Determination of Volatile Organic Compounds from US FDA list of Harmful or Potentially Harmful Compounds in mainstream cigarette smoke by GC-MS

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FDA TPSAC List of HPHCs

- Large number of Volatile and Semi-Volatile Compounds are included in the proposed HPHC list.
- Few methods exist for the analysis of these compounds

Target Compounds

1,3-Butadiene, Acrylonitrile, Benzene, Isoprene, Toluene, Furan, Ethylene oxide, Vinyl chloride, Propylene oxide, Nitromethane, 2-Nitropropane, Vinyl acetate, Ethylbenzene, Nitrobenzene, Acetamide, Acrylamide, Quinoline, Styrene, and Pyridine

Ideal Method for the Analysis of Volatile HPHCs

- Single method for all compounds
- Based on existing method
- Equipment currently in use in the laboratory or industry standard equipment
- Rapid method allowing for the analysis of many samples per day

Can CRM-70 “Analysis of Selected Volatile Organic Compounds” be used as a starting point?

CORESTA Recommended Method 70

- GC-Mass Spectrometry Method
- Volatiles are collected by passing the mainstream smoke of cigarettes through a glass fiber filter disc and into cryogenic traps containing methanol.
- Validated method with collaborative study data
- Method gives results consistent with Tedlar® bag method

Target Compound List:

- 1, 3-butadiene, isoprene, acrylonitrile, benzene, and toluene

CORESTA recommended method 70

- A fused silica capillary column like a DB-624, length 60 m, I.D. 0.25 mm, 1.4 μm film is suggested
- Trapping system consists of two impingers after a filter pad (not analyzed).
- Method recommends number of traps and volume of trapping solution.
- Method recommends one internal standard
- Method can be modified for use with Intense smoking conditions.

Volatile Compounds

Which compounds on the TPSAC list are suitable for analysis using CRM-70?

- Compounds must pass through the filter pad un-retained.

1,3-Butadiene, Acrylonitrile, Benzene, Isoprene, Toluene, Furan, Ethylene Oxide, Vinyl chloride Propylene Oxide, Nitromethane, 2-Nitropropane, Vinyl acetate, Ethylbenzene, Nitrobenzene, Acetamide, Acrylamide, Quinoline, Styrene, and Pyridine

We smoked the 3R4F cigarette under intense conditions with extra clearing puffs and analyzed the pad separate from the impingers.

Compounds in red were detected on the filter pad and not suitable for CRM-70.

Compound Stability

Which of the remaining compounds are suitable for analysis

- Compounds must be stable in the trapping solution long enough to allow for analysis.

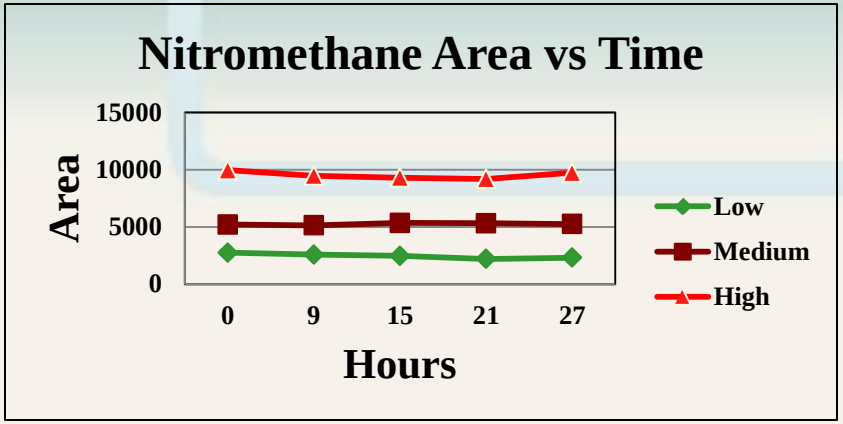
Compound in 3R4F	%Decrease in 36Hrs
1,3-Butadiene	1.7
Ethylene oxide	6.5
Furan	1.7
Acrylonitrile	1.8
Isoprene	3.0
Benzene	0.6
Toluene	1.3

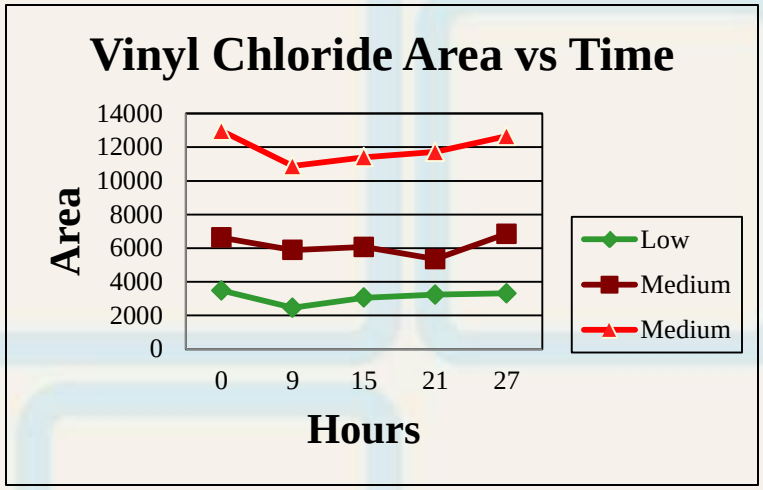
Stability of compounds in trapping solution was determined by measuring % decrease over two days. Samples were placed in sealed autosampler vials with zero headspace. Samples held at room temperature.

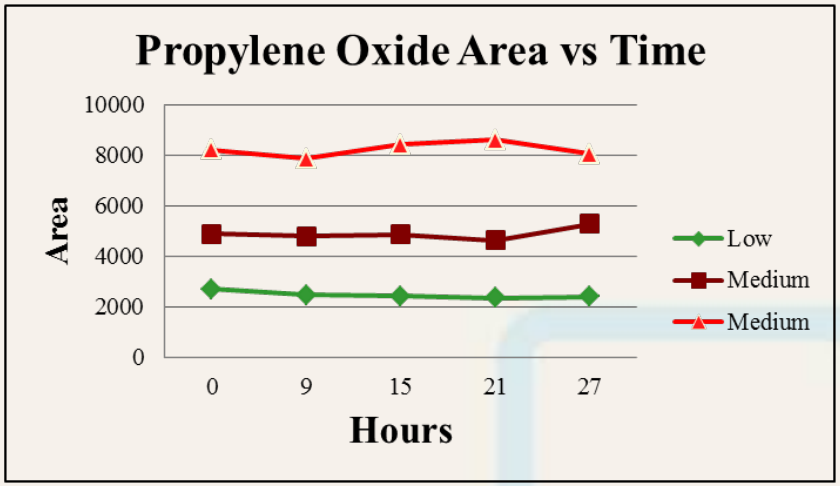
With this approach, it was not possible to measure stability of vinyl chloride, propylene oxide, or nitromethane

Compound Stability

Each compound was spiked into trapping solution and then vapor phase smoke was added to impinger. Samples were held at room temp in autosampler vials.





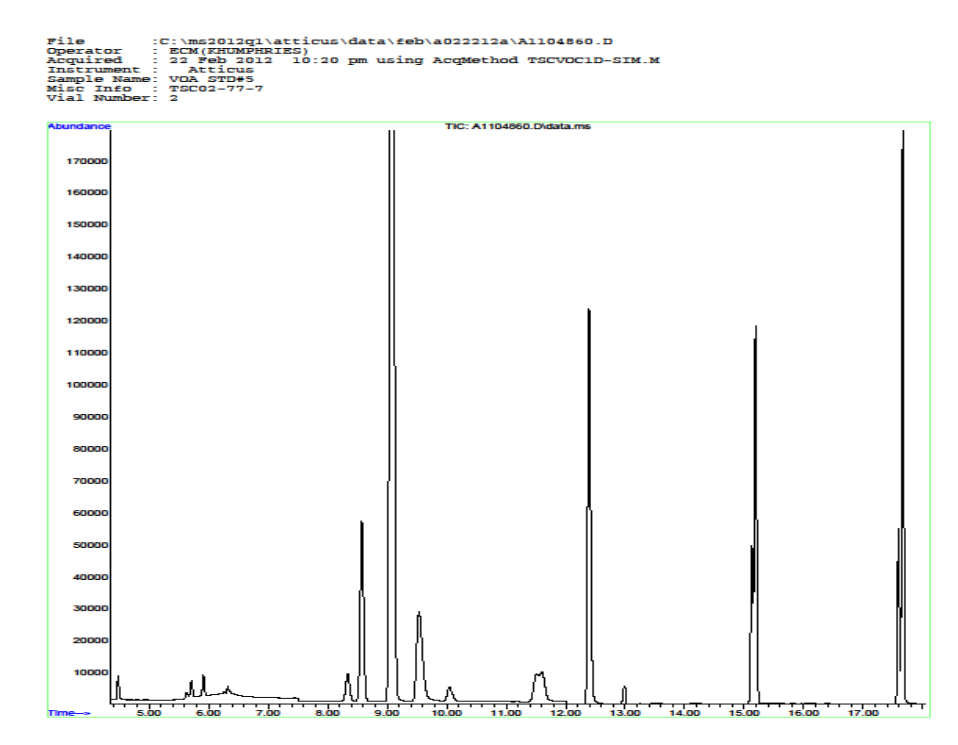


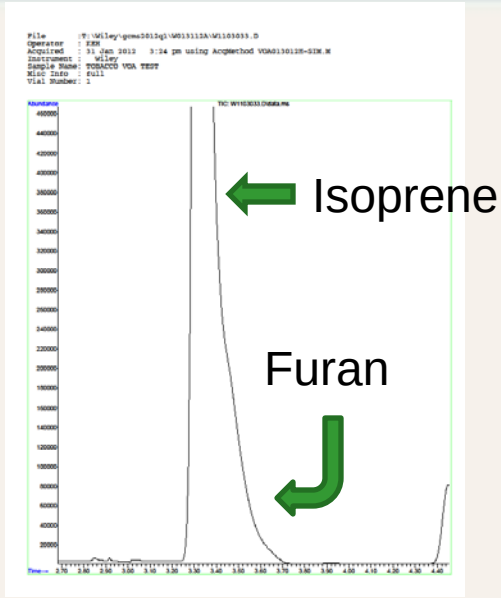
Separation of Compounds by GC-MS

- CRM-70 suggested column DB-624, length 60 m, I.D. 0.25 mm, 1.4 µm film.

Compounds on the CRM-70 list separated on this column, 1,3-Butadiene, Acrylonitrile, Benzene, Toluene as well as Vinyl acetate, Ethylene oxide, Vinyl chloride, Propylene oxide, and Nitromethane. We were however unable to separate Furan and the much larger Isoprene peak.

Separation of Compounds by GC-MS





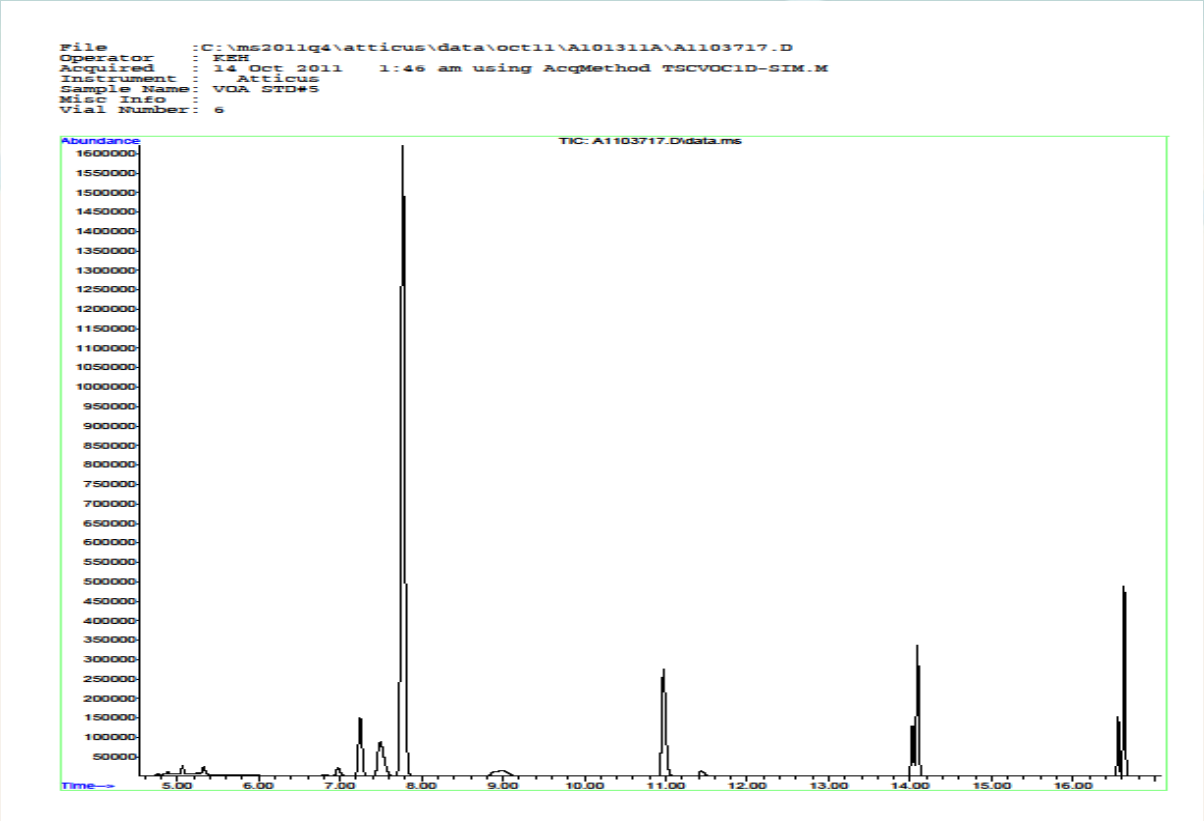
DB-624, length 60 m, I.D. 0.25 mm, 1.4 µm film.

Separation of Compounds by GC-MS

- CRM-70 allows for alternate column selection. We tried a Rxi-1, length 60 m, I.D. 0.25 mm, 1.0 μm film.

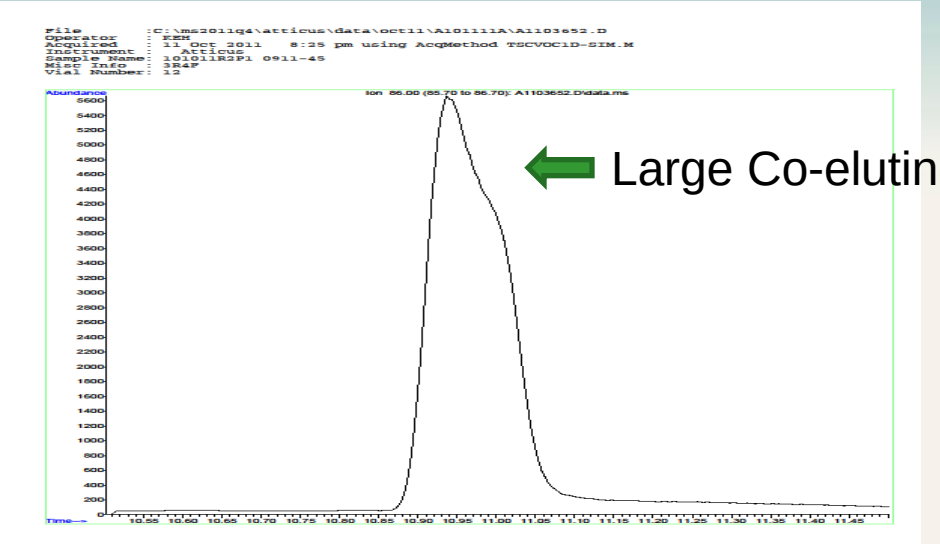
Compounds on the CRM-70 list separated on this column, 1,3-Butadiene, Isoprene, Acrylonitrile, Benzene, Toluene as well as Ethylene oxide, Vinyl chloride, Propylene oxide, Furan, and Nitromethane. We were however unable to separate Vinyl acetate from a co-eluting matrix compound.

Separation of Compounds by GC-MS

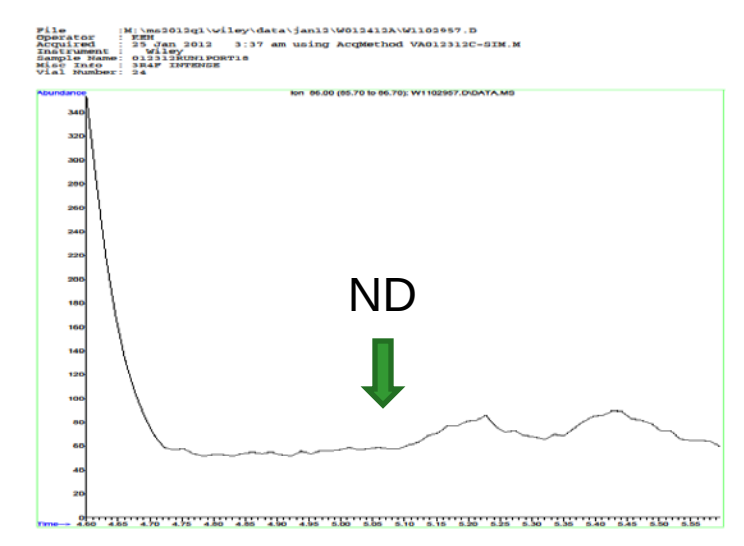


Rxi-1ms, length 60 m, I.D. 0.25 mm, 1.0 µm film.

Separation of Compounds by GC-MS



Vinyl Acetate Ion 86
Rxi-1ms, length 60 m,
I.D. 0.25 mm, 1.0 µm film.



Vinyl Acetate Ion 86
DB-624, length 60 m,
I.D. 0.25 mm, 1.4 µm film

Trapping of Compounds

- CRM-70 recommends two impingers, each with 10 ml of trapping solution (20 ml each intense smoking), -78°C.
- Type and size of impinger is not specified.
- Trapping efficiency was evaluated for each compound using either fritted or capillary impingers inserts.

Breakthrough was evaluated using three impingers placed in series. Each impinger analyzed separately.

Trapping of Compounds

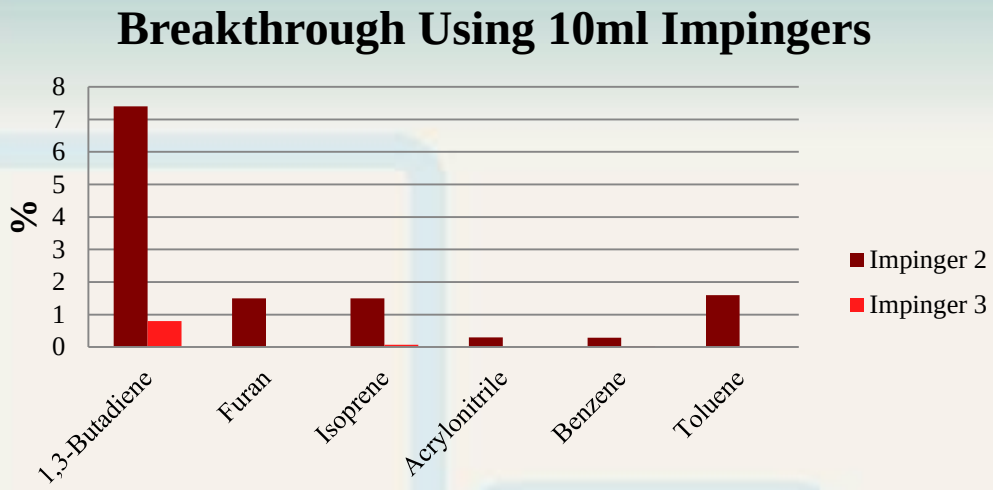
10 ml

20 ml

20 ml

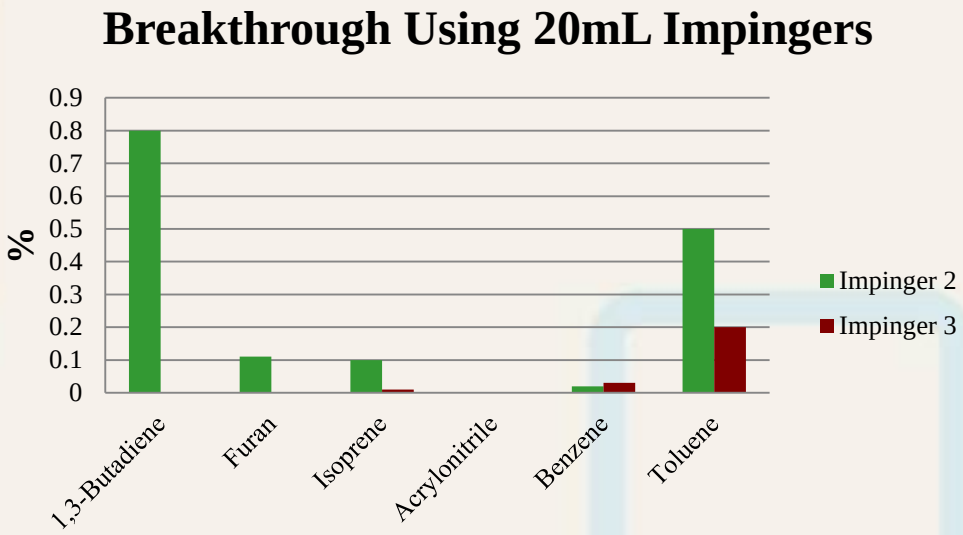
- Our capillary tipped inserts did not efficiently trap gas phase compounds.
- 10 ml of trapping solution did not completely cover our fritted impinger inserts.

Trapping of Compounds



With 10 ml of trapping solution in front impinger, 1,3 butadiene was trapped with 93% efficiency (intense smoking)

With 20 ml of trapping solution in front impinger, 1,3 butadiene was trapped with >99% efficiency (intense smoking). Second and third impinger not needed.



Improving Method Performance

CRM-70: one internal standard, benzene-d6

We found reproducibility was poor for many compounds when based solely on benzene-d6.

We added nitromethane-d3 and toluene-d8 to the method which improved reproducibility

Nitromethane was difficult to add to each impinger, internal standards were added to bulk trapping solution

Method Summary

- Column: Rxi-1ms, length 60 m, I.D. 0.25 mm, 1.0 µm film
- Temperature program: 35°C for 10min., 20°C/min to 250°C.
- Internal Standards: Nitromethane-d3, Benzene-d6, Toluene-d8
- Impingers: Single fritted stem with 20mL trapping solution, -78°C.
- Zero headspace autosampler vials with Teflon® septa.

Method Performance

Detection Limits

Compound Name	Detection Limit (µg/mL)	Method Detection Limit (Five Cigs) (µg/cig)
Vinyl Chloride	0.04	0.16
1,3- Butadiene	0.12	0.48
Ethylene Oxide	0.03	0.12
Propylene Oxide	0.04	0.16
Furan	0.09	0.37
Nitromethane	0.04	0.16

Method Performance

3R4F ISO	Vinyl chloride	Ethylene oxide	Propylene oxide	Furan	Nitromethane
Average	<0.16	11.1	<0.16	20.8	<0.16
SD	NA	0.92	NA	1.2	NA
% RSD	NA	8.3	NA	5.8	NA

3R4F-CI					
Average	<0.27	38.4	<0.27	63.1	<0.27
SD	NA	6.98	NA	4.92	NA
% RSD	NA	18.2	NA	7.8	NA

1R5F ISO					
Average	< 0.16	3.59	< 0.16	6.94	<0.16
SD	NA	0.52	NA	0.57	NA
% RSD	NA	14.4	NA	8.1	NA

All values in μg/cigt

Method Performance

	CRM70 (5 compounds)	TPSAC (5 compounds)	Ratio
	total μg/cigt	total μg/cigt	%
1R5F ISO	148	11	7.13
3R4F ISO	447	32	7.14
3R4F CI	1448	102	7.01

The five compounds that are included in CRM-70 are present in mainstream smoke at much higher concentrations than the 5 additional compounds on the TPSAC list. Ratio of TPSAC compounds to the CRM-70 compounds is constant in the three cigarettes measured for this study.

Summary of Work

- 10 compounds can be analyzed in a single analytical run.
- All compounds were found to be stable in methanol trapping solution for >24 hours.
- Three compounds, nitromethane, vinyl chloride and propylene oxide were not detected at levels >0.2 μg/cigt under Intense smoking.
- Cambridge filter pad traps semi-volatile compounds, might be possible to expand method to include particulate matter.
- Separate method needed for vinyl acetate.