



Designation: D8456 – 22

Standard Test Method for Determination of Nitrosamines in Water by Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)¹

This standard is issued under the fixed designation D8456; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ϵ) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This test method covers the liquid chromatography tandem mass spectrometry (LC-MS/MS) detection and quantitation of N-nitrosamines after direct injection. It has been validated for groundwater, surface water, wastewater influents, and wastewater effluents. This test method is not limited to these aqueous matrices; however, the applicability of this test method to other aqueous matrices must be demonstrated.

1.2 This test method is applicable to nitrosamines that can be chromatographed and detected using a mass spectrometry procedure. [Table 1](#) lists the compounds that have been validated for this test method. This test method is not limited to the compounds listed in [Table 1](#); however, the applicability of the test method to other compounds must be demonstrated.

1.3 Analyte concentrations from 0.05 $\mu\text{g/L}$ up to approximately 5 $\mu\text{g/L}$ may be determined without dilution of the sample. Analytes with insufficient sensitivity will not be detected, but they can be measured with acceptable accuracy and precision when present in sufficient amounts. In addition, newer instruments, or instruments of improved sensitivity may be used to lower detection limits.

1.4 Analytes that are not separated chromatographically, but that have different mass spectra and noninterfering quantitation ions, can be identified and measured in the same calibration mixture or water sample. Analytes that have very similar product ions cannot be individually identified and measured in the same calibration mixture or water sample unless they have different retention times.

1.5 It is the responsibility of the user to ensure the validity of this test method for untested matrices.

1.6 This test method is restricted to use by or under the supervision of analysts experienced in the use of a liquid chromatograph with tandem mass spectrometry (LC-MS/MS).

1.7 Depending on data usage, you may modify this test method but limit to modifications that improve performance

while still meeting method quality acceptance criteria. Shortening the chromatographic run simply to save time is not allowed. Use Practice [E2935](#) or similar statistical tests to confirm that modifications produce equivalent results on non-interfering samples. In addition, use Guide [E2857](#) or equivalent statistics to re-validate the modified test.

1.8 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.9 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety, health, and environmental practices and determine the applicability of regulatory limitations prior to use.*

1.10 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*²

- [D1129 Terminology Relating to Water](#)
- [D1193 Specification for Reagent Water](#)
- [D2777 Practice for Determination of Precision and Bias of Applicable Test Methods of Committee D19 on Water](#)
- [D3370 Practices for Sampling Water from Flowing Process Streams](#)
- [D4448 Guide for Sampling Ground-Water Monitoring Wells](#)
- [D6089 Guide for Documenting a Groundwater Sampling Event](#)
- [D6538 Guide for Sampling Wastewater With Automatic Samplers](#)
- [D6759 Practice for Sampling Liquids Using Grab and Discrete Depth Samplers](#)
- [E2857 Guide for Validating Analytical Methods](#)

¹ This test method is under the jurisdiction of ASTM Committee [D19](#) on Water and is the direct responsibility of Subcommittee [D19.06](#) on Methods for Analysis for Organic Substances in Water.

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² For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

TABLE 1 Analytes Validated for this Method

Sr. No.	Name	Abbreviations	CAS No
1	N-Nitroso dimethylamine	NDMA	62-75-9
2	N-Nitroso Morpholine	NMOR	59-89-2
3	N-Nitroso-N-methyl-4-aminobutyric Acid	NMBA	61445-55-4
4	N-Nitroso pyrrolidine	NPYR	930-55-2
5	N-Nitroso ethylmethylamine	NMEA	10595-95-6
6	N-Nitroso diethylamine	NDEA	55-18-5
7	N-Nitroso piperidine	NPIP	100-75-4
8	N-Nitroso isopropylethylamine	NEIPA	16339-04-1
9	N-Nitroso diisopropylamine	NDIPA	601-77-4
10	N-Nitroso di n-Propyl amine	NDPA	621-64-7
11	N-Nitroso dibutylamine	NDBA	924-16-3
12	N-Nitrosomethylphenylamine	NMPA	614-00-6
13	N-Nitroso diphenylamine	NDPhA	86-30-6
14* ISTD	N-Nitroso dimethylamine-D6	NDMA-D6	17829-05-9
15* ISTD	N-Nitroso diethylamine-D10	NDEA-D10	1219794-54-3

E2935 Practice for Evaluating Equivalence of Two Testing Processes

3. Terminology

3.1 Definitions—For definitions of terms used in this test method, refer to Terminology [D1129](#).

3.2 Definitions of Terms Specific to This Standard:

3.2.1 atmospheric pressure chemical ionization (APCI), *n*—an ionization method used in mass spectrometry which uses a gas-phase ion-molecule reaction at atmospheric pressure coupled with high-performance liquid chromatography (HPLC).

3.2.1.1 Discussion—APCI is a soft ionization method similar to chemical ionization where primary ions are produced on a solvent spray. The main usage of APCI is for mid-polar and relatively less polar thermally stable compounds with molecular weight less than 1500 Da.

4. Summary of Test Method

4.1 Internal standard is added to a known volume of sample. The sample is injected into LC-MS/MS system operated with an APCI source. Alternatively, extract an isotopically labelled analog of each analyte (isotope dilution), if available, and correct for recovery.

4.2 Compounds eluting from the LC column, are identified by comparing their MRM transition and retention times to reference standards. MRM transitions and retention times for analytes are obtained by the measurement of calibration standards under the same conditions used for the samples. The concentration of each identified component is measured by relating the Selected Reaction Monitoring (SRM) response of the SRM produced by that compound to the SRM transition response produced by a compound that is used as an internal standard. Surrogate analytes, whose concentrations are known in every sample, are measured with the same internal standard calibration procedure. Qualitative identity is made by measuring the relative abundance ratios of Multiple Reaction Monitoring (MRM) from the same compound and comparing it to the relevant standard. Quantitative analysis is performed by using the authentic standard(s) to produce a response factor or calibration curve. The calibration data, along with the sample

volume extracted and the final sample extract volume, is used to determine the concentration of a target compound in the sample extract.

5. Significance and Use

5.1 Nitrosamines are a class of nitrogen-containing compounds with a known occurrence in wastewater. They may also be created in deionization and are a potential contaminant in water for reuse. The World Health Organization has issued a guideline for NDMA in drinking water at 0.1 µg/L. NDMA may occur in chlorinated effluents and other wastewaters. Other methods for nitrosamines employ solid phase extraction, which may not be applicable to wastewaters that contain particulate matter or a high organic load. This method analyses nitrosamines directly using LC-MS/MS.

6. Interferences

6.1 Interferences are largely eliminated by use of tandem MSMS technology. Reagents should also be checked for the presence of contaminants. Subtracting blank values from sample results is not permitted.

6.2 Interfering contamination may occur when a sample containing low concentrations is analyzed immediately after a sample containing higher concentrations. After analysis of a sample containing high concentrations of semi-volatile organic compounds, one or more solvent blanks should be analyzed to check for cross contamination. After analyzing a highly contaminated sample, it may be necessary to wash out the system by injection of blanks.

6.3 Nitrosamines may be present in trace amounts in rubber products. Repeat injections from auto-sampler vials with polytetrafluoroethylene coated rubber septa may introduce method analytes into the sample.

7. Apparatus

7.1 Tandem Liquid Chromatography/Mass Spectrometer/Data System (LC-MS/MS):

7.1.1 Liquid Chromatography System—A complete LC system is required to analyze samples, this includes a sample injection system, a solvent pumping system capable of mixing