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Application News

No. GCMS-2004

Gas Chromatography Mass Spectrometry

Oregon Residual Solvent Analysis Method for Cannabis/Hemp using a Single Quad GCMS with Headspace

■ Abstract

Cannabis and hemp production within the United States has expanded exponentially within recent years. Because the legalization of cannabis and hemp is determined by each state, consumer product safety testing requirements are also determined by the state. Typically, consumer product safety for these products include residual solvent screening. A residual solvent method for cannabis or hemp matrices is demonstrated based on the requirements of the State of Oregon (OR). Using a single quadrupole GC-MS with a dedicated headspace autosampler, all thirty-five solvents currently in the screening method were detected and quantified. The limit of detection (LOD) and saturation level for many of the solvents were determined.

■ Introduction

The State of Oregon (OR) mandates the analysis of residual solvents in hemp and cannabis products. In this method, thirty-five solvents are monitored, with limits varying from 2 ppm (by weight; in the following, ppm refers to 1 µg of a given analyte in 1 gram of sample) for benzene, to 5000 ppm for butane.

These solvents are commonly used in manufacturing processes for the extraction and concentration of THC or CBD. Analysis of these solvents can be conducted via GC or GC-MS using universally accepted methods such as USP <467>, a method based on pharmaceutical manufacturing testing requirements. Different sample introduction techniques are used within the industry, with static headspace emerging as a popular technique and detection is generally conducted by either FID or MS. The most commonly used column is the Rxi-624 Sil MS or a similar type. Time is critical to most applications therefore, the ability to heat-ahead samples is important when selecting an appropriate headspace sample introduction device.

■ Samples and Analytical Conditions/Experimental

A Shimadzu GCMS-QP2010 SE was utilized with a HS-20 headspace loop only autosampler in static mode. Method parameters are reported in Table 1.

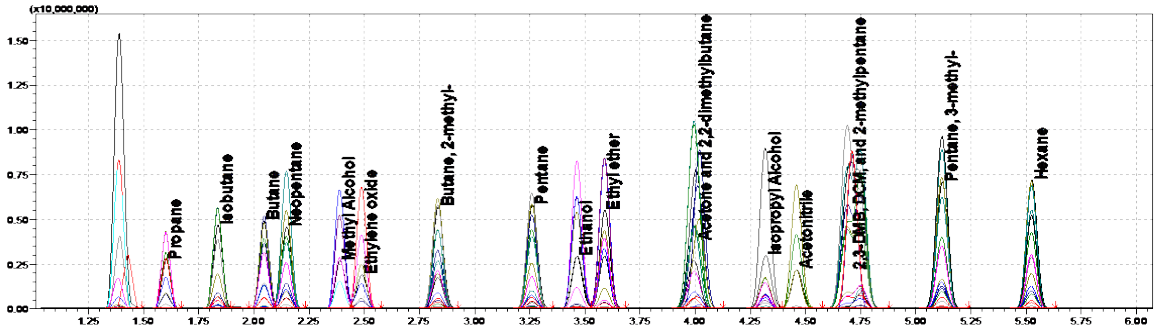
Table 1: Acquisition parameters for headspace GC-MS residual solvent method for the State of Oregon

Headspace	**HS-20 Loop Model**
Operation Mode	Static headspace with heat-ahead
Sample	150µL sample volume 20mL headspace vial
Equilibration	15.00 min at 120°C
Sample Loop	0.2mL loop Vial pressure: 125KPa Pressurizing time: 1.50 min Loop load time: 0.20 min Equilibration: 0.20 min Injection time: 0.20 min
Sample Line Temperature	150°C
Transfer Line Temperature	150°C
Gas Chromatograph	**GC-2010 Plus**
Injection	Split injection from HS-20, with 50:1 split ratio
Column	Rxi-624 Sil MS 30.0m x 0.25 mm x 1.40 um Helium carrier gas Constant linear velocity: 39.9 cm/sec Column flow: 1.24 mL/min Purge flow: 0.0 mL/min
Oven Program	30°C, hold 3.0 min 10°C/min to 140°C hold 0.0 min 45°C/min to 200°C hold 1.0 min Total GC run time: 16.33 min Total GC cycle time: 25.00 min
Detector	**GCMS-QP2010 SE**
Operation Mode	Selected Ion Monitoring Mode (SIM)
Ion Source	200°C, EI mode, 70eV
Solvent Cut Time	0.1 min
MS Interface	300°C

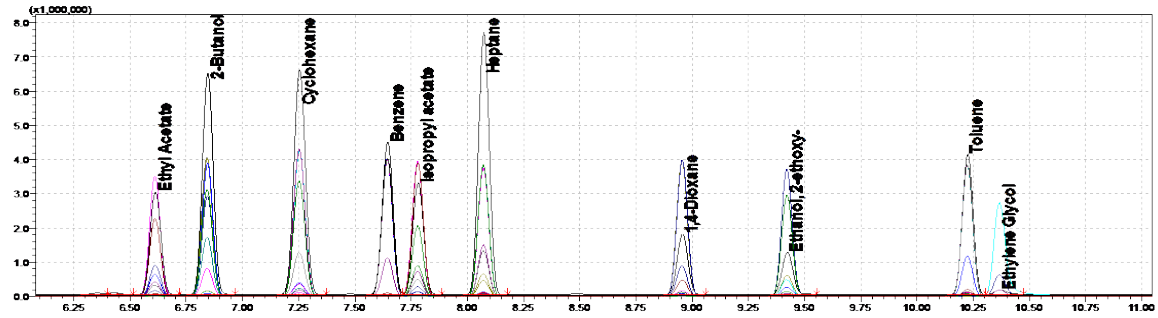
■ Results and Discussion

Measurements were acquired in three different groups within the overall 16-minute SCAN/SIM run displayed in Figure 1.

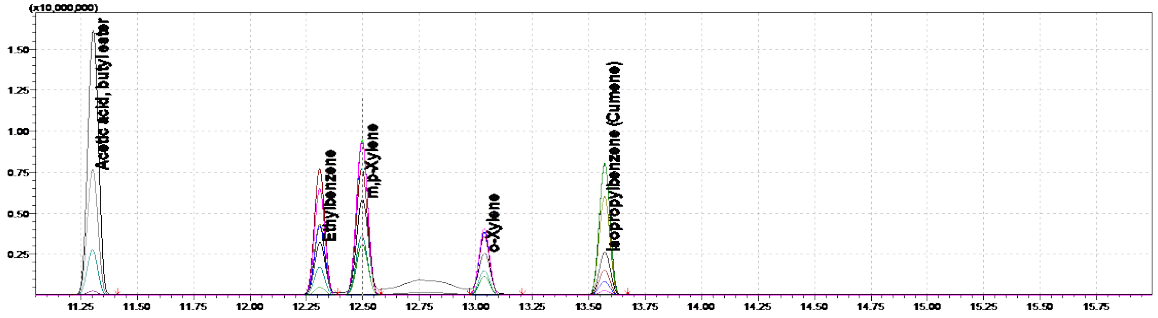
The respective SIM channels used are also plotted in Figure 1 (SCAN data not shown).



Group 1 1-6 min



Group 2 6-11 min



Group 3 11-16 min

Figure 1: Plot of SIM acquisition (1 run, 3 groups) for 35 residual solvents at 150 µg each in the headspace (representing less than 0.1% in a 200 mg sample).

Standards preparation followed a 10-fold serial dilution from 150 µg, using butyl acetate as the dilution solvent.

Specific analytes such as benzene, which has the lowest screening limit in the OR method (2 ppm by weight), were calibrated and determined to have levels well below the screening limit. Figure 2 displays benzene content of approximately 300 ng in the headspace of the vial, which represents 1.5 ppm by weight for a 200 mg sample, with full evaporation assumed.

The calibration range for each analyte was 1.5 ppm to 750 ppm (by weight) and covered by two-fold serial dilutions. A large portion of the analytes demonstrated slight quadratic behavior in this range, most likely attributed to the effects of the chemical environment.

Benzene

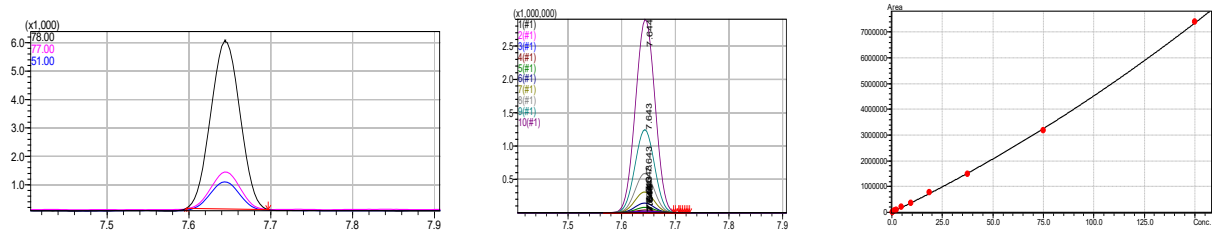


Figure 2: Benzene SIM signal at 300 ng in headspace, calibration peaks, and calibration curve.

Examples of additional analytes can be seen below. Analytes of interest, such as acetonitrile and methanol, are shown in Figure 3 at similar levels in addition to the calibration full range (0.293 µg to 150 µg).

Acetonitrile

Methanol

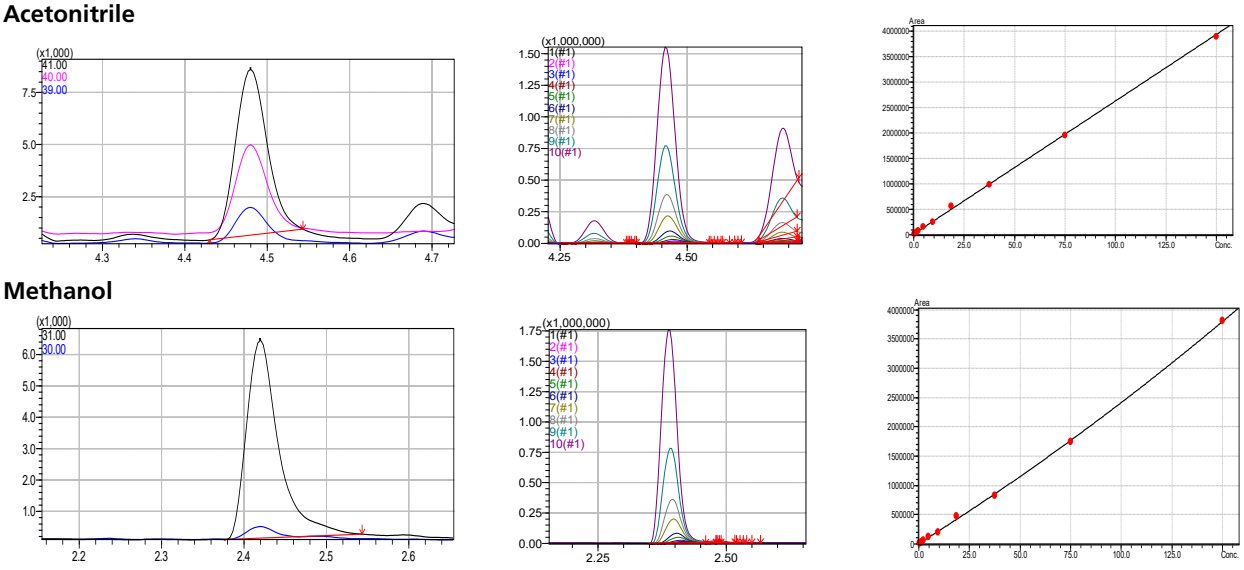


Figure 3: Acetonitrile and methanol SIM signal at 300 ng in headspace, calibration peaks, and calibration curve.

In some sample matrices, ethylene glycol is difficult to determine therefore, it is an analyte of interest. The limit of detection (LOD) achieved with the OR method is 4 µg in 200 mg, which is approximately 30 times better than the screening level. The lowest level of detection is shown in Figure 4.

Ethylene Glycol

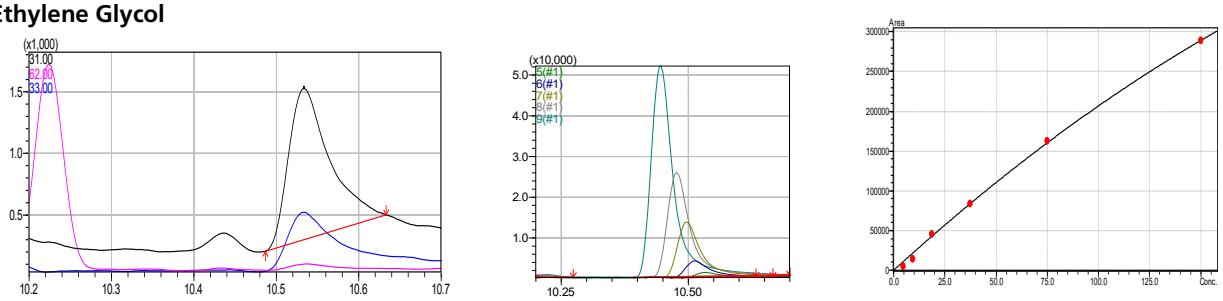


Figure 4: Ethylene glycol SIM signal at 4 µg in headspace, calibration peaks, and calibration curve.

The groups of analytes listed in the OR method, butanes, pentanes, hexanes, and xylenes, are shown in Figures 5, 6, 7, and 8. The screening level shown is approximately 10 µg for all components.

Butane and Isobutane

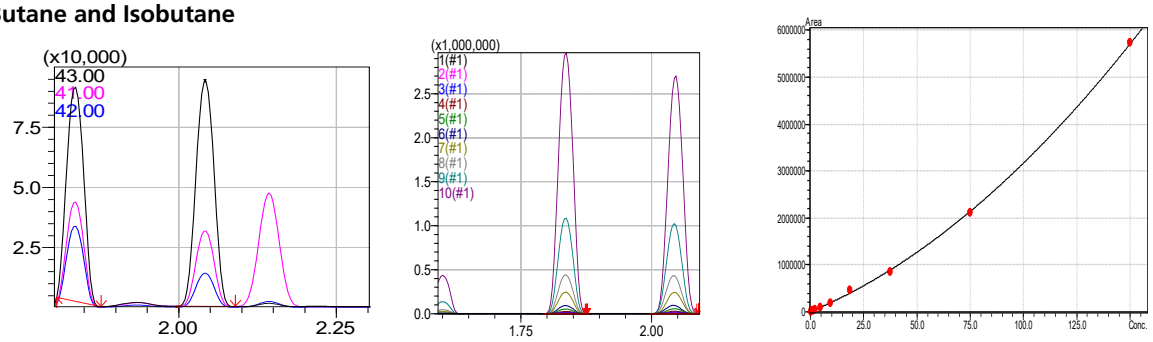
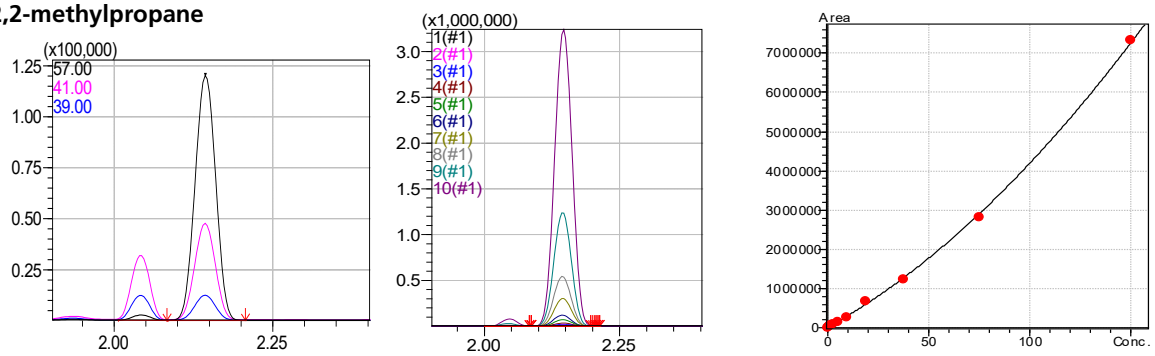
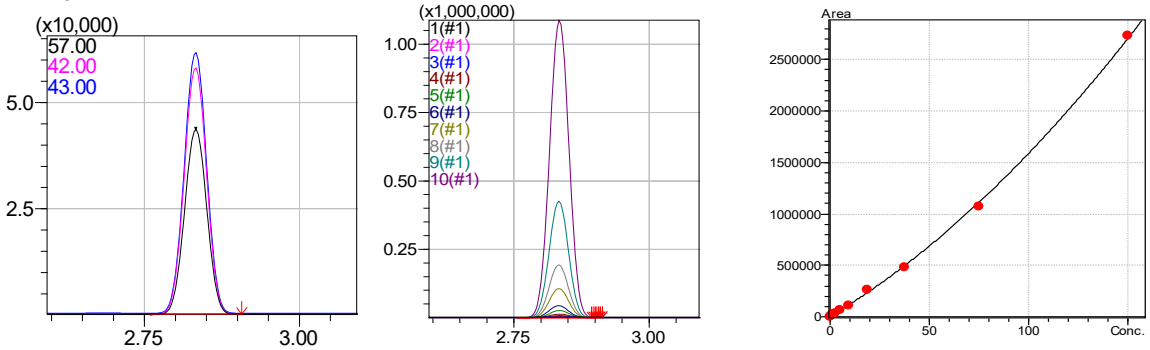


Figure 5: Butane and isobutane SIM signal at 10 µg in headspace, calibration peaks, and calibration curve.

2,2-methylpropane



2-methylbutane



Pentane

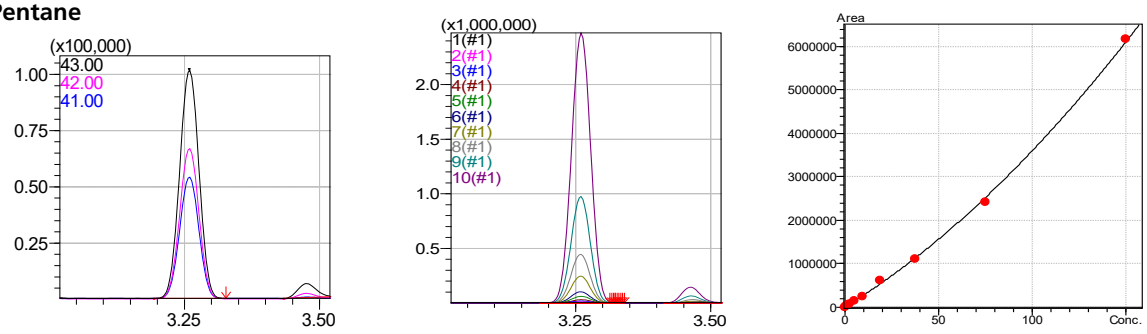
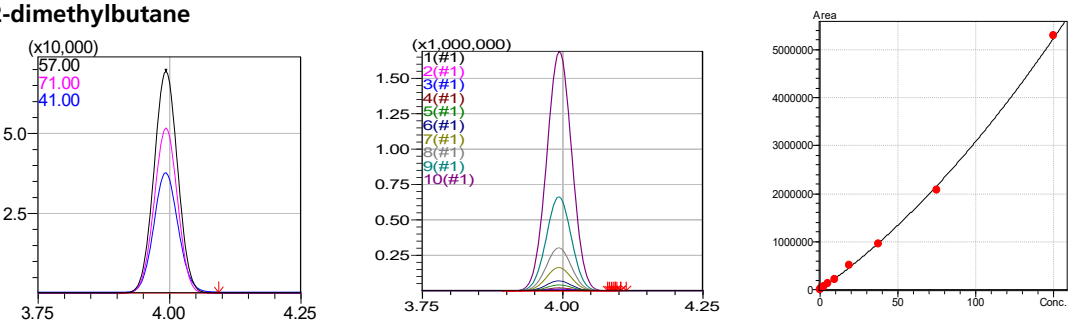
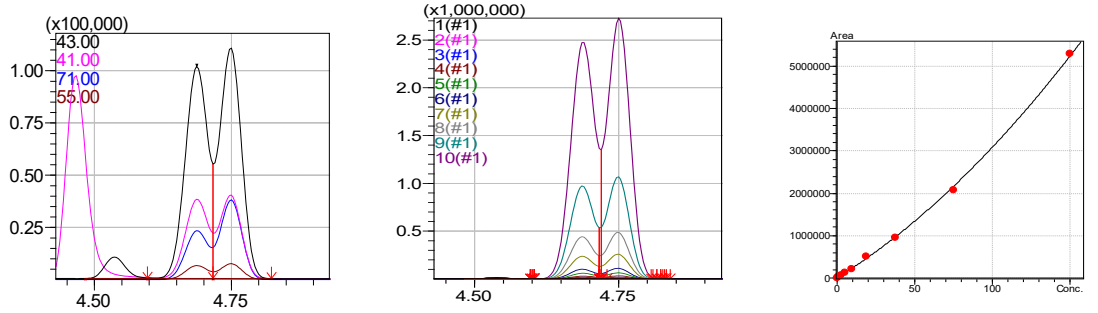


Figure 6: Pentane and isomers SIM signal at 300 ng in headspace, calibration peaks, and calibration curve.

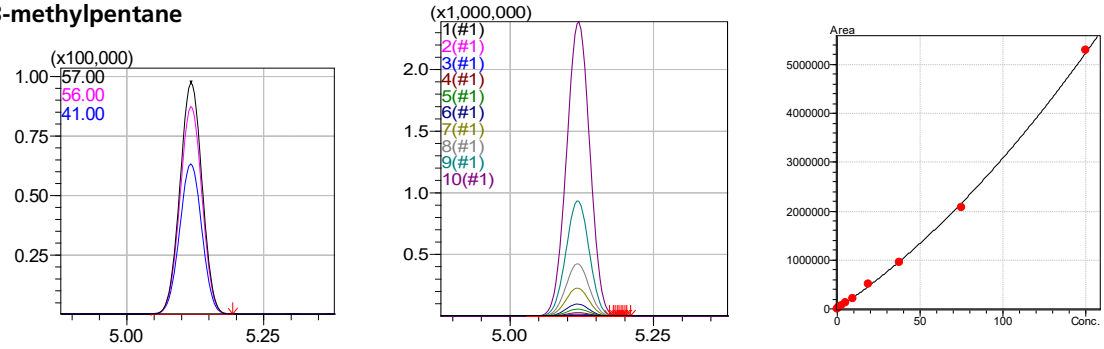
2,2-dimethylbutane



2,3-dimethylbutane and 2-methylpentane



3-methylpentane



Hexane

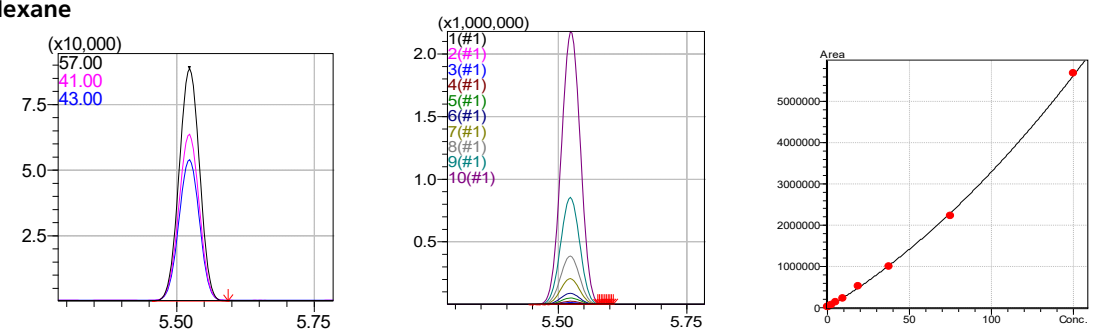
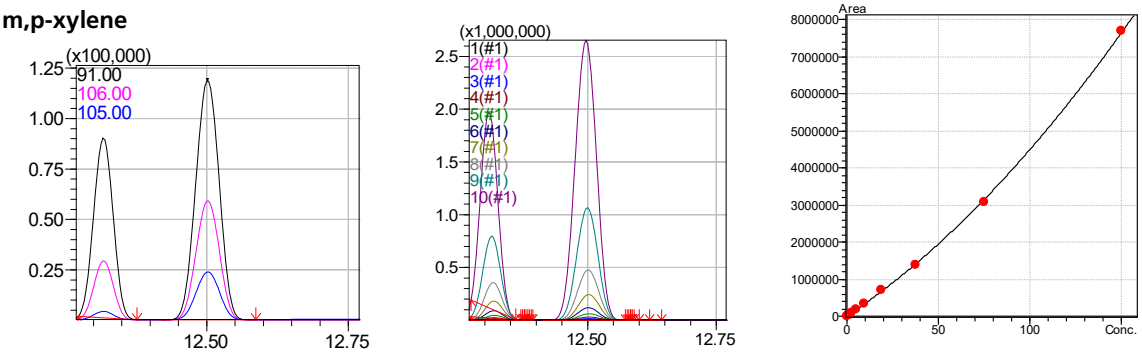
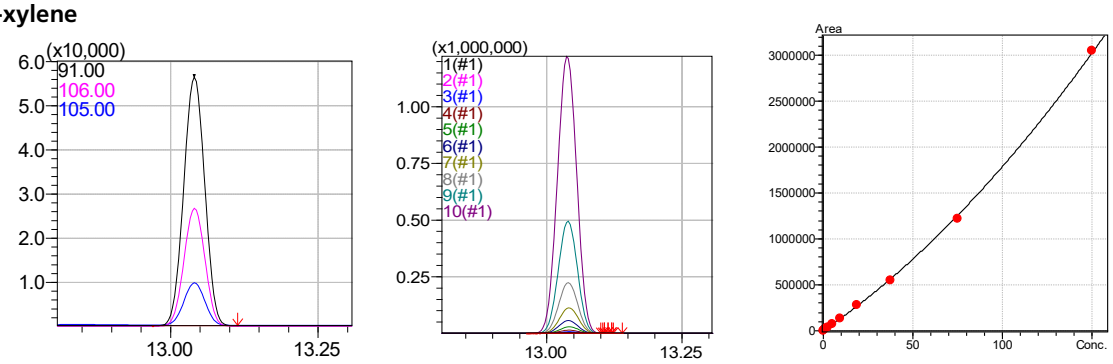


Figure 7: Hexane and isomers SIM signal at 10 µg in headspace, calibration peaks, and calibration curve.

m,p-xylene



o-xylene



Ethylbenzene

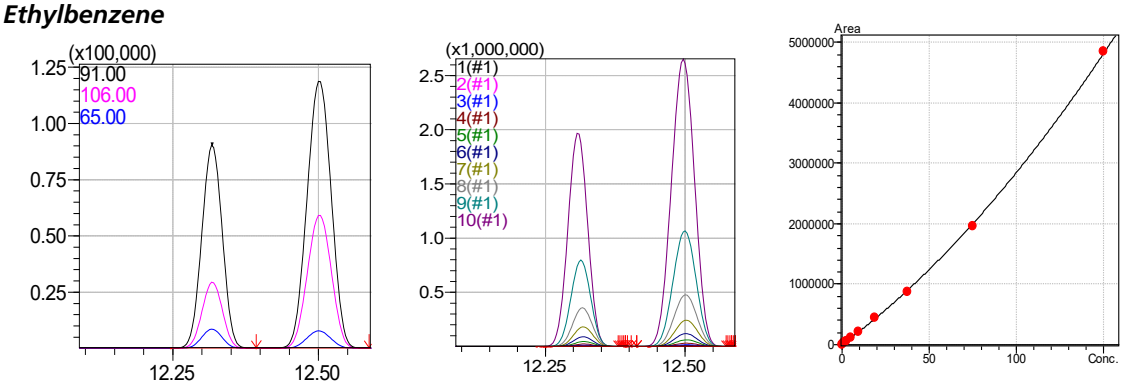


Figure 8: Xylene isomers and ethylbenzene SIM signal at 10 µg in headspace, calibration peaks, and calibration curve.

Table 2 provides a list of required analytes for the determination of residual solvent analysis for the State of Oregon. This includes the screening limit (in micrograms) for a 200 mg sample, in addition to the LOD for low concentration analytes and saturation levels for high concentration analytes.

For example, the screening level for propane in the OR list, 5000 µg/g (ppm by weight), is tabulated as 1000 µg, assuming a 200 mg sample (and similarly for the other analytes).

Table 2: Screening levels for the State of Oregon assuming a 200 mg sample in comparison to performance data of this method using static headspace and GC-MS instrumentation.

Analyte	Screening Level (ug)	LOD by this method (ug)	Saturation Level (ug)
Propane	1000	N/A	2000
Isobutane	1000	N/A	2000
Butane	1000	N/A	2000
2,2-dimethylpropane	1000	N/A	2000
Methanol	600	N/A	2000
Ethylene Oxide	10	0.1	N/A
2-methylbutane	1000	N/A	2000
Pentane	1000	N/A	2000
Ethanol	1000	N/A	2000
Ethyl ether	1000	N/A	2000
2,2-dimethylbutane	58	0.1	N/A
Acetone	1000	N/A	2000
Isopropyl Alcohol	1000	N/A	2000
Acetonitrile	82	0.1	N/A
2,3-dimethylbutane	58	0.1	N/A
Methylene Chloride	120	0.1	N/A
2-methylpentane	58	0.1	N/A
3-methylpentane	58	0.1	N/A
Hexane	58	0.1	N/A
Ethyl Acetate	1000	N/A	2000
2-butanol	1000	N/A	2000
Tetrahydrofuran	144	1	N/A
Cyclohexane	776	0.1	N/A
Benzene	0.4	0.05	N/A
Isopropyl acetate	1000	N/A	2000
Heptane	1000	N/A	2000
1,4-Dioxane	76	0.5	N/A
2-ethoxyethanol	32	0.5	N/A
Toluene	178	0.1	N/A
Ethylene glycol	124	4	N/A
Ethylbenzene	434	0.5	N/A
m,p-Xylene	434	0.5	N/A
o-Xylene	434	0.5	N/A
Isopropylbenzene (cumene)	14	0.5	N/A

■ Conclusion

The Shimadzu GCMS-QP2010 SE with a HS-20 autosampler was used for measuring analytes in the requested ranges. The system was able to measure both low and high concentrations therefore maintaining sensitivity. It was also found that despite high concentrations, the system is not prone to saturations.

The concentration range covered (a factor of 500) can be adapted to better suit both low-level and high-level analytes by focusing on the specific ranges requested for each analyte.

■ Reference

- Oregon Administrative Rule 333-007-0410: Table 4. List of solvents and their action levels

■ Consumables

Rxi®-624Sil MS Column (Terpene and Residual Solvents)	30 m, 0.25 mm ID, 1.40 µm -20 to 300/320 °C	Shimadzu	221-75962-30
Headspace Vials	100 pack - 20 mL	Shimadzu	220-94906-20
Headspace Septum (300C)	Vials, GCMS, HS-10/HS-20 HEAT-RESISTANT SEPTA, 300C MAX, 250/PKG	Shimadzu	220-94906-32
Headspace Caps (300C)	Vials, GCMS, HS-10/HS-20 HEAT-RESISTANT CAPS, 300C MAX, 500/PKG	Shimadzu	220-94906-33
HS-10/HS-20 Vial Rack	HS-20 Vial Rack for 10-mL and 20-mL HS vials	Shimadzu	220-94906-42
0.2mL HS Sample Loop	Deactivated	Shimadzu	225-21889-82

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