Application Note

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Analysis of Phthalates Using the Agilent 5977C GC/MSD with Hydrogen Carrier Gas

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Abstract

An Agilent 8890 GC system coupled with an Agilent 5977C Inert Plus GC/MSD configured with hydrogen carrier gas, and the Agilent Inert Plus Extractor EI source was evaluated for the analysis of 19 phthalates. The system, when used with the method described in this application note, provides excellent peak shape, resolution, and sensitivity. The use of hydrogen carrier and an Agilent J&W HP-5ms column with a 180 µm diameter reduces analysis times by approximately half compared to using helium and a 250 µm column. Calibration curves were linear for 14 of the phthalates, from 1 to 1,000 pg. Bis(2-methoxyethyl) (DMEP) was calibrated from 2.5 to 1,000 pg and required a quadratic fit. Bis(1-butoxyethyl) (DBEP) was calibrated from 1 to 1,000 pg and also required a quadratic fit. Bis(2-ethylhexyl) (DEHP) was linear over the range of 2.5 to 1,000 pg. Diisononyl (DINP) and diisodecyl (DIDP), both mixtures of isomers, were calibrated from 50 to 20,000 pg with a linear fit. Specific attention to the consumables used and their preparation before use is discussed and is important for reaching the lowest calibration levels.

Introduction

Plastics are ubiquitous in the modern world and are used in thousands of applications. To tailor mechanical characteristics of plastics, such as flexibility, transparency, and durability for specific uses, esters of phthalic acid are often added to their formulation. These compounds are not covalently bound to the plastics in which they are mixed, and thus, are easily released into the environment. They are present in a wide range of products including wire insulation, children's toys, packaging, medical devices, pens, and tubing. Many countries now regulate phthalate content in many products. The analytical requirements for phthalate analysis vary depending on the region and products being tested, but GC/MS is usually the preferred measurement technique.

The use of both hydrogen and helium as carrier gas in GC/MS analyses has been demonstrated in previous literature. For example, seven phthalates in polymer materials were successfully analyzed with GC/MS using helium carrier gas and calibrated from 50 to 1,000 ng/mL.[1] The calibration performance for 17 phthalates over the range of 10 to 1,000 ng/mL and for two isomeric mixtures (DINP and DIDP) over the range of 125 to 10,000 ng/mL using helium carrier gas and Agilent JetClean self-cleaning ion source has been detailed.[2] The use of hydrogen carrier gas, the Agilent HydroInert source, and backflushing for analyzing 10 phthalates in electrical cable samples over a calibration range 200 to 5,000 ng/mL has been achieved.[3] Since many laboratories are considering converting from helium to hydrogen carrier gas for GC/MS analyses, it is useful to evaluate the performance of phthalates with hydrogen carrier gas down to low levels (< 10 ng/mL).

This application note focuses on GC/MS in selected ion monitoring (SIM) mode using hydrogen as the GC carrier gas. While helium is generally considered the best carrier gas for GC/MS analysis, its cost and reoccurring shortages have increased demand for applications using hydrogen. When adopting hydrogen for GC/MS analysis, there are several things to consider.

First, hydrogen is a reactive gas and may cause chemical reactions in the inlet, column, and sometimes the mass spectrometer electron ionization (EI) source which can change analysis results. It is important to ensure that there are no chemical reaction problems between analytes and hydrogen at elevated temperatures in the GC/MS.

Second, it is essential to use a reliable source of clean hydrogen gas. Hydrogen generators with a > 99.9999% specification and low individual specs on water and oxygen are often used. Moisture filters are highly recommended for use with hydrogen generators. Chromatographic or research-grade hydrogen cylinders also work well. It is also recommended that anyone working with flammable or explosive gases take a lab safety course covering proper gas handling and use.

Additionally, for GC/MS applications, hardware changes in the gas chromatograph and mass spectrometer may be required when switching to hydrogen. The Agilent EI GC/MS Instrument Helium to Hydrogen Carrier Gas Conversion user guide[4] describes in detail the conversion steps. These steps include the selection of the inlet liner, column, vacuum pump, and EI source. Chromatographic conditions and injection solvent may also have to be adjusted.

One of the advantages observed with hydrogen carrier gas is a reduced need for EI source cleaning. A similar improvement is observed when using Agilent JetClean technology, which uses a low continuous flow of hydrogen into the source during the analysis.[3,5,6,7] A second advantage often observed with hydrogen carrier gas is its ability to decrease the analysis time while maintaining chromatographic resolution.

Phthalates are relatively durable compounds and can therefore be analyzed with hydrogen carrier gas when using the optimized method and following the recommendations described in this application note.

Experimental

The system used in these experiments was configured to minimize the potential problems with hydrogen carrier gas in phthalate analysis. The important parameters used were:

Hydrogen gas: In-house hydrogen with 99.9999% purity specification and low individual specifications on water and oxygen was used as a carrier gas.

Pulsed splitless injection: Used to maximize transfer of the phthalates into the column.

GC column: A J&W HP-5ms Ultra Inert column (20 m × 0.18 mm id, 0.18 µm, part number 19091S-577UI) was used to maintain optimal gas flow and inlet pressure.

Inlet liner: The Agilent Ultra Inert mid-frit liner (part number 5190-5105) was found to give good peak shape and inertness.

MSD EI source: When converting to hydrogen carrier gas, the choice of EI source hardware is an important consideration.[4] For analytes that are subject to hydrogenation, the HydroInert source is strongly recommended because it is constructed of a material that greatly reduces the catalytic activity with hydrogen often seen with the metals typically used in EI sources.[4,8,9]

If the method is used to identify unknown compounds by library searching scan data against, for example, the NIST library, the HydroInert source would again be the source of choice. However, a large percentage of compounds analyzed by GC/MS do not exhibit reactions with hydrogen and can be analyzed using the standard Inert Plus Extractor EI source fitted with the optional 6 or 9 mm extractor lens.[4] For labs that are evaluating hydrogen for the first time, this offers a cost-effective option. If the analysis involves a manageable number of target compounds, it may be worth evaluating their performance with the standard Inert Plus Extractor EI source with the optional 9 mm lens.

In this application there are 19 target phthalates. Experimental data comparing spectral fidelity (based on NIST library match scores) and quantitative performance showed that in this case, the standard Inert Plus Extractor EI source with the 9 mm lens gave results comparable to the HydroInert source and was thus chosen for the method.

Figure 1 shows the system configuration used in this experiment. The instrument operating parameters are listed in Tables 1 and 2.

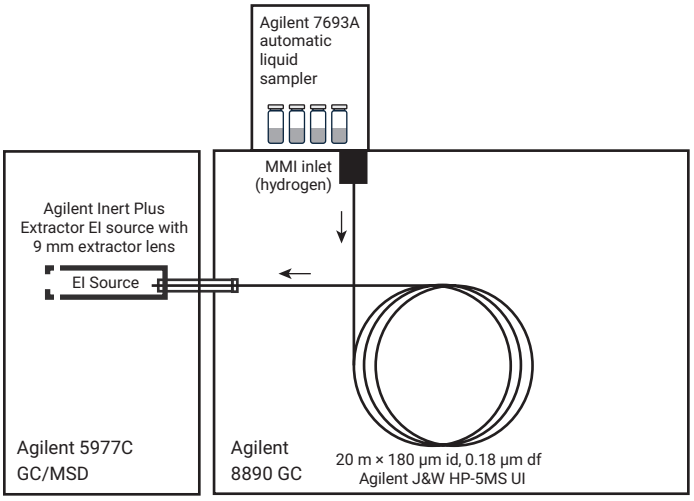

Figure 1. System configuration.

Table 1. GC and MS conditions for phthalate analysis.

Method Parameters	
GC	Agilent 8890 GC with Agilent 7693A automatic liquid sampler and tray
Inlet	Multimode inlet (MMI)
Mode	Pulsed splitless
Injection Pulse Pressure	25 psi until 0.90 min
Purge Flow to Split Vent	50 mL/min at 1.0 min
Injection Volume	1.0 µL
Syringe	10 µL, PTFE tip plunger, dual taper needle (G4513-80203)
Septum	11 mm Advanced Green (p/n 8010-0208)
Inlet Temperature	280 °C
Inlet Liner	Agilent universal Ultra Inert mid-frit liner (p/n 5190-5105)
Column	Agilent J&W HP-5MS UI 20 m × 0.18 mm id, 0.18 µm film (p/n 19091S-577UI)
Column Temperature Program (°C)	60 °C (1.5 min hold), 50 °C/min to 220 °C, (no hold), 12.5 °C/min to 320 °C (0.3 min hold)
Carrier Gas and Flow Rate	Hydrogen, 0.9 mL/min constant flow
MSD	Agilent 5977C Inert Plus GC/MSD
Source	Agilent Inert Plus Extractor EI source with optional 9 mm extractor lens (G3870-20449)
Transfer Line Temperature	280 °C
Ion Source Temperature	300 °C
Quadrupole Temperature	150 °C
EM voltage Gain Mode	Gain, 1.0
Mode	SIM
Tune	ETUNE.U

Table 2. Names, abbreviations, CAS numbers, retention times, and target and qualifiers ions of phthalates studied.

Retention Time	Name	Abbreviation	CAS Number	Target *m/z*	Q1 *m/z*	Q2 *m/z*	Q3 *m/z*
4.177	Dimethyl phthalate	DMP	131-11-3	163	77	194	133
4.530	Diethyl phthalate	DEP	84-66-2	149	177	105	222
4.896	Diallyl phthalate	DAP	131-17-9	149	41	132	189
5.206	1,2-Benzenedicarboxylic acid, bis(2-methylpropyl) ester	DIBP	84-69-5	149	223	167	104
5.480	Dibutyl phthalate	DBP	84-74-2	149	223	205	104
5.602	Bis(2-methoxyethyl) phthalate	DMEP	117-82-8	149	176	104	59
5.876	1,2-Benzenedicarboxylic acid, bis(4-methylpentyl) ester	BMPP	146-50-9	149	251	167	85
5.993	1,2-Benzenedicarboxylic acid, bis(2-ethoxyethyl) ester	DEEP	605-54-9	149	72	104	193
6.128	Diamyl phthalate	DPP	131-18-0	149	237	219	104
6.915	1,2-Benzenedicarboxylic acid, dihexyl ester	DHXP	84-75-3	149	104	233	251
6.971	Benzyl butyl phthalate	BBP	85-68-7	149	91	104	206
7.515	Bis(2-butoxyethyl) phthalate	DBEP	117-83-9	149	193	101	85
7.767	Dicyclohexyl phthalate	DCHP	84-61-7	149	167	104	249
7.858	Bis(2-ethylhexyl) phthalate	DEHP	117-81-7	149	167	113	104
8.777	Di-n-octyl phthalate	DNOP	117-84-0	149	279	104	261
9.292	Bis(2-propylheptyl) phthalate	DPHP	53306-54-0	149	55	167	307
9.779	1,2-Benzenedicarboxylic acid, dinonyl ester	DNP	84-76-4	149	293	275	150
8–10.3	Diisononyl phthalate	DINP	28553-12-0	293	149	167	
8.5–10.7	Diisodecyl phthalate	DIDP	26761-40-0	307	149	167	

Pulsed splitless injections are used to maximize the transfer of the phthalates into the column and to minimize unwanted interactions in the hot inlet. The Ultra Inert mid-frit liner works well for this application. The mid-frit transfers heat to the injected liquid sample and vaporizes it before it enters the column. Note that while the multimode inlet (MMI) temperature-programmable inlet was used, it was operated isothermal at 280 °C. Therefore, the split/splitless inlet would also be applicable.

Phthalate calibration standards were prepared in two separate calibration sets. The first set contained 17 of the 19 phthalates and the second set contained DINP and DIDP phthalate isomers.

A 15-component custom phthalates mix was purchased from Ultra (now Agilent). The concentration of each component was 1,000 µg/mL in isooctane. Diallyl phthalate (DAP), DINP, and DIDP were purchased in pure form from Agilent. Pure bis(2-propylheptyl) phthalate (DPHP) was purchased from Millipore Sigma.

Calibration standards were prepared for 17 phthalates at 11 concentration levels: 1, 2.5, 5, 10, 20, 50, 100, 250, 500, 800, and 1,000 ng/mL in isooctane. Calibration standards for the DIDP and DINP isomers were dissolved in isooctane at 11 concentration levels: 50, 100, 250, 500, 750, 1,000, 2,500, 5,000, 7,500, 10,000, and 20,000 ng/mL. See Table 2 and Figure 2 for compound identifications. All quantitative measurements were performed with Agilent MassHunter Quantitative Analysis software, version 11.1.

Results and discussion

Figure 2 shows the SIM chromatograms of the 50 ng/mL calibration standard at *m/z* 163 for DMP and *m/z* 149 for the rest of the 17 calibration components. With the parameters used here, the peak shapes are excellent. Figure 3 shows the SIM chromatograms for the 1,000 ng/mL DINP and DIDP phthalate standard. Due to the combination of hydrogen carrier gas and a smaller diameter column, the run time with the current method (14.5 minutes) is approximately half of that with helium and a 250 µm column.[2]

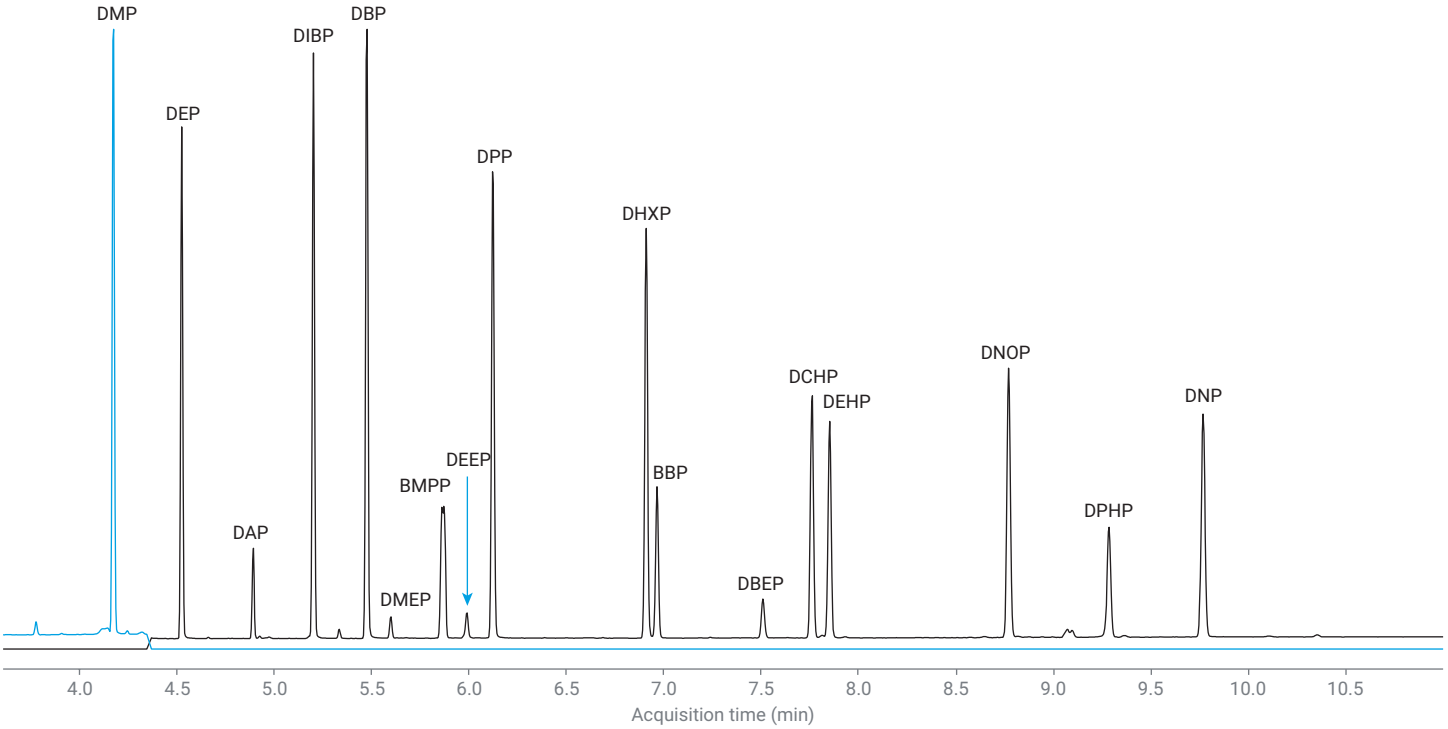

Figure 2. A 50 ng/mL phthalate standard. Blue trace: SIM *m/z* 163 quantifier for DMP. Black trace: SIM *m/z* 149 quantifier for all others.

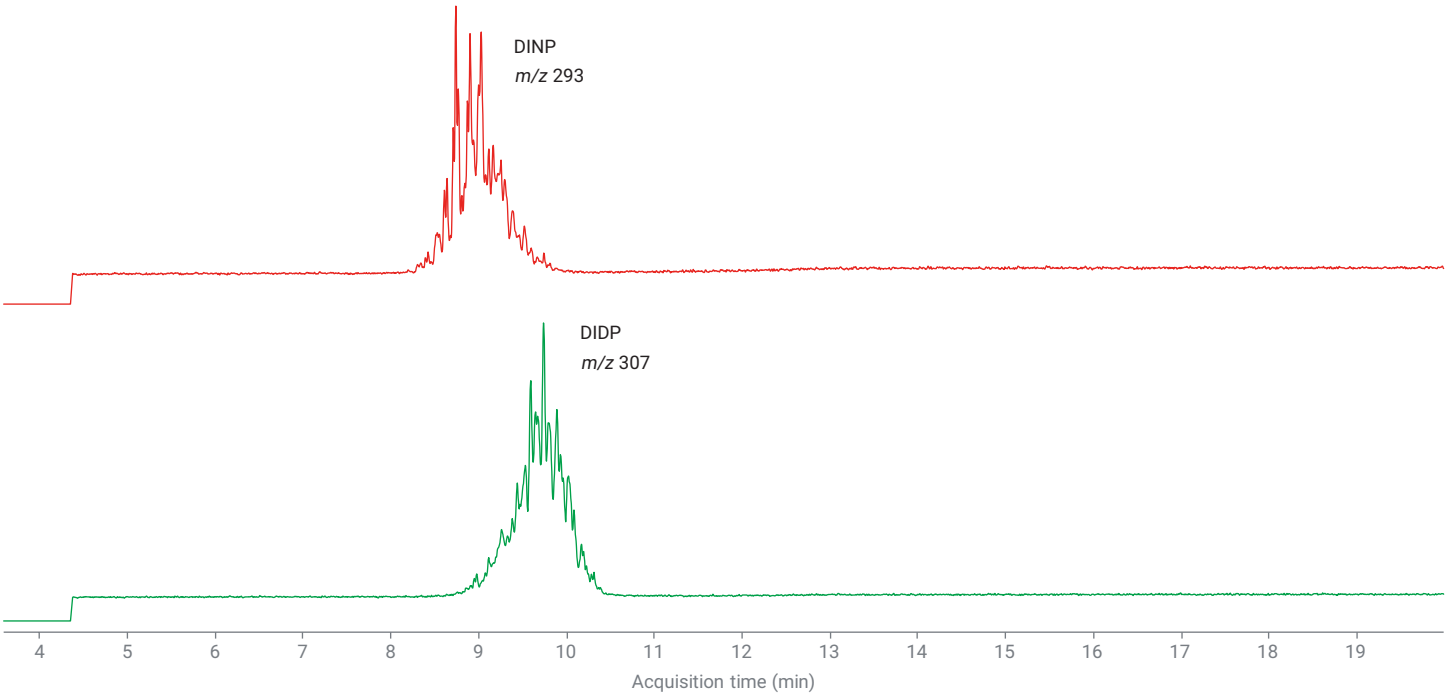

Figure 3. The 1,000 ng/mL DINP and DIDP phthalate standard.

Interferences and contamination

The sensitivity of the GC/MS method employed here is sufficient to see the 17 individual phthalates at low pg levels (ng/mL). However, interferences and contamination initially limited calibration at the lowest concentrations. The interferences were identified as silicone peaks, and the contamination resulted from low levels of common phthalates found in the consumables and glassware used.

Figure 4 shows an example of the problems encountered when first running isooctane solvent blanks.

The blue trace that ends at 4.3 minutes is the SIM quantifier ion for DMP. Although there are a few peaks present in the blank, they are resolved from DMP and do not interfere.

In the black SIM *m/z* 149 trace, multiple problems are evident. Significant responses for 1,2-benzenedicarboxylic acid (DIBP), dibutyl phthalate (DBP), and diethyl phthalate (DEP) are present, as are smaller ones for DEHP and DPHP. In addition, a series of peaks identified using scan data as siloxanes (labeled Si) are also observed. The DPHP peak is small and is obscured by the broadened siloxane ghost peak from a previous injection.

Aliquots of approximately 75 µL of each calibration standard or blank isooctane were placed in autosampler vials with a 400 µL silanized flat bottom glass insert (part number 5183-2086). It was found that a significant portion of the phthalate contaminants in blanks was removed by baking the vials, vial inserts, vial septa, and the disposable Pasteur pipettes (used for aliquoting) overnight at 130 °C in a glassware oven.

However, the interfering siloxanes were still evident. The vial septa initially used were of the common sandwich type consisting of 1 mm of silicone rubber with a layer of PTFE on the bottom side facing the sample liquid (part number 5185-5820). It was determined that each time the autosampler syringe needle pierced the septum, a microscopic particle of silicone rubber was deposited into the sample. The solvent then leached the siloxanes from the particles.

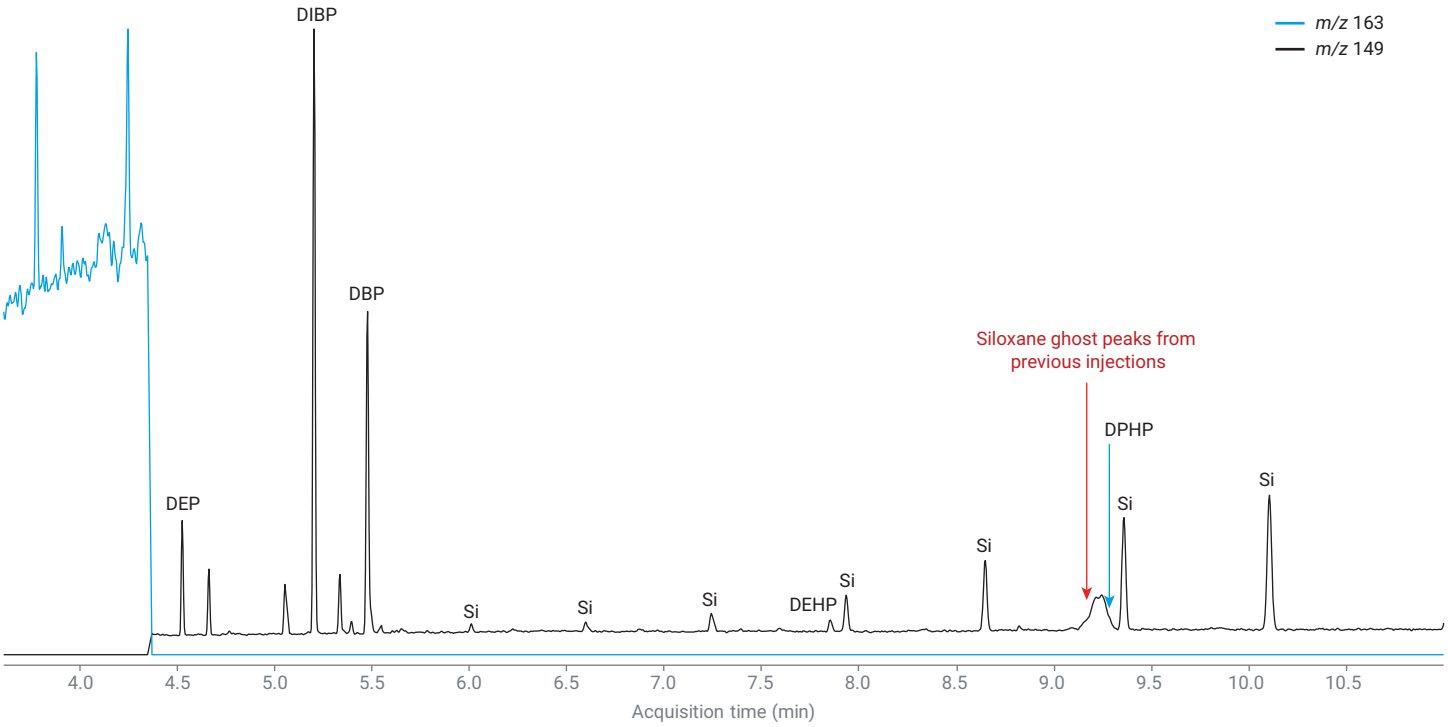

Figure 4. Example of interferences and contaminants initially observed in isooctane solvent blanks. Blue trace: SIM *m/z* 163 quantifier for DMP. Black trace: SIM *m/z* 149 quantifier for all others.

Figure 5 shows two sequential blank solvent runs made from the same vial. Note that the injection parameters are such that the needle only pierces the septum once per injection (with no sample washes), using four syringe pumps instead. By the second injection, prominent siloxane responses were observed. The oven temperature ramp was extended to 320 °C and the final hold was extended to 7.3 minutes to determine how far out the siloxane peaks eluted. As shown in Figure 5, they continued out to at least 20 minutes. This is why the broadened ghost peaks appeared when the GC run ended at 13 minutes.

While Figure 5 shows only very small siloxane responses in the first run, their response is variable and can sometimes interfere with the lowest calibration standards. Therefore, two alternative vial caps were evaluated. Figure 6 shows the polyurethane snap caps and the PTFE crimp caps tested.

Both types of caps exhibited no siloxane peaks and very low levels of phthalate contamination. The polyurethane snap caps are elastomeric and reseal after a needle puncture, allowing multiple injections from a sample. They do, however, have solvent compatibility limitations. For example, while they performed well with the isooctane solvent, they swelled to the point of unsealing with dichloromethane.

Figure 6. Alternative Agilent vials and caps tested for reducing siloxane interferences. (A) polyurethane caps and snap cap vials. (B) Aluminum/PTFE crimp caps and crimp cap vials.

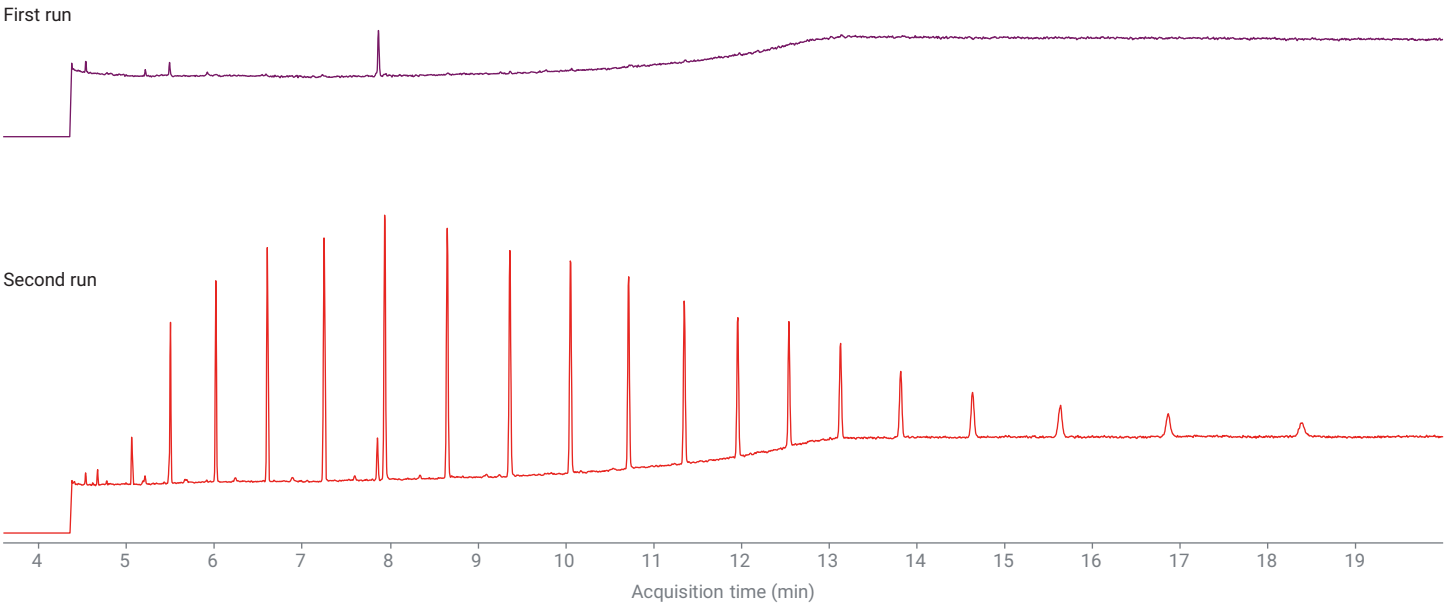

Figure 5. Sequential isooctane solvent blank injections showing siloxane interferences from the vial septa at SIM *m/z* 149.

The PTFE crimp caps also performed well. Since PTFE has very little elasticity, the caps do not reseal after a needle puncture. It is best to use one injection per vial. Repeat injections, if necessary, should be done immediately to reduce problems with evaporation. One advantage of the PTFE crimp caps is that they can be baked overnight in the glassware oven at 130 °C with the other consumables. Note that the PTFE crimp caps are not recommended for long term sample storage as they do not seal as completely due to their relative inelasticity.

Another possible source of phthalate (and other) contamination is the needle support insert (G4513-40525) in the Agilent 7693A automatic liquid sampler, shown in Figure 7. Over time, the support can become contaminated with residue from highly concentrated standards and/or high matrix samples. The support can be cleaned by placing it in a vial with roughly 20 mL of methanol, vortexing, and letting it soak overnight. After soaking, it should be thoroughly air dried before reinstallation. Note that the needle support is a consumable, and it should be replaced at least yearly, and possibly more often with heavy use. In this work, a new needle support was washed as described previously, and installed.

Figure 8 shows the SIM *m/z* 149 chromatograms of the 1 ng/mL (1 pg) calibration standard and blank using the baked consumables, polyurethane caps, and new washed needle support. Note that the scale is the same for both chromatograms, but the blank has been offset for clarity. While there are still some small amounts of contamination evident, they are much lower and should permit calibration down to low ppb concentrations. The use of the PTFE crimp caps gave similar results. Figure 9 shows the SIM *m/z* 163 chromatograms from the same runs, showing that the blank level of DMP is also very low.

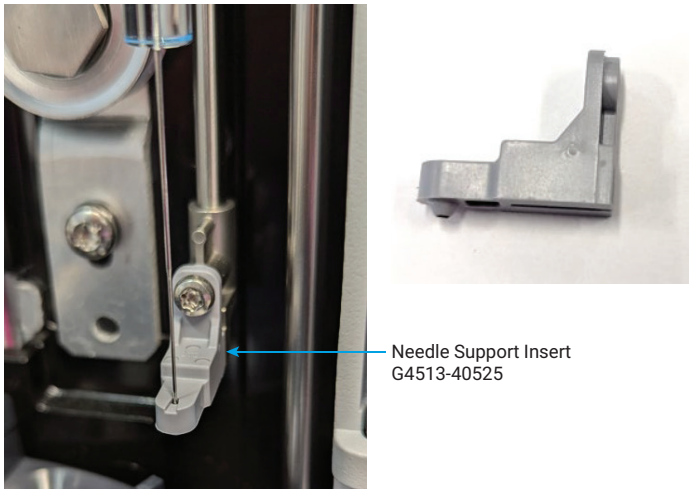

Figure 7. Autosampler needle support insert in the Agilent 7693A automatic liquid sampler.

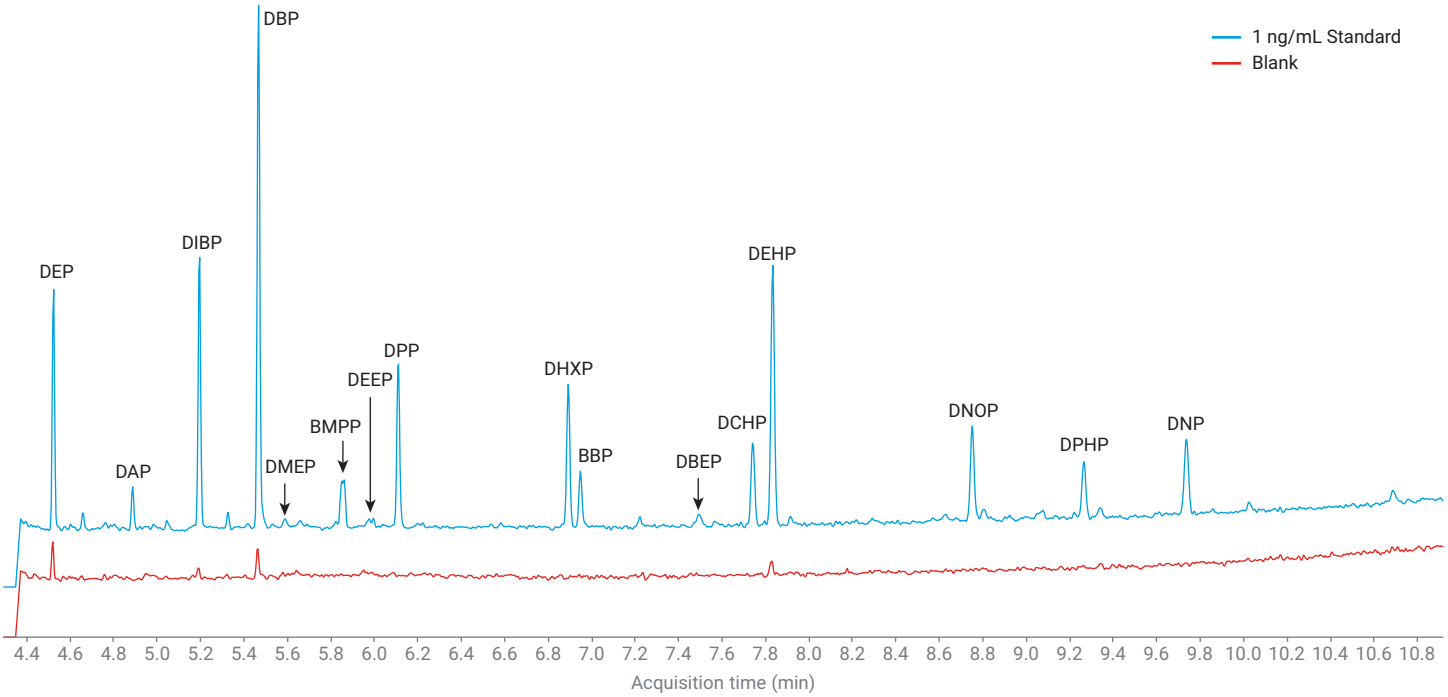

Figure 8. SIM *m/z* 149 chromatograms of 1 ng/mL calibration standard and blank using the baked consumables, polyurethane caps, and new washed needle support.

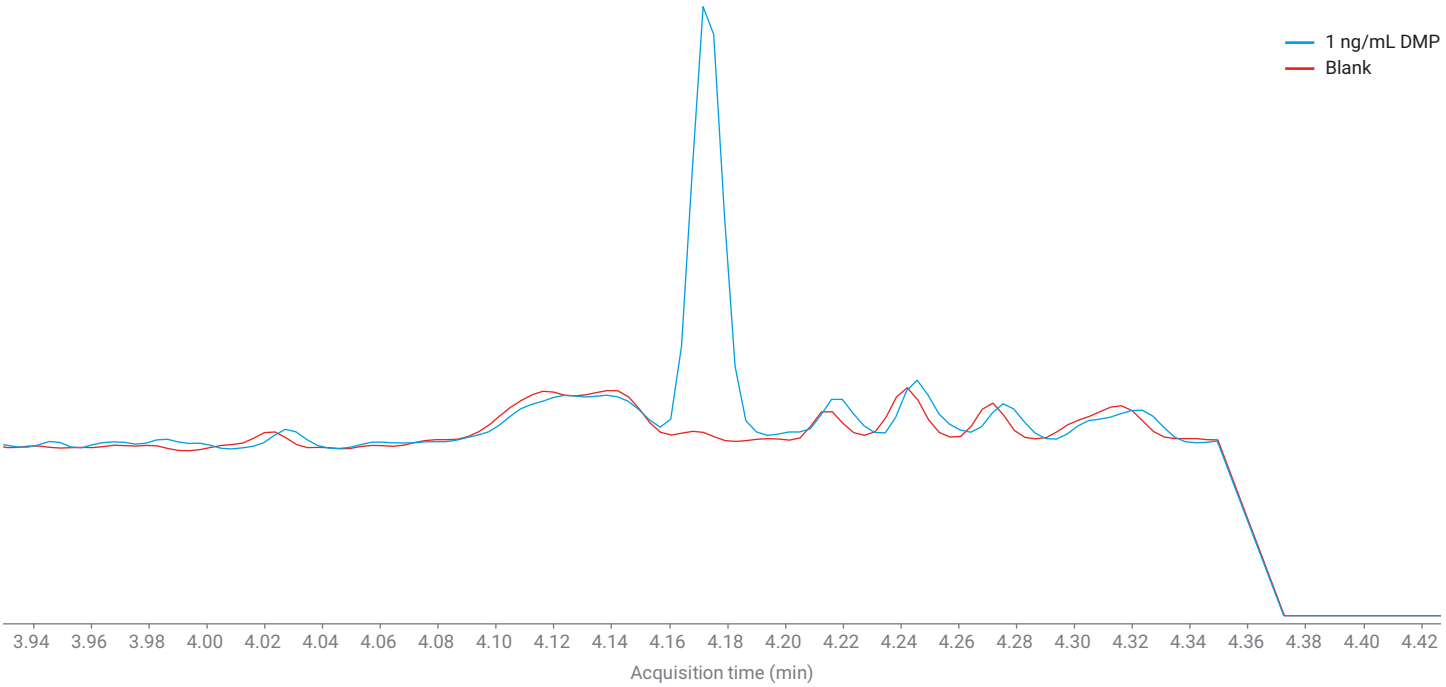

Figure 9. SIM 163 chromatogram (DMP) of 1 ng/mL calibration standard and blank using the baked consumables, polyurethane caps, and new washed needle support.

Initial calibration

Calibration curves were linear for 14 of the individual phthalates from 1 to 1,000 pg. DMEP was calibrated from 2.5 to 1,000 pg and required a quadratic fit. DBEP was calibrated from 1 to 1,000 pg and also required a quadratic fit. DEHP was linear over the range of 2.5 to 1,000 pg. Table 3 and Figures 10 and 11 show the calibration results of the system with 11 levels from 1 to 1,000 pg for 17 of the phthalates and the separate calibration of DINP and DIDP from 50 to 20,000 pg.

If necessary, the relative standard error (RSE) value was used to guide selection of a quadratic fit and/or removal of the lowest calibration points to achieve an RSE value of < 20%.

Instrument detection limits

An instrument detection limit (IDL) study was performed after completion of the initial calibration. Eight trials were performed with the 1 pg calibration standard for the 17 individual phthalates. The calculated IDLs were obtained by applying Equation 1. For compounds with lower signal-to-noise ratios (DMEP and DEEP), eight trials were performed at the concentration of 2.5 pg. Eight trials were performed with the 50 pg calibration standard for DINP and DIDP. Table 3 lists the calculated IDLs.

Equation 1. Formula for IDL calculations.

$$IDL = s \times t(n - 1, 1 - \alpha = 99) = s \times 2.998$$

Where:

$t(n - 1, 1 - \alpha)$ = t value for the 99% confidence level with n – 1 degrees of freedom

n = number of trials (eight)

s = standard deviation of the eight trials

Table 3. Results for 11 level SIM mode calibration over a range of 1 to 1,000 pg.

Compound Method									
Retention Time	Name	CF	CF Limit Low	CF Limit High	CF Weight	RSE	CF R2	Conc. IDL	IDL (ppb)
4.175	DMP	Linear	1	1,000	1/x	9.5	1.000	1	0.20
4.524	DEP	Linear	1	1,000	1/x	9.9	0.999	1	0.21
4.892	DAP	Linear	1	1,000	1/x	11.6	0.999	1	0.23
5.200	DIBP	Linear	1	1,000	1/x	7.3	0.999	1	0.60
5.471	DBP	Linear	1	1,000	1/x	5.4	1.000	1	0.60
5.594	DMEP	Quadratic	2.5	1,000	1/x	14.1	0.999	2.5	0.40
5.865	BMPP	Linear	1	1,000	1/x	7.7	0.999	1	0.17
5.985	DEEP	Linear	1	1,000	1/x	14.9	0.998	2.5	0.56
6.119	DPP	Linear	1	1,000	1/x	10	0.999	1	0.16
6.899	DHXP	Linear	1	1,000	1/x	11.1	0.999	1	0.19
6.955	BBP	Linear	1	1,000	1/x	11.3	0.999	1	0.18
7.498	DBEP	Quadratic	1	1,000	1/x	14.3	0.999	1	0.73
7.751	DCHP	Linear	1	1,000	1/x	11.7	0.999	1	0.26
7.841	DEHP	Linear	2.5	1,000	1/x	9.6	0.999	1	0.61
8.758	DNOP	Linear	1	1,000	1/x	11.3	0.999	1	0.27
9.274	DPHP	Linear	1	1,000	1/x	10.1	0.999	1	0.30
9.745	DNP	Linear	1	1,000	1/x	11.8	0.999	1	0.31
8.754	DINP	Linear	50	20,000	1/x	11.3	0.998	50	7.08
9.762	DIDP	Linear	50	20,000	1/x	11.7	0.998	50	7.13

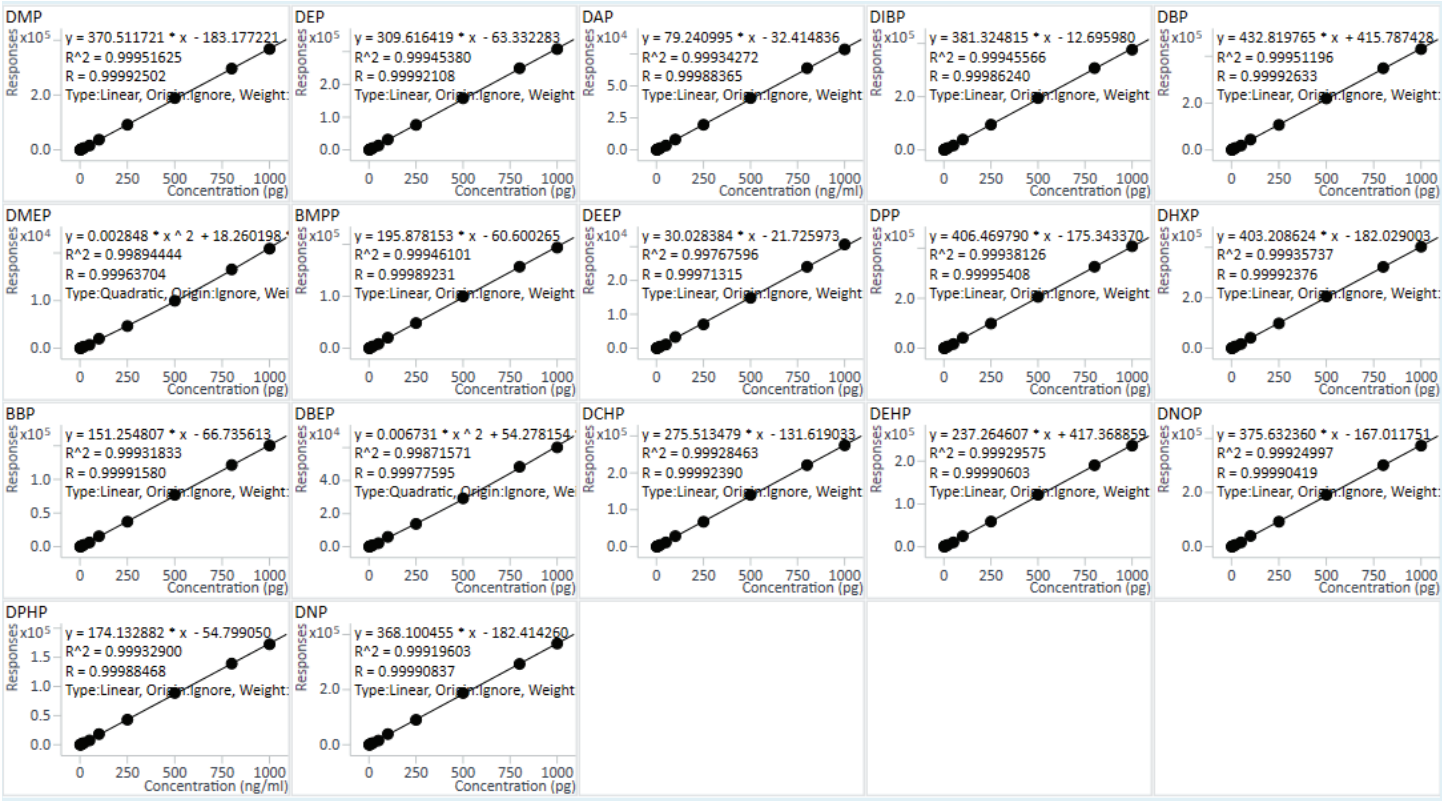

Figure 10. Calibration plots for 11 level SIM mode calibration over a range of 1 to 1,000 pg for the 17 individual phthalates.

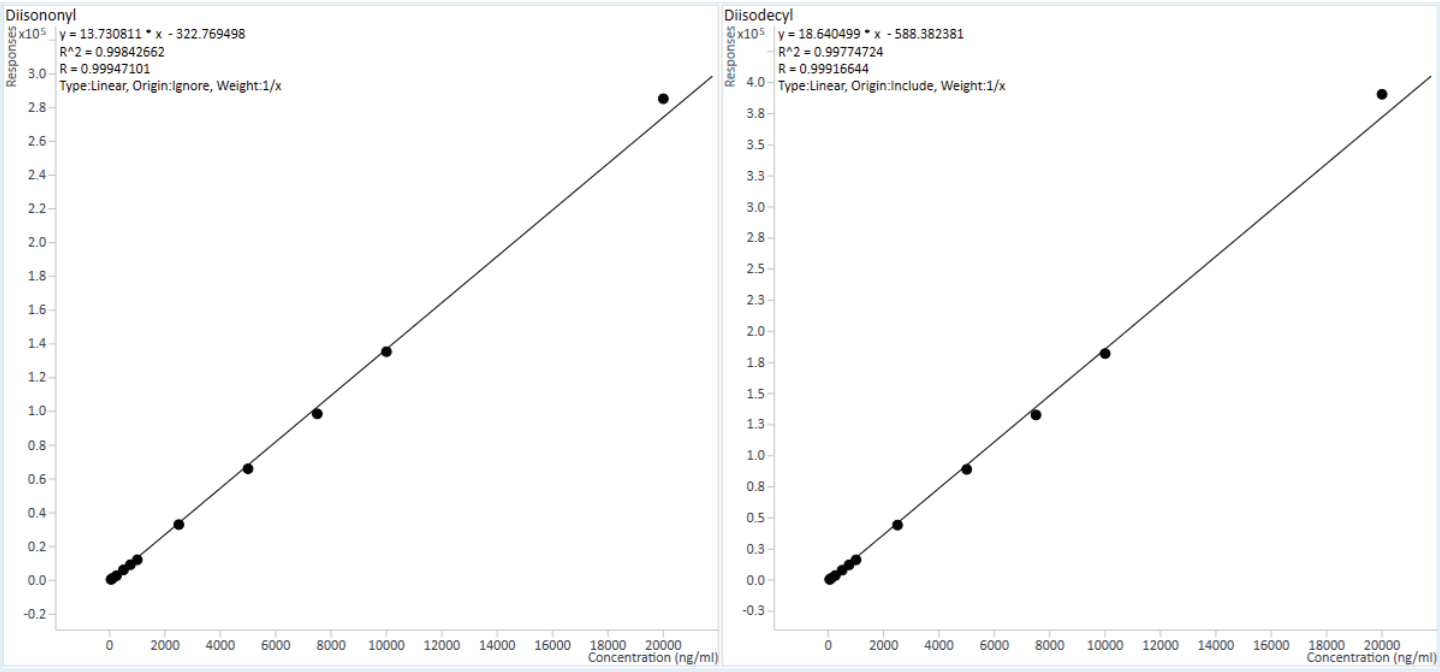

Figure 11. Calibration plots for 11 level SIM mode calibration over a range of 50 to 20,000 pg for DINP and DIDP.

Conclusion

The Agilent 5977C GC/MSD and 8890 GC, when used with the method described in this application note, provide excellent peak shape, resolution, and sensitivity. The combination of hydrogen carrier and the Agilent J&W HP-5ms 180 µm diameter column allowed for reduced analysis times relative to helium. Calibration curves were linear for 14 of the phthalates from 1 to 1,000 pg. DMEP and DBEP required quadratic curve fits, and DMEP and DEHP were calibrated from 2.5 to 1,000 pg. DINP and DIDP were calibrated from 50 to 20,000 pg with a linear fit. Specific attention to the consumables used and their preparation before use is important for reaching the lowest calibration levels.

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