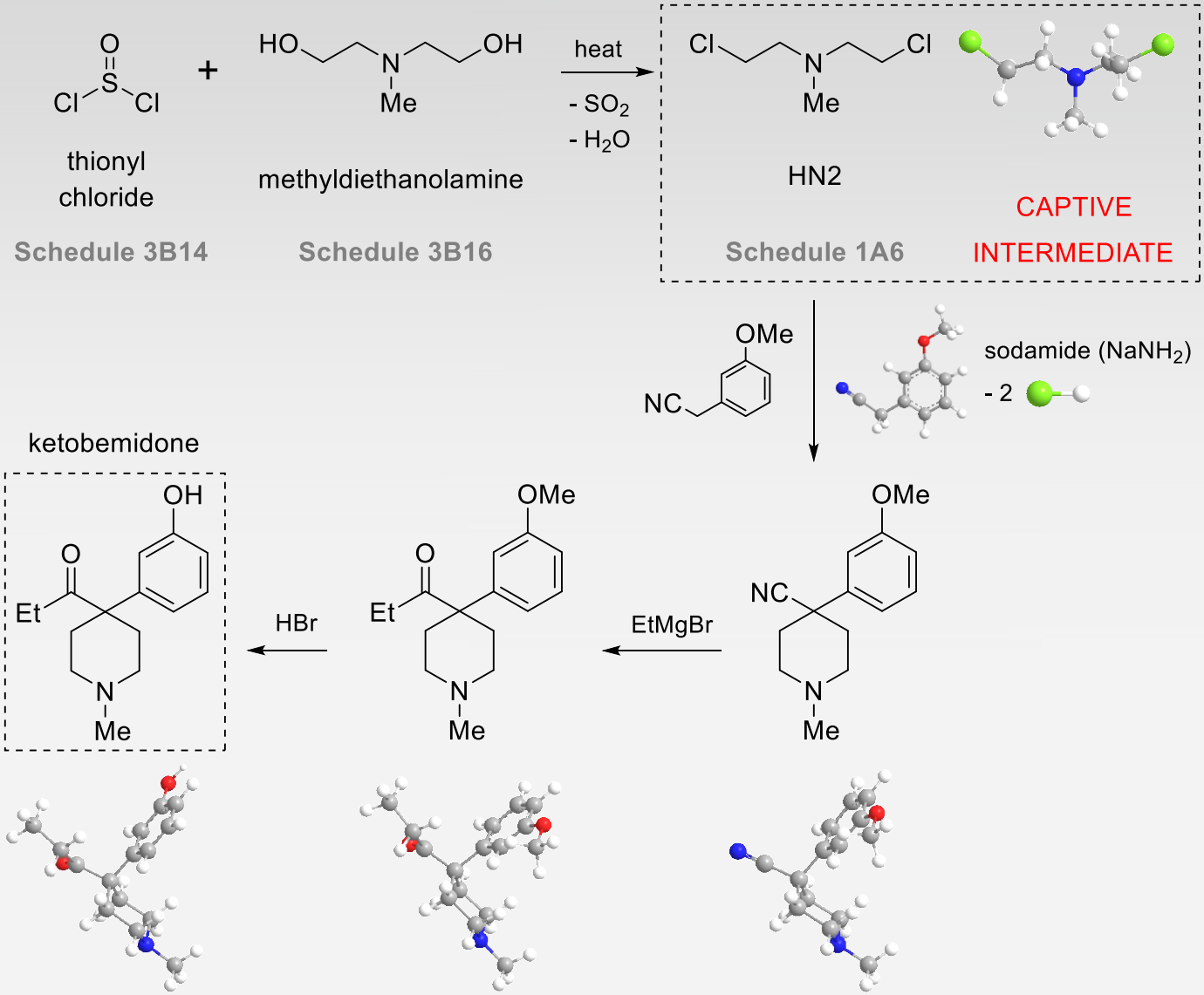


J. Chem. Soc. 1950, 1469-1471


thionyl chloride
Schedule 3B14
methyldiethanolamine
Schedule 3B16
heat
- SO2
- H2O
HN2
Schedule 1A6
CAPTIVE INTERMEDIATE
sodamide (NaNH2)
- 2
ketobemidone
HBr
EtMgBr

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)

Production of Schedule 1 chemical

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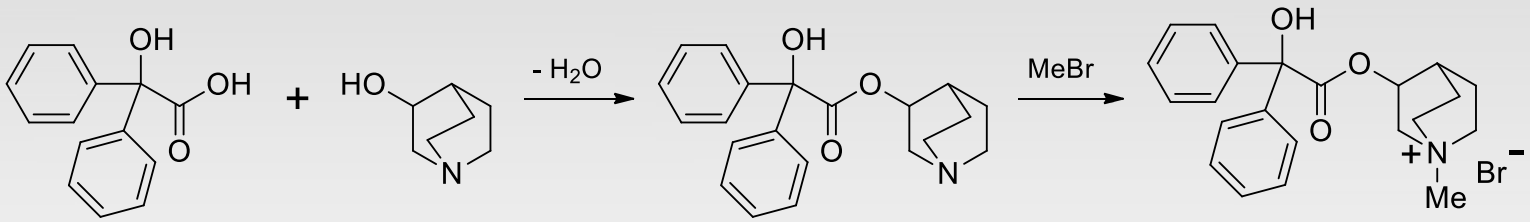
Decision of OPCW CSP (C-10/DEC.12 dated 10 November 2005)

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

BZ as a captive intermediate

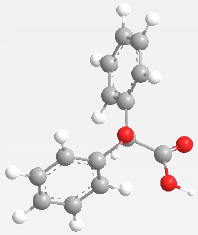


2,2-Diphenyl-2-hydroxyacetic acid

Quinuclidin-3-ol

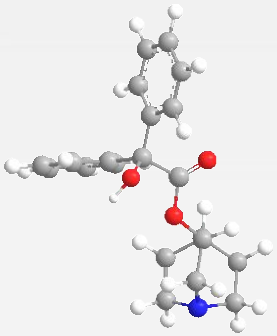
3-Quinuclidinyl benzilate (BZ)

Clinidium bromide (pharmaceutical)

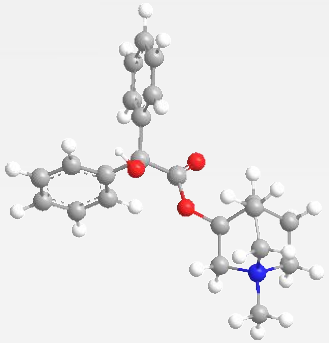


Schedule 2B8

Schedule 2B9



Schedule 2A3



Not scheduled

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

Unintended by-products

Unintended by-products

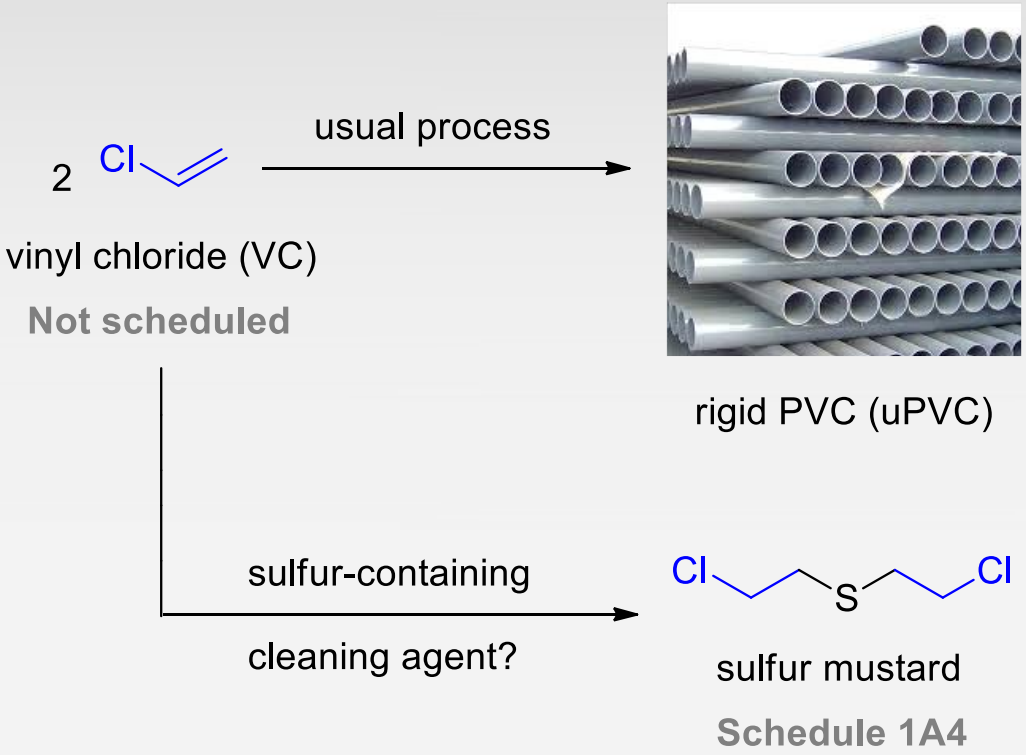
An unintended by-product is a Schedule 1 or 2 chemical formed unintentionally during a sequence of planned chemical reactions

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

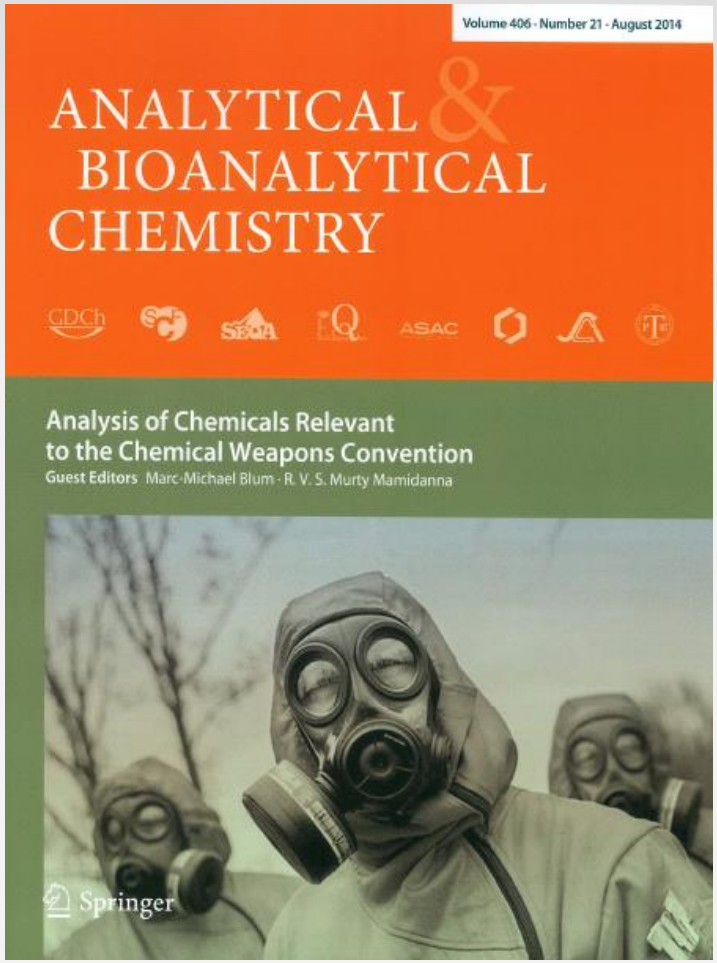
C Curty, J Ducry, S Mogl. Schedule 1 chemicals as captive intermediates or unavoidable by-products in chemical production: technical feasibility assessment based on literature review, LN 2013-01-CC, Spiez Laboratory, Switzerland, 2013.

Unintended Schedule 1 production



Employees experienced skin blistering, burns and respiratory problems

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)

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