

# Analysis of N-nitrosodimethylamine (NDMA) in Water using GC Triple Quadrupole Mass Spectrometry

## Application Note

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### Abstract

A method was developed on the Agilent 7890A Series GC and an Agilent 7000B Triple Quadrupole GC/MS mass spectrometer in positive chemical ionization (PCI) mode that provides sensitivity of one part per trillion (ppt) and lower for N-nitrosodimethylamine (NDMA). The method further provides an acceptable alternative to the commonly used ion trap MS method for those laboratories that do not have an ion trap instrument. The limit of detection (LOD) was 0.20 ppt, and the limit of quantitation (LOQ) was determined to be 0.56 ppt.



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## Introduction

Chloramination is used in wastewater treatment facilities to reduce trihalomethanes (THMs) which have been associated with an increased risk of bladder cancer and are released into water sources through both industrial and anthropogenic sources. However, nitrosamines like NDMA are inadvertent by-products of wastewater treatment through chloramination. NDMA itself has been classified by national and international regulatory authorities as a probable human carcinogen, and numerous laboratory animal studies have linked NDMA exposure to various cancers.

NDMA is considered a priority pollutant, but few regulatory limits exist for the concentration of NDMA in the environment and drinking water in particular. However, a number of international, national and subnational authorities have set regulatory guidelines or assessment levels for nitrosamines in drinking water. In 1989, NDMA was found in a drinking water well in northern California and the state has since established a notification level of 10 ng/L (ppt), and a response level of 300 ng/L, at which removal of the water source from service is recommended. Internationally, in 2008 the World Health Organization (WHO) added NDMA to its guidelines for drinking water quality. In March 2010, Health Canada proposed a maximum acceptable concentration for NDMA in drinking water of 40 ng/L.

As of October 2009, the US Environmental Protection Agency (EPA) listed five nitrosamines, including NDMA, on its candidate list of priority drinking water contaminants for which the EPA will research whether regulations are needed. If NDMA or other nitrosamines become regulated drinking water contaminants, robust, sensitive analytical methods will be required for compliance monitoring [1].

This application note describes a GC/MS/MS method that yields an LOD of 0.20 ppt and an LOQ of 0.56 ppt.

## Experimental

### Standards and Reagents

NDMA standard was obtained from Supelco, and d6-NDMA surrogate and N-nitroso-di-n-propylamine-d14 (NDPA- d14) internal standard were obtained from Cambridge Isotope Laboratories Inc. Standards were made up by weight in dichloromethane. Coconut charcoal SPE cartridges, 80/120 mesh, were obtained from Restek. Dichloromethane and methanol were obtained from Fisher Scientific. HPLC grade water was used to prepare the calibration standards.

### Instruments

This method was developed on an Agilent 7890A Series GC equipped with an S/SL inlet and coupled to an Agilent 7000B Triple Quadrupole GC/MS in positive chemical ionization (PCI) mode. Table 1 lists the instrument conditions.

Table 1. Agilent 7890A Series Gas Chromatograph and Agilent 7000B Triple Quadrupole Mass Spectrometer Conditions

GC run conditions	
Analytical columns	DB-WAXETR 30 m × 0.25 mm, 0.25 µm (p/n 122-7332)
Inlet temperature	200 °C
Injection mode	Splitless 5-µL injection.
Flow	Constant flow at 1.7 mL/min
Oven program	40 °C for 3 minutes then 10 °C/min to 110 °C for 0 minutes then 15 °C/min to 200 °C for 0 minutes then 40 °C/min to 240 °C for 0 minutes
Carrier gas	Helium Ultra High Purity. Constant flow.
Transfer line temperature	240 °C
PCI MS conditions	
Tune	PCI Autotune
EMV gain	15
Acquisition parameters	PCI positive mode with single reaction monitoring (SRM)
Reagent gas	Ammonia, 20 % flow
Collision gas	Nitrogen, constant flow, 1.5 mL/min
Quench gas	Helium, constant flow, 2.25 mL/min
Solvent delay	6.0 minutes
MS temperatures	Source 200 °C; Quadrupole 150 °C

## Sample Preparation

One-half liter of each water sample spiked with NDMA standard at a given concentration was extracted using solid phase extraction (SPE) procedures similar to those described elsewhere [1]. NDMA-d6 was added to samples as a surrogate prior to sample preparation to monitor extraction efficiency. The eluent from the SPE column was reduced to 0.5 mL using a gentle stream of nitrogen at room temperature. The sample was then brought to 1.0 mL with dichloromethane. The final concentration factor was 500 fold. NDPA-d14 was then added as an internal standard.

## Acquisition Parameters

The mass spectrometer single reaction monitoring (SRM) acquisition parameters are given in Table 2.

Table 2. Agilent 7000B Triple Quadrupole GC/MS Acquisition Parameters

Nitrosamine	RT (min)	SRM	PCI with ammonia mode		
			Dwell time (ms)	Collision energy (EV)	Gain
N-Nitrosodimethylamine (NDMA)	9.141	92 → 75	30	12	15
Deuterated N-Nitrosodimethylamine (NDMA-d6)	9.133	98 → 81	30	12	15
Deuterated N-Nitrosodi-n-propylamine (NDPA-d14)	11.862	162 → 50	30	12	15
		162 → 145	30	12	15

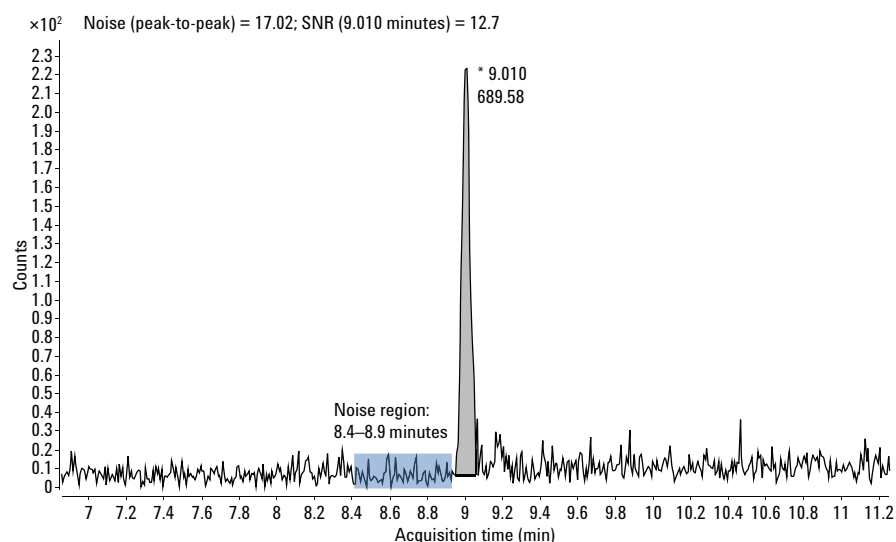


Figure 1. Single Reaction Monitoring (SRM) chromatogram of 0.56 ppt NDMA standard.

## Results and Discussion

### PCI with Ammonia

Using the 7000 Triple Quadrupole GC/MS in positive chemical ionization (PCI) mode with ammonia as the reagent gas and single reaction monitoring (SRM) enables the low detection limits that may be required to monitor NDMA in environmental water samples. Figure 1 illustrates an LOQ with a signal-to-noise (S/N) ratio of 12:1 for NDMA at 0.56 ppt (height, peak-to-peak, 30 second noise region over 8.4–8.9 minutes).

Figure 2 shows an overlay of the SRM chromatograms of the seven calibration levels and Figure 3 illustrates the corresponding calibration curve with a linear correlation coefficient of > 0.999.

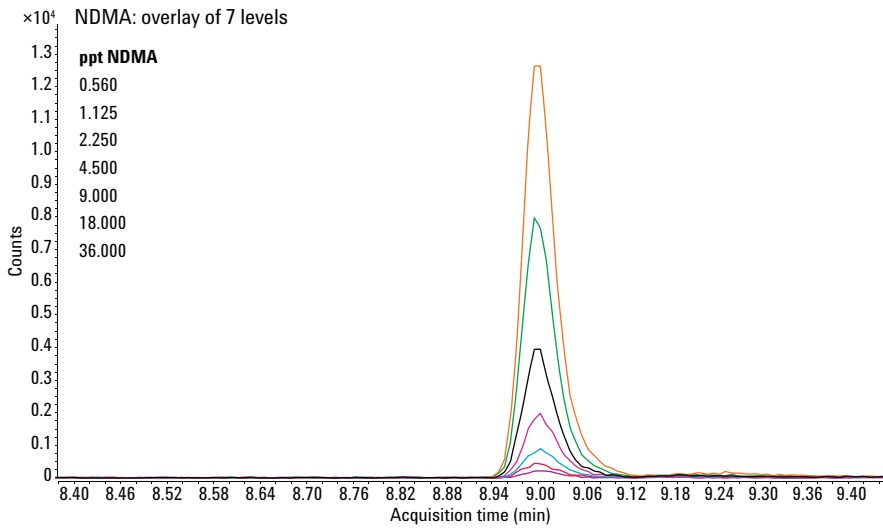


Figure 2. Overlaid SRM chromatograms of NDMA standards.

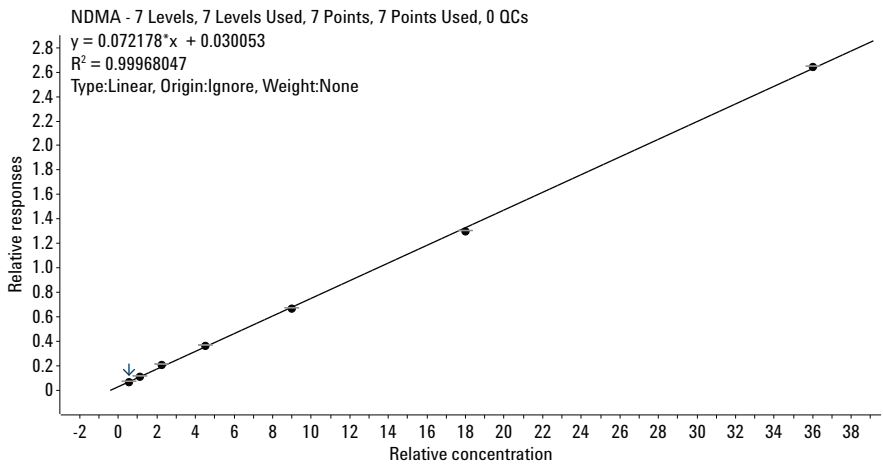


Figure 3. Calibration curve for NDMA standards from 0.56 to 360 ppt in PCI Ammonia mode, after accounting for 500 fold concentration during sample preparation.

With this data, minimum reportable limits such as the LOD and LOQ were determined as 0.20 ppt and 0.56 ppt, respectively at the 95% confidence level for 10 replicate injections by using a one-tail Student-T test with n-1 degrees of freedom. Figure 4 shows typical lab and field blank detection

levels of NDMA. Figure 5 illustrates the NDMA and NDMA-d6 SRM channels of dichloromethane solvent blank and actual drinking water sample from a city in the western United States that was determined to contain 3.4 ppt NDMA.

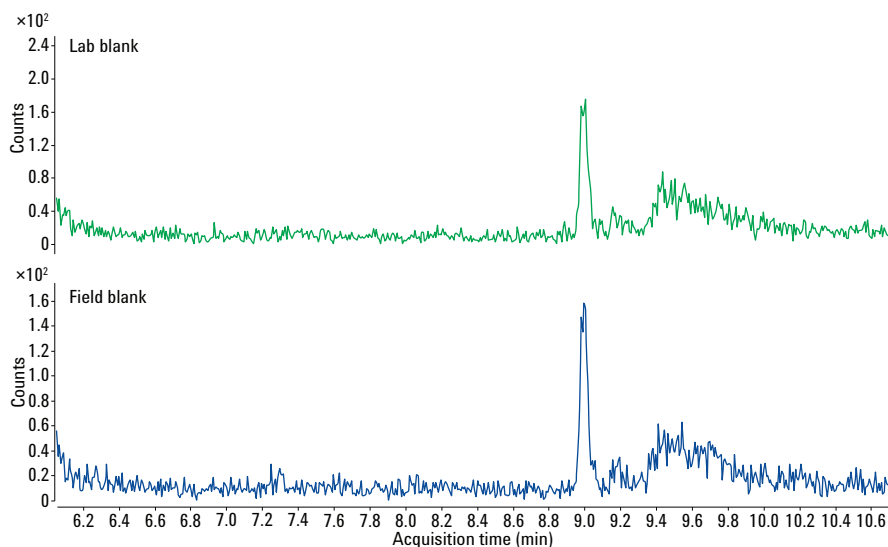


Figure 4. NDMA SRM chromatograms of lab and field blanks.

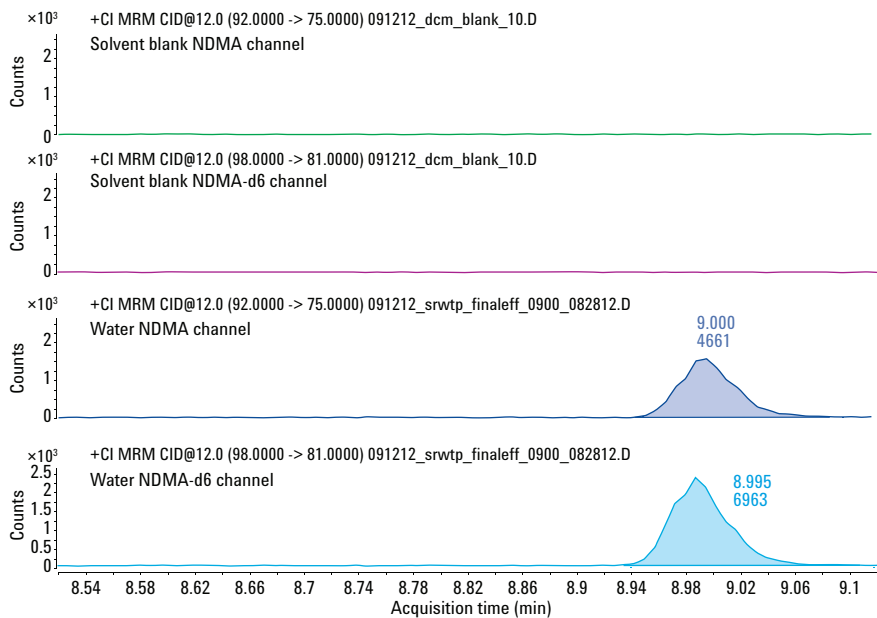


Figure 5. NDMA and NDMA-d6 SRM channels of dichloromethane solvent blank and water sample illustrating clean solvent background and 3.4 ppt NDMA detected in the water sample.

## Conclusion

This method, using the Agilent 7890A GC and 7000B Triple Quadrupole GC/MS system, yields limits of detection and quantification of less than 1 ppt NDMA in water matrices.

## Reference

1. J.W. Munch, M.V. Basset. US EPA Method 521, Version 1. September, 2004.

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