ARE WE MISREPORTING TOXAPHENE?

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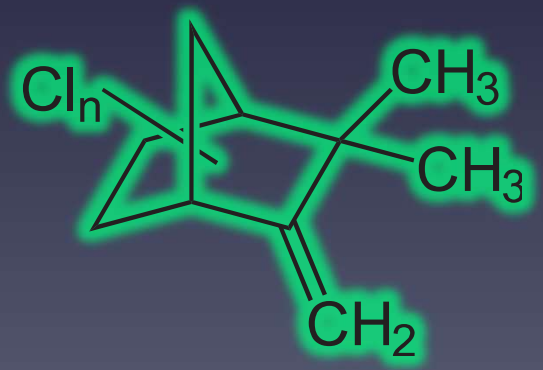
Outline

- Toxaphene "101"
- Analytical Approaches
- Exposure & Risk
- Path(s) Moving Forward
- Q & A

TOXAPHENE

1. Challenging analytical "problem"
2. "The *underestimated* pesticide"
3. What method should we use?
4. What are we to report anyway?



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Toxaphene "101"

Physical & Chemical Properties
History, Sources, & Uses
Transport and Fate
Nomenclature

One of the most heavily used insecticides in U.S. in 1970's
All uses banned in 1990 in U.S. & 2001 Stockholm Convention
Still persistent!

Physical & Chemical Properties

- Complex mixture of chlorinated terpenes
  - Produced by chlorination of camphene
  - 67 to 69 percent chlorine by wt.
  - Comprised of chlorinated bornanes, bornenes, bornadienes, camphenes, and dihydrocamphenes
  - Theoretically >tens of thousands compounds
  - Few hundred constituents present at "significant" concentrations in technical toxaphene

$C_{10}H_{18-n}Cl_n$ or $C_{10}H_{16-n}Cl_n$ where *n* is 6 to 10

Physical & Chemical Properties, cont.

MW: 413.8 to 431.8

Melting point: 65 – 90 °C

Boiling point: NA

Density at 25 °: ~1.65 kg/L

Sol. (water): ~0.55 mg/L

- Freely sol. in aromatic HCs
- Readily in organic solvents
- Readily in petroleum oils

Partition Coefficients:

Log K_{ow}: ~3.3 – 6.64[1]

Low K_{oc}: ~3 – 5

Vapor Pressure[1,2]:

~6.69 x10^{-6} mm Hg at 20 °C

Henry's Law Constant:

~6.69 x10^{-6} atm-m^3/mol at 20 °C

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[1] Estimated comparable to HCB

[2] <PCB mixtures, > DDx's; BCF high

Properties are for technical mixture and not congeners

History, Sources, & Uses

- Introduced by Hercules Company
  - First produced in late 1940's as insecticide
  - Many product names; produced > 180 companies
  - One of the most widely used products in U.S.
    - Livestock dips (miticide) & piscicide in lakes
    - Agriculture: cotton (~75% use in in south and south central U.S), cereals, fruits, soybeans, nuts, vegetables
    - Control of tsetse-flies in tropics
  - **Was often mixed with xylenes, diesel fuel, and other insecticides (e.g., DDT)**

History, Sources, & Uses, cont.

- Cumulative production volumes:
  - ~454,000 tonnes in U.S. (IPCS 1995)
  - ~181,000 tonnes other countries (IPCS 1995)
- Suspected carcinogen; most uses banned 1982 and completely in 1990 in U.S.
- Manufactured in China, Pakistan, and Nicaragua (FAO/UNEP 1995)
- Possibly still being used in parts of the world (e.g., China and Russia?)

Transport and Fate

- A problem POP:
  - Half-life in soil from ~100 d to ~12 yrs. (anaerobic)
  - Aerobic half-life in soil ~0.8 to 14 yrs.
  - Persistent in soil and sediment (K_{oc})
  - Low water solubility (K_{ow})
  - Photolysis not significant
  - In air and warm-blooded organisms, degradation is rapid (half-life's of 15 and 3 days, respectively)

Transport and Fate, cont.

- Vapor pressure (P) and Henry's Law constant (H):
  - Atmospheric transport largest vector
  - Cold "condensation effect"; aerosols
  - Global distribution
- Persistent degradation products
- Microbial degradation is enhanced in anaerobic soil and sediment
- Bioaccumulates in fish, crustaceans, molluscs, phytoplankton, zooplankton, algae, etc.

Nomenclature

- What is toxaphene?
  - Comprised of chlorinated bornanes, bornenes, bornadienes, camphenes, and dihydrocamphenes
  - Technical mixture, congeners, & enantiomers
  - Many trade names have been used
  - At least > 30,000 congeners possible
- Non-uniform nomenclature; incorrect citation of IUPAC conventions

Nomenclature, cont.

- Generally five systematic conventions:
  - Parlar (1993): numbered selected compounds from 11 to 69 based on RT; frequently used but has issues
  - Nikiforov (1995): Binary coding and ordered by IUPAC order and 13-digit binary number
  - Oehme & Kallenborn (1995): Binary numbering system to decimal code (based on Nikiforov convention)
  - Andrews & Vetter (1995): conversion of structure into code (i.e., AV code) via computer; order of preference by IUPAC rules
  - Wester, et al. (1997): mixture of above, but with deduction of structural information

Analytical Approaches

- Most routine methods include:
  - GC/ECD (e.g., Method 8081B)
  - GC-NICI-MS or GC-ECNI-MS (e.g., Method 8276)
- Many different quantitative approaches:
  - Selected peaks (e.g., 5 to 9)
  - Total area under curve (TAUC)
  - Selected congeners (and combinations thereof)

Analytical Approaches, cont.

Other analytical approaches have included:

- GC/MS/MS
- HRGC/HRMS
- GC/HRMS-SIM (magnetic sector)
- GC/MS EI (e.g. Method 8270D)
- Ion Trap HRGC-EI-MS/MS
- GC x GC -TOFMS
- Multi Dimensional GC/ECD
- GC-EI-MS & GC-CI-MS (EPA 1976); early years!
- GC/QQQ MS in EI mode: the future?
- Are there more?

EPA-600/3-76-076
August 1976

Ecological Research Series

ANALYSIS AND GC-MS CHARACTERIZATION OF TOXAPHENE IN FISH AND WATER

ABSTRACT

Sensitive methods for the detection and identification of toxaphene in water and fish were described. Polyurethane foam, gel permeation and silicic acid chromatography were utilized to permit accurate quantitation of multi-component toxaphene residues. A method for characterization of changes in isomer composition of toxaphene residues in fish was reported. The chemical composition of toxaphene was examined by electron impact and chemical ionization mass spectrometry. Chemical ionization gas chromatography-mass spectrometry was particularly applicable to the analysis and confirmation of toxaphene residues in environmental samples.

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Analytical Approaches, cont.

- What are the pros and cons?
  - So many analytical choices, which to use?
  - What is most useful qualitative method(s)?
  - How do we quantify a meaningful concentration?
  - Let's not forget the degradation products!
  - GC/QQQ MS becoming more common and, realistically, an option to seriously consider
  - Are there other viable options?

Analytical Approaches, cont.

- Few thoughts on ID & quantification:
  - Complex mixture of $Cl_6 - Cl_{10}$ camphenes
  - No two "standards" are identical
  - Selective weathering (abiotic and biotic matrices)
  - Enhancement of lower chlorinated products
  - Persistent degradation products such as Hx-Sed, Hp-Sed, P-26, P-50, & P-62

Analytical Approaches, cont.

- Pattern matching by GC/ECD biased low & often ND's (okay if report as "technical toxaphene")
- GC/ECD problematic - interferences
- Issue with congener approach due to limited availability of standards
- Current congener approach also biased low
- Reporting of degradation products more meaningful & useful for assessing potential risk

Following set of slides are presented to illustrate the qualitative and quantitative issues of concern.

Due to time constraints cannot discuss information in great detail, but perhaps we can discuss later?

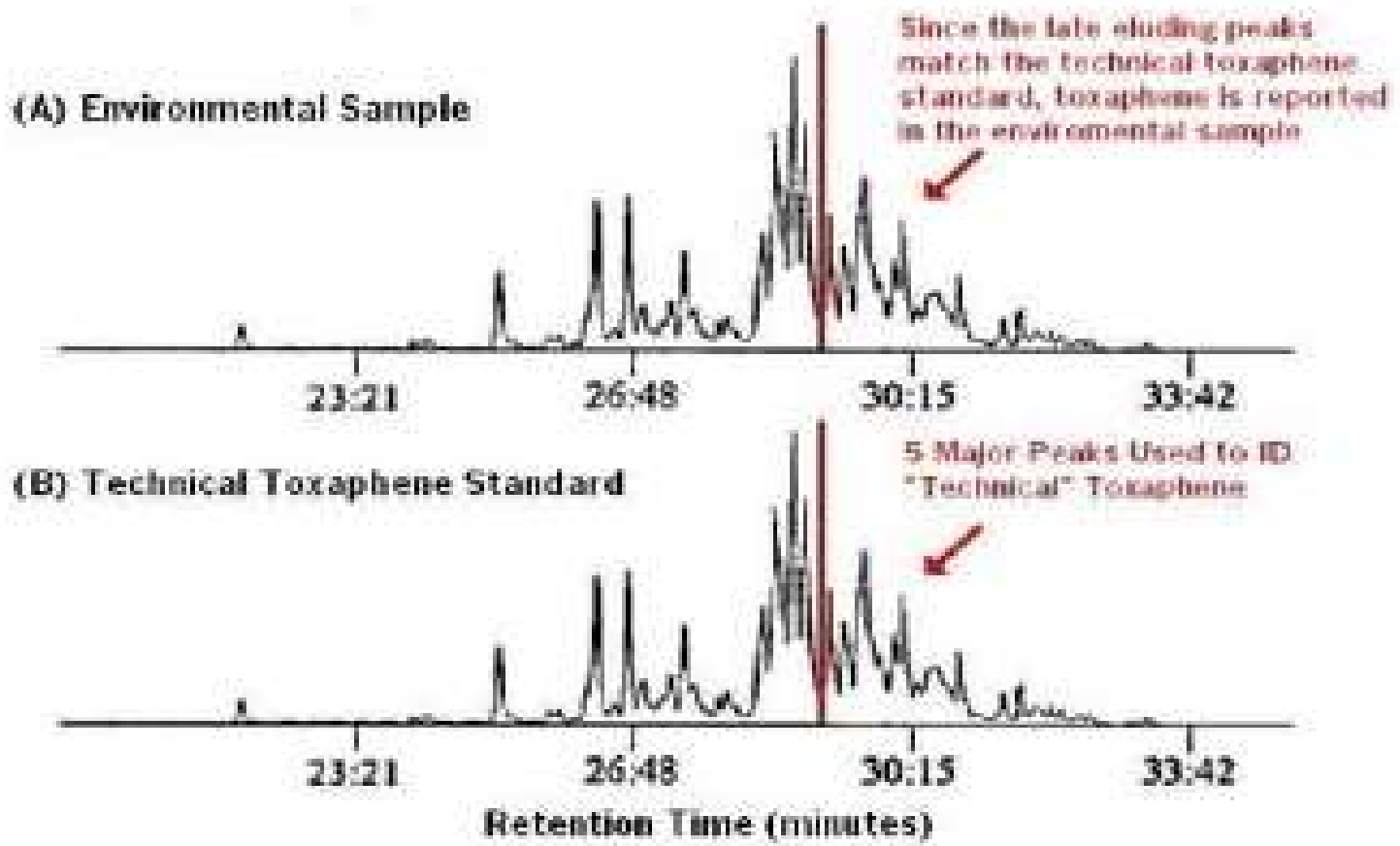


Figure 2: GC/ECD Chromatograms of Technical Toxaphene

EPA Method 8081 Does Not Identify Toxaphene Degradation Products

Source: Office of Inspector General. Ombudsman Report: More Information Is Needed on Toxaphene Degradation Products (USEPA 2005)

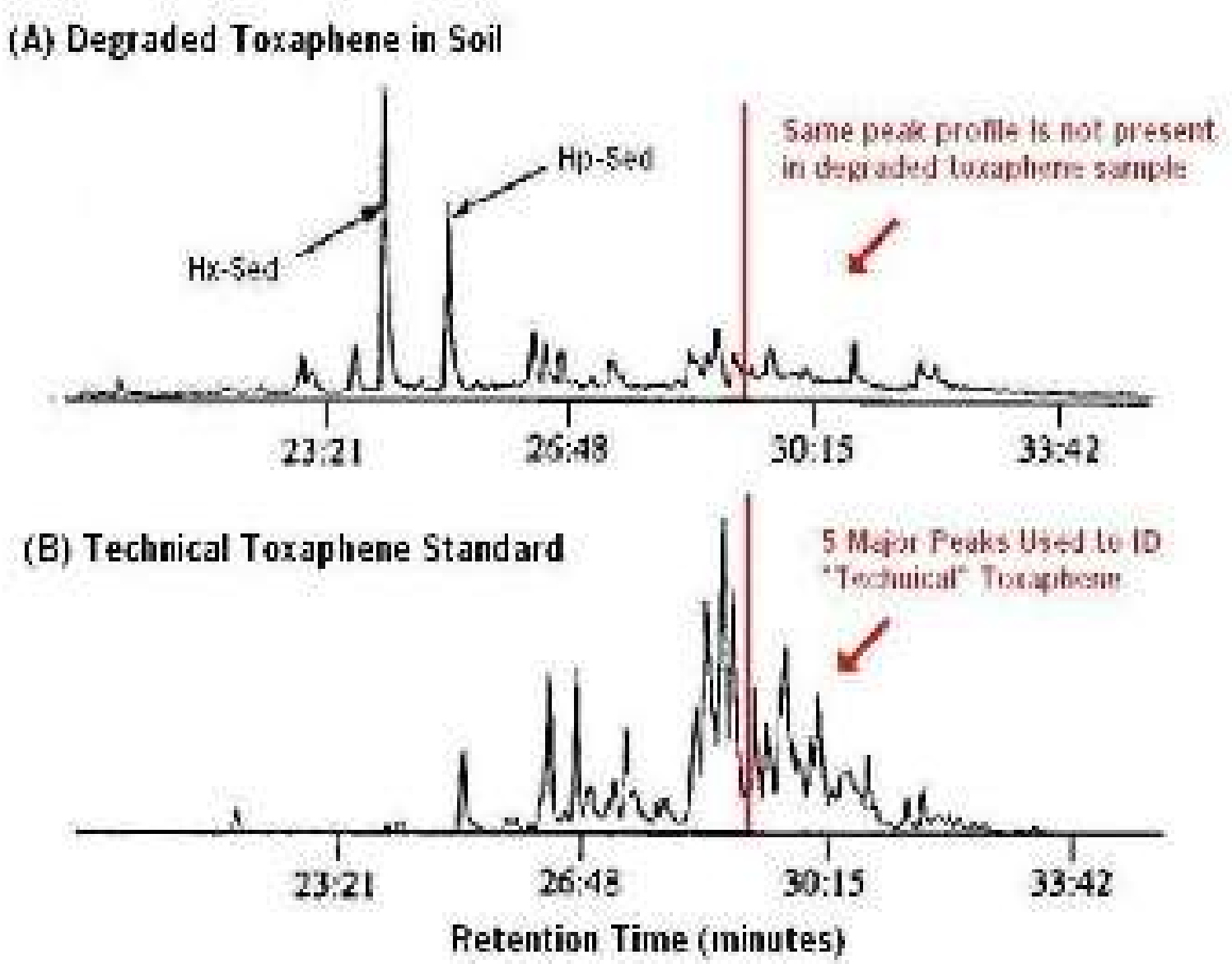


Figure 3: EPA Method 8081 Analyzes for Only Technical Toxaphene

Source: Office of Inspector General. Ombudsman Report: More Information Is Needed on Toxaphene Degradation Products (USEPA 2005)

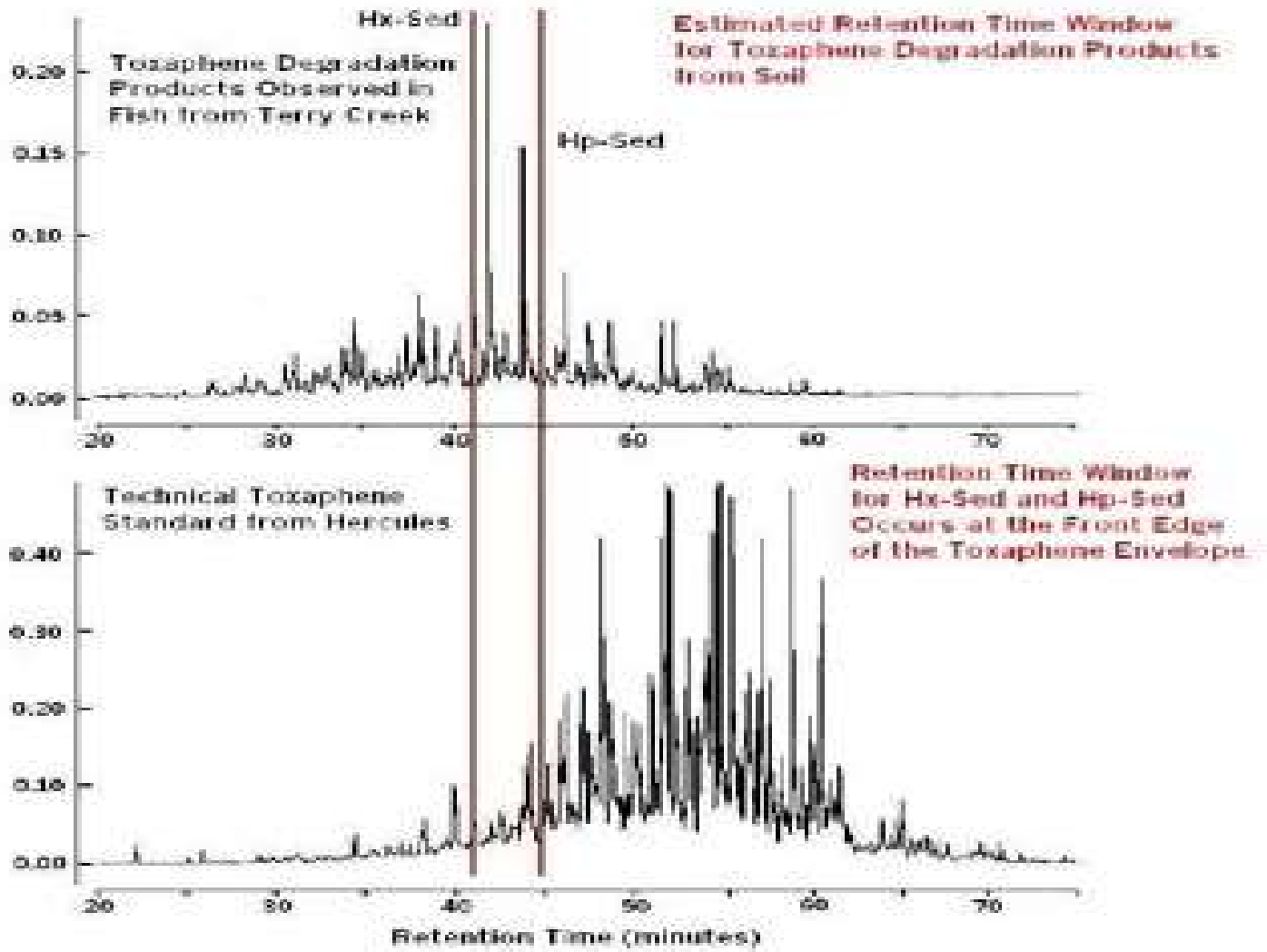
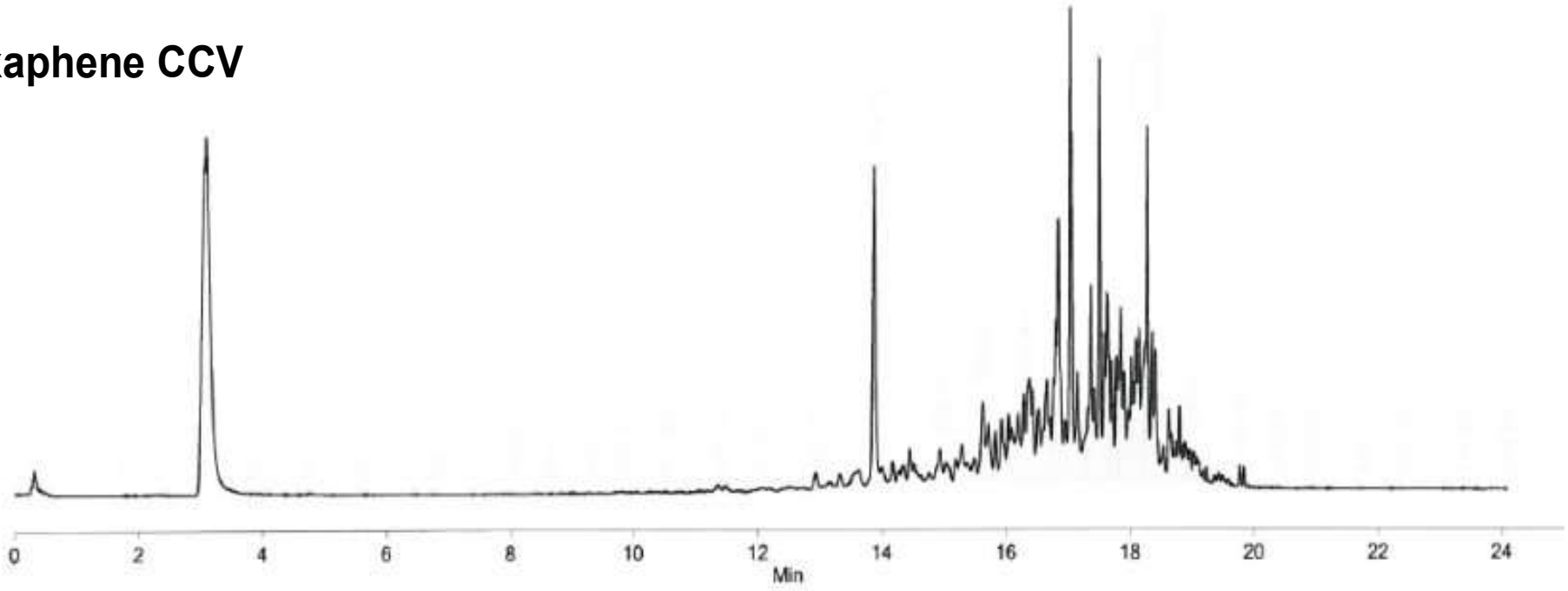


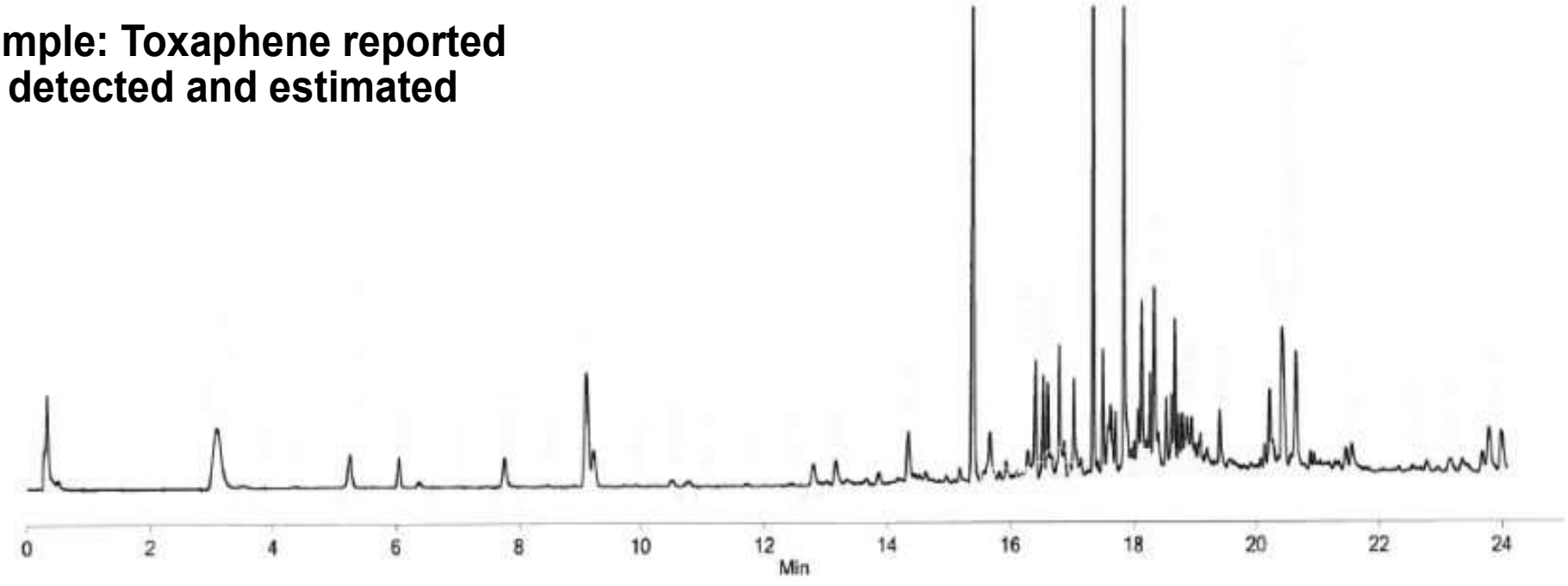
Figure 4: Estimated Retention Time Window for Hx-sed and Hp-sed

Source: Office of Inspector General. Ombudsman Report: More Information Is Needed on Toxaphene Degradation Products (USEPA 2005)

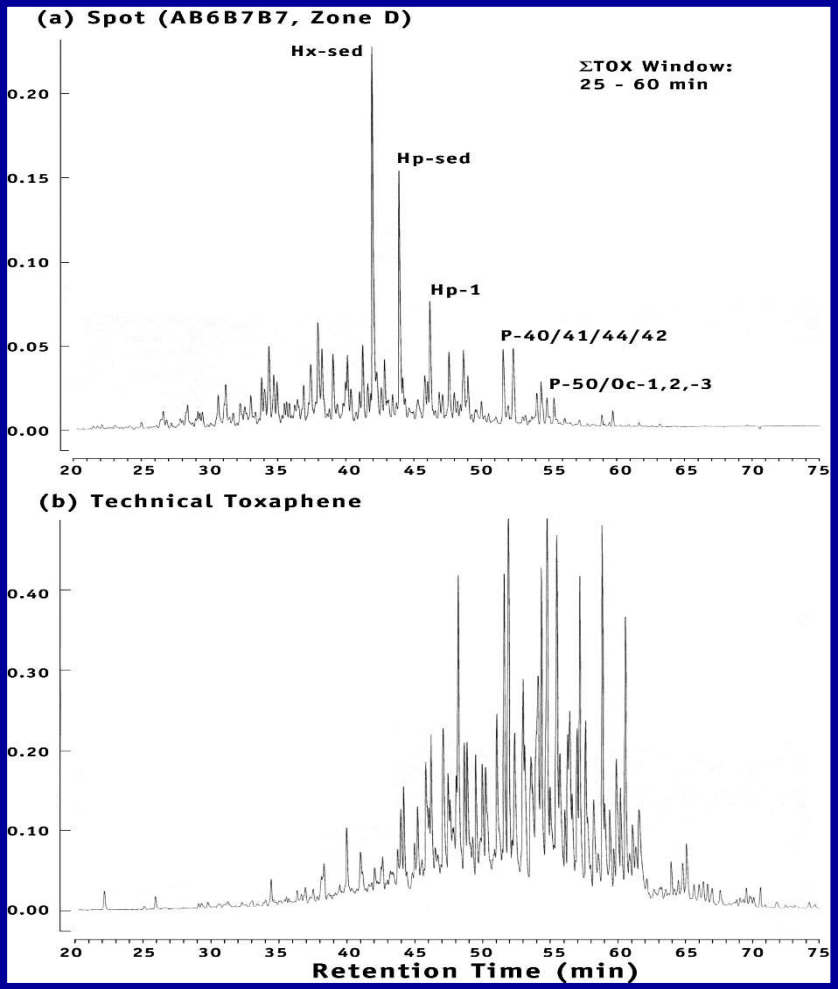
Toxaphene CCV



Sample: Toxaphene reported as detected and estimated



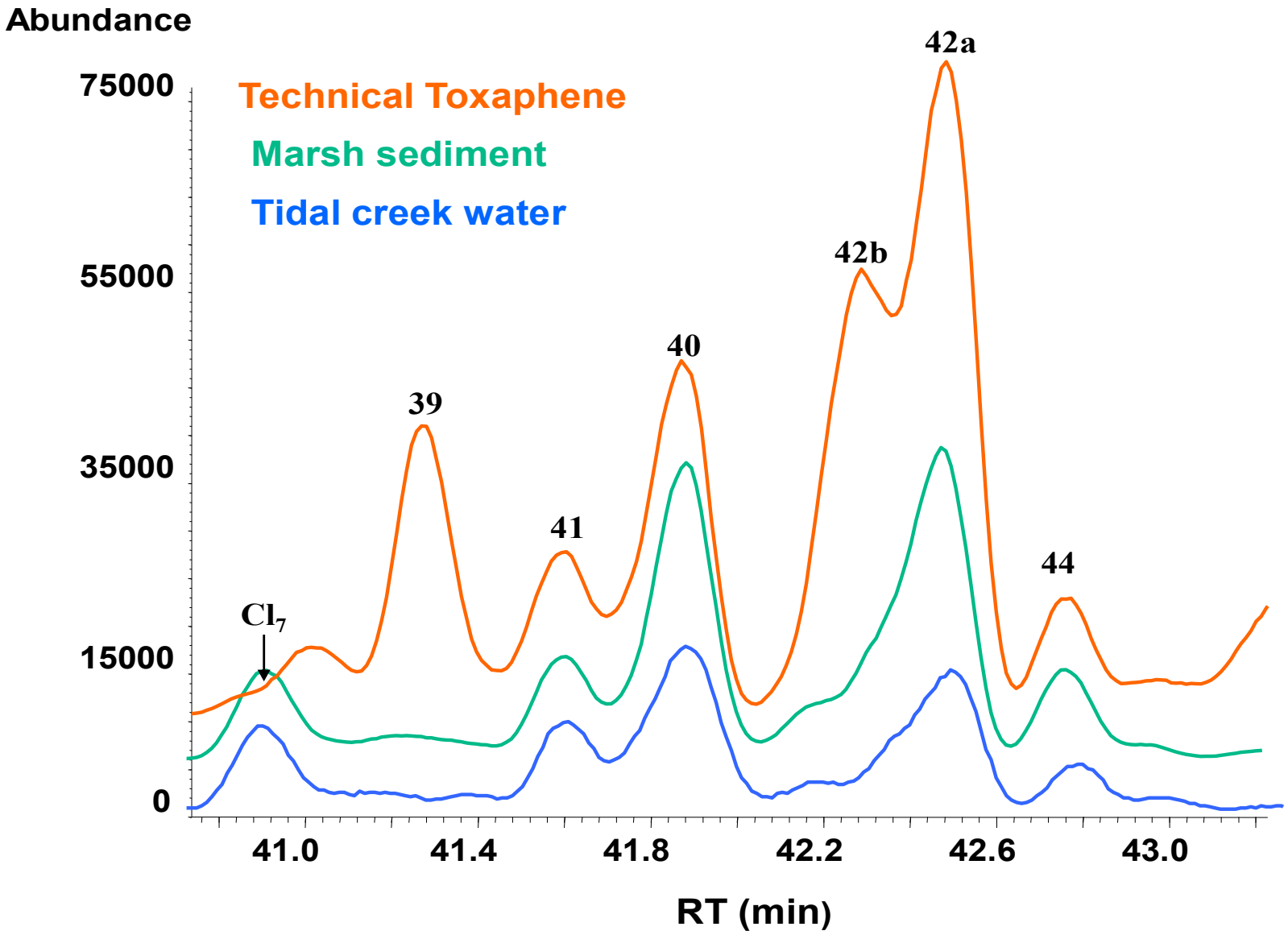
Weathering of toxaphene



- TTX *transformed* in aquatic environment (Williams & Bidleman 1978)
- GC shift to *lower chlorinated* homologs
- Dominated by *Hx- and Hp-Sed* (Stern et al. 1996)
- Many *unidentified* residue congeners (e.g. Hp-1; Oc-1)

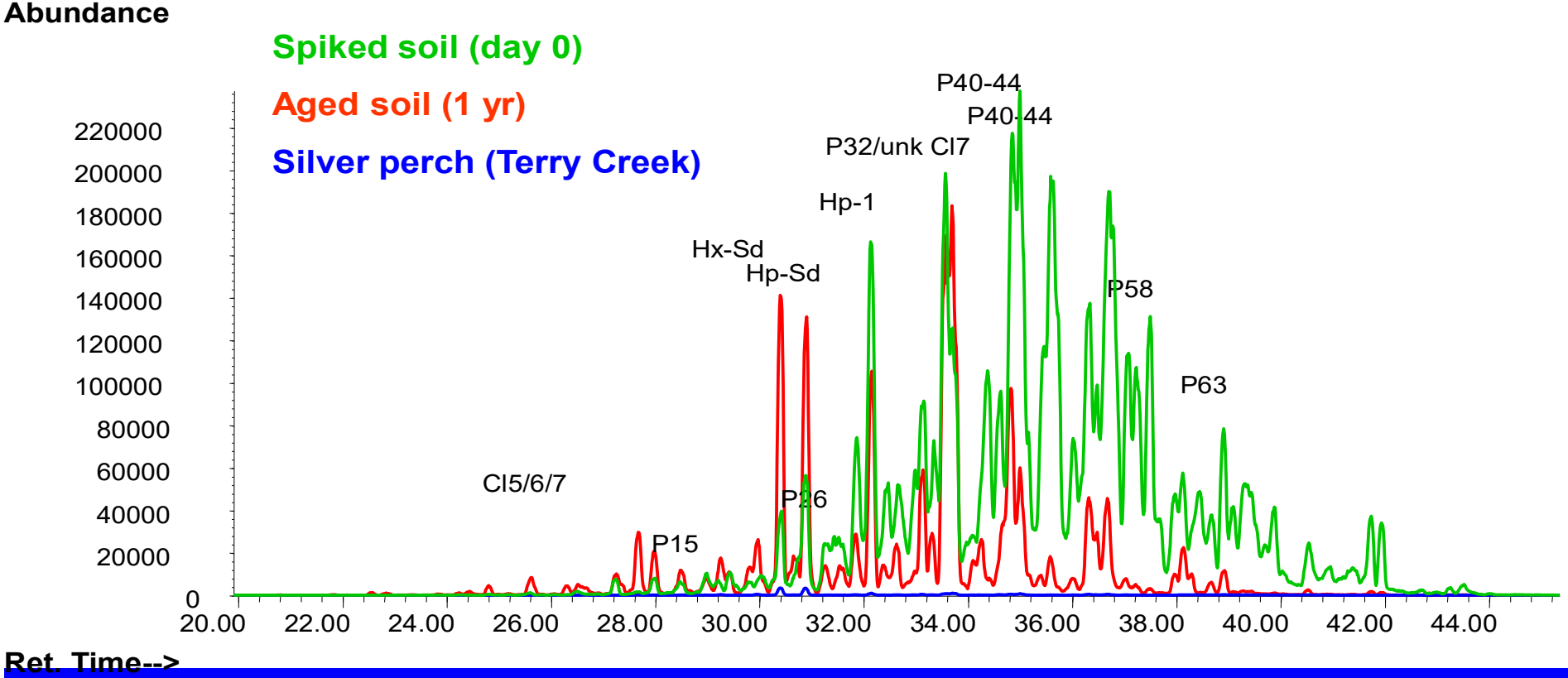
- *What is toxaphene and how do we measure it?*

Source: Dr. Keith Maruya, Southern California Coastal Water Research Project (SCCWRP), with permission (personal communication, July 13, 2016). Source: Maruya et al. (2001)



Source: Dr. Keith Maruya, SCCWRP, with permission (personal communication, July 13, 2016).
Source: Maruya, unpublished data

GC-ECNI-MS TICs showing *soil degradation pattern after 1 yr*



Source: Dr. Keith Maruya, SCCWRP, with permission (personal communication, July 13, 2016). Data adapted from study described by Young et al. (2009)

Exposure and Risk

- Via air, soil, sediment, & aquatic organisms
- Typically report technical toxaphene, but…
- Degradation products are the concern
- Limited science-based regulatory action levels and risk information (ATSDR 1998)
- Hx-Sed, Hp-Sed, P-26, P-50, & P-62 predominant, but need to look at more?

Exposure and Risk, cont.

Analyte:	Toxaphene

Resident Soil (mg/kg)	Industrial Soil (mg/kg)	Resident Air (ug/m^3)	Industrial Air (ug/m^3)	Tapwater (ug/L)	MCL (ug/L)	Risk-based SSL (mg/kg)	MCL-based SSL (mg/kg)	Source
1.2E+01	1.2E+02	8.0E-01		6.0E-01				EPA-2004
4.9E-01	2.1E+00	8.8E-03	3.8E-02	7.1E-02	3.0E+00	1.1E-02	4.6E-01	EPA-Aug. 2016

By congener (P-26, P-50, and P-62):

∑3PC RfD = 2E-05 mg/Kg-day

Source: Simon & Manning (2006)

Exposure and Risk, cont.

- Other congeners in Method 8276 are P-40, P-41, & P-44 (expand this list?)
- Is RfD based on toxicity of P-26, P-50, & P-62 sufficient?
- Toxic to aquatic organisms (saltwater fish more sensitive)
- Is more wide-spread monitoring of residues in fish and other biotic matrices needed?
- So much more to discuss here…

Path Moving Forward

- Analytical Improvement and Consistency
  - Let's just go to triple quad GC/MS!
  - Need more congener standards
  - Produce an SRM/CRM of weathered toxaphene?
  - More consistency in qualitative and quantitative approaches amongst laboratories
- Physical and Chemical Properties
  - More information on other congeners to facilitate more reliable prediction of fate and transport?

Path Moving Forward, cont.

- Environmental Fate, Exposure, & Risk
  - Better understanding of biotransformation, bioavailability, & bioaccumulation?
  - Better understanding of fate and transport of additional congeners?
  - Should more congeners be included in assessment of risk?

Path Moving Forward, cont.

- Insufficient data to evaluate carcinogenicity risks to humans (MATT reports)?
- What are reasonable maximum residue levels in fish and other biotic organisms?
- More cooperation and data sharing amongst global scientific and regulatory community?
- Establish a portal where data from around the globe can be stored and accessed?

Data Validation and DQA

- Qualify results as estimated (*UJ, J, or NJ*) reported by GC/ECD?
  - USGS acknowledges altered toxaphene difficult, so detects assigned "E" code
- Any other ideas?

We should better educate all data users, laboratory staff, and regulators as to what "Toxaphene" means based on the data reported and the method used!

“An Interested Mind Brooks No Delay”

A quote by ”Cameca” to Dr. Who
The Aztecs (original airdate: May 23, 1964)
Episode 2, Garden of Peace

Acronyms

- ATSDR – Agency for Toxic Substances and Disease Registry
- CI – chemical ionization
- ECD – electron capture detection
- EI – electron impact
- ECNI – electron capture negative ionization
- GC – Gas Chromatography
- GC/MS – Gas Chromatography/Mass Spectrometry
- HR – high resolution
- IUPAC – International Union of Pure and Applied Chemistry
- MS – mass spectrometry
- MATT – Monitoring, Analysis and Toxicity of Toxaphene
- NEMC – National Environmental Monitoring Conference
- NI – negative ion
- NICI – negative ion chemical ionization
- POP – persistent organic pollutant
- QQQ – triple quadrupole
- RfD – reference dose
- SIM – Selected Ion Monitoring
- TAUC – total area under curve
- TNI – The NELAC Institute
- TOF – time-of-flight
- USEPA – U.S. Environmental Protection Agency

References

If you are interested in the extensive list of references used to help prepare this presentation, please contact me at jjmcateer@msn.com

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- Laboratories we have worked with throughout our careers
- Our client(s)
- Agilent, Shimadzu, Thermo Fisher Scientific, and Waters

DISCLAIMER

The views and opinions expressed in this presentation are those solely of the presenters and do not reflect the opinions, official policy, or position of any client, regulatory agency, laboratory, or other individuals.

Thank You!

Any Questions?

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