Application Note

Environmental, Food Testing and Agriculture

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Tetra- Through Octa-Chlorinated Dioxins and Furans Analysis in Water by Isotope Dilution GC/MS/MS

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Abstract

Dioxins are pollutants that originate from industrial processes, and are highly monitored by environmental agencies. The U.S. Environmental Protection Agency (EPA) developed Method 1613, Revision B (Method 1613B) for determining polychlorinated dibenzo-*p*-dioxins and dibenzofurans (CDDs/CDFs) in environmental matrices using high-resolution GC/MS (GC/HRMS)[1]. The magnetic sector GC/MS is the approved technology for Method 1613B, but the instrument is expensive to maintain, and requires a high skill set for operation. This Application Note investigates triple quadrupole GC/MS (GC/MS/MS) for the analysis of CDDs/CDFs following Method 1613B criteria. Maintenance is lower with GC/MS/MS compared to the GC/HRMS, and it is easier to operate. With GC/MS/MS, mass resolution and distinction of isomers were achieved for the toxic isomers, 2,3,7,8-TCDD and 2,3,7,8-TCDF. Performance criteria were met for Method 1613B. Excellent correlation was observed in spiked water samples when analyzed by GC/HRMS and GC/MS/MS.

Introduction

CDDs and CDFs, collectively known as dioxins, are persistent organic pollutants of great concern due to their adverse health effects from trace level chronic exposure, persistence in the environment, and bio-accumulation in the food chain[2]. The U.S. EPA Office of Science and Technology developed Method 1613B for the determination of the 17 toxic 2,3,7,8-substituted tetra- through octa-chlorinated CDDs/CDFs in aqueous, solid, and tissue matrices by isotope dilution GC/HRMS. Although Method 1613B is a performance-based method, a high mass resolution of ≥10,000 is required, and this can only be achieved by GC/HRMS. However, GC/HRMS is expensive to maintain and requires a highly specialized skill set for operation. This study compares the analysis of a GC/HRMS to GC/MS/MS, which is lower in cost and easier to operate than GC/HRMS.

This Application Note investigates all 17 toxic 2,3,7,8-substituted CDDs/CDFs in Method 1613B (Table 1). Each 2,3,7,8-substituted CDD and CDF is assigned a Toxicity Equivalency Factor (TEF), International Toxicity Equivalency Factor (I-TEF), and World Health Organization TEF (WHO_{2005}-TEF) to estimate the risk associated with exposure to complex mixtures of CDDs and CDFs[3,4]. The TEF values are used to calculate toxic equivalency (TEQ), which the EPA uses to account for the varying toxicity of dioxin and dioxin-like compounds[5]. TEQ is calculated by multiplying the weight (in grams) of each dioxin/dioxin-like compound in the mixture by its corresponding TEF, then adding up the results (Equation 1). This final sum (grams TEQ) indicates that the grams in the mixture are as toxic as the grams TEQ of the two most toxic compounds in the category, which, in this case, would be 2,3,7,8-TCDD and 2,3,7,8-TCDF.

Method 1613B requires the following criteria to be met for CDDs/CDFs investigated in environmental matrices:

- GC retention time window defining solution
- Isomer specificity
- MRM transition
- Relative retention time (RRT)
- Ion abundance ratio
- Signal-to-noise ratio (S/N)

Table 1. Compounds investigated.

CDD/CDF	CDD/CDF isomer[1]	I-TEF[2]	WHO_{2005}-TEF[3]
CDDs	2,3,7,8-TCDD	1	1
	1,2,3,7,8-PCDD	0.5	1
	1,2,3,4,7,8-HxCDD	0.1	0.1
	1,2,3,6,7,8-HxCDD	0.1	0.1
	1,2,3,7,8,9-HxCDD	0.1	0.1
	1,2,3,4,6,7,8-HpCDD	0.01	0.01
	1,2,3,4,6,7,8,9-OCDD	0.001	0.0003
CDFs	2,3,7,8-TCDF	0.1	0.1
	1,2,3,7,8-PCDF	0.05	0.03
	2,3,4,7,8-PCDF	0.5	0.3
	1,2,3,4,7,8-HxCDF	0.1	0.1
	1,2,3,6,7,8-HxCDF	0.1	0.1
	1,2,3,7,8,9-HxCDF	0.1	0.1
	2,3,4,6,7,8-HxCDF	0.1	0.1
	1,2,3,4,6,7,8-HpCDF	0.01	0.01
	1,2,3,4,7,8,9-HpCDF	0.01	0.01
	1,2,3,4,6,7,8,9-OCDF	0.001	0.0003

Table 2. Isomer abbreviations.

TCDD	Tetrachlorodibenzo-*p*-dioxin
PeCDD	Pentachlorodibenzo-*p*-dioxin
HxCDD	Hexachlorodibenzo-*p*-dioxin
HpCDD	Heptachlorodibenzo-*p*-dioxin
OCDD	Octachlorodibenzo-*p*-dioxin
TCDF	Tetrachlorodibenzofuran
PeCDF	Pentachlorodibenzofuran
HxCDF	Hexachlorodibenzofuran
HpCDF	Heptachlorodibenzofuran
OCDF	Octachlorodibenzofuran

[1] Abbreviations for CDDs and CDFs isomers are listed in Table 2.
[2] I-TEF stands for International Toxic Equivalence Factor.
[3] WHO2005-TEF stands for World Health Organization Toxic Equivalence Factor.

$$TEQ = \sum_{i=1}^{17} [CDD/CDF]_i \left(\frac{ng}{L}\right) \times TEF_i \left(\frac{TEQ\ ng}{L}\right)$$

Equation 1. Toxic equivalency (TEQ). [CDD/CDF] refers to the concentration or weight of CDD or CDF. TEF is the toxic equivalency factor assigned to each CDD and CDF (Table 1).

GC retention time window defining solution

Method 1613B requires the use of window-defining compounds to define the beginning and ending retention times for the dioxin and furan isomers[1]. The window-defining compounds are also used to demonstrate the isomer specificity of GC columns for the determination of 2,3,7,8-TCDD and 2,3,7,8-TCDF. In this study, the last eluted HxCDD used was 1,2,3,7,8,9-HxCDD instead of 1,2,3,4,6,7-HxCDD, as in Method 1613B (Table 3).

Table 3. Retention time window-defining solution.

CDD/CDF	First eluted	Last eluted
TCDF	1,3,6,8-	1,2,8,9-
TCDD	1,3,6,8-	1,2,8,9-
PeCDF	1,3,4,6,8-	1,2,3,8,9-
PeCDD	1,2,4,7,9-	1,2,3,8,9-
HxCDF	1,2,3,4,6,8-	1,2,3,4,8,9-
HxCDD	1,2,4,6,7,9-	1,2,3,7,8,9-*
HpCDF	1,2,3,4,6,7,8-	1,2,3,4,7,8,9-
HpCDD	1,2,3,4,6,7,9-	1,2,3,4,6,7,8-

* Method 1613B uses 1,2,3,4,6,7-HxCDD as the last eluted compound.

Isomer specificity

The height of the valley between the 2,3,7,8-substituted isomer and the closest eluted isomer must be <25 %. The order of TCDD isomers is slightly different on the Agilent J&W DB-5ms Ultra Inert column used in the current study compared to the Agilent J&W DB-5 column used Method 1613B. The elution order of CDDs and CDFs using the DB-5ms Ultra Inert column were published in peer reviewed articles by The DOW Chemical Company[6-8]. Using the DB-5 column, the elution order for 2,3,7,8-TCDD and 1,2,3,9-TCDD is swapped compared to the DB-5ms UI column. The order for isomer specificity is listed in Table 4 using TCDD specificity test standards.

Table 4. Order of isomer specificity using TCDD specificity test standards.

Agilent J&W DB-5 column (Method 1613B)	Agilent J&W DB-5ms UI column (Current method)
1,2,3,7/1,2,3,9-TCDD	1,2,3,7/1,2,3,9-TCDD
2378-TCDD*	1239-TCDD
1239-TCDD	2378-TCDD*

MRM transitions, relative retention time, ion abundance ratios, and S/N

Method 1613B has criteria for relative retention time (RRT), ion abundance ratios, and S/Ns. The MRM transitions used to analyze dioxins in Method 1613B by GC/MS/MS analysis were adapted from Agilent dioxin analyzer for Food and Feed[9]. In 2014, the European Union (EU) Regulation 709/2014 enabled the use of GC/MS/MS for the analysis of CDDs, CDFs, dioxin-like PCBs, and nondioxin-like PCBs in food and feed[10]. The RRT between the CDDs/CDFs and labeled compounds must be within the limits described in Method 1613B. The ion abundance ratio must be within the QC limits of ±15 % around the theoretical ion abundance ratio. The S/N for all CDDs/CDFs in calibration standards must be ≥10. For CDDs and CDFs detected in a sample, the S/N must be ≥2.5.

This Application Note analyzed a spiked water sample following Method 163B criteria, and comparisons were made between GC/MS/MS and GC/HRMS.

Methods

Sample preparation

No changes were made to the sample preparation of water described in Method 1613B. One liter of water was filtered. The filter paper and filtrate were extracted using Soxhlet extraction and liquid/liquid extraction, respectively. The extracts were combined, and cleanup was achieved using a silica, alumina, florisil, or carbon column. After cleanup, the extract was split for analysis using GC/HRMS and GC/MS/MS. ^{13}C internal standard, cleanup standard, and injection standards were added before extraction, cleanup, and GC/HRMS or GC/MS/MS analysis, respectively.

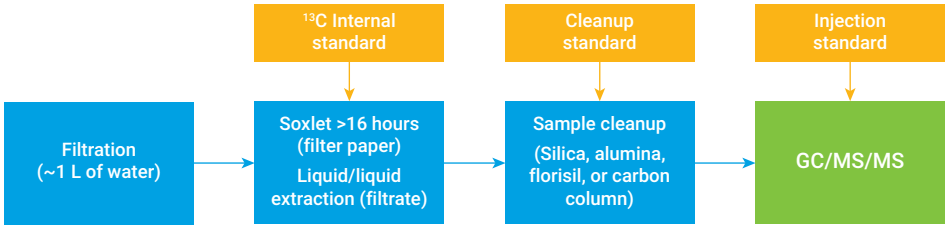


Figure 1. Sample preparation workflow for Method 1613B.

GC/MS/MS parameters

Table 5 lists GC and MS/MS parameters. Table 6 lists MRM transitions, parameters, and collision energies. Figure 2 shows a pictorial GC/MS/MS configuration.

Results and discussion

Calibration standards were used to investigate dioxins and furans analysis by GC/MS/MS following Method 1613B criteria before the analysis of real water samples. The two transitions and collision energies were adopted from Agilent Food and Feed Analyzer[9]. GC retention time window-defining solution, isomer specificity, RRT, ion abundance ratios, and S/N were investigated for all CDDs and CDFs based on Method 1613B criteria.

Table 5. GC and MSD parameters.

Agilent 7890B GC	
Inlet parameters	
Injection volume	1 µL
Liner	Dimpled, splitless, Ultra Inert, 200 µL (Agilent 5190-2297)
Inlet	Multimode inlet
Mode	Pulsed splitless
Pressure	21.954 psi
Total flow	43.056 mL/min
Septum purge flow	2 mL/min
Septum purge flow mode	Switched
Temperature	Initial 62 °C (0.31 minutes)
	Ramp at 600 °C/min to 330 °C (5 minutes)
Gas saver	20 mL/min after 2 minutes
Injection pulsed pressure	30 psi until 1 minute
Run time	57 minutes
Postrun time	1 minute

Oven parameters	
Column	Agilent J&W DB-5ms Ultra Inert (Agilent 122-5562UI)
Column dimensions	60 m × 250 µm, 0.25 µm
Column configuration	Inlet to MSD
Pressure	21.954 psi
Flow	1.056 mL/min
Flow mode	Constant flow
Average velocity	27.099 cm/s
Oven temperature	Initial: 100 °C (2 minutes) Ramp at 30 °C/min to 220 °C (16 minutes) Ramp at 2 °C/min to 240 °C (5 minutes) Ramp at 5 °C/min to 270 °C (4 minutes) Ramp at 15 °C/min to 330 °C (6 minutes)
Equilibration time	0.25 minutes
Collision cell	
He quench gas	4 mL/min
N_2 collision gas	1.5 mL/min
7010 Triple quadrupole MS	
Transfer line temperature	350 °C
Source	300 °C
Quadrupole 1	150 °C
Quadrupole 2	150 °C

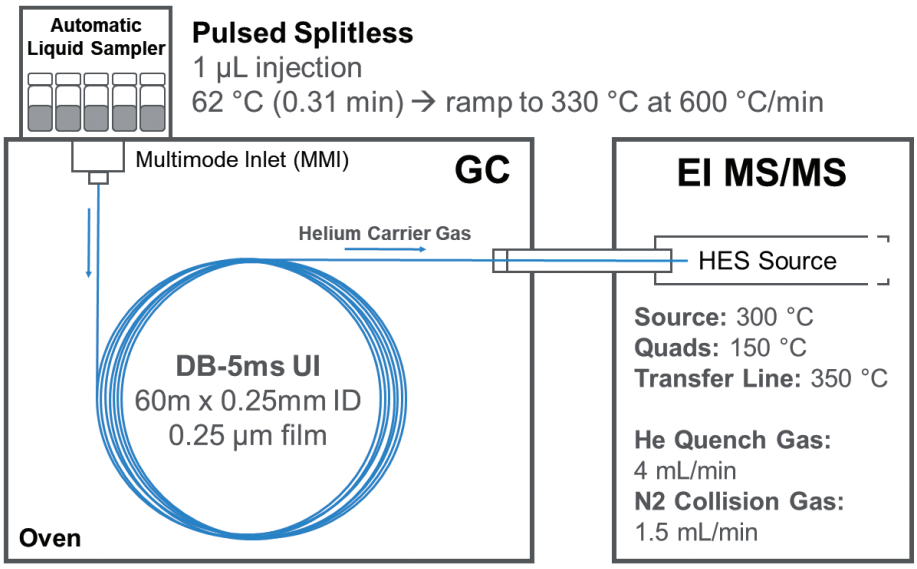


Figure 2. GC/MS/MS configuration.

Table 6. MRM parameters and collision energy.

Segment	Analyte	Precursor ion[1]	Product ion[1]	Dwell	CE[2]
1 Toxic TCDD/TCDF	^{13}C-TCDD	333.9	269.9	50	26
	^{13}C-TCDD	331.9	267.9	50	26
	TCDD	321.9	258.9	100	26
	TCDD	319.9	256.9	100	26
	^{13}C-TCDF	317.9	253.9	50	40
	^{13}C-TCDF	315.9	251.9	50	40
	TCDF	305.9	242.9	100	40
	TCDF	303.9	240.9	100	40
2 Nontoxic TCDD/TCDF[3]	^{13}C-PeCDF	351.9	287.9	25	40
	^{13}C-PeCDF	349.9	285.9	25	40
	PeCDF	339.9	276.9	75	40
	PeCDF	337.9	274.9	75	40
	^{13}C-TCDD	333.9	269.9	25	26
	^{13}C-TCDD	331.9	267.9	25	26
	TCDD	321.9	258.9	75	26
	TCDD	319.9	256.9	75	26
	^{13}C-TCDF	317.9	253.9	25	40
	^{13}C-TCDF	315.9	251.9	25	40
	TCDF	305.9	242.9	75	40
	TCDF	303.9	240.9	75	40
3 PeCDD/PeCDF	^{13}C-PeCDD	367.9	302.9	50	26
	^{13}C-PeCDD	365.9	301.9	50	26
	PeCDD	355.9	292.9	100	26
	PeCDD	353.9	290.9	100	26
	^{13}C-PeCDF	351.9	287.9	50	40
	^{13}C-PeCDF	349.9	285.9	50	40
	PeCDF	339.9	276.9	100	40
	PeCDF	337.9	274.9	100	40

Segment	Analyte	Precursor ion[1]	Product ion[1]	Dwell	CE[2]
4 HxCDD/HxCDF	^{13}C-HxCDD	403.9	339.9	50	25
	^{13}C-HxCDD	401.9	337.9	50	25
	HxCDD	391.8	328.8	100	25
	HxCDD	389.8	326.8	100	25
	^{13}C-HxCDF	387.9	323.9	50	40
	^{13}C-HxCDF	385.9	321.9	50	40
	HxCDF	375.8	312.8	100	40
	HxCDF	373.8	310.8	100	40
5 HpCDD/HpCDF	^{13}C-HpCDD	437.8	373.8	50	24
	^{13}C-HpCDD	435.8	371.8	50	24
	HpCDD	425.8	362.8	100	24
	HpCDD	423.8	360.8	100	24
	^{13}C-HpCDF	421.8	357.8	50	40
	^{13}C-HpCDF	419.8	355.8	50	40
	HpCDF	409.8	346.8	100	40
	HpCDF	407.8	344.8	100	40
6 OCDD/OCDF	^{13}C-OCDD	471.8	407.8	50	24
	^{13}C-OCDD	469.8	405.8	50	24
	OCDD	459.7	396.7	100	24
	OCDD	457.7	394.7	100	24
	^{13}C-OCDF	455.8	391.8	50	40
	^{13}C-OCDF	453.8	389.8	50	40
	OCDF	443.7	380.7	100	40
	OCDF	441.7	378.7	100	40

[1] Wide resolution for precursor and product ions.

[2] Collision energies were adapted from Agilent Food and Feed Analyzer[9].

[3] Segment 2 was added to account for the last eluted TCDD/TCDF and first eluted PeCDD/PeCDF. The retention time of the congeners is too close to TCDD/TCDF in segment 1 and PeCDF in segment 3. The compounds in segment 2 are for investigating nontoxic CDDs/CDFs, and are optional if investigating only the toxic compounds.

Isomer specificity (GC/MS/MS versus GC/HRMS)

Isomer specificity for each of the CDDs and CDFs was investigated by GC/MS/MS based on the Method 1613B criteria. The isomer specificity criteria states that analytes must elute between the first and last eluted compound in the window-defining solution. The height of the valley between the most closely eluted isomers and the 2,3,7,8-substituted isomers must be <25 %.

All CDDs and CDFs eluted within the defined retention time window, and <25 % valley isomeric separation was achieved with GC/MS/MS. A <25 % valley separation was observed between toxic 2,3,7,8-TCDD and its closest isomer, 1,2,3,9-TCDD (Figure 3A). The DB-5ms UI column aids in the separation of nontoxic and toxic 2,3,7,8-TCDF, the coelution of which is usually observed with a DB-5 column (Figure 3B).

According to the RRT criteria, the RRT reference for 1,2,3,7,8,9-HxCDD is ^{13}C-1,2,3,6,7,8-HxCDD, and 1,2,3,7,8,9-HxCDD is quantified using the average response for ^{13}C-1,2,3,4,7,8 and ^{13}C-1,2,3,6,7,8-HxCDD (Figure 3C).

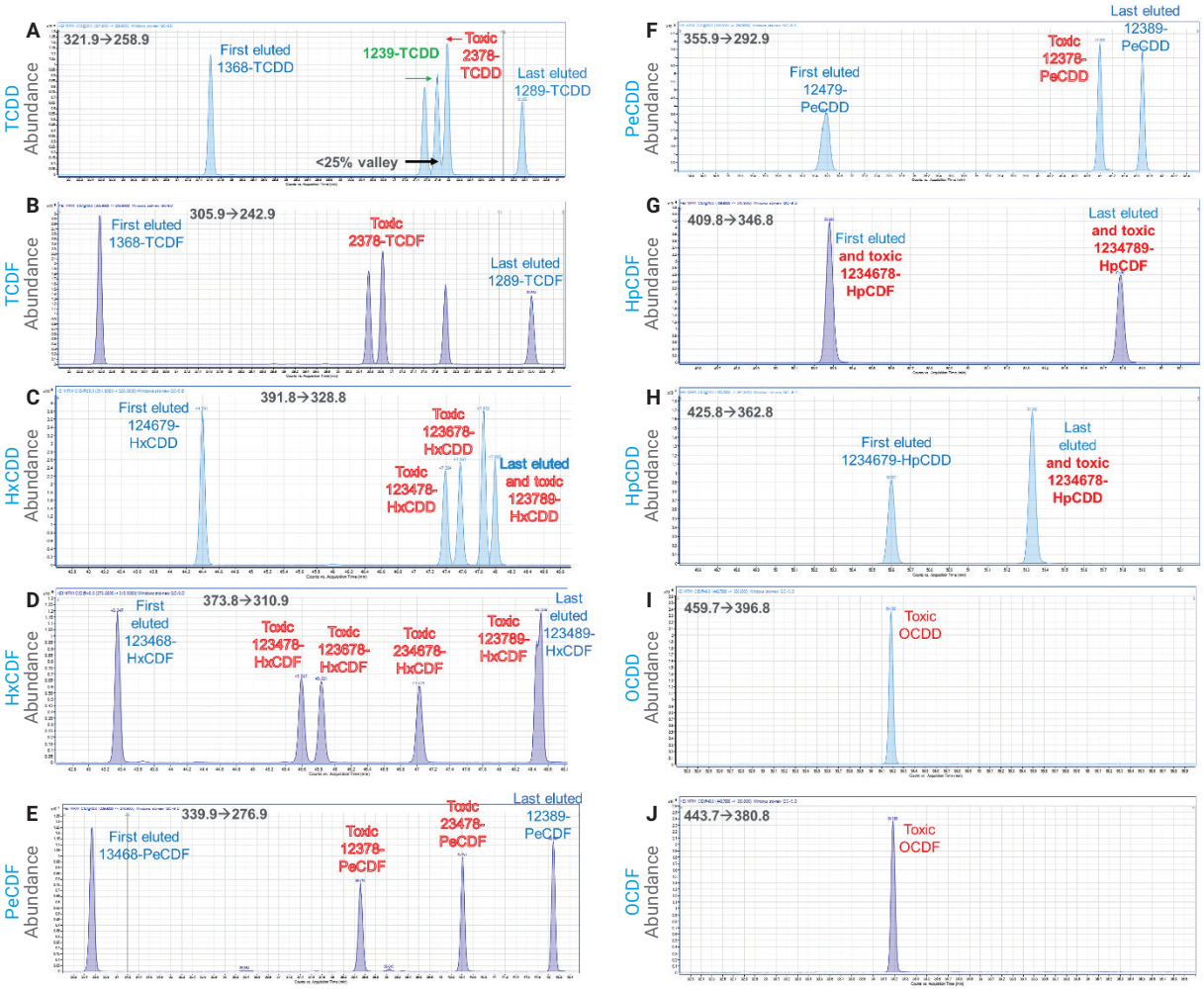


Figure 3. CDDs/CDFs by GC/MS/MS.

Toxic 1,2,3,7,8,9-HxCDF cannot be separated with a <25 % valley from its closest/last eluted isomer 1,2,3,4,8,9-HxCDF using a DB-5ms UI column (Figure 3D). The same observation was also seen in the GC/HRMS analysis (Figure 4). A shoulder in the combined peak is observed in GC/MS/MS and GC/HRMS. 1,2,3,7,8,9-HxCDF is the correct peak due to the RRT with the ^{13}C internal standard. The peak is split and integrated using the estimated maximum concentration (EMPC).

Penta, hepta, and octa CDDs and CDFs had no coelution, and were all well separated (Figures 3E–J).

Transitions, RRT, ion abundance, and S/N

RRT, ion abundance ratio, and S/N criteria were evaluated. All CDDs/CDFs passed the Method 1613B criteria. An example is demonstrated for ^{13}C-2,3,7,8-TCDD and 2,3,7,8-TCDD to show how each of the CDDs/CDFs were evaluated (Figure 5). Two transitions were analyzed for ^{13}C-2,3,7,8-TCDD and 2,3,7,8-TCDD. The RRT between ^{13}C-2,3,7,8-TCDD and 2,3,7,8-TCDD was 1.001 outside of the criteria, since the range of 0.999–1.002 was stated in Method 1613B. The ion abundance ratio for ^{13}C-2,3,7,8-TCDD and 2,3,7,8-TCDD are 106.1 and 104.8, which are both within a ±15 % window around the theoretical ion abundance ratio of 90.2–122.0 and 88.9–120.2, respectively. The S/N for ^{13}C-2,3,7,8-TCDD and 2,3,7,8-TCDD in the verification standard are 543 and 2,569, respectively, which satisfies the Method 1613B criteria of >10. The same evaluations for RRT, ion abundance ratio, and S/N were applied to all CDDs and CDFs in Method 1613B.

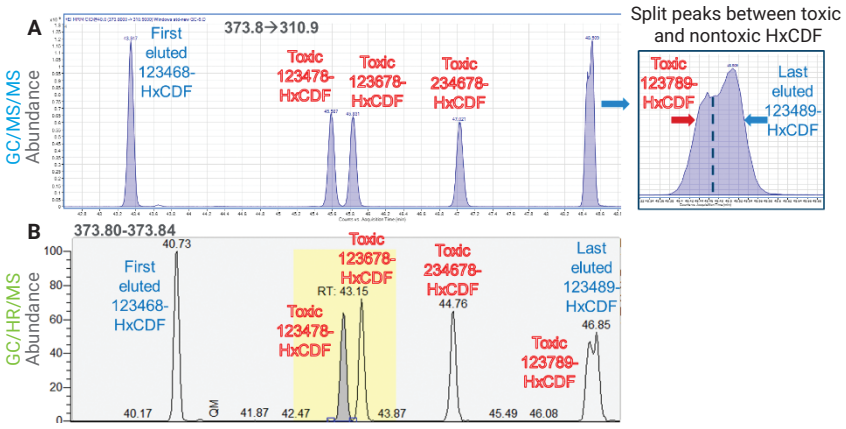


Figure 4. HxCDF analysis by GC/MS/MS and GC/HRMS.

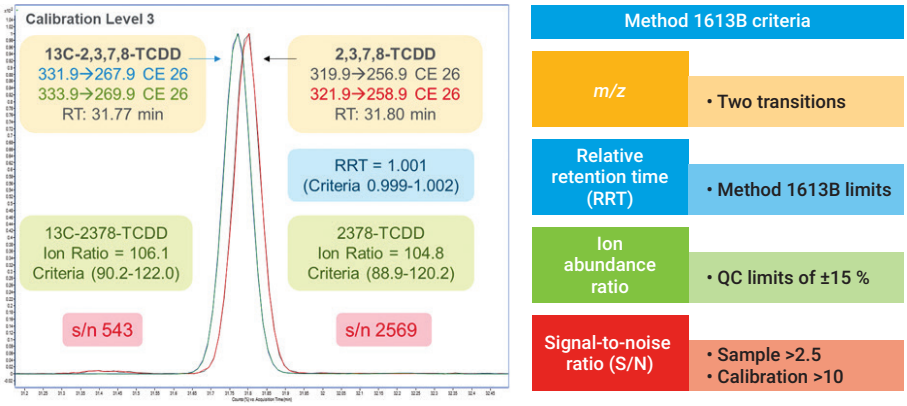
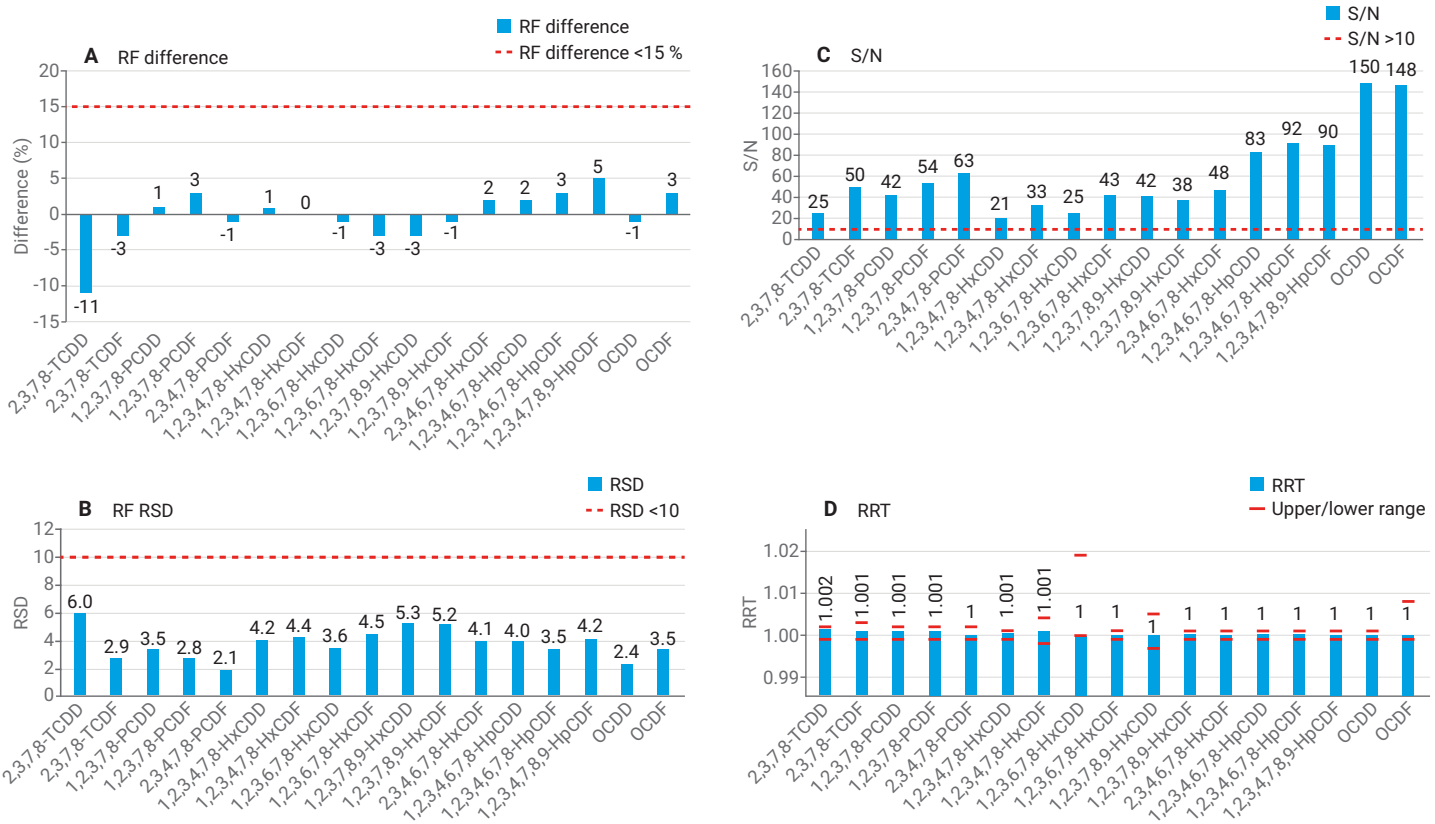


Figure 5. Meeting Method 1613 criteria for RRT, ion abundance ratio, and S/N.

Calibration

All 17 dioxins were calibrated by an isotope dilution approach, using a response factor (RF) for quantification after verifying that all analytes elute within the defined time window and that isomer specificity was achieved. The calibration concentrations investigated were 0.2, 0.5, 1, 4, 10, 50, 250, 1,000, and 2,500 ng/mL. Calibration standard 1 (CS1) in Method 1613B was used for calibration, which consisted of compounds starting at 0.5 ng/mL. All analytes met the acceptance criteria.

The average RF differences were all below the criteria of <15 % (Figure 6A). All CDDs and CDFs met the criteria for RF RSD of <10 (Figure 6B). The S/N for all analytes was >10 (Figure 6C), and the RRT was within the range stated in Method 1613B (Figure 6D).



*Blue bars represent recoveries of tetra CDDs/CDFs at 0.5 ng/mL, penta, hexa, and hepta CDDs/CDFs at 2.5 ng/mL, and octa CDDs/CDFs at 5.0 ng/mL. Red lines in A and B indicate the upper limit. Red lines in C indicate the lower limit. Red lines in D indicate the lower and upper limits.

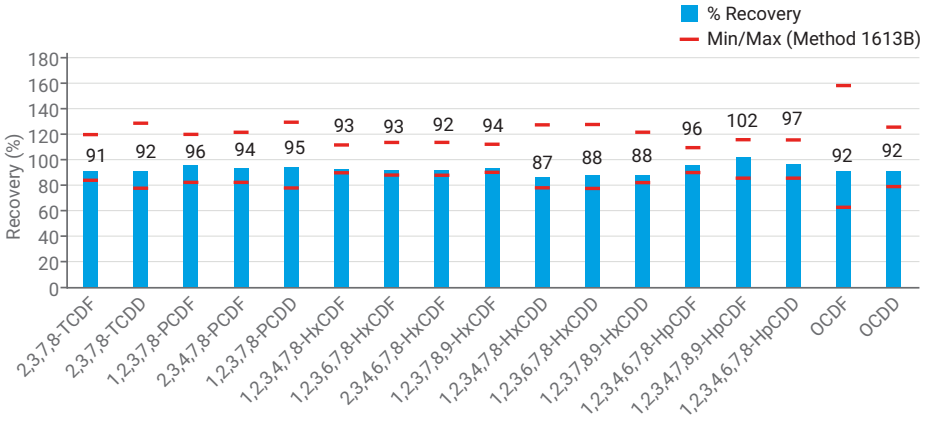
Figure 6. RF, S/N, and RRT of CDDs/CDFs at CS1.

Verification standard (VER) recoveries

The midpoint calibration standard (CS3) was used to verify the calibration. Recoveries for all CDDs and CDFs fall within the acceptance criteria range stated in Method 1613B (Figure 7).

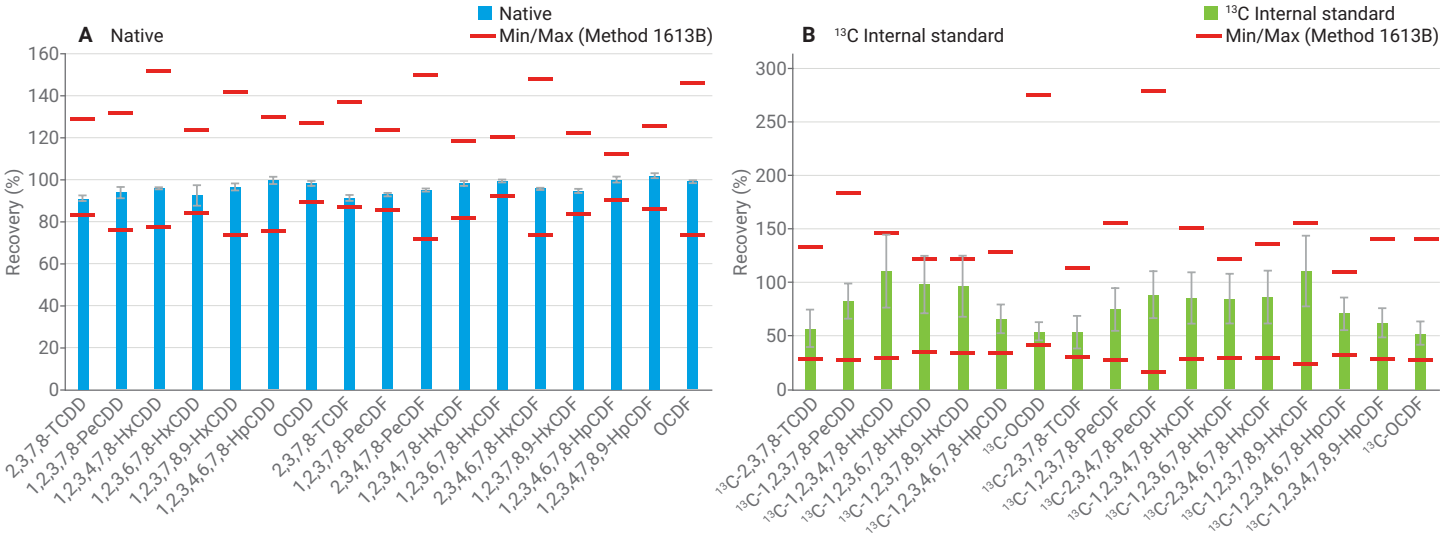
Initial precision and recovery (IPR)

IPR was used to establish the ability to generate acceptable precision and recovery. All native and labeled CDDs and CDFs meet the corresponding limits for IPR (Figure 8).



*Blue bars represent recoveries of tetra CDDs/CDFs at 10 ng/mL, penta, hexa, and hepta CDDs/CDFs at 50 ng/mL, and octa CDDs/CDFs at 100 ng/mL. Red lines indicate the acceptance criteria for VER.

Figure 7. VER recovery for CDDs and CDFs.



Bars represent recoveries, and error bars represent standard deviation for native (A) and labeled (B) CDDs and CDFs. Recovery and standard deviation are calculated based on four 1 L aliquots of reagent water spiked with native and labeled CDDs/CDFs. The test concentration for IPR consisted of tetra CDDs/CDFs at 10 ng/mL, penta, hexa, and hepta CDDs/CDFs at 50 ng/mL, octa CDDs/CDFs at 100 ng/mL, ^{13}C tetra through hepta CDDs/CDFs at 100 ng/mL, ^{13}C-OCDD at 200 ng/mL, and cleanup standard ^{37}Cl-2,3,7,8-TCDD at 10 ng/mL.

Figure 8. IPR recovery for native and labeled CDDs and CDFs.

Spiked water sample

Excellent correlation was observed with GC/HRMS and GC/MS/MS analyses of spiked water samples, following Method 1613B (Figure 9), with pg/mL of native and labeled CDDs/CDFs.

Conclusion

GC/MS/MS is a highly promising technique for the analysis of water when following Method 1613B. Isomeric separation was achieved for all analytes monitored in Method 1613B. All CDDs/CDFs eluted within the defined retention time window. Quantifier and qualifier MRM transitions passed the RRT, ion abundance ratio, and S/N criteria. Calibration was verified, and IPR met the method criteria. Excellent correlation was observed between GC/HRMS and GC/MS/MS in the spiked water samples.

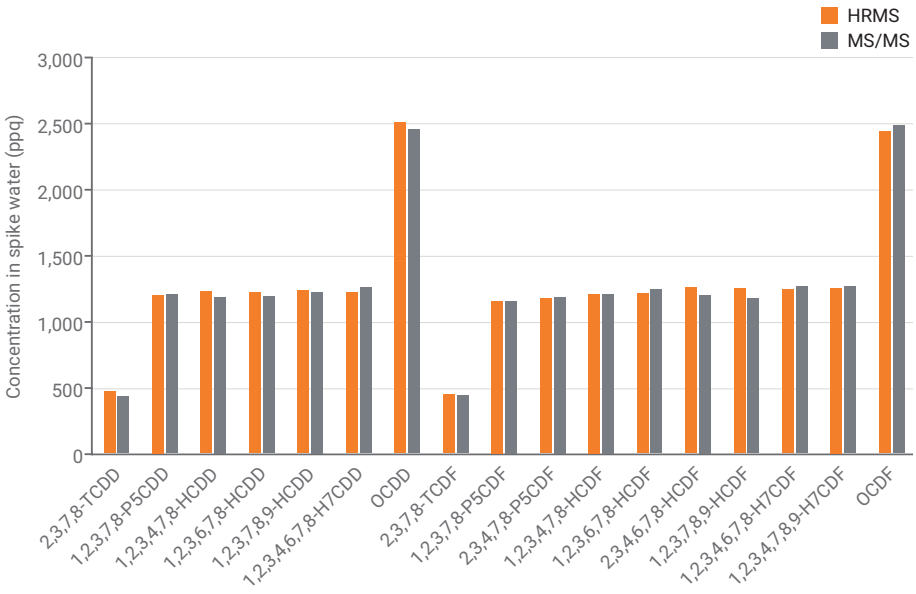


Figure 9. GC/HRMS and GC/MS/MS analysis of a spiked water sample.

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