Application Note

Chemicals

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Development of GC/TQ Methods for the Analysis of Hazardous Chemicals

Agilent MassHunter Optimizer enables rapid development of MRM data acquisition methods

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Abstract

The European Registration, Evaluation, Authorization, and Restriction of Chemicals (REACH) Regulations for the control of hazardous chemical substances include 219 Substances of Very High Concern (SVHCs) in the candidate list. When the candidate list is updated every six months to include new compounds, labs must revisit their analytical methods and develop multiple reaction monitoring (MRM) transitions. This application note describes how the Agilent MassHunter Optimizer software for GC Triple Quad (GC/TQ) can help generate MRM transitions for newly added compounds using an Agilent 8890 GC coupled to an Agilent 7000D GC/TQ system. The time, effort, and expertise required to set up methods and analyze the resulting data is decreased dramatically using Optimizer. After optimization of MRMs, the acquisition method can be saved as a time-segment MRM method, a dynamic MRM (dMRM) method, or exported in the form of a database. The MRMs that were developed in this study were used to create a dMRM method for 170 compounds. Linearity was plotted for a range of concentrations from 0.1 to 10 mg/L and the method was evaluated by analyzing polymer samples.

Introduction

REACH is a European Union regulation (EC No. 1907/2006) that affects many different industries throughout the world.[1] REACH is often described as one of the most complex and stringent set of regulations for the control of chemical substances. The candidate list of SVHCs is updated frequently to include new chemicals of concern. Since its inception, the SVHC list has been updated several times and currently includes 219 substances. SVHCs can be introduced into consumer products from raw materials or during the manufacturing process. To comply with the regulations, manufacturers and importers are required to test and screen their products for SVHCs.

Like multiresidue pesticide analysis, all compounds cannot be analyzed using a single technique. However, several SVHCs can be analyzed using gas chromatography with mass spectrometric detection (GC/MS). According to the "Compendium of analytical methods recommended by the forum to check compliance with REACH annex XVII restrictions", GC/MS is a preferred technique for many of the analytes.[2]

A frequent challenge faced by REACH-testing labs is the number of compounds to be determined in different products, that is often further complicated due to interfering compounds. Multiple MRM transitions may help to avoid the interference by using alternative MRM transitions during data acquisition. The development of GC/TQ MRM transitions is a challenging and time-consuming multistep process that often becomes more complicated due to analyte coelution and matrix interferences. MassHunter Optimizer for GC/TQ enables end-to-end automated optimization of MRM transitions and drastically decreases the time required for method development. When MRM data are collected in dMRM mode, the requirement to set up complicated time segment-based methods can be eliminated. Compared to time segment MRM methods, dMRM methods can achieve similar sensitivity, linear dynamic range, and quantitative accuracy, with better precision.

In this application note, a dynamic MRM data acquisition method was developed for 170 compounds belonging to different chemical classes. The optimized MRMs could easily be saved in the format of a dMRM-based acquisition method, ready to be used for the analysis of real samples. Initially, the data acquisition MRM method was developed using a conventional approach and included 100 compounds. In this work, the MassHunter Optimizer for GC/TQ was used to develop MRM transitions for 70 more compounds, which were added to the existing method.

Experimental

Sample preparation

Two fortified polymer samples for multiple groups of analytes and one fortified polymer sample for phthalates and alkylphenol were analyzed using the GC-TQ method developed in this study. The samples were cut into pieces (2 cm × 2 cm). The extraction solvent consisted of a mixture of hexane:acetone (1:1). A portion of 0.5 g sample was extracted with 5 mL of extraction solvent mixture at 50 °C for 1 hour. A portion of 1 µL of the sample extract was injected into the GC/TQ. The compounds in the samples were quantified against external calibration curves generated for 70 compounds. If the response of the analytes determined in the sample was higher than the calibration range, the sample was further diluted.

Standard preparation

The stock standards were grouped according to their chemical classes. They were then mixed appropriately in extraction solvent to obtain a series of calibration solutions containing 0.1, 0.2, 0.5, 1, 2, 5, and 10 µg/mL of each compound.

Instrumentation

An 8890 GC equipped with an Agilent 7693A automatic liquid sampler was coupled to a 7000D triple quadrupole GC/TQ. The method was developed in a post-column backflush setup. From the inlet, an Agilent J&W HP-5ms GC capillary column (30 m × 0.25 mm, 0.25 µm) was connected to the purged Agilent Ultimate union. From the purged Ultimate union, a 0.7 m × 0.15 mm deactivated capillary was connected to the MS. The objective of the method was to include multiple analytes in a single analysis to reduce the total sample turnaround time. The GC operating parameters are shown in Table 1. Analytical performance of the tested analytes are found to be satisfactory in J&W DB-35ms GC Column (30 m × 0.25 mm, 0.25 µm) and it may also be used as an alternative column.

MS acquisition method

The MRMs for all the compounds were developed using the MRM optimizer tool within MassHunter Optimizer. The TQ operating parameters listed in Table 2 were used for data acquisition.

Results and discussion

The MRMs for this method were developed using two approaches: a conventional approach (for 100 compounds) and MassHunter Optimizer for GC/TQ (for 70 compounds). A dynamic MRM based acquisition method was created with the MRMs for the 100 compounds.

Automated MRM development was used to obtain the optimized MRMs of 70 compounds using the Start from scan data workflow option within the MassHunter Optimizer software. The process for automated MRM development is described elsewhere.[3] The optimized MRMs can be saved in a data acquisition method format, ready for implementation. The optimized MRMs for the 70 compounds were exported to the method containing MRMs for the 100 compounds that had been developed previously. Sample acquisition was then carried out.

Steps for automated development of MRMs

Figures 1 to 3 describe the steps involved in the automated development of MRMs. The optimization is performed in a sequence of steps, as follows:

1. Acquisition of full scan data to identify target compounds
2. Precursor ion identification
3. Product ion identification
4. Collision energy (CE) optimization

The Optimizer software for GC/TQ uses spectral deconvolution to identify compounds and for precursor ion selection. The software correctly identifies target analytes and enables the reliable selection of precursor ions, even in the presence of chromatographic interferences such as column bleed, coeluting analytes, or matrix interferences.

Table 1. Agilent 8890 GC parameters.

Parameter	Value	
MMI Injection Mode	Splitless	
Inlet Temperature	280 °C	
Oven Temperature Program	60 °C (1 min) 40 °C/min to 170 °C (0 min) 10 °C/min to 310 °C (10 min)	
Postrun	5 min	
Total Run Time	32.75 min	
MS Transfer Line Temperature	310 °C	
Injection Volume	1 µL	
Configuration	MMI + 30 m + PUU + restrictor + MS	
Column	1	2
	Agilent HP-5ms Ultra Inert, 30 m × 0.25 mm, 0.25 µm (p/n 19091S-433UI)	Fused silica, deactivated, 0.7 m × 0.15 mm (p/n 160-2625-1)
Control Mode	Constant Flow	Constant Pressure
Flow	1.2 mL/min	2.624 mL/min
Inlet Connection	Multimode Inlet (MMI)	PSD (PUU)
Outlet Connection	PSD (PUU)	MSD
Postrun Flow (Backflushing)	–1.55	
Carrier Gas	Helium, 1.2 mL/min (constant flow) Inlet pressure 2 psi (during backflush)	
Restrictor Pressure	1 psi (during analytical run) 35 psi (during post run)	

Table 2. Agilent 7000D TQ MS parameters.

Parameter	Value
Tune File	atunes.eiex.tune.xml
Mode	Electron impact, 70 eV
Source Temperature	280 °C
Quadrupole Temperature	Q1 and Q2 = 150 °C
MRM Mode Conditions	
Collision Gas Flow	Nitrogen at 1.5 mL/min
Quenching Gas Flow	Helium at 2.25 mL/min

The next step (Figure 2) is the identification of product ions. A coarse determination of CE is performed where up to four different CEs can be defined by the user when Optimizer is acquiring Product Ion Scan data.

The next step is CE optimization, which can be performed around the value chosen in the previous step or over a user-defined range. In this optimization experiment, optimization of CEs was done across the range from 0 to 60 eV in steps of 2 eV (Figure 3).

The entire MRM development process was fully automated from compound identification to CE optimization, with no user intervention needed. MRMs were developed for compounds shown in Table 3 that belong to several classes, including phthalates, amines, organotin compounds (after derivatization with $NaBEt_4$), organosilicon, organonitrogen, PAHs, flame retardants, etc. The developed MRMs were used in the data acquisition methods to analyze both standards and samples.

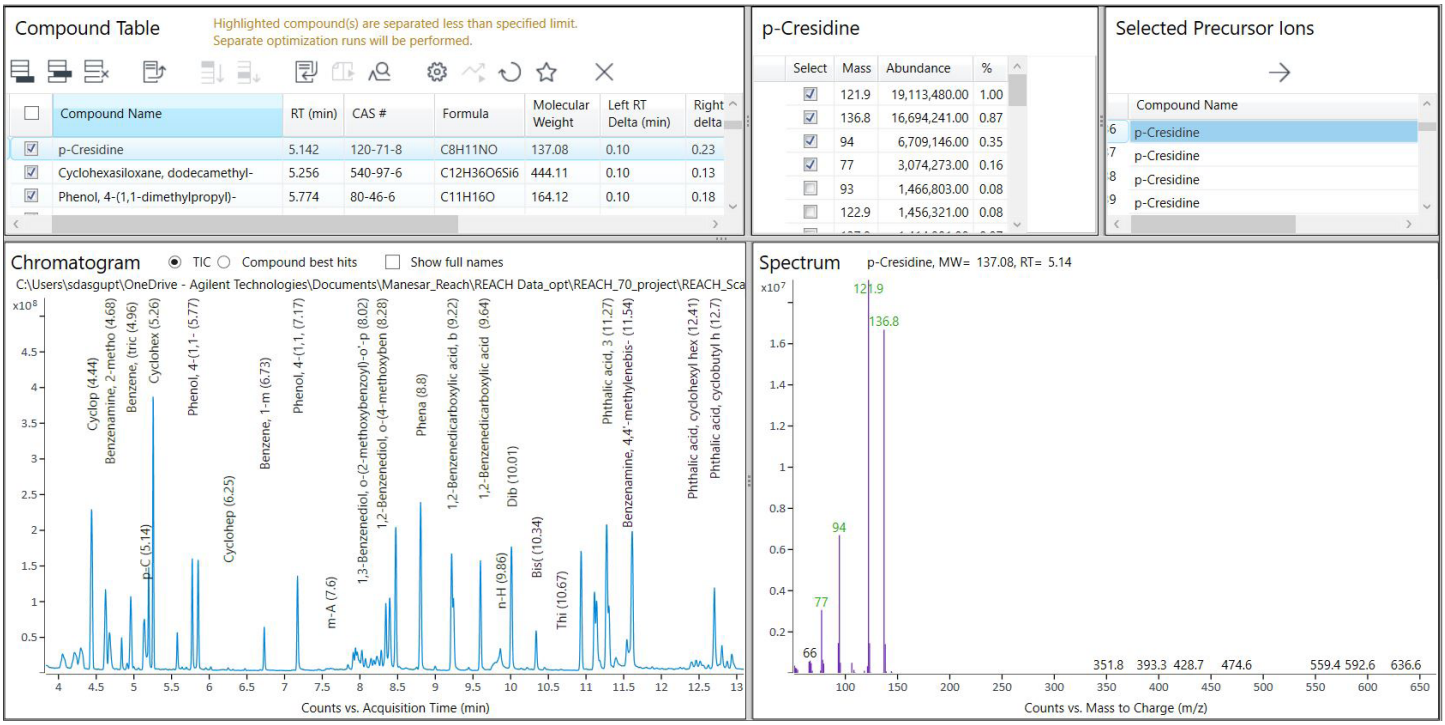

Figure 1. Step 1 and 2 in MRM development with the *Start from scan data* workflow, retention time determination, and selection of precursor ions. The deconvoluted compounds are identified and listed in the compound table (top-left pane) and the best choices for precursor ions are automatically selected and displayed in the adjacent pane. The chromatogram and spectrum are also displayed. The user may also modify precursor ions from selection displayed in the pane adjacent to the compound table.

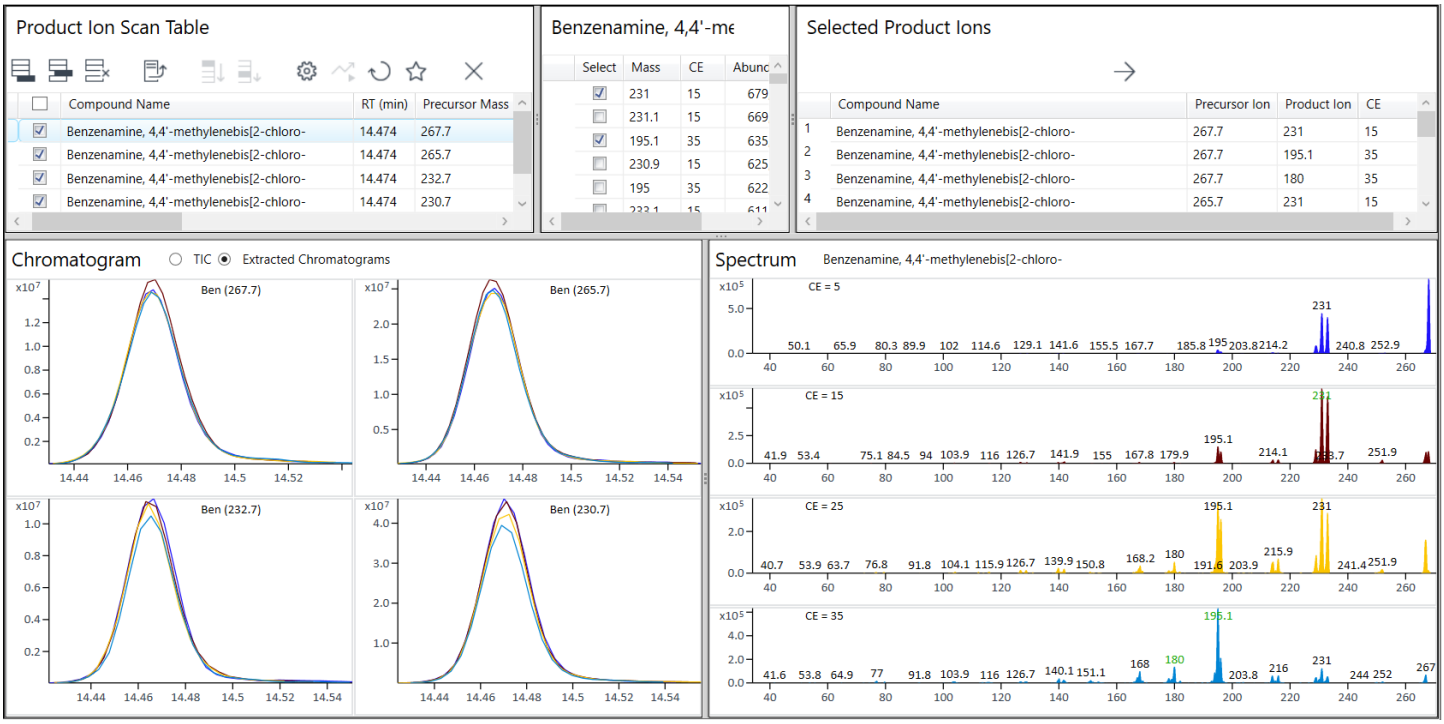

Figure 2. Step 3 in MRM development with the *Start from scan data* workflow, identification of product ions. For each precursor identified in the previous step, a product ion scan is performed with up to four different CEs. In this experiment 5, 15, 25, and 35 V was used. The selection of product ions is done automatically, and the list of selected product ions is displayed (top right). The chromatogram and spectrum are displayed on the bottom. The user may review and modify the selection.

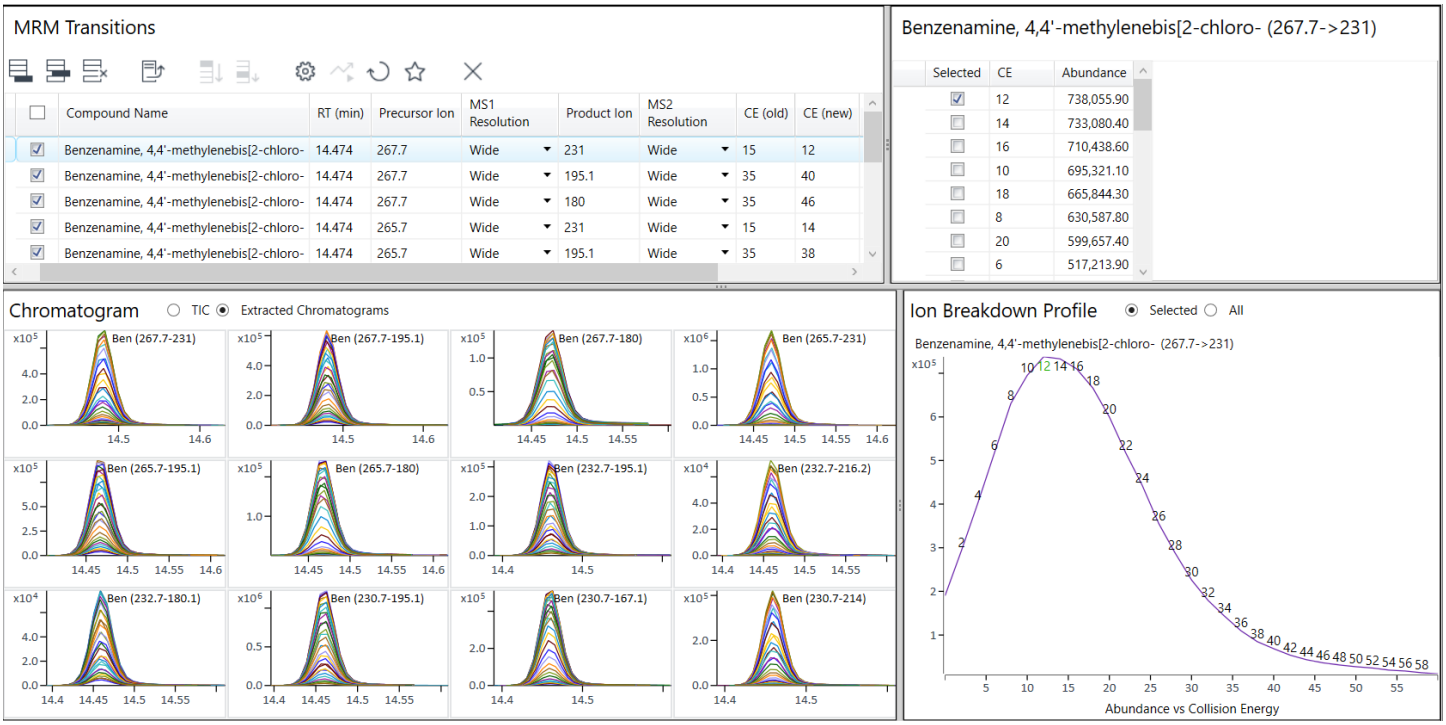

Figure 3. Step 4 in MRM development with the *Start from scan data* workflow, optimization of collision energy. The window includes an MRM transitions list, collision energies with abundances for the highlighted MRM transition, chromatogram of each MRM transition at different CEs, and ion breakdown profile. The ion breakdown is a plot of the MRM transition abundance versus collision energy. The peak of this plot corresponds to the optimized CE value for each corresponding MRM transition.

Table 3. List of compounds with CAS numbers included in the data acquisition method. The initial GC/TQ method included 100 compounds with MRM transitions developed previously using a conventional approach. Seventy new compounds were added to the method and the MRM transitions for the compounds were developed using the Optimizer for GC/TQ.

No.	Compound Name	CAS No.
1	2-Ethoxyethanol†	110-80-5
2	2-Ethoxyethyl acetate†	111-15-9
3	1,2,3-Trichloropropane†	96-18-4
4	*bis*(2-Methoxyethyl) ether†	111-96-6
5	Octamethylcyclotetrasiloxane (D4)†	556-67-2
6	2-Chlorotoluene	95-49-8
7	3-Chlorotoluene	108-41-8
8	4-Chlorotoluene	106-43-4
9	Phenol	108-95-2
10	Dichlorobenzene, 1,3-	541-73-1
11	Dichlorobenzene, 1,4-	106-46-7
12	*o*-Toluidine	95-53-4
13	Dichlorobenzene, 1,2-	95-50-1
14	Benzene, nitro-†	98-95-3
15	Aniline	62-53-3
16	Decamethylcyclopentasiloxane (D5)†	541-02-6
17	2,6-Dimethyl phenol	576-26-1
18	2,3-Dichlorotoluene	32768-54-0
19	2,4-Dichlorotoluene	95-73-8
20	2,5-Dichlorotoluene	19398-61-9
21	Trichlorobenzene, 1,2,4-	120-82-1
22	2-Methoxyaniline, *o*-Anisidine†	90-04-0

No.	Compound Name	CAS No.
23	3,4-Dichlorotoluene	95-75-0
24	2,6-Dichlorotoluene	118-69-4
25	1,2-*bis*(2-methoxyethoxy)ethane (TEGDME, triglyme)†	112-49-2
26	2-Chlorophenol	95-57-8
27	Trichlorobenzene, 1,2,3-	87-61-6
28	α,α,α-Trichlorotoluene†	98-07-7
29	3-Chlorophenol	108-43-0
30	Naphthalene†	91-20-3
31	Dibutyl tin*	683-18-1
32	4-Chlorophenol	106-48-9
33	Trichlorobenzene, 1,3,5-	108-70-3
34	6-Methoxy-*m*-toluidine (*p*-cresidine)†	120-71-8
35	2,4 Xylidine	95-68-1
36	2,6 Xylidine	87-62-7
37	Dodecamethylcyclohexasiloxane(D6)†	540-97-6
38	Tri-*n*-Propyl tin*	2279-76-7
39	2,3-Dichlorophenol	576-24-9
40	2,4,5 Trichlorotoluene	6639-30-1
41	2,3,6-Trichlorotoluene	2077-46-5
42	2,4-Dichlorophenol	120-83-2
43	2,5-Dichlorophenol	583-78-8
44	Tetrachlorobenzene, 1,2,3,5-	634-90-2

No.	Compound Name	CAS No.
45	2,6-Dichlorophenol	87-65-0
46	Chloroaniline, 4-	106-47-8
47	*n*-Butyl tin*	1118-46-3
48	*p*-(1,1-Dimethylpropyl)phenol (PTAP)†	80-46-6
49	4-Methyl-*m*-phenylenediamine (toluene-2,4-diamine)†	95-80-7
50	Trimethylaniline, 2,4,5-	137-17-7
51	3,4-Dichlorophenol	95-77-2
52	4-Chlorobenzo trichloride†	5216-25-1
53	Tetrachlorobenzene, 1,2,4,5-	95-94-3
54	Tetrachlorobenzene, 1,2,3,4-	634-66-2
55	3,5-Dichlorophenol	591-35-5
56	4-Chloro-*o*-Toluidine	95-69-2
57	2,4,5-Trichlorophenol	95-95-4
58	2,3,4-Trichlorophenol	15950-66-0
59	Phenylenediamine, *p*-	106-50-3
60	Tetrachlorotoluene	2136-89-2
61	Acenaphthylene†	208-96-8
62	Acenaphthene†	83-32-9
63	2,3,5-Trichlorophenol	933-78-8
64	2,3,6-Trichlorophenol	933-75-5
65	2,6,α,α-Tetrachlorotoluene	81-19-6
66	2,4,6-Trichlorophenol	88-06-2
67	Tributyl tin*	1461-22-9
68	3,4,5-Trichlorophenol	609-19-8
69	2,4-Dinitrotoluene (2,4-DNT)†	121-14-2
70	Pentachlorobenzene	608-93-5
71	Diethyl phthalate†	84-66-2
72	Tri-*n*-Octyl tin*	2587-76-0
73	4-(1,1,3,3-Tetramethylbutyl)phenol (4-ter-OctylPhenol)†	140-66-9
74	Fluorene†	86-73-7
75	2,3,5,6-Tetrachlorophenol	935-95-5
76	2-Phenylphenol	90-43-7
77	2,3,4,5-Tetrachorophenol	4901-51-3
78	Tetrabutyl tin*	1461-23-2
79	2,3,4,6-Tetrachlorophenol	58-90-2
80	2,4 Diamino anisole	615-05-4
81	4-Nonylphenol, branched and linear†	--
82	4-Bromodiphenyl ether	101-55-3
83	2,3,4,5,6-Pentachlorotoluene	877-11-2
84	4-Bromodiphenyl	92-66-0
85	4 -Phenylphenol	92-69-3
86	Tribromophenol, 2,4,6-	118-79-6
87	Hexachlorobenzene	118-74-1
88	Naphthylamine, 2-	91-59-8
89	4-*n*-Octylphenol	1806-26-4
90	Tris 2-Chloro ethyl phosphate†	115-96-8
91	Diisopropyl phthalate	131-16-8

No.	Compound Name	CAS No.
92	[1,1'-Biphenyl]-4-amine†	92-67-1
93	Benzyl benzoate†	120-51-4
94	Benzene-1,2,4-tricarboxylic acid 1,2 anhydride (trimellitic anhydride)(TMA)†	552-30-7
95	Phenanthrene†	85-01-8
96	5-Nitro-*o*-toluidine	99-55-8
97	Anthracene†	120-12-7
98	Dinoseb (6-sec-butyl-2,4-dinitrophenol)†	88-85-7
99	Pentachlorophenol†	87-86-5
100	Tetrachloroguaiacol	2539-17-5
101	Diisobutyl phthalate†	84-69-5
102	4-*n*-Nonylphenol	104-40-5
103	5-*tert*-Butyl-2,4,6-trinitro-*m*-xylene (Musk xylene)†	81-15-2
104	Diphenyl tin*	1135-99-5
105	Di-*n*-Butyl phthalate†	84-74-2
106	*bis*(2-Methoxyethyl) phthalate†	117-82-8
107	4,4'-Dibromodiphenyl Ether	2050-47-7
108	4,4'-Dibromodiphenyl	92-86-4
109	Diisopentylphthalate†	605-50-5
110	Fluoranthene†	206-44-0
111	4-Aminoazobenzene†	60-09-3
112	*n*-Octyl tin*	3091-25-6
113	N-pentyl-isopentylphthalate†	776297-69-9
114	4,4'-oxydianiline†	101-80-4
115	Pyrene†	129-00-0
116	4,4'- Diaminodiphenylmethane (MDA)†	101-77-9
117	Dipentyl phthalate (DPP)†	131-18-0
118	2,4,5-Tribromodiphenyl	115245-07-3
119	2,3,4-Tribromodiphenyl Ether	147217-78-5
120	Methylpyrene	2381-21-7
121	*o*-Aminoazotoluene†	97-56-3
122	4,4'-methylenedi-*o*-toluidine†	838-88-0
123	Triphenyl tin*	639-58-7
124	Dihexyl phthalate†	84-75-3
125	Butyl benzyl phthalate†	85-68-7
126	2,2'4,5'-Tetrabromobiphenyl	60044-24-8
127	3,3'4,4'-Tetrabromobiphenyl	77102-82-0
128	N,N,N',N'-tetramethyl-4,4'-methylenedianiline (Michler's base)†	101-61-1
129	1,2-Benzenedicarboxylic acid, di-C6-8-branched alkyl esters, C7-rich (DHNUP C7-C11 or Diisoheptyl phthalate)†	71888-89-6
130	Benz[a]anthracene†	56-55-3
131	Chrysene†	218-01-9
132	Benzidine	92-87-5
133	2-Benzotriazol-2-yl-4,6-di-tert-butylphenol (UV-320)†	3846-71-7
134	Tricyclohexyl tin*	3091-32-5
135	2,2'-Dichloro-4,4'-methylenedianiline (MOCA)†	101-14-4
136	2-(2H-benzotriazol-2-yl)-4-(*tert*-butyl)-6-(*sec*-butyl)phenol (UV-350)†	36437-37-3

No.	Compound Name	CAS No.
137	2,2',4,4'-Tetra bromodiphenyl ether	5436-43-1
138	Dicyclohexyl phthalate (DCHP)†	84-61-7
139	1,2-Benzenedicarboxylic acid, di-C7-11-branched and linear alkyl esters (Heptyl undecyl phthalate)†	68515-42-4
140	*bis*(2-ethylhexyl) phthalate†	117-81-7
141	2,2'4,5'6-Pentabromobiphenyl	59080-39-6
142	Di-*n*-Octyltin*	3542-36-7
143	2-(2H-benzotriazol-2-yl)-4,6-ditertpentylphenol (UV-328)†	25973-55-1
144	Dimethyl benzidine, 3,3'-	119-93-7
145	Di-*n*-Octyl Phthalate†	117-84-0
146	Benzo[b]fluoranthene†	205-99-2
147	2,2',4,4',5-Penta bromodipheyl ether	60348-60-9
148	Benzo[j]fluoranthene	205-82-3
149	Diisononyl Phthalate†	68515-48-0
150	4,4' Thiodianiline	139-65-1
151	Benzo[k]fluoranthene†	207-08-9
152	3,3'-Dichlorobenzidiene	91-94-1
153	Benzo[e]pyrene	192-97-2
154	3,3'-Dimethoxy benzidiene	119-90-4

No.	Compound Name	CAS No.
155	4,4'-*bis*(dimethylamino)benzophenone (Michler's ketone)†	90-94-8
156	Benzo[a]pyrene†	50-32-8
157	Dinonyl phthalate	84-76-4
158	Diisodecyl phthalate†	26761-40-0
159	3,3'4,4'5,5'-Hexabromobiphenyl	60044-26-0
160	2,2'4,4'5,5'-Hexabromobiphenyl	59080-40-9
161	2,2',4,4',5,5'-Hexa bromodiphenyl ether	68631-49-2
162	HBCDD†	25637-99-4
163	Indeno[1,2,3-cd]pyrene†	193-39-5
164	Dibenz[a,h]anthracene†	53-70-3
165	Benzo[g,h,i]perylene†	191-24-2
166	2,2',3,4,4',5',6' Heptabromodipheyl ether	207122-16-5
167	Benzo[a,l]pyrene	191-30-0
168	Dodecachloropentacyclo[12.2.1.16,9.02,13.05,10]octadeca-7,15-diene (*bis*(hexachlorocyclopentadieno)cyclooctane)†	-
169	Dibenz[a,e]pyrene	192-65-4
170	Benzo[a,h]pyrene	189-64-0

† MRM for marked compounds has been developed using TQ Optimizer
* After derivatization with $NaBEt_4$
** After acetylation with acetic anhydride in the presence of NaOH

A mixture of 170 compounds listed in Table 4 was analyzed by GC/TQ using the developed data acquisition method. Figure 4 demonstrates the extracted MRM chromatograms of the compound mixture.

Table 4. List of 70 compounds with R^2, and detected amounts in tested samples.

No.	Compound Name	R^2	Concentration Detected (ppm)		
			Polymer Sample 1	Polymer Sample 2	Polymer Sample 3
1	2-Ethoxyethanol	0.999			
2	2-Ethoxyethyl acetate	0.990			
3	1,2,3-Trichloropropane	0.999			
4	*bis*(2-Methoxyethyl) ether	0.999			
5	Octamethylcyclotetrasiloxane(D4)	0.999	6.45	2.17	
6	Benzene, nitro-	0.999			
7	Decamethylcyclopentasiloxane (D5)	0.999	7.95	35.85	
8	2-Methoxyaniline, o-Anisidine	0.999	13.20	5.31	
9	1,2-*bis*(2-Methoxyethoxy)ethane (TEGDME,triglyme)	0.998	8.55	5.23	
10	α,α,α-Trichlorotoluene	0.999	7.30	–	
11	Naphthalene	0.999			
12	6-Methoxy-*m*-toluidine (p-cresidine)	0.999	12.90	5.89	
13	Dodecamethylcyclohexasiloxane(D6)	0.999	41.60	84.21	
14	*p*-(1,1-dimethylpropyl)phenol (PTAP)	0.999			
15	4-Methyl-*m*-phenylenediamine (toluene-2,4-diamine)	0.998	11.10		
16	4-Chlorobenzo trichloride	0.999	8.20	7.01	
17	Acenaphthylene	0.999			

No.	Compound Name	R^2	Concentration Detected (ppm)		
			Polymer Sample 1	Polymer Sample 2	Polymer Sample 3
18	Acenaphthene	0.999			
19	2,4-Dinitrotoluene (2,4-DNT)	0.992	10.15	–	
20	Diethyl phthalate	0.998			
21	4-(1,1,3,3-Tetramethylbutyl)phenol (4-*ter*-octylphenol)	0.995	10.80	2.02	33.60
22	Fluorene	0.997			
23	4-Nonylphenol, branched and linear	0.989	13.40	6.43	
24	Tris 2-Chloro ethyl phosphate	0.987	13.25	8.09	
25	[1,1'-Biphenyl]-4-amine	0.992			
26	Benzyl benzoate	0.999	14.65	9.66	
27	Benzene-1,2,4-tricarboxylic acid 1,2 anhydride (trimellitic anhydride)(TMA)	0.978	6.85	9.81	
28	Phenanthrene	0.999			
29	Anthracene	0.998			
30	Dinoseb (6-*sec*-butyl-2,4-dinitrophenol)	0.975	16.20	10.86	
31	Pentachlorophenol	0.987			
32	Di-*n*-butyl phthalate	0.999	13.55	6.24	
33	5-*tert*-Butyl-2,4,6-trinitro-m-xylene (Musk xylene)	0.982	6.55	8.83	
34	Diisobutyl phthalate	0.998	13.55	11.87	168.50
35	*bis*(2-Methoxyethyl) phthalate	0.997	13.60	11.76	163.80
36	Diisopentylphthalate	0.994	10.70	9.74	8.05
37	Fluoranthene	0.999			
38	4-Aminoazobenzene	0.991	11.10	9.74	
39	N-pentyl-isopentylphthalate	0.999	10.90	7.99	80.50
40	4,4'-oxydianiline	0.972	14.70	9.68	
41	Pyrene	0.999			
42	4,4'- Diaminodiphenylmethane (MDA)	0.986	13.90	6.61	
43	Dipentyl phthalate (DPP)	0.999	10.90	6.94	118.00
44	*o*-Aminoazotoluene	0.995	12.45	9.63	
45	4,4'-Methylenedi-o-toluidine	0.978	10.15	9.41	
46	Dihexyl phthalate	0.997	10.20	10.31	121.40
47	Butyl benzyl phthalate	0.997	11.10	10.40	119.90
48	N,N,N',N'-tetramethyl-4,4'-methylenedianiline (Michler's base)	0.999	10.20	–	
49	1,2-Benzenedicarboxylic acid, di-C6-8-branched alkyl esters, C7-rich (DHNUP C7-C11 or Diisoheptyl phthalate)	0.987	10.15	11.62	
50	Benz[a]anthracene	0.999			
51	Chrysene	0.999			
52	2-Benzotriazol-2-yl-4,6-di-*tert*-butylphenol (UV-320)	0.996	7.00	–	
53	2,2'-Dichloro-4,4'-methylenedianiline (MOCA)	0.994	14.00	9.39	
54	2-(2H-benzotriazol-2-yl)-4-(*tert*-butyl)-6-(*sec*-butyl)phenol (UV-350)	0.989	6.85	11.02	
55	Dicyclohexyl phthalate (DCHP)	0.995	9.60	9.45	123.80
56	1,2-Benzenedicarboxylic acid, di-C7-11-branched and linear alkyl esters (Heptyl undecyl phthalate)	0.989	7.30	11.20	128.50
57	*bis*(2-Ethylhexyl) phthalate	0.997	9.25	9.82	154.40
58	2-(2H-Benzotriazol-2-yl)-4,6-ditertpentylphenol (UV-328)	0.993	5.90	11.13	
59	Di-*n*-octyl phthalate	0.991	10.05	9.40	130.60
60	Benzo[b]fluoranthene	0.999			
61	Diisononyl phthalate	0.976	9.65	13.73	
62	Benzo[k]fluoranthene	0.999			

No.	Compound Name	R^2	Concentration Detected (ppm)		
			Polymer Sample 1	Polymer Sample 2	Polymer Sample 3
63	4,4'-*bis*(Dimethylamino)benzophenone (Michler's ketone)	0.971	8.05	11.88	
64	Benzo[a]pyrene	0.999			
65	Diisodecyl phthalate	0.975			
66	HBCDD	0.995			
67	Indeno[1,2,3-cd]pyrene	0.999			
68	Dibenz[a,h]anthracene	0.999			
69	Benzo[g,h,i]perylene	0.999			
70	Dodecachloropentacyclo[12.2.1.16,9.02,13.05,10]octadeca-7,15-diene (bis(hexachlorocyclopentadieno)cyclooctane)	0.984	7.55	12.14	

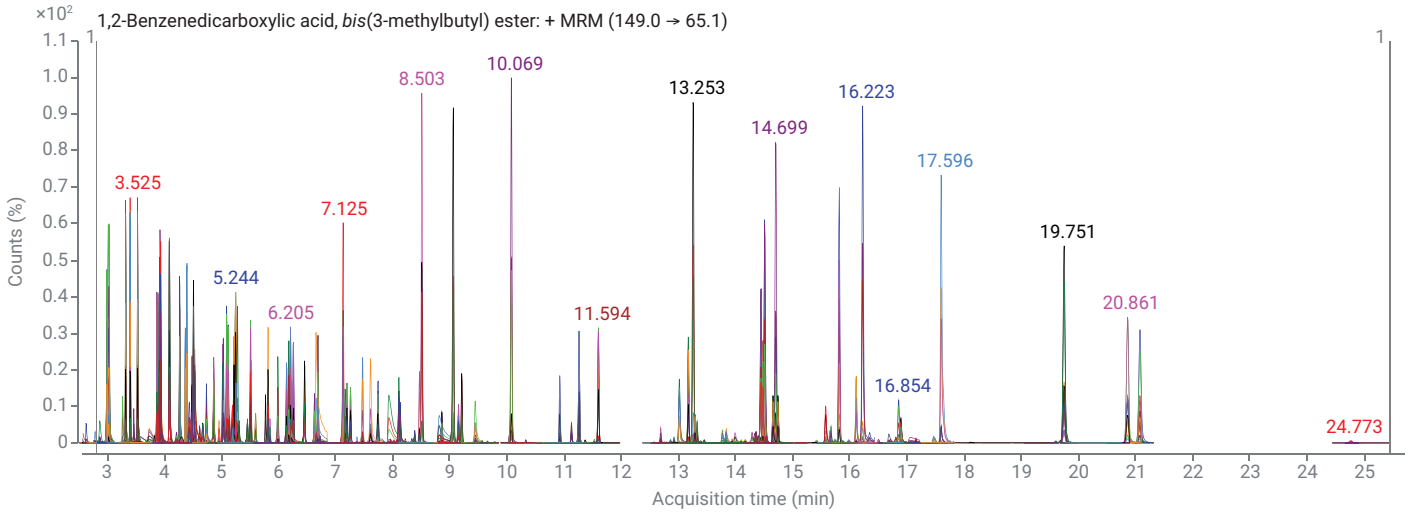

Figure 4. Extracted MRMs of 170 compounds (phthalates, aryl amines, PAHs, etc.).

Sample analysis

The three sample extracts were analyzed using the GC/TQ method. Chromatograms of one of the samples and the 0.5 mg/L mixed-compound standard are displayed in Figures 5 to 8.

Seventy compounds were selected for targeted analysis of the tested samples. Calibration curves were generated for the compounds using an external standard method with seven calibration points at 0.1, 0.2, 0.5, 1, 2, 5, and 10 mg/L. Linear regression coefficients were greater than 0.97 for most compounds across the concentration range. The calibration equations and R^2 data are listed in Table 4.

For compounds such as nonylphenol (linear and branched) where a cluster of peaks eluted, the total area under the peak cluster was considered for construction of the calibration curve. For other compounds that eluted as a cluster with baseline separation such as 1,2-benzenedicarboxylic acid, di-C7-11-branched and linear alkyl esters (heptyl undecyl phthalate), the compound math feature was used. The response was calculated as total sum peak areas of all the individual peaks and plotted against the concentration. A few representative calibration curves for compounds belonging to different compound classes are shown in Figure 9.

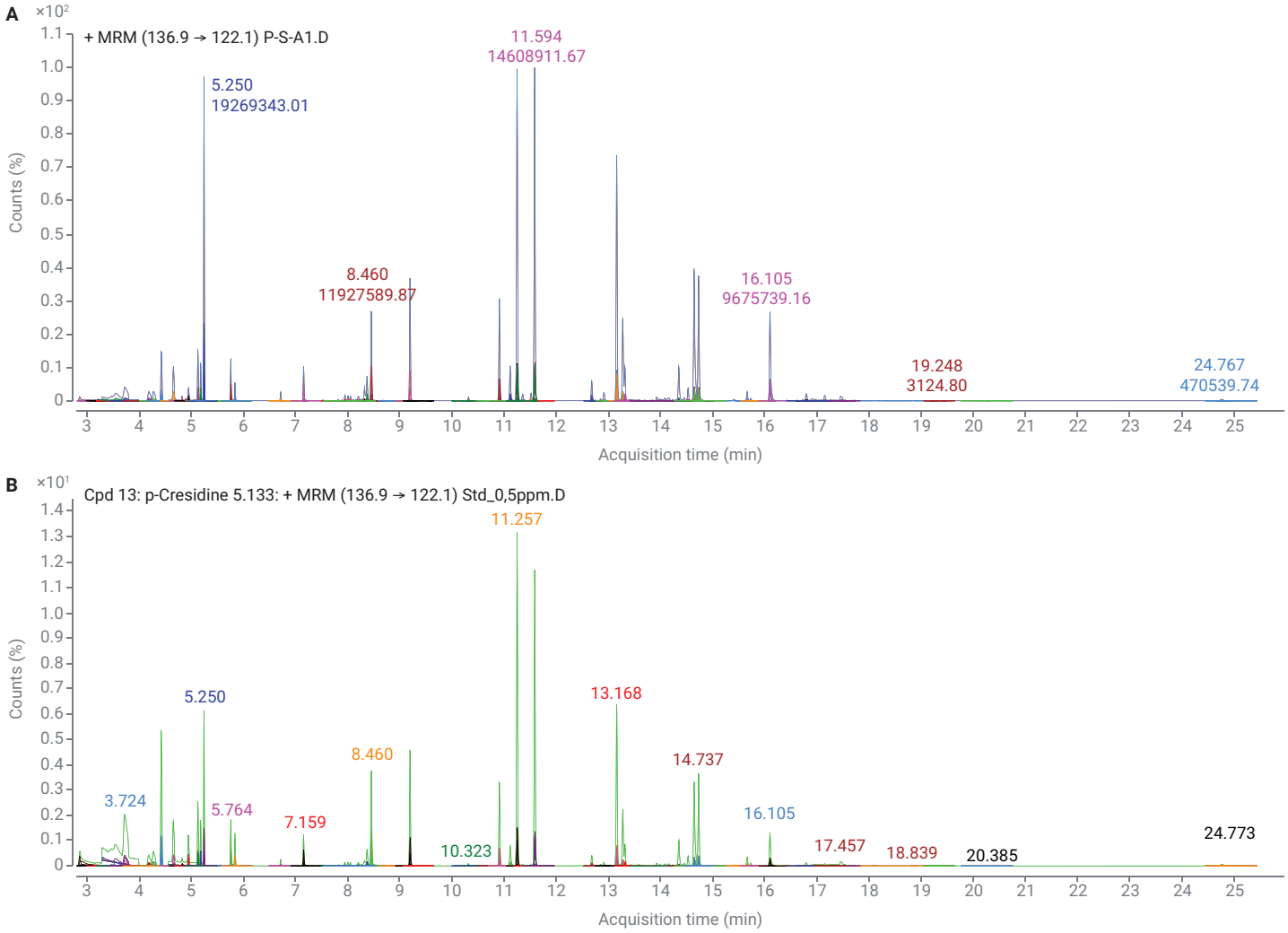

Figure 5. Extracted MRM chromatograms of compounds in the real-world sample (A) and 0.5 mg/L standard (B).

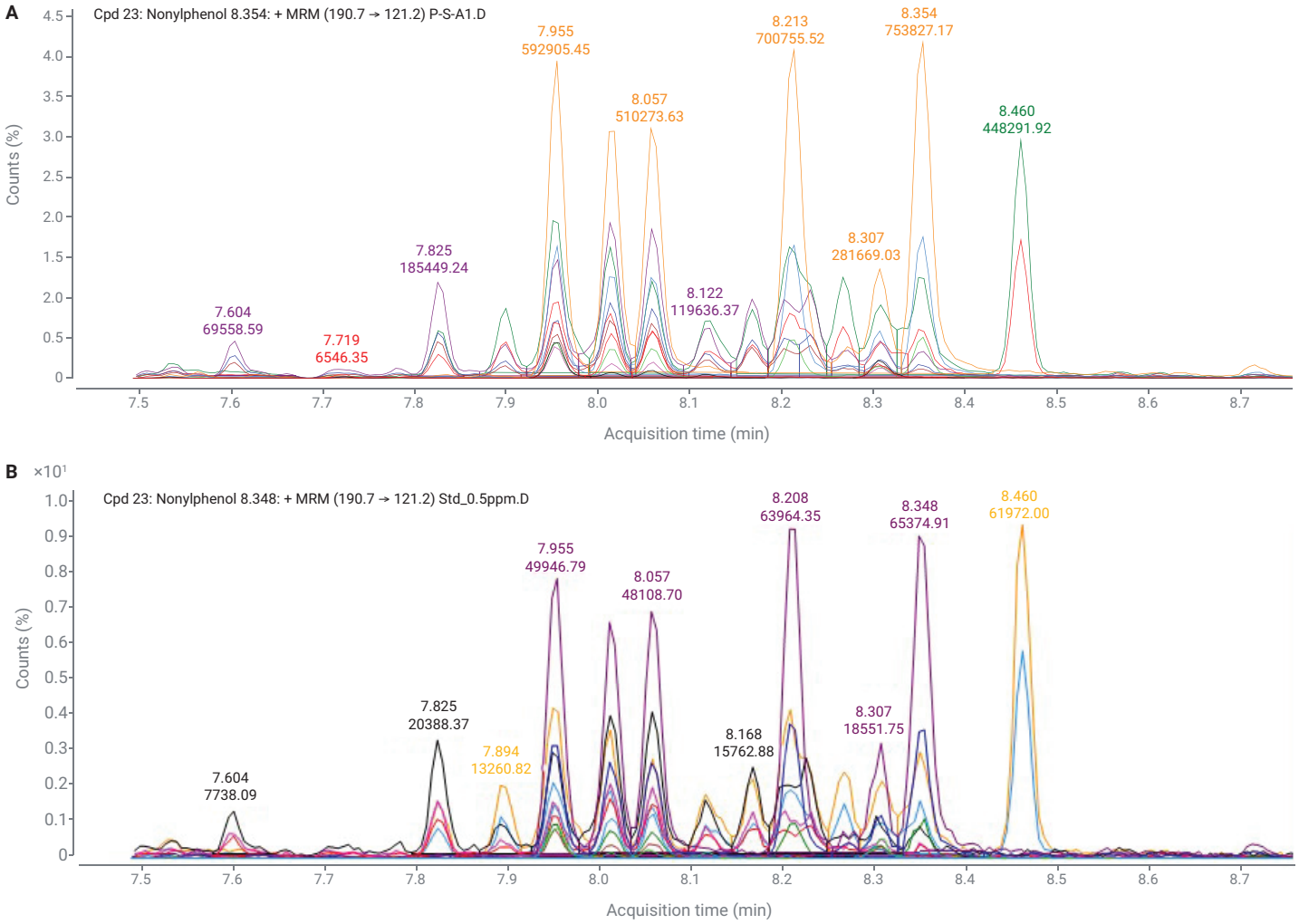

Figure 6. Nonylphenol, branched and linear, in sample (A) and a 0.5 mg/L standard (B).

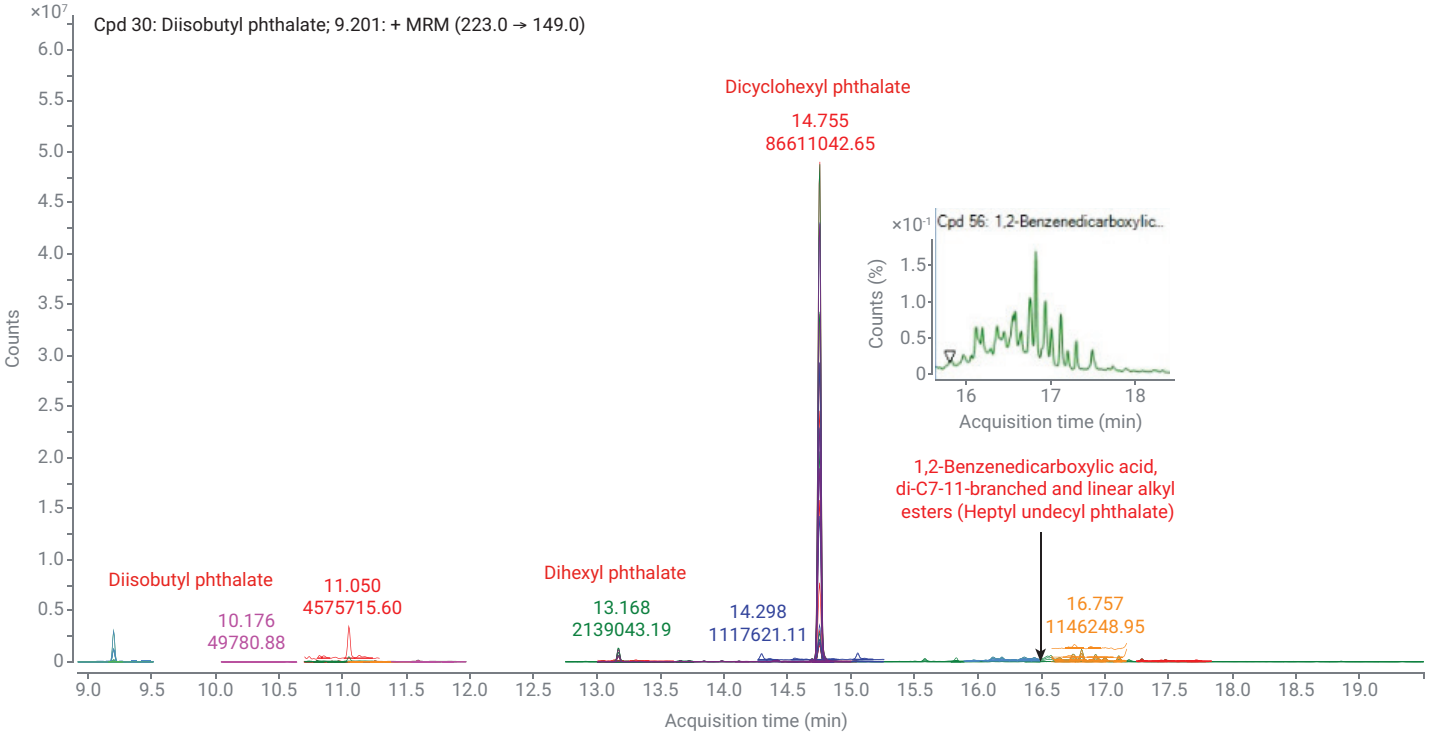

Figure 7. Some of the phthalate compounds detected in one of the samples.

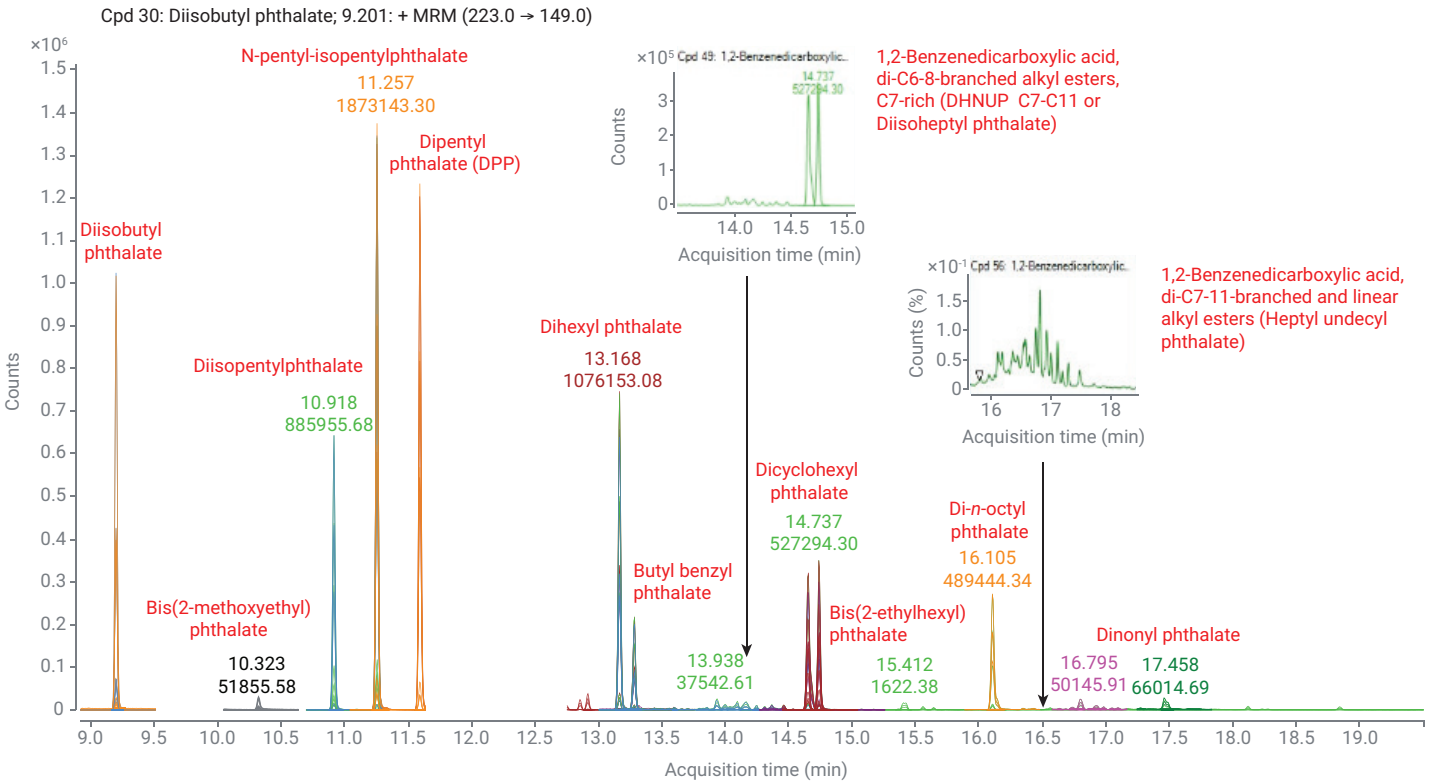

Figure 8. Phthalate esters in the 0.5 mg/L standard mixture.

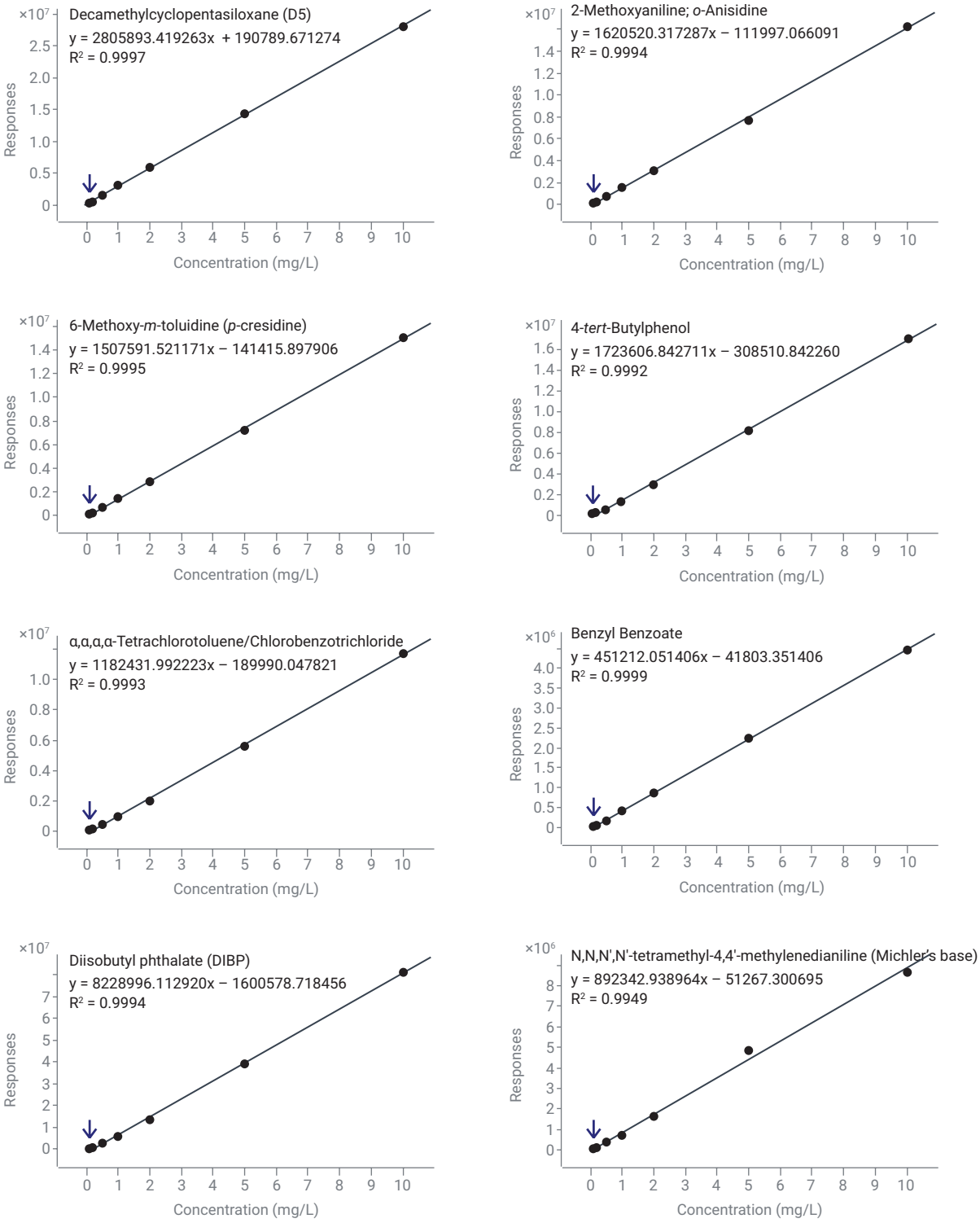

Figure 9. Example calibration results for a selection of compounds from different compound classes.

Conclusion

The Agilent MassHunter Optimizer for GC/TQ greatly reduces the time and effort required for MRM transition development. For complex mixtures of compounds such as SVHCs, the selectivity of MRM greatly enhances method performance and reduces the need for complicated review of samples.

The list of the MRMs generated can either be exported as a dynamic MRM method, time segment-based MRM method, or saved as a database. Alternative MRM transitions can be used to confidently confirm the presence or absence of a target analyte, along with accurate quantitation.

Using the Optimizer tool, MRM transitions for 70 compounds were developed using the *Start from Scan data* workflow. The newly developed MRMs were added to the MRM data acquisition method that already included 100 MRMs. The 100 MRMs had been developed using a conventional approach.

Previously, the time required for the development of MRMs using a conventional method was more than a week. Using MassHunter Optimizer with the Agilent 8890 GC and Agilent 7000D TQ, the total time taken to develop the MRMs was less than 24 hours, including data analysis. A total of 41 chromatographic runs (one scan run, plus 20 runs for product ion identification, plus 20 runs for CE optimization) were acquired – all automatically, without any user intervention. This workflow significantly reduces the time and effort required to build complex multicompound MRM methods.

The method provided acceptable calibration data for 70 compounds that are regulated in the REACH regulations. The MRM acquisition method was also used for trace-level quantitation of the 70 compounds in three tested samples.

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2. Forum methodology for recommending analytical methods to check compliance with REACH Annex XVII restrictions
3. Andrianova, A.; Quimby, B.; Churley, M. Automated MRM Method Development for US EPA Method 8270 with the Agilent MassHunter Optimizer for GC/TQ. *Agilent Technologies application note*, publication number 5994-2086EN, **2020**.

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