METHOD 557: DETERMINATION OF HALOACETIC ACIDS, BROMATE, AND DALAPON IN DRINKING WATER BY ION CHROMATOGRAPHY ELECTROSPRAY IONIZATION TANDEM MASS SPECTROMETRY (IC-ESI-MS/MS)

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METHOD 557

DETERMINATION OF HALOACETIC ACIDS, BROMATE, AND DALAPON IN DRINKING WATER BY ION CHROMATOGRAPHY ELECTROSPRAY IONIZATION TANDEM MASS SPECTROMETRY (IC-ESI-MS/MS)

1. SCOPE AND APPLICATION

1.1 Method 557 is a direct-inject, ion chromatography, negative-ion electrospray ionization, tandem mass spectrometry (IC-ESI-MS/MS) method for the determination of haloacetic acids in finished drinking water. Bromate and dalapon (2,2-dichloropropionic acid) may be measured concurrently with the haloacetic acids. Real time, chromatographic separation of common anions in drinking water (matrix elimination) is a key feature of this method. Acceptable method performance has been demonstrated for matrix ion concentrations of 320 mg/L chloride, 250 mg/L sulfate, 150 mg/L bicarbonate and 20 mg/L nitrate. Method 557 requires the use of MS/MS in Multiple Reaction Monitoring (MRM) mode to enhance selectivity. Precision and accuracy data have been generated for the detection of nine haloacetic acids, bromate, and dalapon in reagent water, synthetic sample matrix, and finished drinking water from both ground water and surface water sources. The single laboratory Lowest Concentration Minimum Reporting Level (LCMRL) has also been determined in reagent water. Method 557 is applicable for the measurement of the following analytes:

Analyte	Chemical Abstracts Services Registry Number (CASRN)
Bromate (BrO_3^-)	15541-45-4 (BrO_3^- anion)
Bromochloroacetic acid (BCAA)	5589-96-8
Bromodichloroacetic acid (BDCAA)	71133-14-7
Chlorodibromoacetic acid (CDBAA)	5278-95-5
Dalapon	75-99-0
Dibromoacetic acid (DBAA)	631-64-1
Dichloroacetic acid (DCAA)	79-43-6
Monobromoacetic acid (MBAA)	79-08-3
Monochloroacetic acid (MCAA)	79-11-8
Tribromoacetic acid (TBAA)	75-96-7
Trichloroacetic acid (TCAA)	76-03-9

1.2 The chromatographic and MRM mass spectrometry conditions described in this method were developed using commercially available IC-ESI-MS/MS systems.

1.3 The single laboratory LCMRL is the lowest spiking concentration such that the probability of spike recovery in the 50% to 150% range is at least 99%. Single laboratory LCMRLs for the analytes in this method ranged from 0.042 to 0.58 microgram per liter (µg/L), and are listed in Table 5. The procedure used to determine the LCMRL is described elsewhere.[1]

1.4 Laboratories using this method are not required to determine LCMRLs, but they must demonstrate that the Minimum Reporting Level (MRL) for each analyte meets the requirements described in Section 9.2.4.

1.5 Detection Limit (DL) is defined as the statistically calculated minimum concentration that can be measured with 99% confidence that the reported value is greater than zero.[2] The DL is dependent on sample matrix, fortification concentration, and instrument performance. Determining the DL for analytes in this method is optional (Sect. 9.2.6). DLs for method analytes fortified into reagent water ranged from 0.015 to 0.20 µg/L (Table 6).

1.6 This method is intended for use by analysts skilled in the operation of IC-ESI-MS/MS instrumentation and the interpretation of the associated data.

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.

2. SUMMARY OF METHOD

Residual chlorine present in drinking water samples is reacted with ammonium chloride to form chloramines, effectively preventing chlorine-mediated formation of method analytes during storage. In addition, the combined chlorine residual prevents microbial degradation in the sample. Prior to analysis, isotopically enriched analytes (monochloroacetic acid-*2*-^{13}C, monobromoacetic acid-*1*-^{13}C, dichloroacetic acid-*2*-^{13}C, and trichloroacetic acid-*2*-^{13}C) are added to the samples as internal standards. An aliquot of the sample is injected without cleanup or concentration onto an ion exchange column specifically designed to separate method analytes from the following common anions (matrix components) in drinking water: chloride, carbonate, sulfate, and nitrate. The matrix components in the column eluate are monitored via conductivity detection and then diverted to waste; the analytes of interest are directed into the ESI-MS/MS system. Acetonitrile is added post-column to enhance desolvation of the method analytes in the ESI interface. Each

method analyte is qualitatively identified via a unique mass transition, and the concentration is calculated using the integrated peak area and the internal standard technique.

3. DEFINITIONS

3.1 ANALYSIS BATCH – A sequence of samples, analyzed within a 30-hour period, including no more than 20 field samples. Each Analysis Batch must also include all required QC samples, which do not contribute to the maximum field sample total of 20. The required QC samples include:

Laboratory Reagent Blank (LRB),
Continuing Calibration Check (CCC) Standards,
Laboratory Fortified Sample Matrix (LFSM), and
Laboratory Fortified Sample Matrix Duplicate or Laboratory Duplicate (LFSMD or LD).

3.2 CALIBRATION STANDARD – An aqueous solution of the method analytes prepared from the Primary Dilution Standard (Sect. 3.21) solution. The calibration standards are used to calibrate the instrument response with respect to analyte concentration.

3.3 CONTINUING CALIBRATION CHECK – A calibration standard containing the method analytes and internal standards, which is analyzed periodically to verify the accuracy of the existing calibration.

3.4 DETECTION LIMIT (DL) – The minimum concentration of an analyte that can be identified, measured, and reported with 99% confidence that the analyte concentration is greater than zero. This is a statistical determination (Sect. 9.2.6), and accurate quantitation is not expected at this level.

3.5 DIVERT WINDOW – The period of time during which the column eluate is directed to waste for the purpose of diverting matrix components away from the ESI-MS/MS system.

3.6 ELUTION WINDOW – The period of time during which the column eluate is directed to the ESI-MS/MS system for the purpose of measuring the method analytes.

3.7 INTERNAL STANDARD – A pure compound added to all standard solutions and samples in a known amount. Each internal standard is assigned to a specific analyte or multiple analytes, and is used to measure relative response.

3.8 ION SUPPRESSION/ENHANCEMENT – An observable loss or increase in analyte response in complex (field) samples as compared to the response obtained in standard solutions.

3.9 LABORATORY DUPLICATES (LDs) – Two sample aliquots (LD_1 and LD_2) taken in the laboratory from a single sample bottle, and analyzed separately with identical procedures. By cancelling variation contributed from sample collection, preservation, and storage

procedures, Laboratory Duplicates provide an estimate of precision associated specifically with the analytical determination.

3.10 LABORATORY FORTIFIED BLANK (LFB) – An aliquot of reagent water, containing the method preservative, to which known quantities of the method analytes are added. The LFB is used during the IDC to verify method performance for precision and accuracy.

3.11 LABORATORY FORTIFIED SAMPLE MATRIX (LFSM) – An aliquot of a field sample to which known quantities of the method analytes are added. The LFSM is processed and analyzed as a sample, and its purpose is to determine whether the sample matrix contributes bias to the analytical results.

3.12 LABORATORY FORTIFIED SAMPLE MATRIX DUPLICATE (LFSMD) – A second aliquot of the field sample used to prepare the LFSM which is fortified and analyzed identically to the LFSM. The LFSMD is used instead of the Laboratory Duplicate to assess method precision when the method analytes are rarely found at concentrations greater than the MRL.

3.13 LABORATORY FORTIFIED SYNTHETIC SAMPLE MATRIX (LFSSM) – Aliquots of the Laboratory Synthetic Sample Matrix (Sect. 3.15) fortified with known quantities of the method analytes. The LFSSM is analyzed at the beginning of each Analysis Batch to verify that the matrix components elute within the divert windows, and to ensure that no portion of an analyte peak is inadvertently diverted to waste. The LFSSM also serves as a QC sample for the purpose of estimating precision and accuracy during the IDC.

3.14 LABORATORY REAGENT BLANK (LRB) – An aliquot of reagent water that contains the preservative and internal standards. The LRB is used to determine if the method analytes or other interferences are introduced from the laboratory environment, the reagents or glassware, and to test for cross contamination.

3.15 LABORATORY SYNTHETIC SAMPLE MATRIX (LSSM) – For this method, the LSSM is a solution of common anions prepared at high concentrations relative to their typical occurrence in drinking water. Guidance for preparation of the LSSM is provided in Section 7.2.

3.16 LOWEST CONCENTRATION MINIMUM REPORTING LEVEL (LCMRL) – The single laboratory LCMRL is the lowest spiking concentration such that the probability of spike recovery in the 50% to 150% range is at least 99%.[1]

3.17 MATERIAL SAFETY DATA SHEETS (MSDS) – Written information provided by vendors concerning a chemical's toxicity, health hazards, physical properties, fire and reactivity data, storage instructions, spill response procedures, and handling precautions.

3.18 MINIMUM REPORTING LEVEL (MRL) – The minimum concentration that can be reported by a laboratory as a quantified value for the method analyte in a sample following analysis. This concentration must meet the criteria defined in Section 9.2.4 and must be no

lower than the concentration of the lowest calibration standard for each method analyte. A laboratory may be required to demonstrate a specific MRL by a regulatory body if this method is being performed for compliance purposes.

3.19 MULTIPLE REACTION MONITORING (MRM) – A mass spectrometric technique in which a precursor ion (Sect. 3.20) is first isolated, then subsequently fragmented into a product ion(s) (Sect. 3.23). Quantitation is accomplished by monitoring a specific product ion. As described in Section 10.2.2, MS parameters must be optimized for each precursor ion and product ion.

3.20 PRECURSOR ION – The precursor ion is the gas-phase species corresponding to the method analyte produced in the ESI interface. In MS/MS, the precursor ion is mass selected and fragmented by collision-activated dissociation to produce distinctive product ions of smaller mass/charge (*m/z*) ratio.

3.21 PRIMARY DILUTION STANDARD (PDS) – An aqueous solution containing the method analytes (or internal standards) prepared from Stock Standard Solutions and diluted as needed to prepare calibration standards and sample fortification solutions.

3.22 PROCEDURAL CALIBRATION – A calibration technique in which calibration standards are processed through the entire method, including sample preparation and addition of preservatives.

3.23 PRODUCT-ION – For the purpose of this method, a product ion is one of the fragment ions produced in MS/MS by collision-activated dissociation of the precursor ion.

3.24 QUALITY CONTROL SAMPLE (QCS) – A solution containing the method analytes at a known concentration, which is obtained from a source external to the laboratory and different from the source of calibration standards. The purpose of the QCS is to verify the accuracy of the primary calibration standards.

3.25 REAGENT WATER – Purified water that does not contain any measurable quantity of the method analytes or interfering compounds at or above 1/3 the MRL.

3.26 STOCK STANDARD SOLUTION (SSS) – A concentrated solution containing one or more of the method analytes that is prepared in the laboratory using assayed reference materials or purchased from a reputable commercial source, so that the concentration and purity of analytes are traceable to certificates of analysis.

4. INTERFERENCES

4.1 GLASSWARE – During method development, no problems with stability of the method analytes, interferences, or cross contamination related to glass containers were observed. Sample collection bottles and vials containing samples and standards may be reused after thorough rinsing with reagent water. Dry glassware in an oven or air dry. Teflon-faced septa, if not punctured, may be cleaned and reused. Vials containing PDS solutions must be

rinsed with methanol before reuse and the septa discarded. It is recommended that autosampler vials and septa be discarded after a single use.

4.2 REAGENTS AND EQUIPMENT – Method interferences may be caused by contaminants in solvents and reagents (including reagent water). All laboratory reagents must be routinely demonstrated to be free from interferences (less than 1/3 the MRL for the method analytes) under the conditions of the analysis. This may be accomplished by analyzing LRBs as described in Section 9.3.1.

4.3 MATRIX INTERFERENCES – Matrix interferences are caused by contaminants that are present in the sample. The extent of matrix interferences will vary considerably from source to source depending upon the nature of the water. Matrix components may directly interfere by producing a signal at or near the retention time of an analyte peak. Matrix components may also suppress or enhance the signal of the method analytes. (Suppression and enhancement effects occur during the ionization process in the electrospray source when a co-eluting contaminant influences the ionization of the analyte of interest.) Common anions present in drinking water matrices, which would cause matrix suppression, are diverted from the MS. In addition, the internal standards recommended in this method performed well in a variety of matrices. However, these measures may not compensate for all potential matrix effects. The analysis of Laboratory Fortified Sample Matrix (Sect. 9.3.5) provides evidence for the presence (or absence) of matrix effects.

4.4 INTERFERENCE FROM SYSTEM CONTAMINANTS – Contaminants in the mobile phase, autosampler, column, or other system components may produce a signal at or near the retention time of a method analyte. Such an interfering signal may be observed as a shoulder on an analyte peak or detected as an analyte peak in the Laboratory Reagent Blank. If this occurs, attempt to eliminate the interference. If unsuccessful, investigate alternate MRM transitions.

4.5 INTERFERENCE FROM INTERNAL STANDARDS – Depending on the source and purity, labeled haloacetic acid internal standards may contain a small percentage of the corresponding native analyte. Usually, such contributions are insignificant when performing the method within the normal calibration range of 0.25 to 20 µg/L. However, the contribution may be significant when attempting to determine LCMRLs and DLs. The labeled internal standards must meet the purity requirements stated in the IDC (Section 9.2.1).

4.6 BREAKDOWN OF DALAPON, CDBAA, AND TBAA IN AQUEOUS MEDIA – Under the conditions described in Section 8, the method analytes are stable in aqueous media within the stated holding time. However, during method development, dalapon, CDBAA, and TBAA—in both standards and drinking water samples—degraded while awaiting analysis in conventional autosamplers that may reach temperatures between 25° and 30 °C during operation. For this reason, refrigerated autosamplers, capable of maintaining samples at a temperature of less than or equal to 10 °C, are required for use with Method 557.

4.7 ION SUPPRESSION IN THE PRESENCE OF CHLORITE – The chlorite anion (ClO_2^-) may be present in drinking water distribution systems employing chlorine dioxide (ClO_2) as a disinfectant. During method development studies, severe signal suppression of MCAA and excessive band broadening of the MCAA chromatographic peak profile were observed in the presence of 1 mg/L ClO_2^-, the maximum contaminant level (MCL). As depicted in Figure 4, the ClO_2^- anion co-eluted with MCAA. Method 557 is not applicable to drinking water treated with ClO_2 unless the laboratory demonstrates alternate chromatographic conditions (other than those used to develop the method, Section 17, Table 1) that eliminate the suppression. That is, chlorite must be resolved chromatographically from MCAA and the other method analytes. Alternately, the laboratory must demonstrate that the chlorite anion is not present in the sample matrix.

4.8 SIGNAL SUPPRESSION DUE TO EXCESSIVE BACKGROUND CONDUCTIVITY – The ESI interface is sensitive to the background conductivity of column eluate. The analyst should observe the background conductivity prior to starting an analysis sequence each day. If using a concentration gradient, make this observation at the initial eluent concentration. At the maximum concentration in the gradient, the background conductivity will increase compared to the conductivity at the initial concentration. In this region of the chromatogram, the potential for suppression from the background conductivity is greatest. Such suppression may be evidenced by difficulty detecting TBAA, or by peak areas that are low compared to historical values when the background conductivity was lower. Section 11.3.2 provides guidance on corrective action if background conductivity is problematic.

4.9 PEAK TAILING – Peak tailing may be observed as the column ages. Peak tailing will limit the analyst's ability to separate matrix components from the method analytes. Peak tailing should be minimal with a properly configured ion chromatography system when using a new column. (See Figure 2.) If tailing is observed with continued column use, original performance can usually be restored by replacing the guard column.

4.10 EFFECT OF TEMPERATURE ON ANALYTE STABILITY – MBAA CDBAA, and TBAA degrade readily in aqueous eluent at high pH. Such conditions may exist in the mobile phase of ion exchange columns. The reaction is temperature dependent. For this reason, the separation is performed at subambient temperature, specifically 15 °C. At 15 °C, degradation in the column eluent is minimized.

4.11 MANAGING DIVERT WINDOWS – Analyte retention times may slowly shift toward lower values as the column ages or becomes fouled. Because this method employs multiple divert windows, the analyst must monitor peak locations on a daily basis to ensure that each analyte peak elutes entirely within the MS/MS elution windows. Guidance for verifying elution/divert windows is provided in Section 10.2.5. To avoid loss of column capacity, follow the manufacturer's instructions for proper operating temperature and for storage conditions when the column is not in use.

4.12 BAND BROADENING AND RETENTION TIME (RT) SHIFTS IN HIGH IONIC STRENGTH MATRICES – Method performance has not been evaluated for matrix ion concentrations exceeding 320 mg/L chloride, 250 mg/L sulfate, 150 mg/L bicarbonate and 20

mg/L nitrate. Near these limits, the analyte peaks will widen, peak height will decrease, and retention times will decrease slightly. These effects are compound dependent, but affect all analytes to some degree. Such effects were minimal in the drinking water matrices evaluated, but were more pronounced in Laboratory Synthetic Sample Matrix. [Compare Figure 3 (fortified tap water) and Figure 4 (fortified synthetic matrix).] Note that the concentrations of common anions in the LSSM are at the limits listed above. This method requires the analyst to verify method performance in LSSM during the IDC, and to verify elution/divert windows on a daily basis in LFSSM to ensure that these windows are properly set to compensate for the potential effects of high ionic strength matrices.

5. SAFETY

5.1 The toxicity and carcinogenicity of each reagent used in this method has not been precisely defined. Each chemical should be treated as a potential health hazard and exposure to these chemicals should be minimized. Each laboratory is responsible for maintaining an awareness of OSHA regulations regarding safe handling of chemicals used in this method.[3] The OSHA laboratory standards can be found online at http://www.osha.gov/SLTC/laboratories/standards.html. A reference file of MSDSs should be made available to all personnel involved in the chemical analysis.

5.2 Pure standard materials and stock standard solutions of the method compounds should be handled with suitable protection for skin, eyes, etc.[4]

6. EQUIPMENT AND SUPPLIES

References to specific brands or catalog numbers are included as examples only and do not imply endorsement of the product. Such reference does not preclude the use of other vendors or suppliers.

6.1 SAMPLE CONTAINERS – Amber glass bottles fitted with polytetrafluoroethylene (PTFE) -lined screw caps with sufficient volume to allow preparation of all required sample and QC aliquots.

6.2 VIALS FOR SAMPLE PREPARATION – Amber glass vials with PTFE/silicone septa for use preparing field samples and QC samples. Forty-milliliter (mL) volatile organic analysis (VOA) vials (I-Chem Cat. No. S146–0040 or equivalent) were used during method development.

6.3 AUTOSAMPLER VIALS – Glass vials with PTFE/silicone septa.

6.4 MICRO SYRINGES – Suggested sizes include 50, 100, and 1000 microliters (µL).

6.5 VOLUMETRIC PIPETTES – Class A, for preparing calibration standards, and for measuring aliquots of field samples and QC samples.

6.6 AUTOMATIC PIPETTE – Electronic, with polypropylene tips (Eppendorf Research Pro or equivalent). An automatic pipette is recommended for fortifying samples with internal standards.

6.7 ANALYTICAL BALANCE – Capable of weighing to the nearest 0.0001 gram (g).

6.8 TOP-LOADING BALANCE – Capable of weighing to the nearest 0.01 g. A top-loading balance and disposable pipettes may be used to measure aqueous sample volumes and to prepare aqueous calibration standards.

6.9 DESOLVATION GAS – High-purity gas (nitrogen or zero-air) for use in the ESI interface. The specific type of gas, purity and pressure requirements will depend on the instrument manufacturer's specifications.

6.10 COLLISION GAS – High-purity gas (nitrogen or argon) for use in the collision cell of the mass spectrometer. The specific type of gas, purity, and pressure requirements will depend on the instrument manufacturer's specifications.

6.11 DISPOSABLE PASTEUR PIPETTES – Borosilicate glass, used to transfer samples to autosampler vials and for sample preparation.

6.12 ION CHROMATOGRAPHY ELECTROSPRAY IONIZATION TANDEM MASS SPECTROMETRY SYSTEM (IC-ESI-MS/MS) – The following specifications are based on use of a Dionex Corporation AS24 ion exchange column and a hydroxide-based eluent system. Other columns and eluent systems are permitted providing that the basic chromatographic elements of the method are retained (Sect. 1.7).

6.12.1 IC SYSTEM WITH SUPPRESSED CONDUCTIVITY DETECTION – An analytical system (Dionex ICS-3000 or equivalent) consisting of a refrigerated autosampler, pump module, anion trap, guard column, anion separator column, a six-port injection valve, sample loop, conductivity suppressor, conductivity detector, post-column divert valve, and a data acquisition and management system. The laboratory must be able to acquire and store conductivity data for the purpose of monitoring matrix components and establishing elution/divert windows.

6.12.1.1 ELUENT GENERATION – Reagent-free electrolytic eluent generation (Dionex ICS-3000 EG or equivalent) or manually prepared reagents may be used. Care must be exercised with manually prepared hydroxide eluent to prevent formation of carbonate in the eluent from exposure to the atmosphere, which could cause analyte retention times to drift.

6.12.1.2 ANION TRAP – A continuously regenerated anion trap column (Dionex CR-ATC or equivalent).

6.12.1.3 SAMPLE LOOP – 100-µL size. A 100-µL sample loop was used to generate the data presented in this method. Smaller injection volumes may be used as long as the Initial Demonstration of Capability (Sect. 9.2), calibration, and sample analyses are performed using the same injection volume. The laboratory must be able to meet the MRL verification criteria (Section 9.2.4) using the selected injection volume.

6.12.1.4 GUARD COLUMN – IonPac® AG24, 2 x 50 millimeters (mm) (Dionex Part No. 064151 or equivalent). The guard column is generally packed with the same resin as the analytical column.

6.12.1.5 ANALYTICAL COLUMN – IonPac® AS24, 2 x 250 mm (Dionex Part No. 064153 or equivalent). Any column that provides on-line separation of common anions (chloride, carbonate, sulfate, and nitrate) from the method analytes and symmetrical peak shapes may be used. The column must have sufficient capacity to minimize retention time shifts in high ionic strength matrices.

6.12.1.6 COLUMN COMPARTMENT – Temperature controlled and capable of subambient operation.

6.12.1.7 CONDUCTIVITY SUPPRESSOR – An electrolytic suppressor operated with an external source of regeneration water (Dionex Anion Self Regenerating Suppressor Model No. ASRS®-300, 2-mm, Part No. 064555 or equivalent). Chemical conductivity suppressors, although not prohibited, have not been evaluated for use with Method 557.

6.12.1.8 CONDUCTIVITY DETECTOR – A flow-through detector with an internal volume that does not introduce analyte band broadening.

6.12.1.9 POST-COLUMN DIVERT VALVE – A two-position, six-port valve may be used. All wetted parts must be of polyetheretherketone (PEEK) construction. The proper placement of the divert valve in the sample path is illustrated in Figure 1.

6.12.2 AUXILIARY PUMP – Pump capable of precisely delivering flow rates between 0.2 and 0.3 mL/minute. This pump is used to mix acetonitrile into the suppressed eluent post-column. (Dionex high performance metering pump, Model No. AXP-MS or equivalent). See Figure 1 for placement of the pump in the sample path.

6.12.3 STATIC MIXING TEE – High pressure, microbore mixing tee. (Upchurch Scientific, Oak Harbor, WA, Part No. U-466 or equivalent). The proper placement of the mixing tee in the sample path is illustrated in Figure 1.

6.12.4 ELECTROSPRAY IONIZATION – TANDEM MASS SPECTROMETER (ESI – MS/MS) – The mass spectrometer interface must be able to operate in the negative-ion electrospray ionization mode. The system must be capable of performing MS/MS to produce unique product ions for the method analytes within specified retention time windows. Method performance data presented in Section 17 were collected using a Waters Quattro Premier XE ESI-MS/MS system.

6.12.5 MS/MS DATA SYSTEM – An interfaced data system is required to acquire, store, and output MS data. The computer software must have the capability of processing stored data by recognizing a chromatographic peak within a given retention time window. The software must allow integration of the ion abundance of any specific ion between

specified time or scan number limits. The software must be able to construct a linear regression or quadratic calibration curve and calculate analyte concentrations using the internal standard technique.

7. REAGENTS AND STANDARDS

7.1 REAGENTS AND SOLVENTS – Reagent grade or better chemicals must be used. Unless otherwise indicated, it is intended that all reagents will conform to the specifications of the Committee on Analytical Reagents of the American Chemical Society (ACS), where such specifications are available. Other grades may be used if all the requirements of the IDC are met when using these reagents.

7.1.1 ACETONITRILE (CAS No. 75-05-8) – Post-column organic modifier. High purity, demonstrated to be free of analytes and interferences (Honeywell Burdick & Jackson Brand®, Catalog No. 015 or equivalent).

7.1.2 METHYL-TERTIARY-BUTYL ETHER (MtBE, CAS No. 1634-04-4) – High-performance liquid chromatography-grade (Sigma-Aldrich Catalog No. 34875 or equivalent). MtBE is used to prepare dilutions of neat standard materials.

7.1.3 AMMONIUM CHLORIDE (NH_4Cl, CAS No. 12125-02-9) – Method preservative.

7.1.4 SODIUM BICARBONATE (CAS No. 144-55-8) – Laboratory Synthetic Sample Matrix component.

7.1.5 SODIUM CHLORIDE (CAS No. 7647-14-5) – Laboratory Synthetic Sample Matrix component.

7.1.6 SODIUM NITRATE (CAS No. 7631-99-4) – Laboratory Synthetic Sample Matrix component.

7.1.7 SODIUM SULFATE (CAS No. 7757-82-6) – Laboratory Synthetic Sample Matrix component.

7.2 LABORATORY SYNTHETIC SAMPLE MATRIX (LSSM) – Prepare the LSSM at the concentrations listed in the table below. The required concentrations of nitrate (20 mg/L), bicarbonate (150 mg/L), chloride (250 mg/L), and sulfate (250 mg/L) are based on the mass of the anion, not the sodium salt. The NH_4Cl preservative is included in the matrix. LFSSM QC samples (Sect. 3.13) can be prepared by diluting the Analyte PDS (Sect. 7.3.2.2) with the synthetic matrix solution.

Compound	Empirical Formula	Salt (gfw)[a]	Anion (gfw)	Salt Mass (mg)	H_2O, L	Conc. Stock (mg/L)[b]	Conc. LSSM (mg/L)[c]
Ammonium chloride (preservative)	NH_4Cl	53.49		500	0.5	1000	100
Nitrate anion	NO_3^-	84.99	62.00	137		200	20
Bicarbonate anion	HCO_3^-	84.01	61.02	1030		1500	150
Chloride anion	Cl^-	58.44	35.45	2060		2500	250
Sulfate anion	SO_4^{--}	142.04	96.06	1850		2500	250

[a] gfw = gram formula weight of the sodium salt.

[b] Stock concentration = (salt mass)(gfw anion)/(gfw salt)(0.5 L).

[c] 1:10 dilution of stock (e.g., 50 mL to 500 mL), LSSM = Laboratory Synthetic Sample Matrix.

7.3 STANDARD SOLUTIONS – Solution concentrations listed in this section were used to develop this method and are included only as examples. Guidance on the storage stability of Primary Dilution Standards and calibration standards is provided in the applicable sections below.

NOTE: When preparing aqueous solutions from MtBE stock solutions, do not add more than 0.5% of MtBE relative to the total water volume. MtBE has limited water solubility (~5%).

7.3.1 INTERNAL STANDARDS – This method requires four isotopically enriched internal standards. The following table lists the required internal standards and current sources.

Internal Standard	CASRN[a]	Neat Materials Catalog No.	Solution Standards (1000 µg/mL in MtBE), Cat. No.
Monochloroacetic acid-*2*-^{13}C	1633-47-2	Sigma-Aldrich 488526	Dionex Corp. 069406
Monobromoacetic acid-*1*-^{13}C	57858-24-9	Sigma-Aldrich 279331	Dionex Corp. 069407
Dichloroacetic acid-*2*-^{13}C	286367-78-0	Sigma-Aldrich 485489	Dionex Corp. 069408
Trichloroacetic acid-*2*-^{13}C	Not available	Custom synthesis[b]	Dionex Corp. 069409

[a] CASRN = Chemical Abstract Registry Number.

[b] Isotec, a member of the Sigma-Aldrich Group (www.sigma-aldrich.com/isotec).

NOTE: TCAA[1-^{13}C] may NOT be substituted for TCAA[2-^{13}C]. TCAA[1-^{13}C] has been demonstrated to convert to the native TCAA analyte in the ESI interface, theoretically via gas-phase exchange with carbon dioxide-^{12}C in the ionization region of the source. The process is temperature dependent (desolvation gas temperature) and was observed on all MS/MS platforms evaluated during method development.

7.3.1.1 INTERNAL STANDARD STOCK STANDARDS (ISSS) (1000 µg/mL) – Prepare individual solutions of MCAA[2-^{13}C], MBAA[1-^{13}C], DCAA[2-^{13}C], and TCAA[2-^{13}C] by weighing 15 mg of the solid material into a 15-mL vial and adding 15 mL of MtBE. Alternately, obtain the internal standards from outside suppliers as solutions in MtBE at 1000 µg/mL.

7.3.1.2 INTERNAL STANDARD PRIMARY DILUTION STANDARD (Internal Standard PDS) (1.0 µg/mL) – Prepare the Internal Standard PDS by adding enough of each ISSS to a known volume of reagent water to make the final concentration 1.0 µg/mL (e.g., combine 100 µL of each ISSS into 100 mL reagent water). Store the PDS in a

glass vial with a PTFE/silicone septum. During method development, addition of 160 µL of the Internal Standard PDS to each 40-mL field sample, QC sample, or calibration standard produced a final concentration of 4.0 µg/L. Analysts are permitted to use other PDS concentrations and volumes provided all field samples, QC samples, and calibration standards contain the same amount of internal standard, the concentration of the internal standard added provides adequate signal to maintain precision (as defined in the IDC), and the volume added has a negligible effect on the final concentration. The aqueous Internal Standard PDS is stable for 60 days when stored at 4 °C.

7.3.2 ANALYTE STANDARD SOLUTIONS

7.3.2.1 ANALYTE STOCK STANDARD SOLUTION (1000 µg/mL) – Obtain the haloacetic acid analytes listed in the table in Section 1.1 as certified solutions in MtBE. Obtain bromate as a certified aqueous standard. Obtain dalapon as a certified standard in MtBE or in methanol. Representative sources are listed in the table in Section 7.3.2.2.

7.3.2.2 ANALYTE PRIMARY DILUTION SOLUTION (Analyte PDS) (1.0 µg/mL) – Prepare the Analyte PDS by diluting of the Analyte Stock Standard solutions into reagent water. Store the PDS in a glass vial with a PTFE/silicone septum. The Analyte PDS is used to prepare calibration standards, and to fortify QC samples with the method analytes. An example preparation of the Analyte PDS that was used to collect data presented in Section 17 is provided in the table below.

Analyte Stock	Catalogue Number	Stock Concentration (µg/mL)	Stock Volume (mL)	Final Volume (mL reagent water)	Analyte PDS Concentration (µg/mL)
Bromate, aqueous	Ultra Scientific Cat. No. ICC-010	1000 as bromate anion	0.05	50	1.0
Dalapon in methanol	Ultra Scientific Cat. No. HB-140	100	0.50		
Haloacetic acids in methyl-tert-butyl ether	Restek Cat. No. 31896	1000	0.05		

NOTE: Storage stability of the Analyte PDS was evaluated during method development at a single concentration of 1.0 µg/mL. The aqueous Analyte PDS is stable for 60 days when stored at 4 °C. Other PDS concentrations may be selected. However, it is recommended that the laboratory independently assess the stability of the aqueous PDS to determine safe storage time.

7.3.2.3 CALIBRATION STANDARDS – This method uses a procedural calibration technique. Prepare procedural calibration standards by diluting the Analyte PDS into reagent water containing 100 mg/L NH_4Cl (preservative). A calibration range of 0.25 to 20 µg/L is recommended as a starting point and is adequate for most drinking water sources. The lowest concentration calibration standard must be at or below the

MRL. A constant amount of each internal standard is added to each calibration standard. The calibration standards may also be used as CCCs. An example of the dilutions (starting with the Analyte PDS) necessary to prepare the calibration standards is provided in the table below.

Dilution Aliquot	Starting Concentration (µg/L)	Final Volume (mL, 100 mg/L ammonium chloride, aqueous)	Final Concentration (µg/L)	Internal Standard Concentration[a] (µg/L)
2 mL Analyte PDS	1000	50	40 (WS)[a]	4.0
20 mL of WS	40	40	20	4.0
10 mL of WS	40	40	10	4.0
5 mL of WS	40	40	5.0	4.0
2 mL of WS	40	40	2.0	4.0
1 mL of WS	40	40	1.0	4.0
4 mL of 5 µg/L std.	5.0	40	0.50	4.0
2 mL of 5 µg/L std.	5.0	40	0.25	4.0

[a] Internal standards added at the rate of 160 µL to 40 mL by use of an Eppendorf Research Pro pipette:

(0.16 mL)(1.0 µg/mL)/(0.040 liter) = 4.0 µg/L internal standard concentration

[b] WS = working standard; not analyzed.

NOTE: The stability of calibration standards was evaluated during method development at concentrations of 2.0 and 5.0 µg/L. The aqueous calibration standards are stable for 14 days when stored at 4 °C in glass vials with PTFE/silicone septa. It is recommended that the laboratory independently assess the stability of the aqueous calibration standards to determine safe storage time.

8. SAMPLE COLLECTION, PRESERVATION, AND STORAGE

The preservation requirements for Method 557 are identical to those stipulated in EPA Method 552.3, *Determination of Haloacetic Acids and Dalapon in Drinking Water by Liquid-Liquid Microextraction, Derivatization, and Gas Chromatography with Electron Capture Detection*.[5]

8.1 SAMPLE BOTTLE PREPARATION

8.1.1 SAMPLE CONTAINERS – Amber glass bottles with PTFE-lined screw caps and sufficient capacity to allow subsequent preparation of all required sample and QC aliquots.

8.1.2 ADDITION OF PRESERVATIVE – Prior to shipment to the field, add crystalline or granular NH_4Cl to the sample containers to produce a concentration of 100 mg/L in the field sample. For example, a 250-mL sample requires 25 mg of NH_4Cl.

8.2 SAMPLE COLLECTION – Grab samples must be collected in accordance with conventional sampling practices.[6] Fill sample bottles taking care not to flush out the ammonium chloride. Because the method analytes are not volatile, it is not necessary to ensure that the sample bottles are completely headspace-free.

8.2.1 SAMPLING FROM A TAP – When sampling from a cold water tap, remove the aerator, open the tap, and allow the system to flush until the water temperature has stabilized (approximately three to five minutes). Collect a representative sample from the flowing system using a beaker of appropriate size. Use this bulk sample to generate individual samples as needed. Invert the vials several times to mix the sample with the preservation reagent.

8.3 SAMPLE SHIPMENT AND STORAGE – Samples must be chilled during shipment and must not exceed 10 °C during the first 48 hours after collection. Samples must be confirmed to be at or below 10 °C when they are received at the laboratory. In the laboratory, samples must be stored at or below 6 °C and protected from light until analysis. Samples must not be frozen.

8.4 SAMPLE HOLDING TIMES – Samples must be analyzed within 14 days of collection. Chlorinated field samples that are preserved in accordance with the method guidance should not exhibit biological degradation of analytes during the allotted 14-day storage time. **The residency time in the autosampler must be included when calculating the holding time from collection until analysis.**

9. QUALITY CONTROL

9.1 QC requirements include the IDC and ongoing QC requirements. This section describes each QC parameter, its required frequency, and the performance criteria that must be met in order to satisfy EPA quality objectives. The QC criteria discussed in the following sections are summarized in Section 17, Tables 11 and 12. These QC requirements are considered the minimum acceptable QC program. Laboratories are encouraged to institute additional QC practices to meet their specific needs.

9.2 INITIAL DEMONSTRATION OF CAPABILITY (IDC) – The IDC must be successfully performed prior to analyzing any field samples. The IDC must be repeated if changes are made to analytical parameters not previously validated during the IDC, for example, selection of an alternate MRM transition or changing the internal standard assignment of an analyte. Prior to conducting the IDC, the analyst must verify proper timing of elution windows and divert windows (Section 10.2.5), and meet the calibration requirements outlined in Sections 10.2 and 10.3.

9.2.1 DEMONSTRATION OF LOW SYSTEM BACKGROUND – Analyze an LRB. Confirm that the blank is free of contamination as defined in Section 9.3.1.

NOTE: Depending on the source and purity, labeled haloacetic acid internal standards may contain a small percentage of the corresponding native analyte. Therefore, the analyst must demonstrate that the internal standards do not contain the unlabeled analytes at a concentration $\geq$1/3 of the MRL when added at the appropriate concentration to samples. An internal standard concentration of 4.0 µg/L was used during method development. Lower concentrations may be used providing the internal standard QC criteria (Sect. 9.3.4) are met.

NOTE: The method must be checked for cross contamination (commonly referred to in the environmental laboratory community as "carryover") by analyzing an LRB immediately following the highest calibration standard. If this LRB does not meet the criteria outlined in Section 9.3.1, then carryover is present and the cause must be identified and eliminated.

9.2.2 DEMONSTRATION OF PRECISION – Prepare and analyze seven replicate LFBs and seven replicate LFSSMs. Fortify these samples near the midrange of the initial calibration curve. The NH_4Cl preservative must be added to the LFBs as described in Section 8.1.2. The percent relative standard deviation (RSD) of the concentrations of the replicate analyses must be ≤20% for all method analytes.

$$\%\,\mathrm{RSD} = \frac{\text{Standard Deviation of Measured Concentrations}}{\text{Average Concentration}} \times 100$$

9.2.3 DEMONSTRATION OF ACCURACY – Using the same sets of replicate data generated for Section 9.2.2, calculate the average percent recovery. The average percent recovery of the replicate analyses must be within ±30% of the true value.

$$\%\,\mathrm{Recovery} = \frac{\text{Average Measured Concentration}}{\text{Fortified Concentration}} \times 100$$

9.2.4 MINIMUM REPORTING LEVEL (MRL) CONFIRMATION – Establish a target concentration for the MRL based on the intended use of the method. Analyze an initial calibration following the procedures in Section 10.3. The lowest calibration standard used to establish the initial calibration (as well as the low-level CCC) must be at or below the concentration of the MRL. Establishing the MRL concentration too low may cause repeated failure of ongoing QC requirements. Confirm the MRL following the procedure outlined below.

9.2.4.1 Fortify and analyze seven replicate LFBs at or below the proposed MRL concentration. The LFBs must contain the method preservative as specified in Section 8.1.2. Calculate the mean (*Mean*) and standard deviation for these replicates. Determine the Half Range for the Prediction Interval of Results (HR_{PIR}) using the equation

$$HR_{PIR} = 3.963S$$

where S is the standard deviation and 3.963 is a constant value for seven replicates.[1]

9.2.4.2 Confirm that the Upper and Lower limits for the Prediction Interval of Results ($PIR = Mean \pm HR_{PIR}$) meet the upper and lower recovery limits as shown below.

The Upper PIR Limit must be ≤150 percent recovery.

$$\frac{Mean + HR_{PIR}}{Fortified\,Concentration} \times 100 \leq 150\%$$

The Lower PIR Limit must be ≥50 percent recovery.

$$\frac{Mean - HR_{PIR}}{Fortified\,Concentration} \times 100 \geq 50\%$$

9.2.4.3 The MRL is validated if both the Upper and Lower PIR Limits meet the criteria described above. If these criteria are not met, the MRL has been set too low and must be confirmed again at a higher concentration.

NOTE: These equations are only valid for seven replicate samples.

9.2.5 QUALITY CONTROL SAMPLE (QCS) – Analyze a mid-level Quality Control Sample (Sect. 9.3.7) to confirm the accuracy of the primary calibration standards.

9.2.6 DETECTION LIMIT DETERMINATION *(optional) – While DL determination is not a specific requirement of this method, it may be required by various regulatory bodies associated with compliance monitoring. It is the responsibility of the laboratory to ascertain whether DL determination is required based upon the intended use of the data.*

Analyses for this procedure must be done over at least three days. Prepare at least seven replicate LFBs at a concentration estimated to be near the DL. This concentration may be estimated by selecting a concentration at two to five times the noise level. The NH_4Cl preservative must be added to the samples as described in Section 8.1.2. Process the seven replicates through all steps of Section 11.

NOTE: If an MRL confirmation data set meets these requirements, a DL may be calculated from the MRL confirmation data, and no additional analyses are necessary.

Calculate the DL using the following equation:

$$DL = S \times t_{(n-1,1-\alpha = 0.99)}$$

where

$t_{(n-1,1-\alpha = 0.99)}$ = Student's t value for the 99% confidence level with n-1 degrees of freedom (for seven replicate determinations, the Student's t value is 3.143 at a 99% confidence level),

n = number of replicates, and

S = standard deviation of replicate analyses.

NOTE: Do not subtract blank values when performing DL calculations.

9.3 ONGOING QC REQUIREMENTS – This section describes the ongoing QC elements that must be included when processing and analyzing field samples. Table 12 summarizes these requirements.

9.3.1 LABORATORY REAGENT BLANK (LRB) – Analyze an LRB during the IDC and with each Analysis Batch. The LRB must contain the NH_4Cl preservative and the internal standards at the same concentration used to fortify all field samples and calibration standards. Background from method analytes or contaminants that interfere with the measurement of method analytes must be <1/3 the MRL. If method analytes are detected in the LRB at concentrations equal to or greater than this level, then all data for the problem analyte(s) must be considered invalid for all samples that yielded a positive result. **Subtracting blank values from sample results is not permitted.**

NOTE: Although quantitative data below the MRL may not be accurate enough for data reporting, such data are useful in determining the magnitude of background interference. Therefore, blank contamination levels may be estimated by extrapolation when the concentration is below the MRL.

9.3.2 CONTINUING CALIBRATION CHECK (CCC) – Analyze CCC standards at the beginning of each Analysis Batch, after every ten field samples, and at the end of the Analysis Batch. See Section 10.4 for concentration requirements and acceptance criteria for CCCs.

9.3.3 LABORATORY FORTIFIED BLANK (LFB) – Because this method utilizes procedural calibration standards, which are fortified reagent waters, there is no difference between the LFB and the Continuing Calibration Check standard. Consequently, the analysis of a separate LFB is not required as part of the ongoing QC; however, the term "LFB" is used for clarity in the IDC.

9.3.4 INTERNAL STANDARDS (IS) – The analyst must monitor the peak areas of the internal standards in all injections of the Analysis Batch. The internal standard responses (as indicated by peak areas) for any chromatographic run must not deviate by more than ±50% from the average areas measured during the initial calibration for the internal standards. If an IS area for a sample does not meet this criterion, check the corresponding IS area of the most recent CCC and proceed as follows.

9.3.4.1 If the IS criterion is met in the CCC but not the sample, reanalyze the sample in a subsequent Analysis Batch. If the IS area fails to meet the acceptance criterion in the repeat analysis, but passes in the most recent CCC, report the sample results as "suspect/matrix."

9.3.4.2 If both the original field sample and the CCC fail the IS area criterion, take corrective action (e.g., Sect. 10.4.3). After servicing the instrument, re-inject the sample in a subsequent Analysis Batch. If the IS area fails to meet the acceptance criterion in the

repeat analysis, but passes in the most recent CCC, report the sample results as "suspect/matrix."

9.3.5 LABORATORY FORTIFIED SAMPLE MATRIX (LFSM) – Within each Analysis Batch, analyze a minimum of one LFSM. The background concentrations of the analytes in the sample matrix must be determined in a separate aliquot and subtracted from the measured values in the LFSM. If various sample matrices are analyzed regularly, for example, drinking water processed from ground water and surface water sources, performance data must be collected for each source.

9.3.5.1 Prepare the LFSM by fortifying a sample with an appropriate amount of the Analyte PDS (Sect. 7.3.2.2). Generally, select a spiking concentration that is greater than or equal to the native concentration for most analytes. If the native concentrations of method analytes do not allow this criterion to be met without exceeding the calibration range, dilution with reagent water containing NH_4Cl (100 mg/L) is permitted. Selecting a duplicate aliquot of a sample that has already been analyzed aids in the selection of an appropriate spiking level. If this is not possible, use historical data when selecting a fortifying concentration.

9.3.5.2 Calculate the percent recovery (%R) using the equation:

$$\%R = \frac{(A - B)}{C} \times 100$$

where
A = measured concentration in the fortified sample,
B = measured concentration in the unfortified sample, and
C = fortification concentration.

9.3.5.3 Recoveries for samples fortified at concentrations near or at the MRL (within a factor of two times the MRL concentration) must be within $\pm$50% of the true value. Recoveries for samples fortified at all other concentrations must be within $\pm$30% of the true value. If the accuracy for any analyte falls outside the designated range, and the laboratory performance for that analyte is shown to be in control in the CCCs, the recovery is judged matrix biased. Report the result for the corresponding analyte in the unfortified sample as "suspect/matrix."

NOTE: In order to obtain meaningful percent recovery results, correct the measured values in the LFSM and LFSMD for the native levels in the unfortified samples, even if the native values are less than the MRL. This situation and the LRB are the only permitted uses of analyte results below the MRL.

9.3.6 LABORATORY DUPLICATE OR LABORATORY FORTIFIED SAMPLE MATRIX DUPLICATE (LD or LFSMD) – Within each Analysis Batch, analyze a minimum of one Laboratory Duplicate or one Laboratory Fortified Sample Matrix Duplicate. If the method analytes are not routinely observed in field samples, analyze an LFSMD rather than an LD.

NOTE: The variation due to the addition of internal standards must be included in the precision estimate. Therefore, first split the original sample and then fortify each aliquot with internal standards.

9.3.6.1 Calculate the relative percent difference (RPD) for duplicate measurements (LD_1 and LD_2) using the equation:

$$RPD = \frac{|LD_1 - LD_2|}{(LD_1 + LD_2)/2} \times 100$$

9.3.6.2 RPDs for Laboratory Duplicates must be ≤30%. Greater variability may be observed when Laboratory Duplicates have analyte concentrations that are near or at the MRL (within a factor of two times the MRL concentration). At these concentrations, Laboratory Duplicates must have RPDs that are ≤50%. If the RPD of an analyte falls outside the designated range, and the laboratory performance for the analyte is shown to be in control in the CCC, the precision is judged matrix influenced. Report the result for the corresponding analyte in the unfortified sample as "suspect/matrix."

9.3.6.3 If an LFSMD is analyzed instead of a Laboratory Duplicate, calculate the RPD for the LFSM and LFSMD using the equation:

$$RPD = \frac{|LFSM - LFSMD|}{(LFSM + LFSMD)/2} \times 100$$

9.3.6.4 RPDs for duplicate LFSMs must be ≤30%. Greater variability may be observed when the matrix is fortified at analyte concentrations near or at the MRL (within a factor of two times the MRL concentration). LFSMs at these concentrations must have RPDs that are ≤50%. If the RPD of an analyte falls outside the designated range, and the laboratory performance for the analyte is shown to be in control in the CCC, the precision is judged matrix influenced. Report the result for the corresponding analyte in the unfortified sample as "suspect/matrix."

9.3.7 QUALITY CONTROL SAMPLE (QCS) – A QCS must be analyzed during the IDC, and then at least quarterly thereafter. Fortify the QCS near the midpoint of the calibration range. The acceptance criteria for the QCS are the same as the mid- and high-level CCCs (Sect. 10.4). If the accuracy for any analyte fails the recovery criterion, prepare fresh standard dilutions and repeat the QCS evaluation.

9.4 METHOD MODIFICATION QC REQUIREMENTS – The laboratory is required to perform the procedures in this section if chromatographic conditions and a suppression technique are selected which are different from those utilized to develop the method. Any proposed method modifications must retain the basic chromatographic elements of this new technique (Sect. 1.7). Examples of method modifications include alternate IC columns, an injection volume less than 100 uL, and additional internal standards proposed for use with the method.

9.4.1 Each time method modifications are made, optimize the elution gradient to accomplish separation of the method analytes from matrix components, and then verify elution and divert windows following the guidance in Section 10.2.5. Establish an acceptable initial calibration (Sect. 10.3). Finally, repeat the procedures of the IDC (Sect. 9.2).

9.4.2 The analyst is also required to evaluate and document method performance for the proposed modifications in real matrices that span the range of waters that the laboratory analyzes. This additional step is required because modifications that perform acceptably in the IDC, which is conducted in reagent water and synthetic matrix, could fail ongoing method QC requirements in real matrices. This is particularly important for methods subject to matrix effects, such as IC/MS-based methods. For example, a laboratory may routinely analyze drinking water from municipal treatment plants that process ground water, surface water, or a blend of surface and ground water. In this case, the method modification requirement could be accomplished by assessing precision and accuracy (Sects. 9.2.2 and 9.2.3) in a surface water with moderate to high total organic carbon (e.g., 2 mg/L or greater) and a hard ground water (e.g., 250 mg/L as calcium carbonate ($CaCO_3$) equivalent, or greater).

9.4.3 The results of Sections 9.4.1 and 9.4.2 must be appropriately documented by the analyst and independently assessed by the laboratory's QA officer prior to analyzing field samples. When implementing method modifications, it is the responsibility of the laboratory to closely review the results of ongoing QC, and in particular, the results associated with the LFSM (Sect. 9.3.5), LFSMD (Sect. 9.3.6), CCCs (Sect. 9.3.2), and the internal standard area counts (Sect. 9.3.4). If repeated failures are noted, the modification must be abandoned.

10 CALIBRATION AND STANDARDIZATION

10.1 Demonstration and documentation of acceptable MS calibration and initial analyte calibration are required before performing the IDC and prior to analyzing field samples. Prior to calibration, the analyst must verify the proper timing of divert windows as described in Section 10.2.5. The initial calibration must be repeated each time a major instrument modification or maintenance is performed.

10.2 IC-ESI-MS/MS CALIBRATION AND OPTIMIZATION

10.2.1 MASS CALIBRATION – Method 557 requires the monitoring of low-mass, negatively charged ions within nominal *m/z* range of 35 to 251. Calibrate the mass spectrometer with the calibration compounds and procedures specified by the manufacturer. Verify the mass assignment accuracy for each precursor ion and each product ion by comparing the reported centroid mass to the theoretical mass. (Pay particular attention to the chlorine product ion at nominal *m/z* 35, actual *m/z* 34.97.) Low signal response could result if mass assignments are not centered on the detected mass peaks. If the reported masses differ from the calculated masses and low response is observed, the standard calibration procedure may be inadequate for this method. Consult the MS/MS manufacturer for an

appropriate low-mass calibration procedure. During method development, accurate mass assignments were achieved after calibration via direct infusion of sodium formate (10 nanograms per microliter) in 90:10 2-propanol:water, rather than the sodium iodide and cesium iodide mixture typically employed for Waters MS/MS systems.

10.2.2 OPTIMIZING MS PARAMETERS – Each IC-ESI-MS/MS system will have different optimal conditions, which are influenced by the source geometry and system design. Due to the differences in design, follow the recommendations of the instrument manufacturer when tuning the instrument. During the development of this method, instrumental parameters were optimized for the precursor and product ions listed in Section 17, Table 3. Because the method analytes are relatively small molecules, the selection of precursor and product ions is limited. However, transitions other than those listed exist, and the optimum choice depends on the instrument platform as noted below.

NOTE: Several instrument platforms were investigated during method development. The most abundant precursor ions differed depending on the design of the ESI interface. In particular, the trihaloacetic acids containing bromine tend to undergo neutral loss in the ESI interface. For example, the precursor ions for BDCAA, CDBAA, and TBAA used during method development (Table 3) are 44 mass units less than the molecular ion, corresponding to loss of a carboxyl group (COO^-). However, using other ESI designs, the *m/z* 207 precursor ion for BDCAA was observed, which corresponds to the mass of the molecular ion. BDCAA and TBAA exhibited neutral loss on all ESI-MS/MS systems evaluated. The most abundant product ions also differed between instruments. Although the mass transitions in Table 3 are provided as a guide, the analyst must empirically determine the most abundant precursor and product ions.

10.2.2.1 Optimize the ESI-MS/MS at the analytical flow rate (column eluent plus post-column acetonitrile addition) via split infusion or flow injection analysis (FIA). Use solutions having concentrations between 1 and 5 µg/mL of the method analytes in reagent water for split infusion, and solutions having concentrations between 10 and 100 µg/L (0.01 and 0.1 µg/mL) in reagent water for FIA. Five- or 10-µL sampling loops are recommended for optimizing via FIA. Because the precursor and product ions may be identical for some of the haloacetic acids, individual solutions of the method analytes are recommended for this step.

10.2.2.2 Using Table 3 as a guide, select the most abundant precursor ion. Optimize the response of the precursor ion for each analyte by infusing the prepared solutions (Sect. 10.2.2.1) directly into mobile phase (or via FIA). Vary the ESI parameters (probe orientation, capillary extension, source voltages, source and desolvation temperatures, gas flows, etc.) and the MS parameters until optimal analyte responses are determined. The method analytes may have different optima, thus requiring some compromise. ESI-MS/MS systems are subject to drift, which can affect run-to-run precision. Accordingly, the optimal conditions may be those that yield adequate response while minimizing the potential for drift.

10.2.2.3 Using Table 3 as a guide, select the most abundant product ion. Optimize the response of the product ion for each analyte by infusing the prepared solutions (Sect. 10.2.2.1) directly into the mass spectrometer (or via FIA). Vary the MS/MS parameters (collision gas pressure, collision energy, etc.) until optimal analyte responses are determined.

10.2.3 ION CHROMATOGRAPHY INSTRUMENT CONDITIONS – Follow the column manufacturer's guidelines for calculating the elution gradient to accomplish separation of the method analytes from matrix components. IC operating conditions for the Dionex AS24 column[7] used during method development are summarized in Section 17, Table 1. Establish divert windows for the matrix components and elution windows for the method analytes per the column manufacturer's instructions. Figure 2 presents an example of these windows optimized for the Dionex AS24 column. Conditions different from those described in this method (e.g., IC columns and mobile phases) may be used if the QC criteria in Sections 9.2, 9.3 and 9.4 are met, the column provides reasonable resolution of the method analytes, and chromatographic separation of the method analytes from matrix anions (chloride, carbonate, sulfate, nitrate) is achieved.

10.2.4 ESTABLISH IC-ESI-MS/MS RETENTION TIMES AND MRM SEGMENTS – Inject a mid- to high-level calibration standard under optimized IC-ESI-MS/MS conditions to obtain the retention times of each method analyte. Divide the chromatogram into segments that contain one or more chromatographic peaks. For maximum sensitivity in subsequent MS/MS analyses, minimize the number of MRM (Sect. 3.19) transitions that are simultaneously monitored within each segment. Table 2 presents the assignment of the method analytes and internal standards into each of the three MRM windows used during method development.

10.2.5 VERIFY ELUTION AND DIVERT WINDOWS FOR MATRIX ELIMINATION – Conduct the following tests and verify that the timing of the elution and divert windows meet the stated criteria.

10.2.5.1 Stabilize the chromatographic system and analyze an LFSSM at 10 µg/L. Locate the first and last analyte peak in each elution window. Display the corresponding conductivity trace and note the peak start and peak end times for the chloride, carbonate, sulfate, and nitrate matrix anions. Consider a conductivity signal of ~5 µS as the peak end (return to baseline) after elution of a matrix anion. [Refer to figures 4 and 5 for an example based on use of the Dionex AS24 column. For this column, the chloride anion elutes between elution window 1 and elution window 2. Carbonate, sulfate and nitrate anions elute between elution windows 2 and 3.]

10.2.5.2 For the first analyte in each elution window, calculate a maximum time for the preceding valve switch: RT – (1.5)(peak width at base of the first analyte in the window). For the last analyte in each elution window, calculate a minimum time for the following valve switch: RT + (1.5)(peak width at base of the last analyte in the window). Verify that the valve switch times set in step 10.2.3 do not overlap the calculated times.

NOTE: The actual valve switch times are set in accordance with the column manufacturer's guidelines (Section 10.2.3). These could be wider than the start and end times for the elution windows calculated using the equations in this section.

10.2.5.3 By inspection, verify that matrix peaks have returned to baseline before the calculated valve switch at the beginning of each elution window. By inspection, verify that the valve switch at the beginning of each divert window occurs before a matrix component begins to elute. Finally, verify that each analyte elutes entirely within the established elution windows. If these conditions are not met, consult the column manufacturer's guidelines for adjusting the elution gradient and reset the timing of the divert valve accordingly.

NOTE: Enough time should be allowed for the baseline to stabilize between the valve switch that begins each elution window and the appearance of the subsequent analyte signal. If the valve switch is too close to the analyte, the starting point of the analyte peak may be difficult to distinguish from the baseline disruption, especially for low analyte concentrations.

10.3 INITIAL CALIBRATION

10.3.1 CALIBRATION STANDARDS – Prepare a set of at least five calibration standards as described in Section 7.3.2.3. The analyte concentrations in the lowest calibration standard must be at or below the MRL. Field samples must be quantified using a calibration curve that spans the same concentration range used to collect the IDC data (Sect. 9.2), i.e., analysts are not permitted to use a restricted calibration range to meet the IDC criteria and then use a larger dynamic range during analysis of field samples.

10.3.2 CALIBRATION – Calibrate the IC-ESI-MS/MS system using peak areas and the internal standard technique. Fit the calibration points with either a linear regression or quadratic regression (response vs. concentration). Weighting may be used. Forcing the calibration curve through the origin is not recommended. The MS/MS instrument used during method development was calibrated using inverse concentration-weighted quadratic curves.

NOTE: Internal standard assignments appropriate for the Dionex AS24 column for each method analyte are presented in Table 3, and the mass transitions for the internal standards are provided in Table 4. MCAA must always be referenced to MCAA[2-^{13}C]. MBAA must always be referenced to MBAA[1-^{13}C]. Method 557 was validated with bromate referenced to MBAA[1-^{13}C]; however, MCAA[2-^{13}C] could be used if all requirements in the IDC are met, as well as all ongoing QC requirements.

10.3.3 CALIBRATION ACCEPTANCE CRITERIA – Validate the initial calibration by calculating the concentration of the analytes for each of the analyses used to generate the calibration curve by use of the regression equations. Calibration points that are ≤MRL must calculate to be within ±50% of their true value. All other calibration points must

calculate to be within ±30% of their true value. If these criteria cannot be met, the analyst will have difficulty meeting ongoing QC criteria. In this case, corrective action is recommended such as reanalyzing the calibration standards, restricting the range of calibration, or performing instrument maintenance.

10.4 CONTINUING CALIBRATION CHECKS (CCCs) – Analyze a CCC to verify the initial calibration at the beginning of each Analysis Batch, after every tenth field sample, and at the end of each Analysis Batch. The beginning CCC for each Analysis Batch must be at or below the MRL. This CCC verifies instrument sensitivity prior to the analysis of samples. Alternate subsequent CCCs between the remaining calibration levels.

10.4.1 Verify that the absolute areas of the quantitation ions of each of the internal standards have not changed by more than ±50% from the average areas measured during the initial calibration. If this limit is exceeded, verify that the background conductivity is in control following the guidance in Section 11.3.2. If the background conductivity is normal, remedial action may necessary (Sect. 10.4.3).

10.4.2 Calculate the concentration of each analyte in the CCC. The CCC fortified at ≤MRL must calculate to be within ±50% of its true value. CCCs fortified at all other levels must calculate to be within ±30%. If these limits are exceeded, then all data for the failed analytes must be considered invalid. Any field samples analyzed since the last acceptable CCC that are still within holding time must be reanalyzed after an acceptable calibration has been restored.

10.4.3 REMEDIAL ACTION – Failure to meet CCC QC performance criteria requires remedial action. Acceptable method performance may be restored simply by flushing the column at the highest eluent concentration in the gradient. Following this and other minor remedial action, check the calibration with a mid-level CCC and a CCC at the MRL, or alternatively recalibrate according to Section 10.3. If internal standard and calibration failures persist, maintenance may be required, such as servicing the ESI-MS/MS system and replacing IC columns. These later measures constitute major maintenance, and the analyst must return to the initial calibration step (Sect. 10.3) and verify sensitivity by analyzing a CCC at or below the MRL.

11. PROCEDURE

11.1 This section describes the procedures for sample preparation and analysis. Important aspects of this analytical procedure include proper sample collection and storage (Sect. 8), ensuring that the instrument is properly calibrated (Sect. 10), and that all required QC elements are included (Sect. 9).

11.2 SAMPLE PREPARATION

11.2.1 All field and QC samples must contain the preservative listed in Section 8.1.2, including the LRB. In the laboratory, maintain field samples, QC samples, and calibration

standards at or below 6 °C at all times, including the time these are resident in the autosampler awaiting injection.

11.2.2 Do not filter the samples. Add an appropriate volume of the Internal Standard PDS (Sect. 7.3.1.2) to a known volume of sample, cap, and mix well. The concentration of the internal standards must be the same in the samples as in the calibration standards. Transfer an aliquot of each field or QC sample to an autosampler vial. For example, weigh 40 mL of sample into a 40-mL VOA vial using a top loading balance and a disposable, glass pipette. Add 160 uL of the internal standard PDS (1.0 µg/mL) to achieve a concentration of 4.0 µg/L in the sample. Mix well and transfer 1.5 mL to an autosampler vial by use a disposable pipette.

11.3 SAMPLE ANALYSIS

11.3.1 Establish IC-ESI-MS/MS operating conditions per the guidance in Section 10.2.

11.3.2 Flush the column at the highest eluent concentration in the gradient for at least 15 minutes prior to beginning each analysis sequence. This step is especially important for minimizing background conductivity if the column has been installed in the system and held at the starting eluent concentration for extended periods.

NOTE: During method development, the background conductivity ranged from 0.3 to 2.2 microsiemens (µS). If an internal standard or analyte area response is low due to high background conductivity, flush the column at the maximum eluent concentration in the gradient and observe the conductivity signal until the background stabilizes at less than 2.5 µS. Also, ensure that the suppressor is functioning properly or replace the suppressor to troubleshoot the problem. Occasional overnight flushing of the column will minimize the occurrence of high background conductivity.

11.3.3 VERIFY ELUTION AND DIVERT WINDOWS - Analyze Laboratory Synthetic Sample Matrix fortified at 10 µg/L. Verify the elution and divert windows as specified in Section 10.2.5. This verification must be done *prior to* beginning each Analysis Batch.

11.3.4 THE ANALYSIS BATCH – Establish a valid initial calibration following the procedures outlined in Section 10.3 and confirm that the calibration is valid by analyzing a CCC at or below the MRL as described in Section 10.4. Alternately, verify that an existing calibration, established for a previous Analysis Batch, is still valid by analyzing a CCC at or below the MRL. Next, analyze an LRB. Continue the Analysis Batch by analyzing aliquots of field and QC samples at appropriate frequencies (Section 9.3), employing the optimized conditions used to acquire the initial calibration. Analyze a mid- or high-level CCC after every ten field samples and at the end each Analysis Batch.

NOTE: Each Analysis Batch must begin with the analysis of a CCC at or below the MRL for each analyte that the laboratory intends to report, followed by the analysis of an LRB. This is true whether or not an initial calibration is analyzed. After 20 field samples the low-level CCC and the LRB must be repeated to begin a new Analysis Batch. The

acquisition start time of the mid-level CCC at the end of the Analysis Batch must be within 30 hours of the acquisition start time of the low-level CCC at the beginning of the Analysis Batch. Do not count QC samples (LRBs, LDs, LFSMs, LFSMDs) when calculating the frequency of CCCs that are required during an Analysis Batch.

12. DATA ANALYSIS AND CALCULATIONS

12.1 Establish an appropriate retention time window for each analyte to identify them in QC and field sample chromatograms. Base this assignment on measurements of actual retention time variation for each compound in standard solutions over the course of time. The suggested variation is plus or minus three times the standard deviation of the retention time for each compound for a series of injections. The injections from the initial calibration and from the IDC (Sect. 9.2) may be used to calculate the retention time window. However, the experience of the analyst should weigh heavily on the determination of an appropriate range.

12.2 At the conclusion of data acquisition, use the same software settings established during the calibration procedure to identify peaks of interest in the predetermined retention time windows. Confirm the identify of each analyte by comparison of its retention time with that of the corresponding analyte peak in an initial calibration standard or CCC.

12.3 Calculate analyte concentrations using the multipoint calibration established in Section 10.3. Report only those values that fall between the MRL and the highest calibration standard. Samples with analyte responses that exceed the highest calibration standard require dilution and reanalysis (Sect. 12.7).

NOTE: In validating this method, concentrations were calculated using the product ions listed in Table 3 of Section 17. Other ions may be selected at the discretion of the analyst as discussed in Section 10.2.2.

12.4 Calculations must use all available digits of precision, but final reported concentrations should be rounded to an appropriate number of significant figures (one digit of uncertainty), typically two, and not more than three significant figures.

12.5 Prior to reporting the data, the chromatograms must be reviewed for any incorrect peak identifications or improper integration.

12.6 Prior to reporting data, the laboratory is responsible for ensuring that QC requirements have been met and that any appropriate qualifier is assigned.

12.7 EXCEEDING THE CALIBRATION RANGE – The analyst must not extrapolate beyond the established calibration range. If an analyte result exceeds the range of the initial calibration curve, the sample may be diluted using reagent water containing 100 mg/L NH_4Cl with the appropriate amount of internal standard added to match the original level. Re-inject the diluted sample. Incorporate the dilution factor into final concentration calculations. The resulting data must be annotated as a dilution, and the reported MRLs must reflect the dilution factor.

13. METHOD PERFORMANCE

13.1 PRECISION, ACCURACY, AND DETECTION LIMITS – The method performance data presented in Section 17 were collected using the IC conditions listed in Table 1 and the Waters Quattro Premier XE ESI-MS/MS system. ESI-MS/MS conditions for the Waters system are presented in Table 2. Tables 3 and 4 list the mass transitions for each analyte and internal standard, internal standard assignments, and observed retention times associated with the method performance results. LCMRLs and DLs are presented in Tables 5 and 6. Single laboratory precision and accuracy data are presented for four water matrices: reagent water (Table 7), LSSM (Table 8), chlorinated (finished) ground water (Table 9), and chlorinated (finished) surface water (Table 10). Figure 1 depicts the post-column sample path as previously cited in this document (Sect. 6.12). Figures 2 through 4 are chromatograms of the method analytes in reagent water, drinking water, and LSSM obtained under the conditions employed during method development. Figure 4 was acquired with the inclusion of mass transitions for the chlorite and chlorate anions to mark their position in the chromatogram relative to the method analytes. Figure 5 is a corresponding conductivity trace for the analyte chromatogram presented in Figure 4 showing the location of matrix anions, chlorite anion, and chlorate anion.

13.2 SECOND LABORATORY EVALUATION – The performance of this method was demonstrated by a second laboratory using an API 4000 triple quadrupole mass spectrometer (Applied Biosystems, Foster City, CA) with results similar to those reported in Section 17. The authors wish to acknowledge the Southern Nevada Water Authority (Las Vegas, NV) for their contribution to the method development effort.

14. POLLUTION PREVENTION

14.1 For information about pollution prevention that may be applicable to laboratory operations, consult "Less is Better: Laboratory Chemical Management for Waste Reduction" available from the American Chemical Society's Department of Government Relations and Science Policy, 1155 16th Street N.W., Washington, D.C., 20036, or online at http://www.ups.edu/x7432.xml.

15. WASTE MANAGEMENT

15.1 The analytical procedures described in this method generate relatively small amounts of waste since only small amounts of reagents and solvents are used. The matrix of concern is finished drinking water. However, the Agency requires that laboratory waste management practices be conducted consistent with all applicable rules and regulations, and that laboratories protect the air, water, and land by minimizing and controlling all releases from fume hoods and bench operations. In addition, compliance is required with any sewage discharge permits and regulations, particularly the hazardous waste identification rules and land disposal restrictions. For further information on waste management, see the publications of the American Chemical Society's Laboratory Environment, Health & Safety Task Force on the Internet at http://membership.acs.org/c/ccs/publications.htm. Additional

waste management information can be found in "Laboratory Waste Minimization and Pollution Prevention," Copyright © 1996 Battelle Seattle Research Center, which can be located at http://www.p2pays.org/ref/01/text/00779/ch05.htm.

16. REFERENCES

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17. TABLES, DIAGRAMS, FLOWCHARTS, AND VALIDATION DATA

TABLE 1. ION CHROMATOGRAPHIC CONDITIONS USED TO COLLECT METHOD PERFORMANCE DATA

Parameter	Conditions[a]		
Column	Dionex IonPac® AS24 250 mm x 2 mm i.d.		
Precolumn	Dionex IonPac® AG24 50 mm x 2 mm i.d.		
Column compartment temperature	15 ºC	Autosampler tray temperature	4 ºC
Hydroxide gradient	7 mM for -1 to16.8 min, then 18 mM for 16.8 to 34.2 min, then 60 mM for 34.4 to 51.2 min, then 7 mM for 51.4 to 56 min		
Eluent flow rate	0.30 mL/min		
Post-column solvent	100% acetonitrile at 0.2 mL/min		
Suppressor	Dionex ASRS®300 2 mm, external water mode		
Matrix diversion divert windows	0 to 8 min, 16.5 to 21.2 min, and 33 to 39.2 min		
Sample volume	100-µL loop		

[a] The chromatograms presented in Figures 2, 3, 4, and 5 were obtained under these conditions.

TABLE 2. WATERS QUATTRO PREMIER XE ACQUISITION CONDITIONS USED TO COLLECT METHOD PERFORMANCE DATA[a]

Analyte	Transition (*m/z*)	Dwell (seconds)	Periods	Cone (V)	Collision Energy (V)
IS[b]: Monochloroacetic acid-*2*-^{13}C	94/35	0.4	**MRM Window 1**	-15	-8
Monochloroacetic acid	93/35	1.2		-15	-8
IS: Monobromoacetic acid-*1*-^{13}C	138/79	0.4		-15	-10
Monobromoacetic acid	137/79	0.4		-15	-10
Bromate	127/111	0.4		-25	-18
Dalapon	141/97	0.5	**MRM Window 2**	-18	-8
IS: Dichloroacetic acid-*2*-^{13}C	128/84	0.5		-17	-10
Dichloroacetic acid	127/83	0.5		-17	-10
Bromochloroacetic acid	173/129	0.5		-17	-10
Dibromoacetic acid	217/173	0.5		-18	-12
IS: Trichloroacetic acid-*2*-^{13}C	162/118	0.5	**MRM Window 3**	-16	-8
Trichloroacetic acid	161/117 163/119	0.5		-16	-8
Bromodichloroacetic acid	163/81	1.0		-25	-10
Chlorodibromoacetic acid	207/79	1.0		-28	-10
Tribromoacetic acid	251/79	1.0		-28	-12

[a] Source block: 120 °C, desolvation gas: 350 °C @ 940 liters/hour, capillary: -2.8 V, collision pressure: 5.5×10^{-3} torr (0.15 flow @ 7 psig), cone flow: 100 liters/hour, extractor: -3 V, RF lens: -0.5 V, acetonitrile flow rate: 0.2 mL/min.

[b] IS = internal standard.

TABLE 3. IC-ESI-MS/MS ANALYTE RETENTION TIMES, PRECURSOR AND PRODUCT IONS

Analyte	Retention Time[a] (min)	Internal Standard Assignment	Precursor	Product
Monochloroacetic acid	12.62	MCAA[2-^{13}C]	93	35
Monobromoacetic acid	14.05	MBAA[1-^{13}C]	137	79
Bromate	14.93	MBAA[1-^{13}C]	127	111
Dalapon	23.33	DCAA[2-^{13}C]	141	97
Dichloroacetic acid	24.26	DCAA[2-^{13}C]	127	83
Bromochloroacetic acid	26.16	DCAA[2-^{13}C]	173	129
Dibromoacetic acid	28.89	DCAA[2-^{13}C]	217	173
Trichloroacetic acid	41.08	TCAA[2-^{13}C]	161	117
Trichloroacetic acid (alternate)		TCAA[2-^{13}C]	163	119
Bromodichloroacetic acid	42.89	TCAA[2-^{13}C]	163	81
Chlorodibromoacetic acid	45.50	TCAA[2-^{13}C]	207	79
Tribromoacetic acid	49.22	TCAA[2-^{13}C]	251	79

[a] Dionex AS24 column (used to collect method performance data).

TABLE 4. IC-ESI-MS/MS INTERNAL STANDARD RETENTION TIMES, PRECURSOR AND PRODUCT IONS

Internal Standard	Retention Time[a] (minutes)	Precursor	Product
Monochloroacetic acid-*2*-^{13}C	12.56	94	35
Monobromoacetic acid-*1*-^{13}C	14.05	138	79
Dichloroacetic acid-*2*-^{13}C	24.21	128	84
Trichloroacetic acid-*2*-^{13}C	41.08	162	118

[a] Dionex AS24 column (used to collect method performance data).

TABLE 5. IC-ESI-MS/MS LOWEST CONCENTRATION MINIMUM REPORTING LEVEL (LCMRL)

Analyte	LCMRL Fortification Levels (µg/L)	Calculated LCMRL (µg/L)
Monochloroacetic acid	0.10, 0.25, 0.375, 0.50, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0	0.58
Monobromoacetic acid	0.050, 0.10, 0.25, 0.375, 0.50, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0	0.19
Bromate	0.025, 0.050, 0.10, 0.25, 0.375, 0.50, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0	0.042
Dalapon	0.25, 0.375, 0.50, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0	0.41
Dichloroacetic acid	0.025, 0.050, 0.10, 0.25, 0.375, 0.50, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0	0.13
Bromochloroacetic acid	0.10, 0.25, 0.375, 0.50, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0	0.16
Dibromoacetic acid	0.025, 0.050, 0.10, 0.25, 0.375, 0.50, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0	0.062
Trichloroacetic acid – *m/z* 163/119	0.10, 0.25, 0.375, 0.50, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0	0.25
Bromodichloroacetic acid	0.050, 0.10, 0.25, 0.375, 0.50, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0	0.19
Chlorodibromoacetic acid	0.050, 0.10, 0.25, 0.375, 0.50, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0	0.080
Tribromoacetic acid	0.10, 0.25, 0.375, 0.50, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0	0.27

TABLE 6. IC-ESI-MS/MS DETECTION LIMITS (DL)[a]

Analyte	Fortification Level (µg/L)	Calculated DL (µg/L)
Monochloroacetic acid	0.25	0.20
Monobromoacetic acid	0.10	0.064
Bromate	0.025	0.020
Dalapon	0.25	0.038
Dichloroacetic acid	0.10	0.055
Bromochloroacetic acid	0.25	0.11
Dibromoacetic acid	0.025	0.015
Trichloroacetic acid – *m/z* 163/119	0.10	0.090
Bromodichloroacetic acid	0.050	0.050
Chlorodibromoacetic acid	0.10	0.041
Tribromoacetic acid	0.25	0.067

[a] DLs calculated using data acquired over the course of three days (n=7 sample replicates).

TABLE 7. IC-ESI-MS/MS PRECISION AND ACCURACY OF METHOD ANALYTES FORTIFIED AT 1.0 AND 15 µg/L IN REAGENT WATER

Analyte	Fortified Conc. = 1.0 µg/L (n=7)		Fortified Conc. = 15 µg/L (n=8)	
	Mean % Recovery	Relative Standard Deviation	Mean % Recovery	Relative Standard Deviation
Monochloroacetic acid	101	3.5	101	1.7
Monobromoacetic acid	97.5	3.7	99.8	1.8
Bromate	93.3	2.4	104	7.8
Dalapon	97.4	4.7	100	3.3
Dichloroacetic acid	109	2.6	97.0	6.5
Bromochloroacetic acid	103	2.9	107	4.4
Dibromoacetic acid	104	9.0	111	6.7
Trichloroacetic acid – *m/z* 163/119	99.1	2.3	99.8	3.2
Bromodichloroacetic acid	105	3.7	97.7	2.2
Chlorodibromoacetic acid	90.4	5.9	103	5.4
Tribromoacetic acid	101	5.3	98.9	3.0

TABLE 8. IC-ESI-MS/MS PRECISION AND ACCURACY OF METHOD ANALYTES FORTIFIED AT 1.0 AND 15 µg/L IN SYNTHETIC SAMPLE MATRIX

Analyte	Fortified Conc. = 1.0 µg/L (n=8)		Fortified Conc. = 15 µg/L (n=8)	
	Mean % Recovery	Relative Standard Deviation	Mean % Recovery	Relative Standard Deviation
Monochloroacetic acid	109	4.8	101	4.1
Monobromoacetic acid	97.2	5.3	99.7	4.6
Bromate	117	11	109	11
Dalapon	113	4.5	93.2	6.6
Dichloroacetic acid	89.9	9.3	90.9	8.7
Bromochloroacetic acid	84.9	9.3	82.8	10
Dibromoacetic acid	91.0	14	84.5	10
Trichloroacetic acid – *m/z* 163/119	107	5.4	101	1.1
Bromodichloroacetic acid	91.6	4.7	91.0	4.1
Chlorodibromoacetic acid	98.8	7.2	97.6	6.2
Tribromoacetic acid	94.0	5.4	97.6	2.5

TABLE 9. IC-ESI-MS/MS PRECISION AND ACCURACY OF METHOD ANALYTES FORTIFIED AT 2.5 AND 10 µg/L IN CHLORINATED GROUND WATER[a]

Analyte	Native Conc., µg/L (n=6)	Fortified Conc. = 2.5 µg/L (n=8)		Fortified Conc. = 10 µg/L (n=8)	
		Mean % Recovery[b]	Relative Standard Deviation	Mean % Recovery[b]	Relative Standard Deviation
Monochloroacetic acid	0.57	95.9	4.7	99.6	5.2
Monobromoacetic acid	0.41	101	2.1	101	1.8
Bromate	0.56	107	7.3	102	4.8
Dalapon	0.37	95.5	3.1	98.5	3.0
Dichloroacetic acid	4.3	99.7	6.2	106	1.7
Bromochloroacetic acid	3.4	95.2	5.6	93.5	3.1
Dibromoacetic acid	2.0	95.2	8.1	99.3	6.2
Trichloroacetic acid – *m/z* 163/119	2.6	101	1.8	102	2.8
Bromodichloroacetic acid	2.6	91.2	2.0	99.0	3.6
Chlorodibromoacetic acid	1.7	103	3.6	102	7.2
Tribromoacetic acid	0.24	97.6	1.9	95.8	1.9

[a] Ground water physical parameters: pH = 7.45; total hardness = 308 milligrams/liter (mg/L) (as $CaCO_3$); free chlorine = 0.94 mg/L.

[b] Recoveries corrected for native levels in the unfortified matrix.

TABLE 10. IC-ESI-MS/MS PRECISION AND ACCURACY OF METHOD ANALYTES FORTIFIED AT 2.5 AND 8.0 µg/L IN CHLORINATED SURFACE WATER[a]

Analyte	Native Conc., µg/L (n=6)	Fortified Conc. = 2.5 µg/L (n=8)		Fortified Conc. = 8.0 µg/L (n=7)	
		Mean % Recovery[b]	Relative Standard Deviation	Mean % Recovery[b]	Relative Standard Deviation
Monochloroacetic acid	2.6	97.9	3.5	98.8	3.0
Monobromoacetic acid	0.66	99.3	1.4	101	1.6
Bromate	0.85	99.0	8.8	103	10
Dalapon	0.72	97.8	3.8	96.3	4.8
Dichloroacetic acid	15	79.6	6.3	80.0	6.0
Bromochloroacetic acid	6.4	87.2	9.0	90.2	9.2
Dibromoacetic acid	1.6	106	10	95.8	6.0
Trichloroacetic acid – *m/z* 163/119	11	95.6	2.5	97.1	1.4
Bromodichloroacetic acid	4.7	99.9	4.6	97.9	4.9
Chlorodibromoacetic acid	1.2	102	5.9	102	11
Tribromoacetic acid	0.081	99.5	3.9	103	4.7

[a] Surface water physical parameters: pH = 7.43; total hardness = 154 milligrams/liter (mg/L) (as $CaCO_3$); free chlorine = 2.7 mg/L; total chlorine = 3.7 mg/L.

[b] Recoveries corrected for native levels in the unfortified matrix.

TABLE 11. INITIAL DEMONSTRATION OF CAPABILITY (IDC) QUALITY CONTROL REQUIREMENTS

Method Reference	Requirement	Specification and Frequency	Acceptance Criteria
Section 9.2.1	Demonstration of low system background	Analyze a Laboratory Reagent Blank (LRB) prior to any other Initial IDC steps.	Demonstrate that all method analytes are <1/3 of the Minimum Reporting Level (MRL) and that possible interferences from reagents and glassware do not prevent the identification and quantitation of method analytes.
Section 9.2.1	Test for system carryover	Analyze an LRB after the high calibration standard during the IDC calibration.	Demonstrate that the method analytes are <1/3 of the MRL.
Section 9.2.2	Demonstration of precision	Analyze 7 replicate Laboratory Fortified Blanks (LFBs) and 7 Laboratory Fortified Synthetic Sample Matrix samples (LFSSMs) fortified near the midrange concentration.	Percent relative standard deviation must be ≤20%.
Section 9.2.3	Demonstration of accuracy	Calculate average recovery for replicates used in Section 9.2.2.	Mean recovery within ±30% of the true value.
Section 9.2.4	MRL confirmation	Fortify and analyze 7 replicate LFBs at the proposed MRL concentration. Confirm that the Upper Prediction Interval of Results (PIR) and Lower PIR (Sect. 9.2.4.2) meet the recovery criteria.	Upper PIR ≤ 150% Lower PIR ≥ 50%
Section 9.2.5	Quality Control Sample (QCS)	Analyze mid-level QCS.	Results must be within ±30% of the true value.

TABLE 12. ONGOING QUALITY CONTROL REQUIREMENTS

Method Reference	Requirement	Specification and Frequency	Acceptance Criteria
Section 11.3.3	Verify divert windows	Analyze a Laboratory Fortified Synthetic Sample Matrix (LFSSM) prior to each Analysis Batch.	See Section 10.2.5 for acceptance criteria.
Section 10.3	Initial calibration	Use the internal standard calibration technique to generate a linear or quadratic calibration curve. Use at least five standard concentrations. Validate the calibration curve as described in Section 10.3.3.	When each calibration standard is calculated as an unknown using the regression equations, the lowest level standard must be within ±50% of the true value. All other points must be within ±30% of the true value.
Section 9.3.1	Laboratory Reagent Blank (LRB)	Analyze one LRB with each Analysis Batch.	Demonstrate that all method analytes are below 1/3 the Minimum Reporting Level (MRL), and that possible interference from reagents and glassware do not prevent identification and quantitation of method analytes.
Section 10.4	Continuing Calibration Check (CCC)	Verify initial calibration by analyzing a low-level CCC at the beginning of each Analysis Batch. Subsequent CCCs are required after every 10 field samples, and after the last field sample in a batch.	The lowest level CCC must be within ±50% of the true value. All other points must be within ±30% of the true value. Results for field samples that are not bracketed by acceptable CCCs are invalid.
Section 9.3.4	Internal standard (IS)	Isotopically labeled internal standards are added to all standards and samples.	Peak area counts for each IS must be within ±50% of the average peak areas in the initial calibration.
Section 9.3.5	Laboratory Fortified Sample Matrix (LFSM)	Analyze one LFSM per Analysis Batch. Fortify the LFSM with method analytes at a concentration greater than the native concentrations of most analytes. Calculate LFSM recoveries.	For LFSMs fortified at concentrations ≤2 x MRL, the result must be within ±50% of the true value. At concentrations greater than the 2 x MRL, the result must be within ±30% of the true value.
Section 9.3.6	Laboratory Fortified Sample Matrix Duplicate (LFSMD) or Laboratory Duplicate (LD)	Analyze at least one LFSMD or LD with each Analysis Batch.	For LFSMDs or LDs, relative percent differences must be ≤30%. (≤50% if concentration ≤2 x MRL.)
Section 9.3.7	Quality Control Sample (QCS)	Analyze mid-level QCS at least quarterly.	Results must be ±30% of the true value.

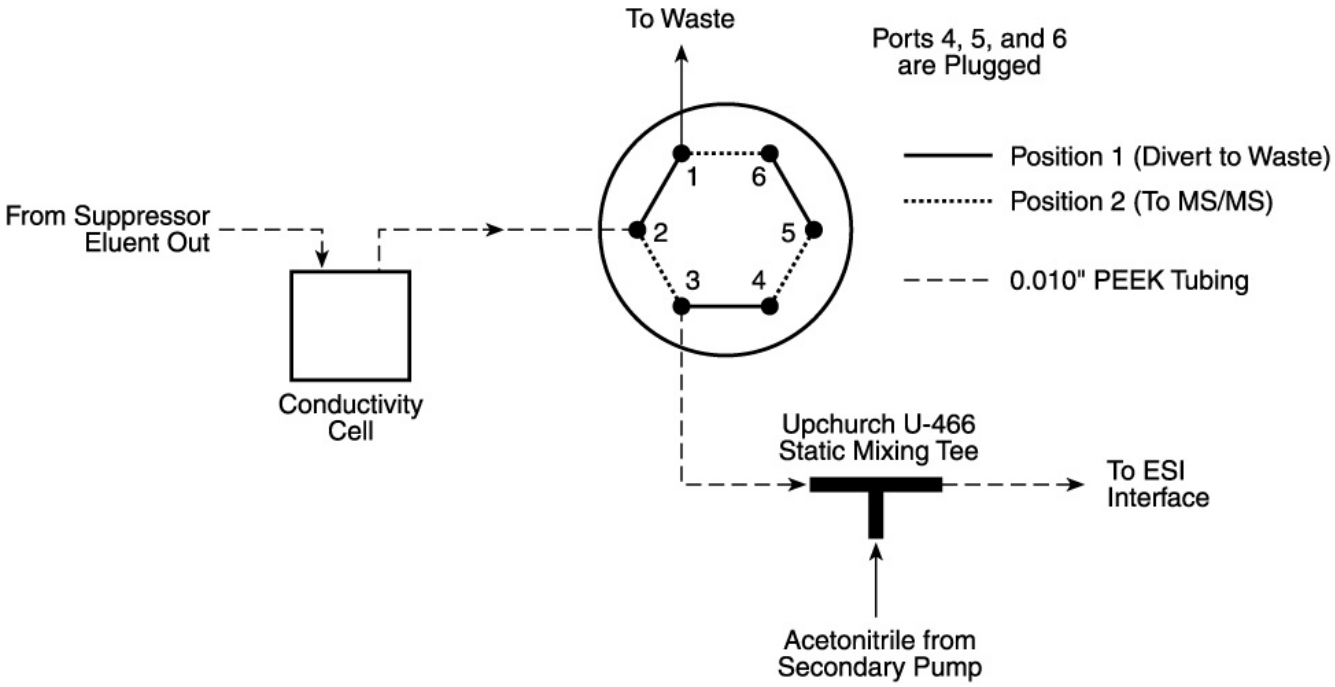

Figure 1. Divert valve placement in sample path.

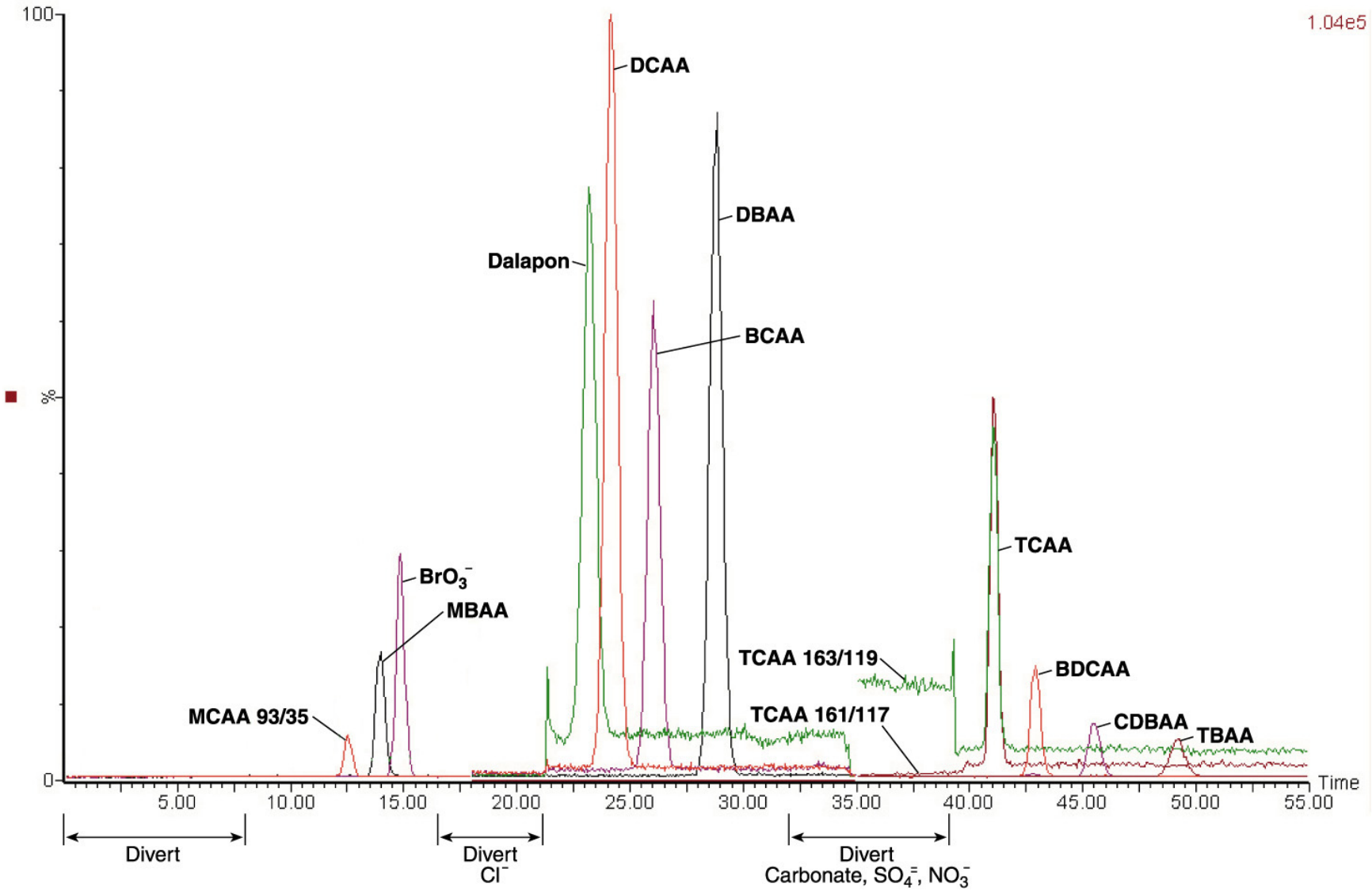

Figure 2. Dionex AS24 column: procedural calibration standard (5 µg/L).

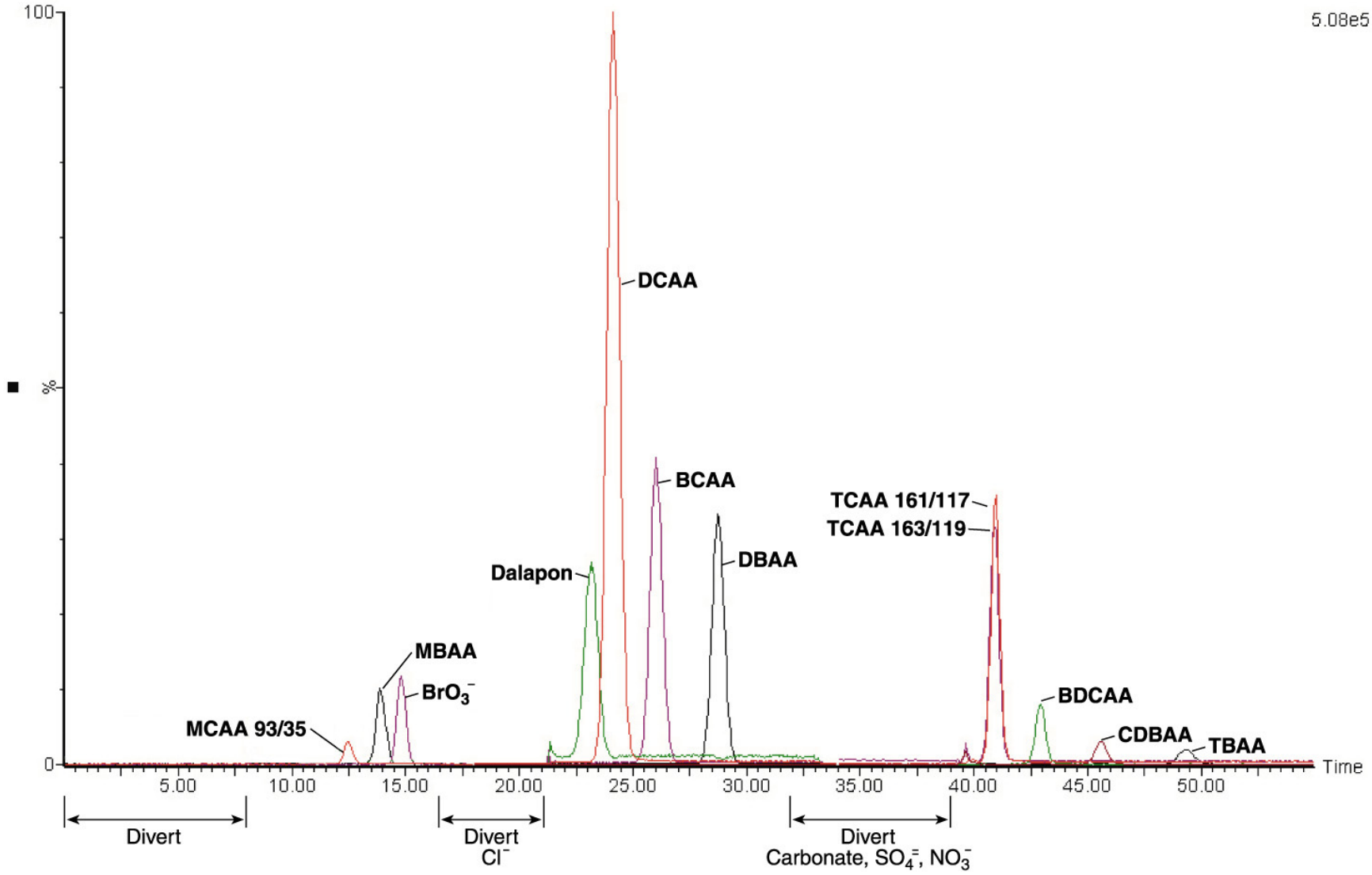

Figure 3. Dionex AS24 column: tap water fortified at 8 µg/L.

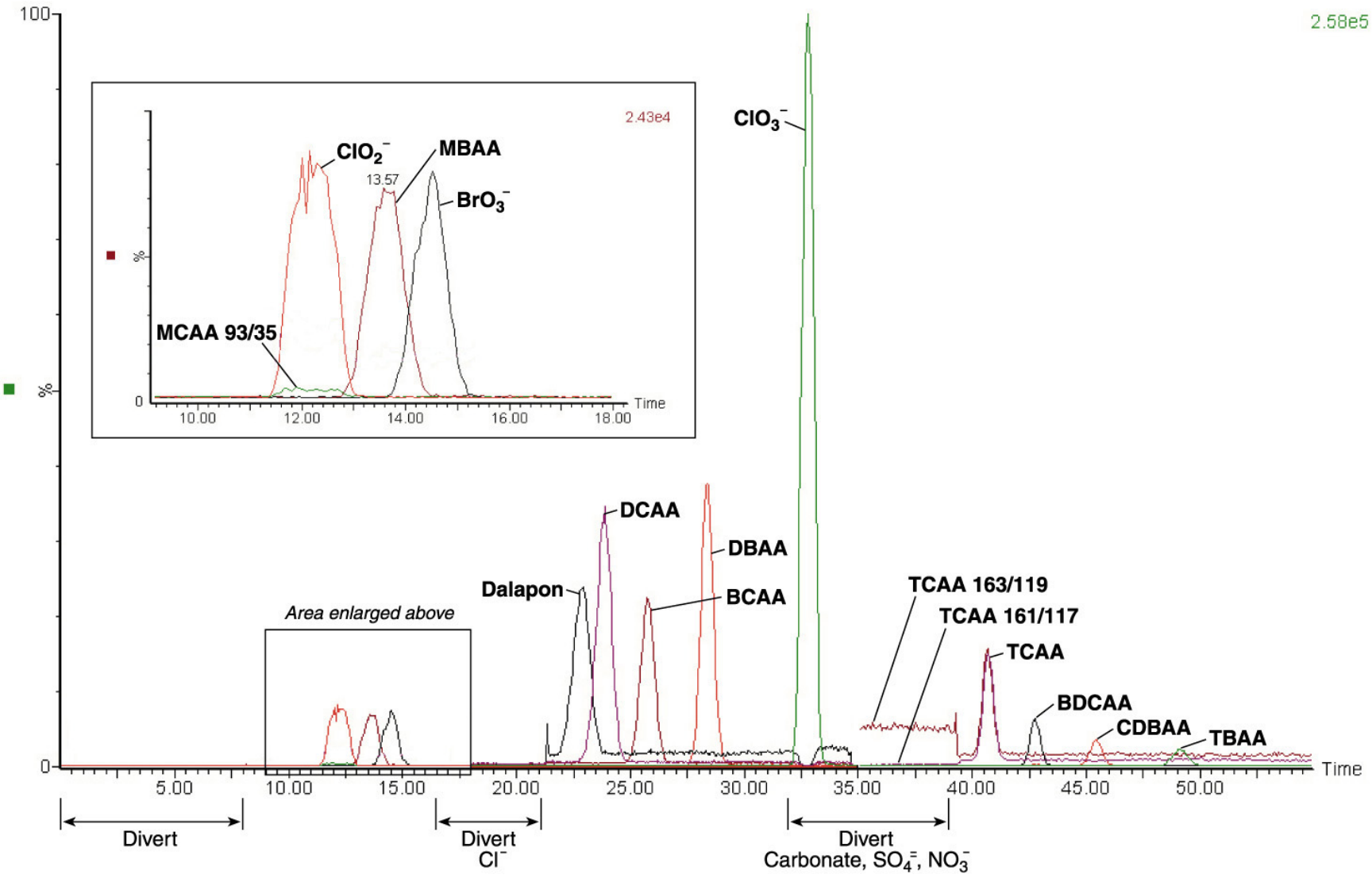

Figure 4. Dionex AS24 column: synthetic sample matrix fortified at 5 µg/L plus chlorite (1 mg/L) and chlorate (0.5 mg/L).

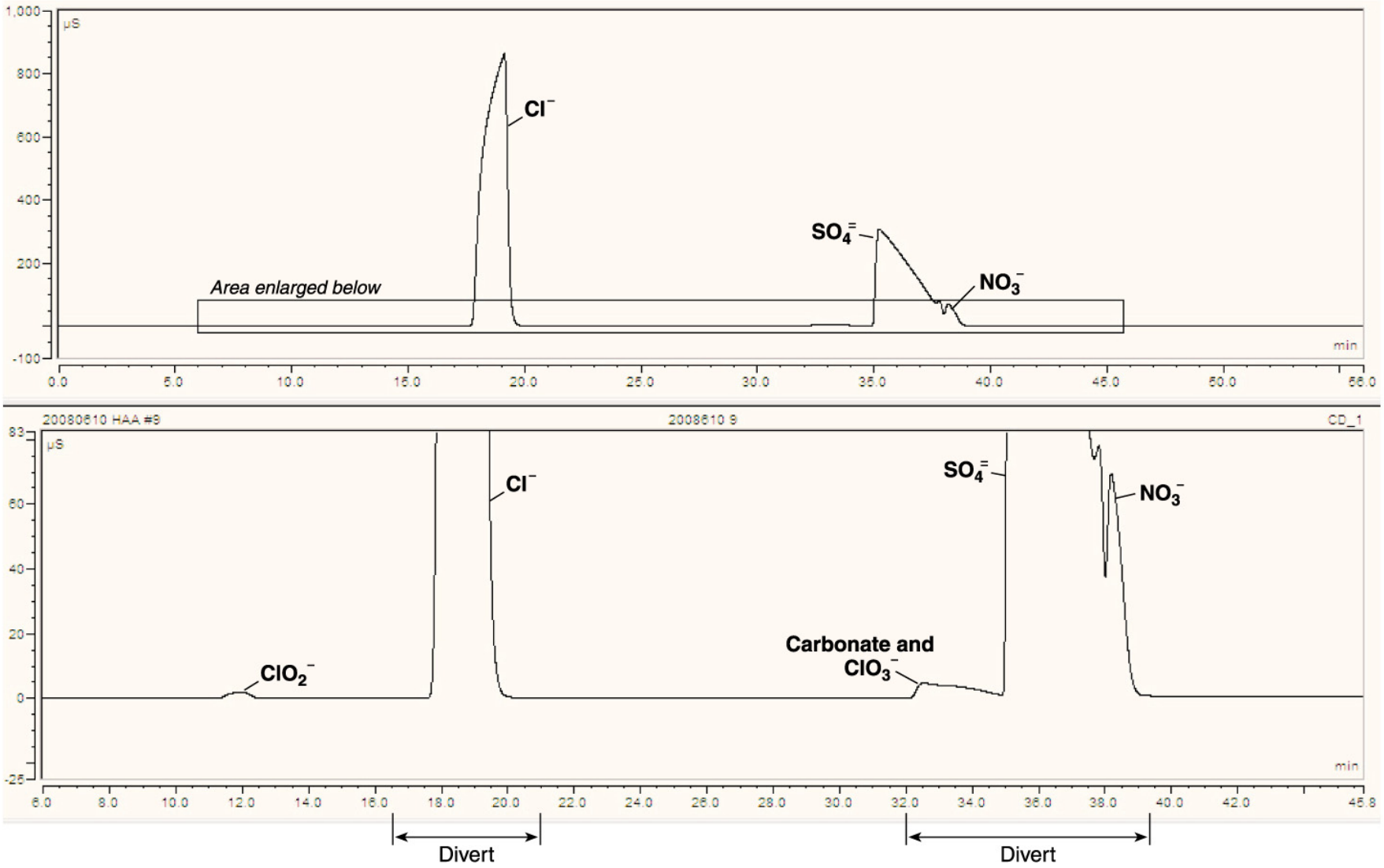

Figure 5. Dionex AS24 column: conductivity trace, synthetic sample matrix plus chlorite (1 mg/L) and chlorate (0.5 mg/L).