SHIMADZU
Excellence in Science

Haloacetic Acids Analysis: Evaluation of alternatives for their improved analysis

Ruth Marfil-Vega, PhD

Senior Market Manager - Environmental

In today's presentation

1. Why HAAs?
2. Approved methods
3. Alternatives
4. Conclusions
5. Q&A

Why HAAs?

Demands for this analysis are only going to become more challenging:

- ✓Updated regulation
- ✓New demands for process control (water reclamation)
- ✓Improved Health & Safety, and waste management measurements
- ✓Streamlined operations

Approved methods HAA5

EPA United States Environmental Protection Agency

April 2019

Analytical Methods Approved for Drinking Water Compliance Monitoring under the Disinfection Byproduct Rules

Analysis for the following disinfectants, contaminants and other parameters shall be conducted in accordance with the methods in the following table, or their equivalent as determined by EPA. The methods are specified in 40 CFR 141.131 and in Appendix A to Subpart C of Part 141. The monitoring requirements are specified in 40 CFR 141.132, 141.135, 141.600-141.603, and 141.620-141.268.

The CFR is the legal reference for approved methods and takes precedence over this table. The table should accurately reflect the analytical methods information published in 40 CFR 141.

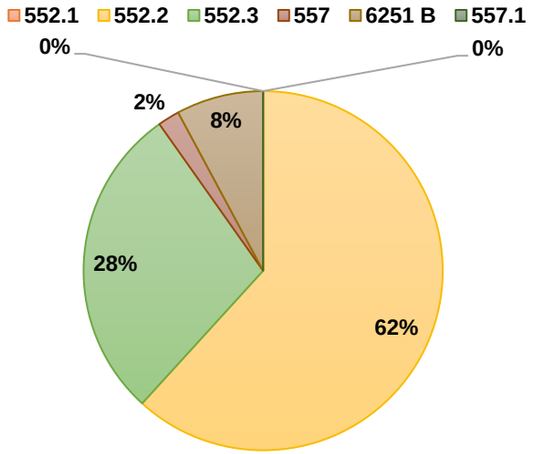
Method	Organization	Date	Analytical Approach
552.1; 552.2; 552.3	EPA	1992, 1995, 2003	GC ECD
557	EPA	2009	IC-ESI-MS/MS
6251 B	SM	1995 – 2017	GC ECD
Thermo Fisher 557.1	Thermo Fisher	2017	2D IC with suppressed conductivity detector

https://nepis.epa.gov/Exe/ZyPDF.cgi?Dockey=P100WD1L.txt

How many labs are accredited?

Method	Organization	Date	# of labs
552.1; 552.2; 552.3	EPA	1992, 1995, 2003	92
557	EPA	2009	2
6251 B	SM	1995 – 2017	8
Thermo Fisher 557.1	Thermo Fisher	2017	0

Source of information: The NELAC Institute (July 2022)



- ✓ 98% of the labs accredited under NELAC use GC/ECD
- ✓ 2% of the labs accredited under NELAC use IC-MS/MS

Let’s break down the steps from each method

GC/ECD

Sample* Analysis - Step	Description
Preparation	Ether extraction at acidic pH Derivatization in acidic methanol (2 h) Extract drying through sodium sulfate Extract neutraliztion
Analysis	Analyze the batch in GC-ECD after confirming status of instrument. Analyze samples twice, in primary and confirmation columns

Time consuming
Multiple opportunities for errors
High risk
Limited number of samples per day

Find Shimadzu's solutions for HAAs analysis by GC-ECD

Let’s break down the steps from each method

IC-MS/MS

Sample* Analysis - Step	Description
Preparation	Add preservatives to QC samples (all other samples: add preservative at collection). Add appropriate amount of internal standard.
Analysis	Analyze the batch in IC-MS/MS after confirming status of instrument.
* Samples, including QC samples, must be maintained at ≤6 ℃ from collection until injection in IC-MS/MS	

Simple

Run time from EPA 557: 50 min

Data do NOT acquire with Shimadzu’s instrument

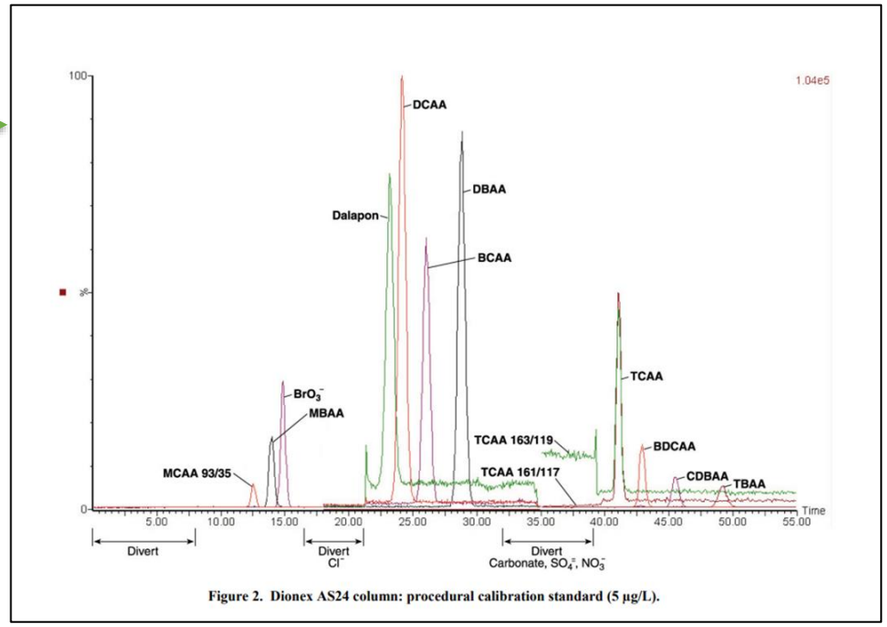


Figure 2. Dionex AS24 column: procedural calibration standard (5 µg/L).

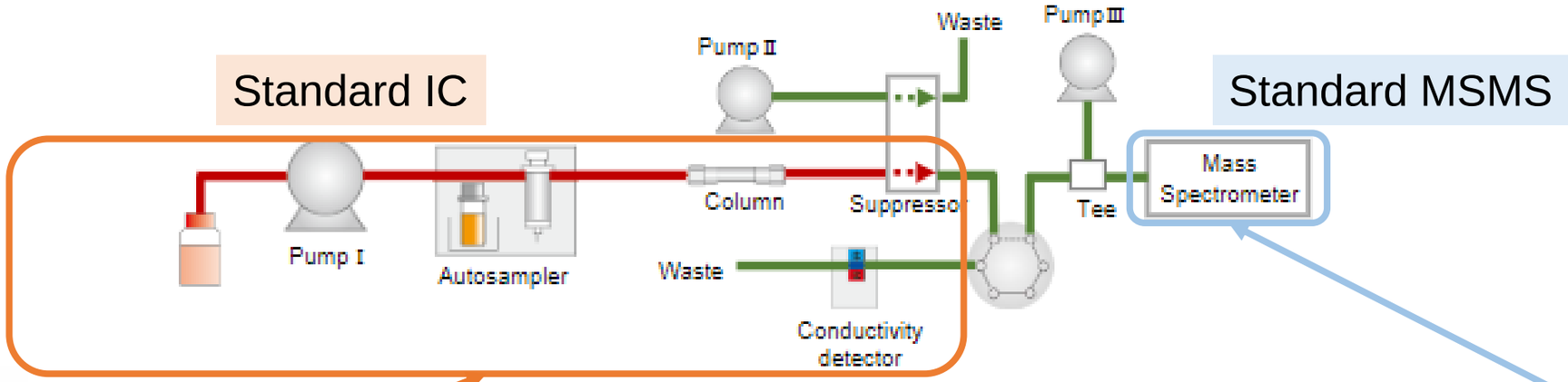
Let’s break down the steps from each method

IC-MS/MS

Additional pumps and valves needed for interfacing IC with MS/MS to:

- Divert mobile phase (high anions concentration)
- Add organic solvent

Complex



Method Comparison

Parameter	GC/ECD	IC-MS/MS
Updated Regulation	☑	☑
New Process Control	☑	☑☑
Health & Safety	☒	☑
Streamlined Operations	☒	☑
Instrument	Common	Uncommon; complex
CAPEX	☑☑☑	☑ to ☑☑
OPEX	☒	☑

☑ Good ☑☑ Very Good ☑☑☑ Extremely Good ☒ Not Good

Method Comparison

Parameter	GC/ECD	IC-MS/MS	Alternative?
Updated Regulation	☑	☑	
New Process Control	☑	☑☑	
Health & Safety	☒	☑	
Streamlined Operations	☒	☑	
Instrument	Common	Uncommon; complex	
CAPEX	☑☑☑	☑ ☑☑	
OPEX	☒	☑	

☑ Good ☑☑ Very Good ☑☑☑ Extremely Good ☒ Not Good

Alternative Method

Simultaneous LC-MS/MS Analysis of Haloacetic Acids, Bromate, Chlorate, and Dalapon

Currently approved for analysis of regulated HAAs in Japan
Viable option for monitoring in the European Union
Routinely used in R&D

Alternative Method

Simultaneous LC-MS/MS Analysis of Haloacetic Acids, Bromate, Chlorate, and Dalapon

Does it meet the method flexibility from EPA 557?

1.7 METHOD FLEXIBILITY – The laboratory is permitted to select IC columns, eluent compositions, eluent suppression techniques, and ESI-MS/MS conditions different from those utilized to develop the method. However, the basic chromatographic elements of the method must be retained. In order to avoid the effects of matrix suppression, the method analytes must be substantially resolved chromatographically from common anions in drinking water. Samples must be analyzed by direct injection. Filtering and pretreatment by use of solid phase extraction are not permitted. At a minimum, the four internal standards prescribed in this method must be used. **Changes may not be made to sample collection and preservation (Sect. 8) or to the quality control (QC) requirements (Sect. 9)**. Method modifications should be considered only to improve method performance. Modifications that are introduced in the interest of reducing cost or sample processing time, but result in poorer method performance, may not be used. In all cases where method modifications are proposed, the analyst must perform the procedures outlined in the Initial Demonstration of Capability (IDC, Sect. 9.2), verify that all QC acceptance criteria in this method (Tables 11 and 12) are met, and verify method performance in a real sample matrix (Sect. 9.4).

NOTE: Single quadrupole instruments are not permitted.

Alternative Method – LC-MS/MS

TARGETS
BrO_3^-
ClO_3^-
MCAA
DCAA
MBAA
BCAA
DBAA
Dalapon
TCAA
BDCAA
CDBAA
TBAA

EPA 557

INTERNAL STANDARDS
MCAA-2-^{13}C
MBAA-1-^{13}C
DCAA-2-^{13}C
TCAA-2-^{13}C

Alternative Method – LC-MS/MS

TARGETS
BrO_3^-
ClO_3^-
MCAA
DCAA
MBAA
BCAA
DBAA
Dalapon
TCAA
BDCAA
CDBAA
TBAA

EPA 557

INTERNAL STANDARDS
MCAA-2-^{13}C
MBAA-1-^{13}C
DCAA-2-^{13}C
TCAA-2-^{13}C

Sample* Analysis - Step	Description
EPA 557 Preparation	Add preservatives to QC samples (all other samples: add preservative at collection). Add appropriate amount of internal standard.
Analysis	Analyze the batch in LC-MS/MS after confirming status of instrument.

EPA 557

* Samples, including QC samples, must be maintained at ≤6 ℃ from collection until injection in LC-MS/MS

Alternative Method – LC-MS/MS

TARGETS
BrO_3^-
ClO_3^-
MCAA
DCAA
MBAA
BCAA
DBAA
Dalapon
TCAA
BDCAA
CDBAA
TBAA

EPA 557

INTERNAL STANDARDS
MCAA-2-^{13}C
MBAA-1-^{13}C
DCAA-2-^{13}C
TCAA-2-^{13}C

Sample* Analysis - Step	Description
EPA 557 Preparation	Add preservatives to QC samples (all other samples: add preservative at collection). Add appropriate amount of internal standard.
Analysis	Analyze the batch in LC-MS/MS after confirming status of instrument.

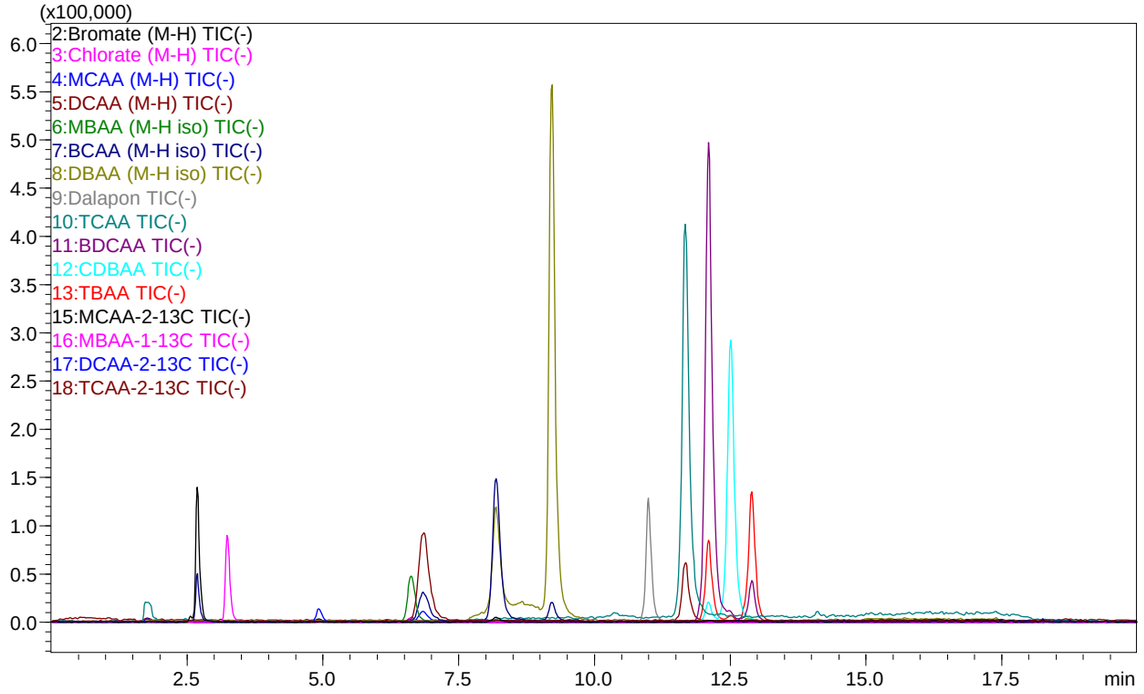
EPA 557

* Samples, including QC samples, must be maintained at ≤6 ℃ from collection until injection in LC-MS/MS

Alternative Method – LC-MS/MS

Nexera HPLC Conditions		
Mobile Phase A	0.05% formic acid in H2O	
Mobile Phase B	0.3% formic acid in 80:20 MeOH:H_2O	
Flow Rate	0.5 mL/min	
Gradient	Time (min) 0-2 6 7 12 16 16.1 20	% B 1 40 60 100 100 1 Stop
Column	Capcell Pak C18 MGIII 150x3mm, 3 µm	
Column Oven Temperature	25°C	
Injection Volume	30 µL	

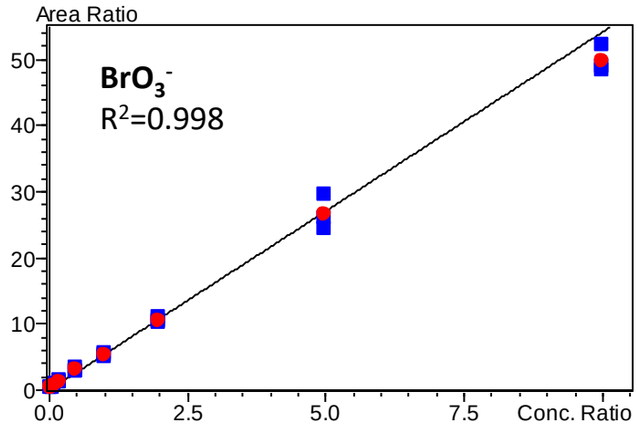
LCMS-8060NX	
Nebulizing Gas	2 L/min
Drying Gas Flow	20 L/min
Interface Temperature	100°C
Heat Block Temperature	75°C

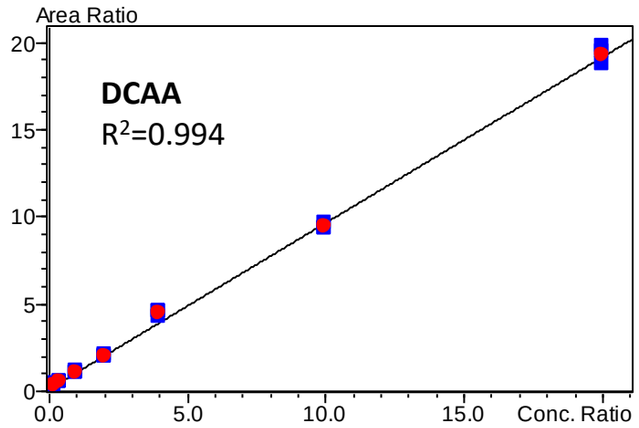


Sample to sample cycle time: 20 min
2 MRMs used for each compound

Synthetic sample matrix with extremely high ionic strength also analyzed to evaluate matrix effect

Alternative Method – LC-MS/MS



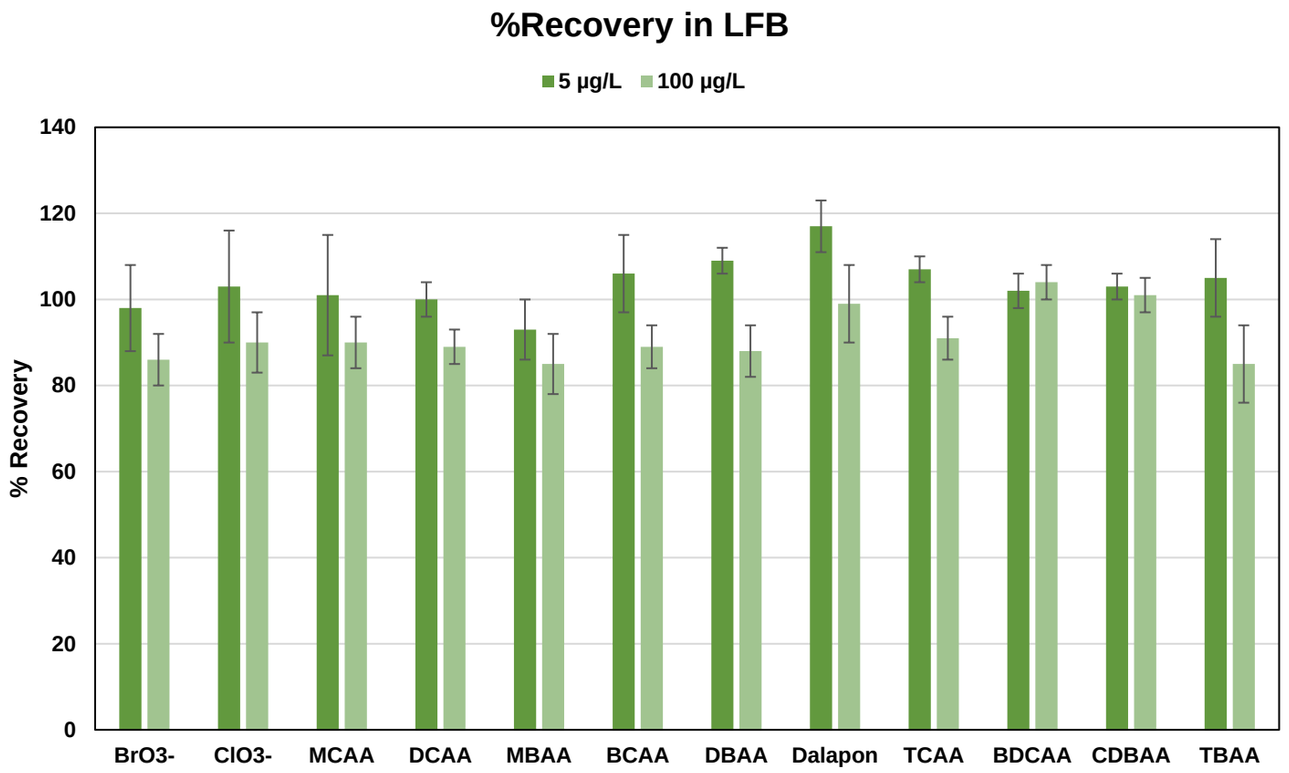


Compound	Linear Range (ug/L)	Equation	R^2
BrO_3^-	0.2 - 100	y = 5.41x + 0.05	0.996
ClO_3^-	1 – 100	y = 14.74x + 0.18	0.999
MCAA	1 – 100	y = 1.90x + 0.05	0.995
DCAA	1 – 100	y = 0.95x + 0.15	0.994
MBAA	1 – 100	y = 2.97x + 0.18	0.994
BCAA	0.5 – 100	y = 0.86x + 0.04	0.997
DBAA	0.2 – 100	y = 3.29x + 0.06	0.997
Dalapon	1 – 100	y = 0.45x - 0.00	0.992
TCAA	0.5 – 100	y = 5.10x + 0.08	0.998
BDCAA	0.1 – 100	y = 6.75x + 0.01	0.998
CDBAA	0.1 – 100	y = 4.34x + 0.01	0.998
TBAA	0.5 - 100	y = 1.65x – 0.00	0.998

Calibration curve:

- acquired in LCMS grade water; each standard analyzed in triplicates
- Linear fitting with a weighting of $1/C^2$
- R^2 >0.99 for all compounds
- Accuracies for calibration points within 80-120%

Alternative Method – LC-MS/MS



Laboratory fortified blank (LFB): LCMS grade water with100 mg/L ammonium chloride
LFB spiked with 5 µg/L and 100 µg/L analyzed with replication (n=6)
%Recovery for all compounds: 85-117%

Alternative Method – LC-MS/MS

Compound	DI Water	Tap Water A	Tap Water B	Tap Water C	River	Stream
BrO_3^-	ND	ND	ND	ND	ND	ND
ClO_3^-	ND	250 ± 20	220 ± 30	400 ± 50	16.1 ± 0.3	ND
MCAA	ND	ND	ND	ND	ND	ND
DCAA	ND	9.8 ± 0.7	ND	ND	ND	ND
MBAA	ND	ND	ND	ND	ND	ND
BCAA	ND	1.2 ± 0.1	ND	ND	ND	ND
DBAA	ND	ND	ND	ND	ND	ND
Dalapon	ND	1.5 ± 0.2	3.2 ± 0.8	ND	ND	ND
TCAA	ND	19 ± 1.0	15.5 ± 0.3	<LOQ	<LOQ	<LOQ
BDCAA	ND	3.6 ± 0.1	1.6 ± 0.1	0.2 ± 0.0	ND	ND
CDBAA	<LOQ	0.4 ± 0.1	<LOQ	<LOQ	ND	ND
TBAA	ND	ND	ND	ND	ND	ND
HAA9	0	34.3	17.2	0.2	0	0

Unspiked samples from different locations analyzed in triplicates
Concentration in µg/L (mean±standard dev) shown in table

SHIMADZU

Method Comparison

Parameter	GC/ECD	IC-MS/MS	LC-MS/MS
Updated Regulation	☑	☑	☑☑ to ☑☑☑
New Process Control	☑	☑☑	☑☑☑
Health & Safety	☒	☑	☑☑
Streamlined Operations	☒	☑	☑☑☑
Instrument	Common	Uncommon; complex	(Less) uncommon
CAPEX	☑☑☑	☑ to ☑☑	☑ to ☑☑
OPEX	☒	☑ to ☑☑	☑ to ☑☑

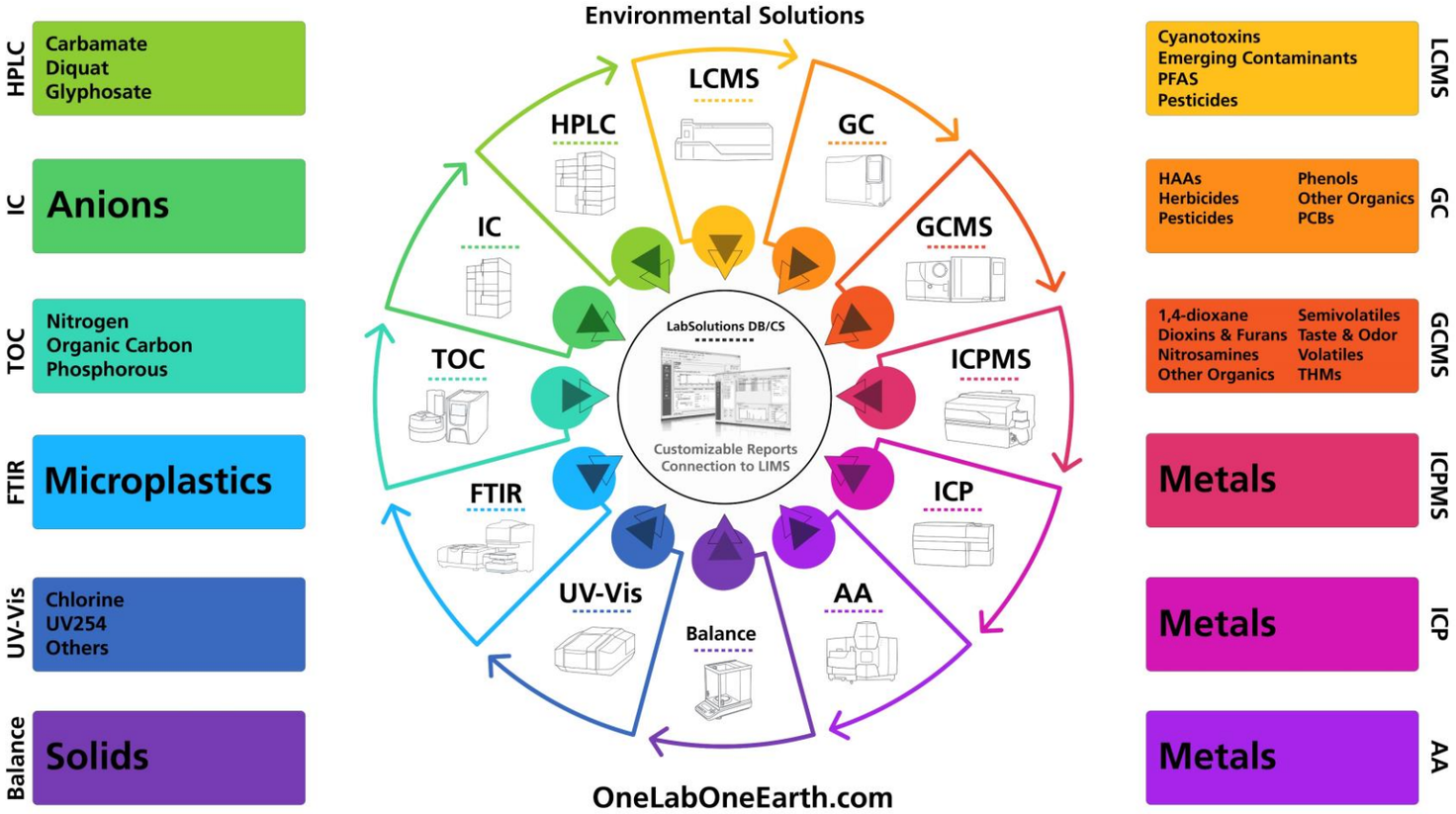
☑ Good ☑☑ Very Good ☑☑☑ Extremely Good ☒ Not Good

Conclusions

- ✓ GC-ECD based method is still the most commonly run for HAAS analysis in accredited laboratories
- ✓ IC based method is available, although with limited implementation in routine labs
- ✓ LC-MS/MS based method is suitable for the analysis and present multiple advantages

Parameter	GC/ECD	IC-MS/MS	LC-MS/MS
Updated Regulation	☑	☑	☑☑ to ☑☑☑
New Process Control	☑	☑☑	☑☑☑
Health & Safety	☒	☑	☑☑
Streamlined Operations	☒	☑	☑☑☑
Instrument	Common	Uncommon; complex	(Less) uncommon
CAPEX	☑☑☑	☑ to ☑☑	☑ to ☑☑
OPEX	☒	☑	☑☑

Q&A



Ruth Marfil-Vega, PhD
rmmarfilvega@shimadzu.com

www.OneLabOneEarth.com