Chemical Analysis in Verification

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OPCW Headquarters
The Hague, The Netherlands

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

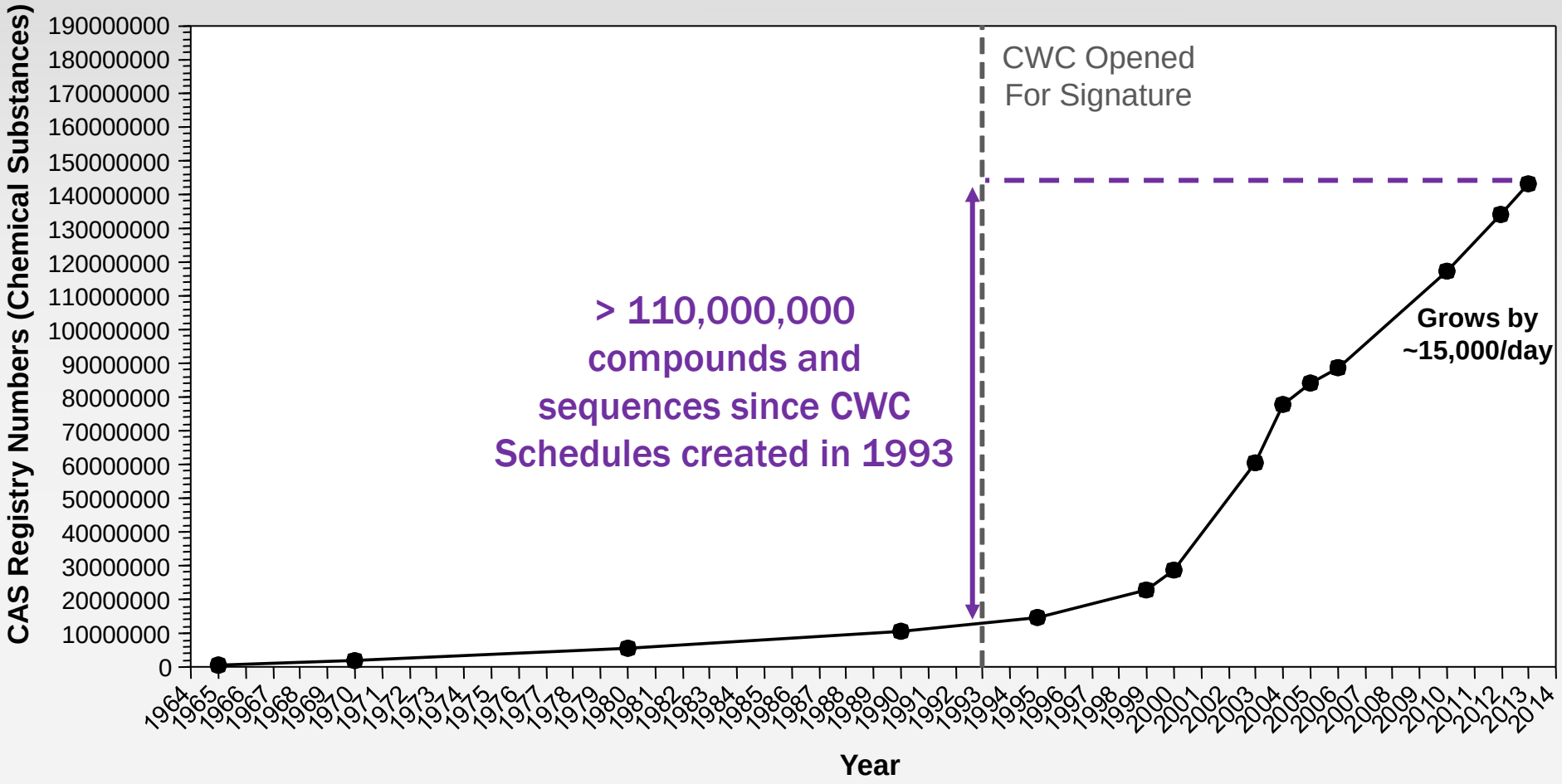
(RC-3/DG.1, dated 29 October 2012)

Director General's Recommendations

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

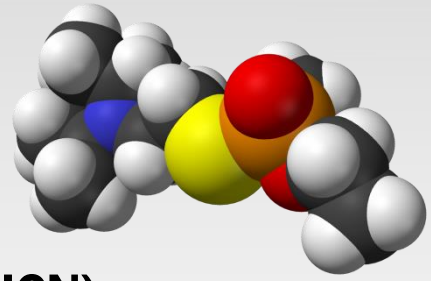
Laboratory Capabilities and Analysis	
"The Secretariat will continue to monitor developments relating to **unscheduled and novel toxic chemicals** and will explore ways in which to augment its **technical capabilities** in this area." "…notes the SAB's views on the **OPCW Central Analytical Database** 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

Reported Chemical Substances 1965-2013

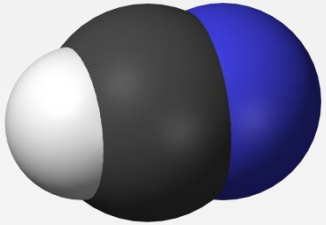


Scheduled Chemicals Span a Broad Range of Properties

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

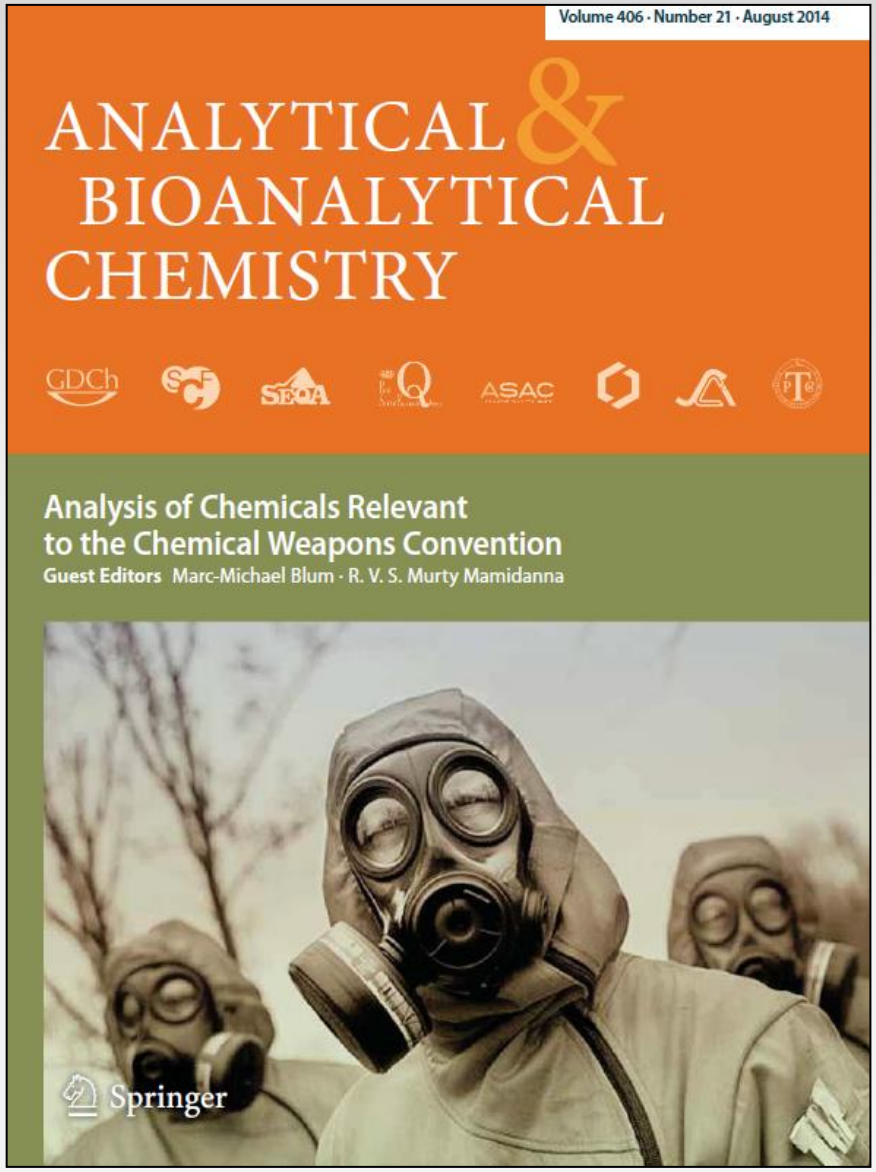


Hydrogen Cyanide (HCN)



Ricin

The Most Appropriate Analytical Method?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Analysis of Chemicals Relevant to the Chemical Weapons Convention
Guest Editors Marc-Michael Blum · R. V. S. Murty Mamidanna
Springer

Chemical Analysis in Verification

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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.).

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

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)

How much is one part per billion (ppb)?

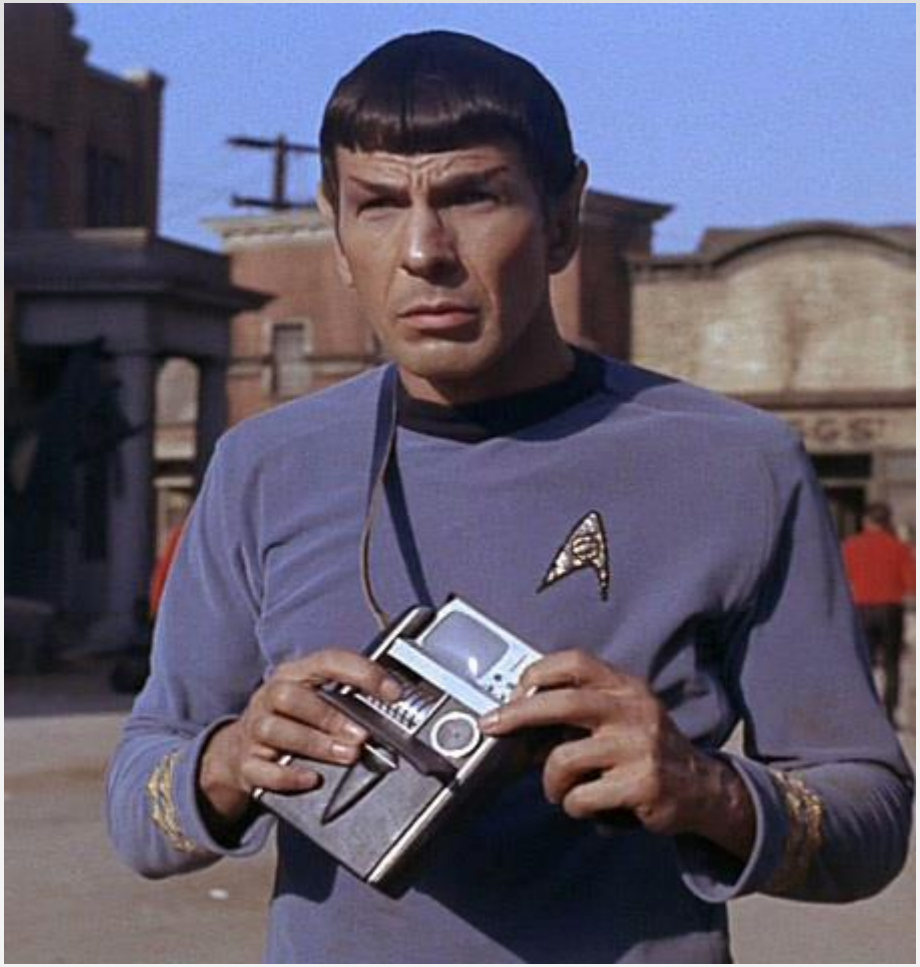
One ppb is like one sheet in a roll of toilet paper stretching from New York to London

- 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

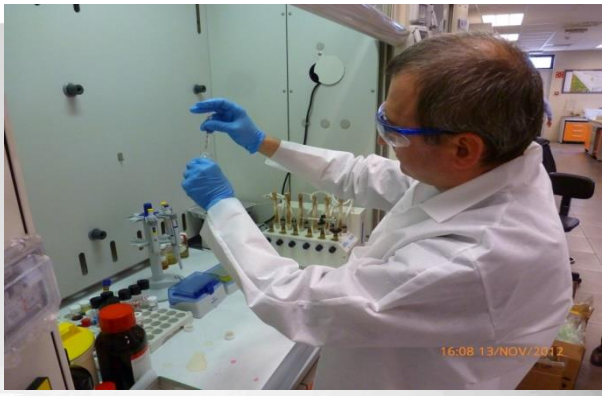
- Instant answers!
- Small, portable!
- Easy to operate!
- No false positives!
- No sampling required, just point and get the answer!

- Cons:
  - Not available for purchase (yet)



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



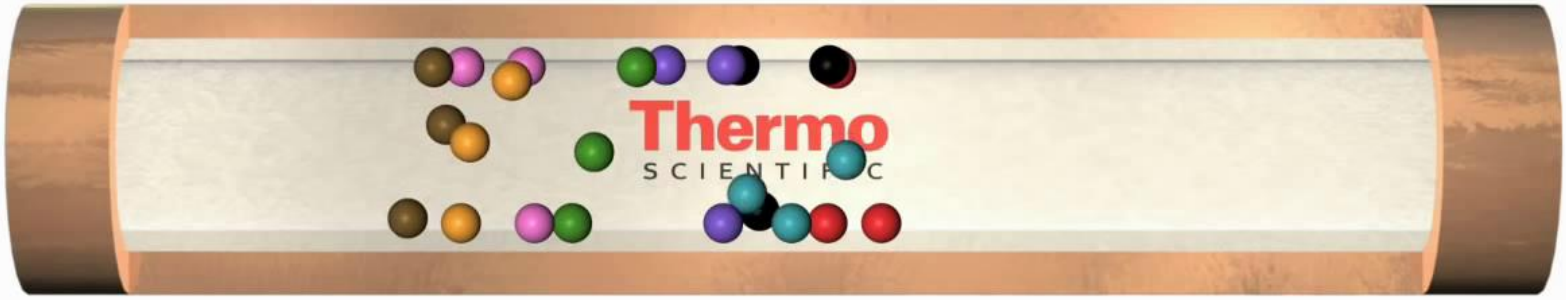
How does a GC-MS work?

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

Animation of how a GC works (courtesy of Thermo)

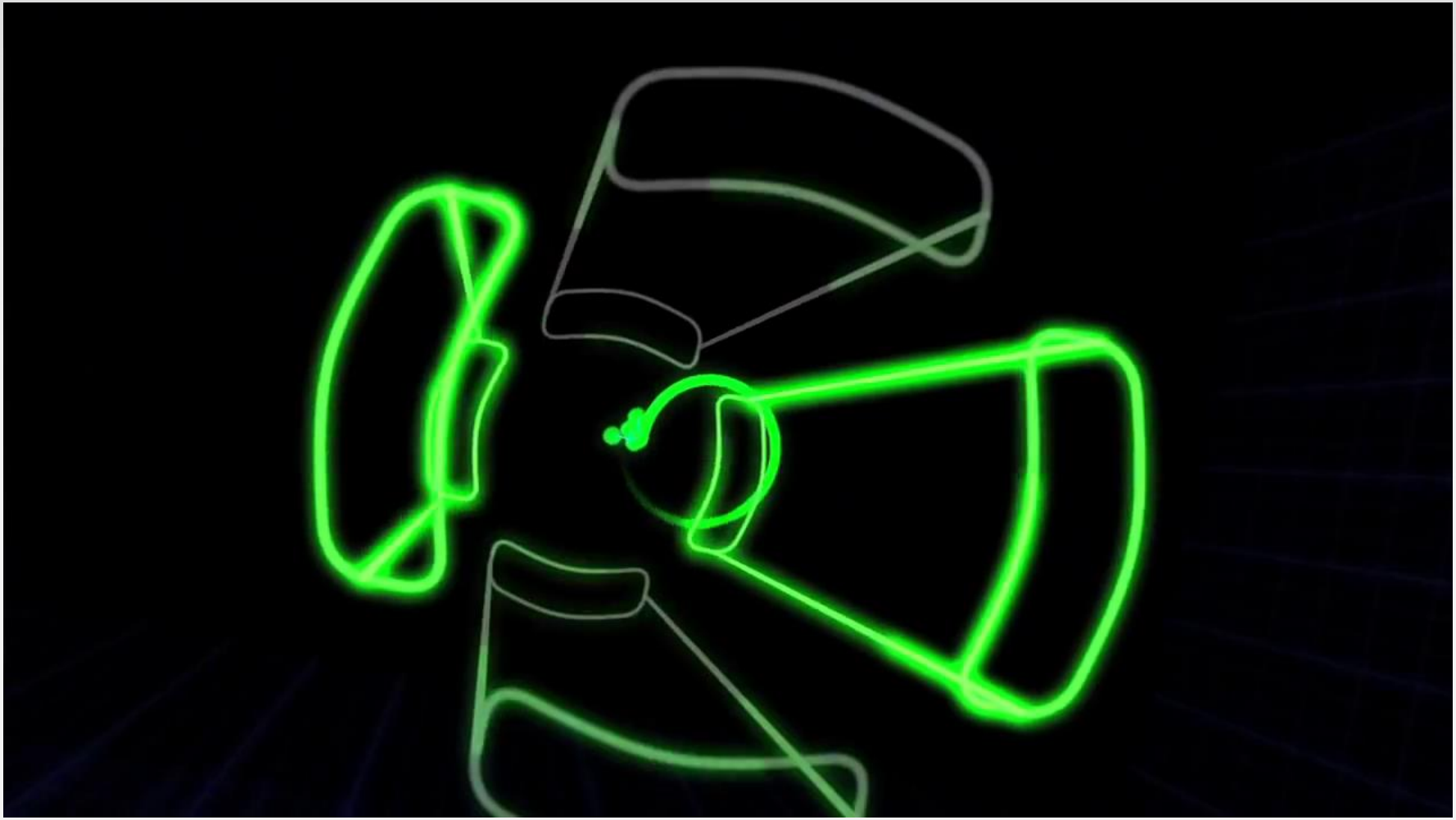


Compound Separation:

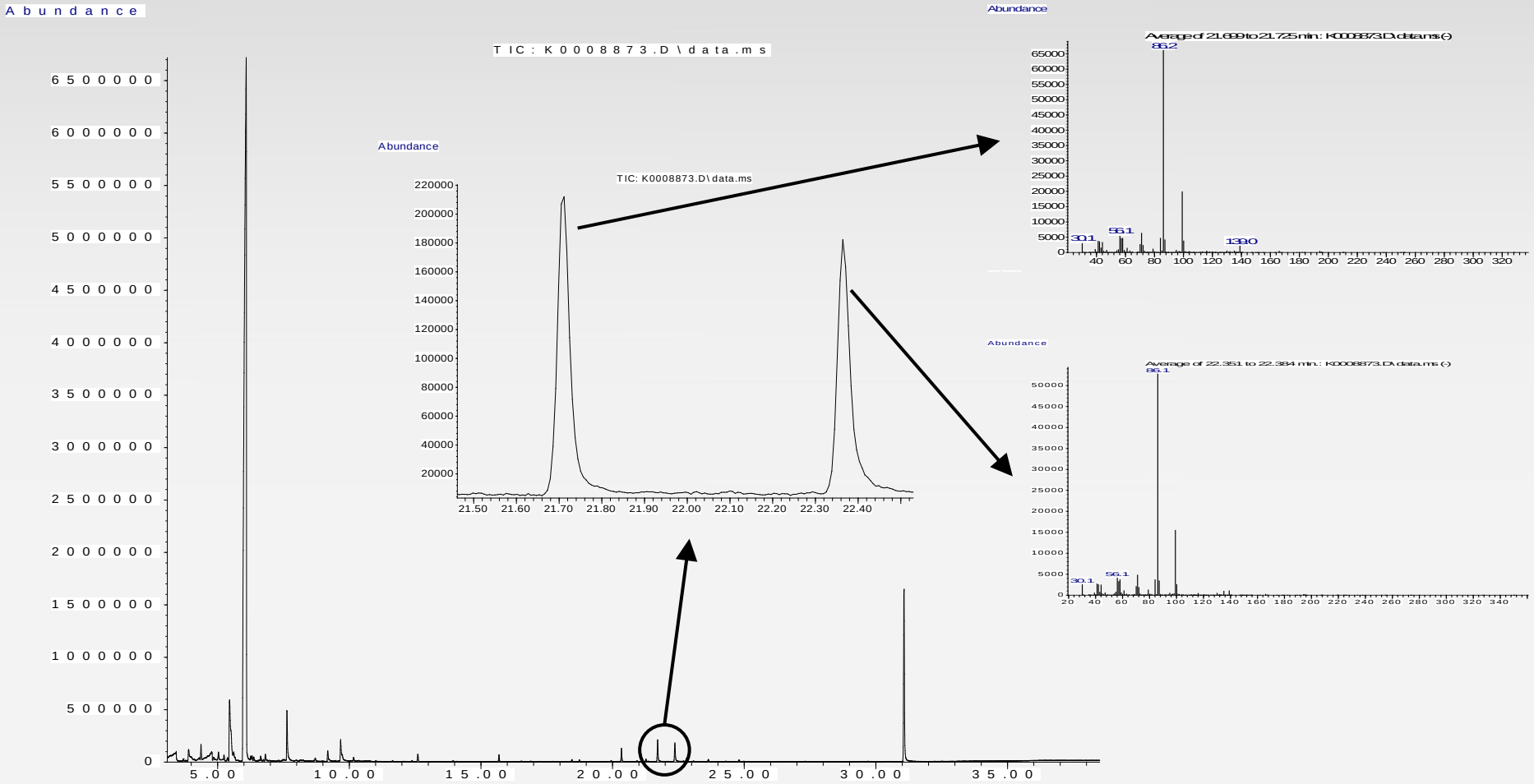
- Compounds separate according to volatility and polarity
- As compounds elute they are quantified by the detector

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

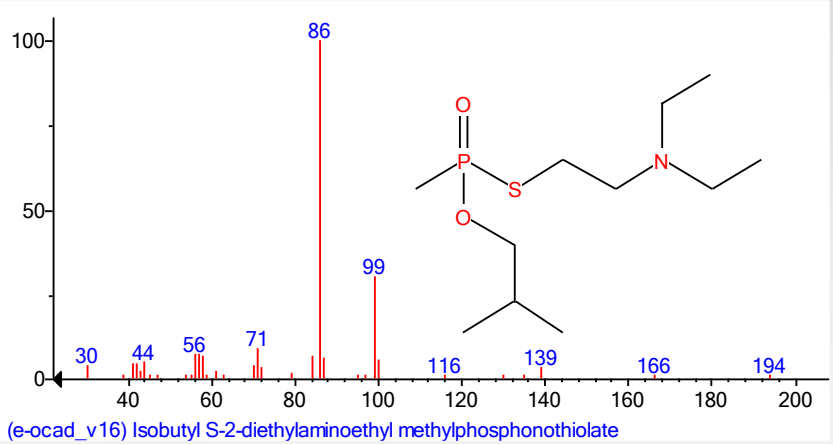
Animation of how a MS works (courtesy of NASA)

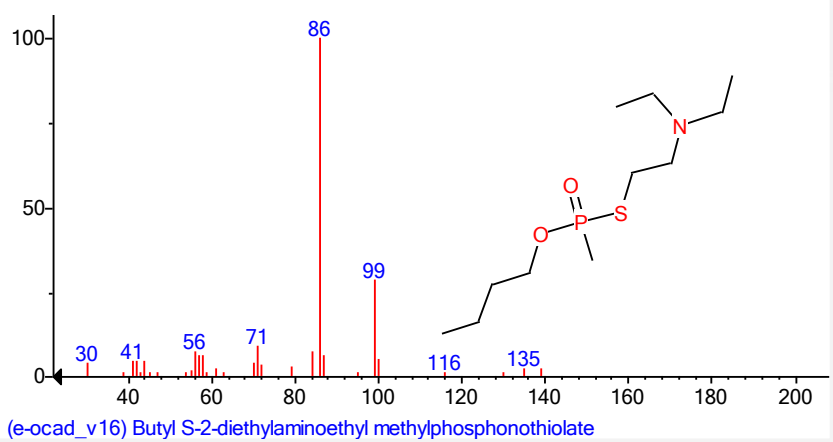


GC-MS data: Chromatograms and Spectra



GC-MS results: Spectra match to library



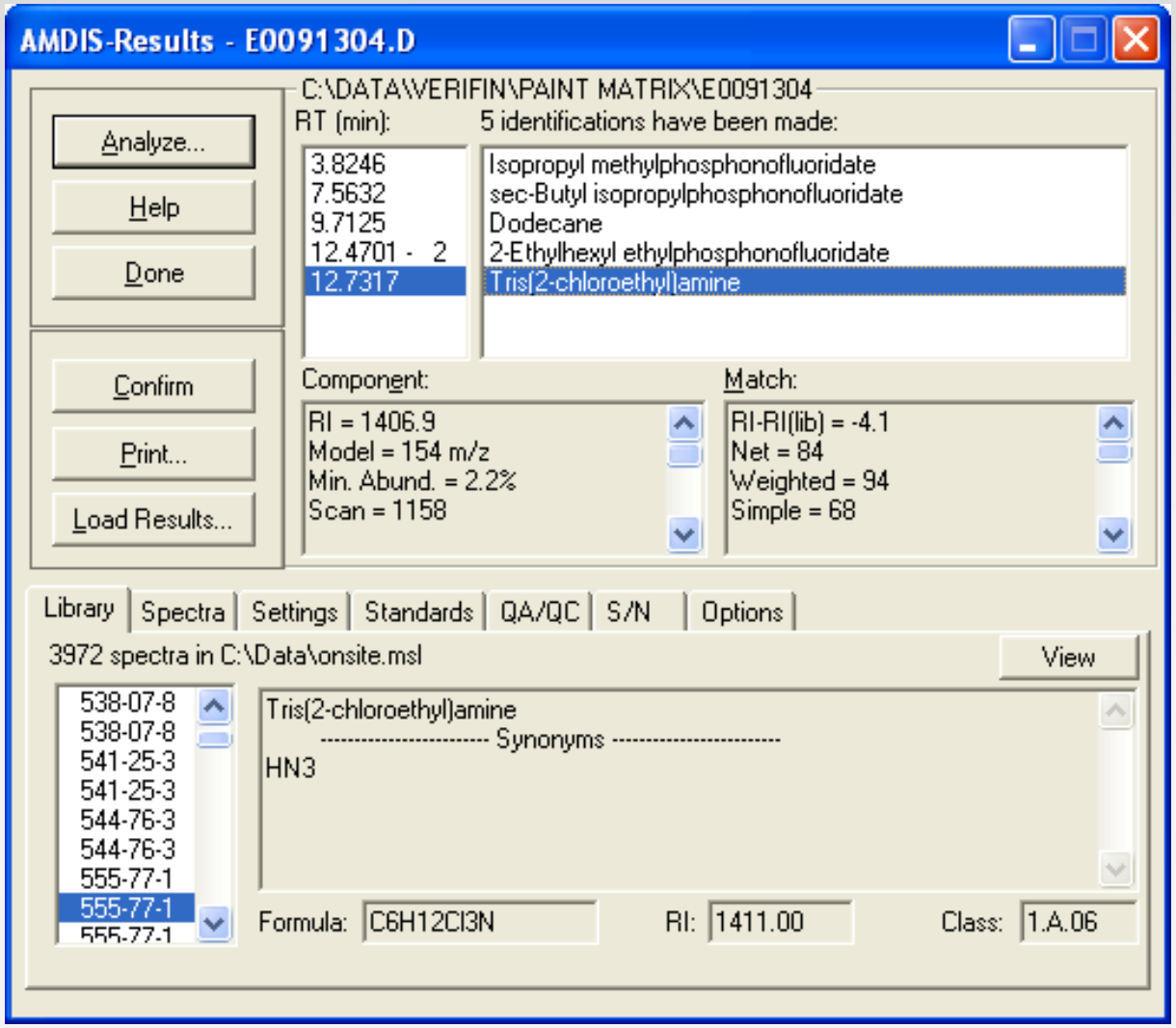


- Note the major ions in both spectra are identical
- Small differences in mass spectra indicate different structures
- The first chromatographic peak matches the top spectra with a match factor of 97 of 100
- Likewise, the second peak and spectrum match at 97
- Both are V-agents

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

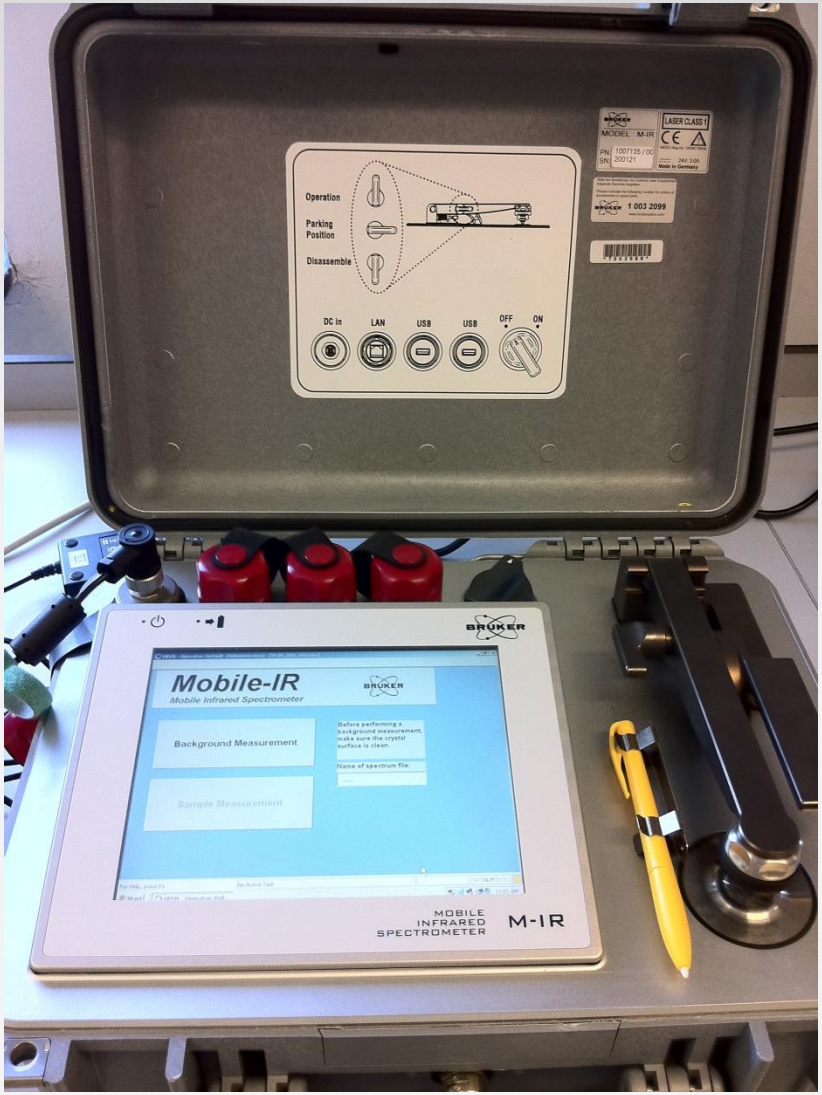
Chemical Identification Information

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

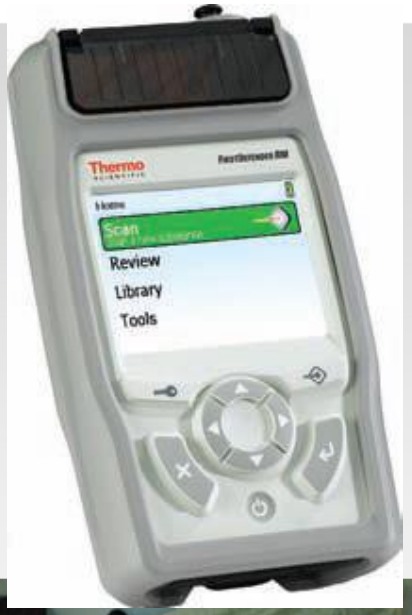


Thermo hand-held FT-IR

- 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

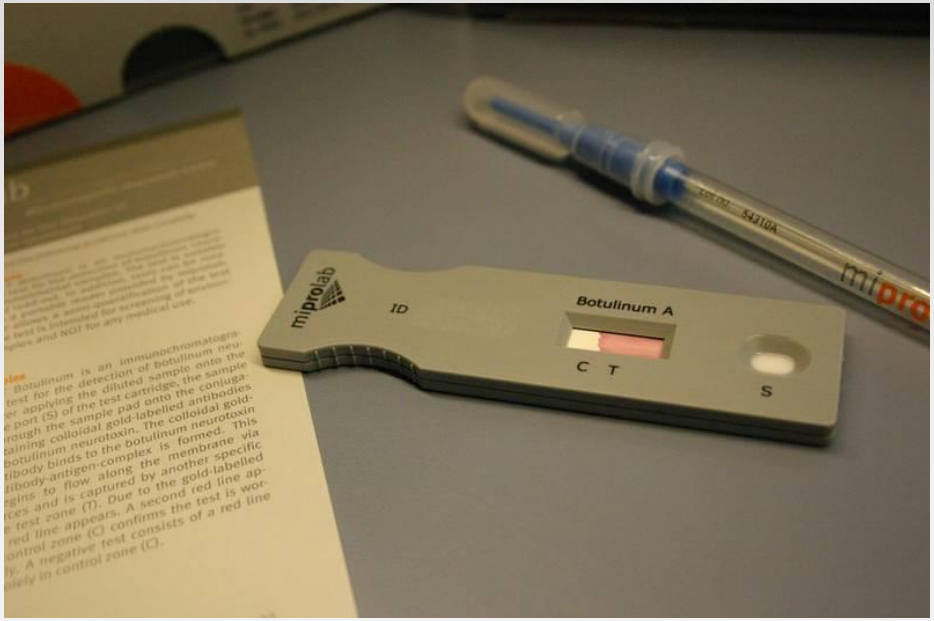


Hapsite mobile GC-MS

- 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

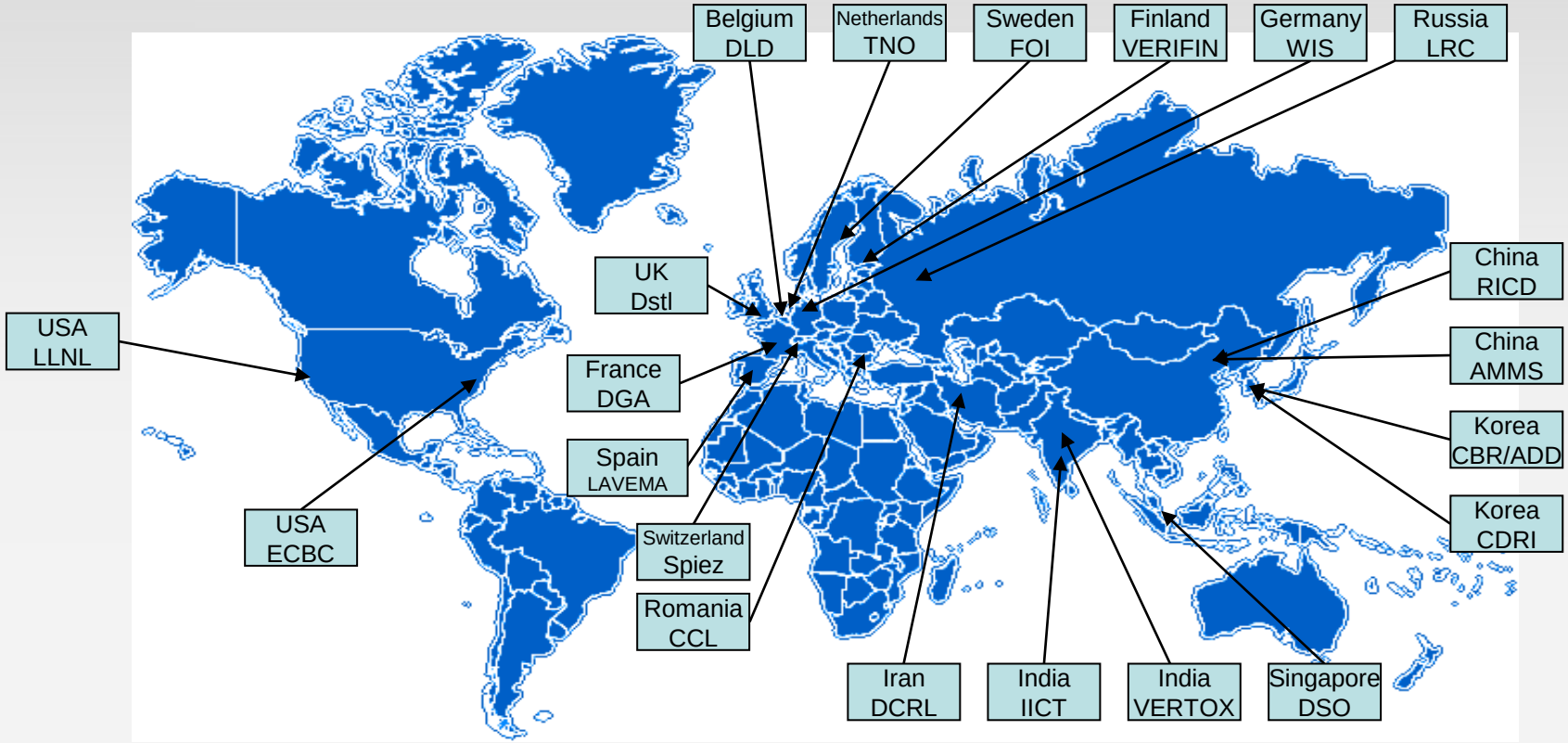
Test kits for "problematic" scheduled chemicals

- Ricin is a protein that cannot be analysed by GC-MS
- Saxitoxin, due to its chemical nature, cannot be analysed 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

OPCW Designated Laboratories



21 Designated Laboratories in 17 countries

as of May 2014

Designated Laboratories: equipment

GC-MS

GC/FTIR

GC/FPD

GC/AED

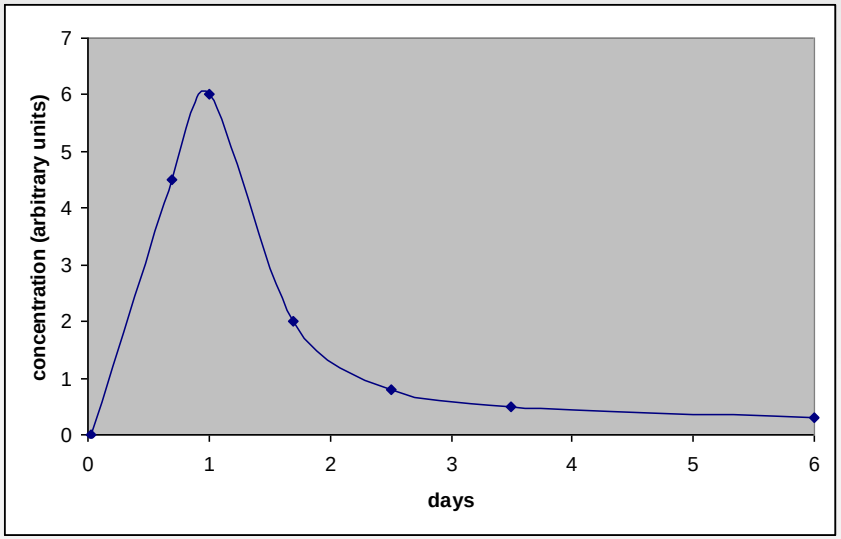
LC/MS

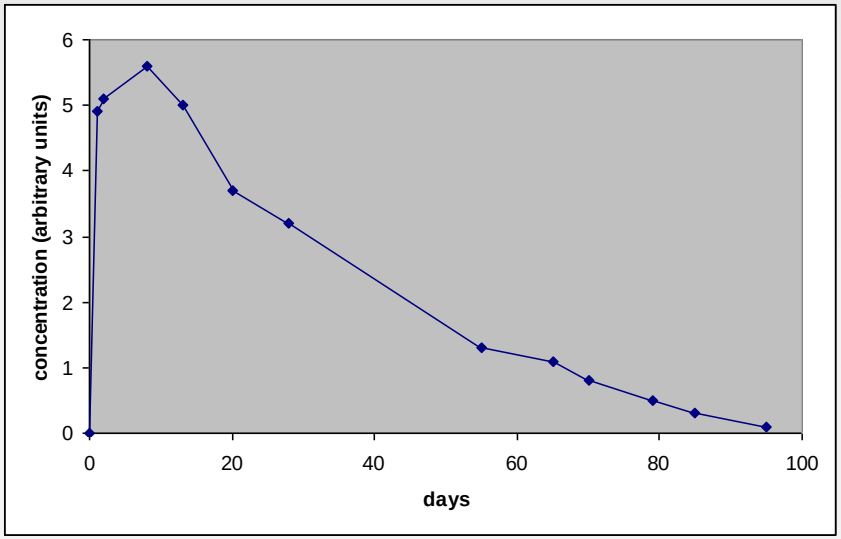
LC/HRMS

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

Syria: Biomedical sampling & analysis

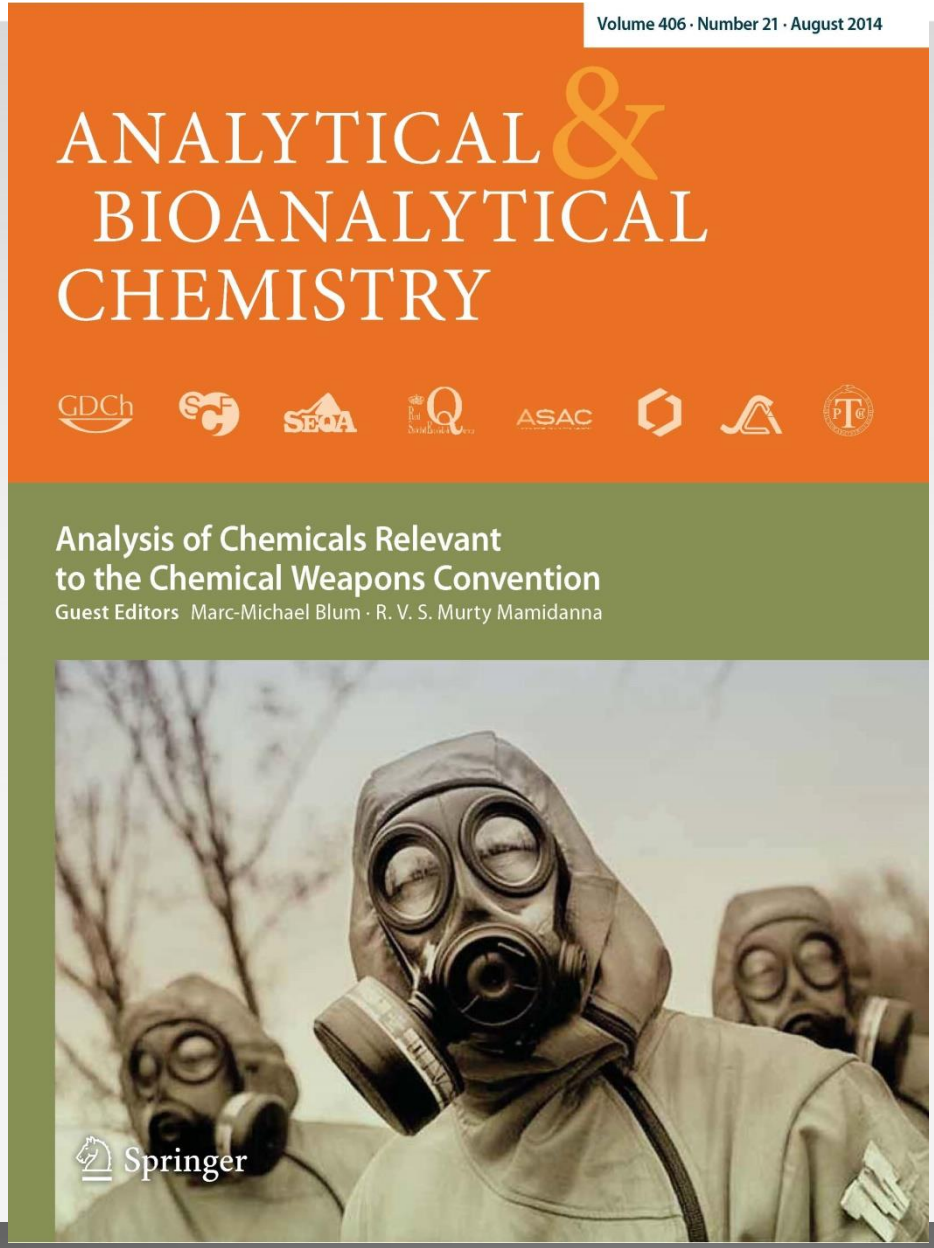
- Sample collection
  - OPCW and WHO staff interviewed victims and collected samples
- Sample splitting
  - Blood samples were centrifuged, plasma separated and refrigerated on-site
  - No splitting on-site – done at OPCW Laboratory
- Sample analysis
  - On-site – not possible
  - Off-site – samples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

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

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