Reference Standards

Cornerstone Solutions in Nitrosamines Analysis for Pharmaceutical Impurities Testing

- World-class reference standards in convenient mixes to streamline your analyses.
- LC and GC solutions to accommodate your unique methodologies.
- Custom solutions, time-saving chromatogram modeling software, and more!

RESTEK Pure Chromatography www.restek.com

Cornerstone Solutions in Nitrosamines Analysis for Pharmaceutical Impurities Testing

The discovery of nitrosamine compounds in pharmaceutical drug products is a worldwide health concern that has prompted laboratories to develop reliable impurity methodologies for these compounds. Due to their carcinogenic potential, the acceptable daily limit (ADL) for nitrosamine compounds is very low per guidelines outlined by the FDA, EMA, and other regulatory authorities. It is imperative for testing laboratories to source reliable standards to ensure data accuracy and product safety.

Comprised of the most frequently targeted nitrosamine compounds for pharmaceutical impurities testing, our new, multicomponent Nitrosamine 7 Standard contains seven key nitrosamines in a single ampul, significantly reducing the complexity in sourcing the compounds laboratories need. Take advantage of our seven-in-one nitrosamine certified reference standard (CRM) and internal standard to simplify sourcing, reduce standard preparation, and to help ensure the accuracy of your data. Features of our nitrosamine standard offering include:

- Seven critical nitrosamines in a single ampul.
- Formulated for optimal stability with a concentration of 100 µg/mL for each analyte, allowing for flexibility in constructing calibration curves.
- Two independently manufactured lots available with verified lot-to-lot agreement.
- Internal standard available at a concentration of 1000 µg/mL.

Streamline Your Nitrosamines Analysis with Our Nitrosamines 7 Standard

Nitrosamines 7 Standard

Contains the following key compounds:

N-Ethyl-N-nitroso-2-propanamine (NEIPA) (16339-04-1)

N-Nitrosodi-n-butylamine (NDBA) (924-16-3)

N-Nitrosodiethylamine (NDEA) (55-18-5)

N-Nitrosodiisopropylamine (NDIPA) (601-77-4)

N-Nitrosodimethylamine (NDMA) (62-75-9)

N-Methyl-N-nitrosoaniline (NMPA) (614-00-6)

N-Nitroso-N-methyl-4-aminobutyric acid (NMBA) (61445-55-4)

Catalog No.	Concentration	Solvent	Volume	Units
36025	100 µg/mL	Acetonitrile	1 mL/ampul	ea.

N-Nitrosodimethyl-d6-amine Standard

For use as an internal standard in nitrosamines analysis.

Catalog No.	Concentration	Solvent	Volume	Units
36026	1000 µg/mL	Acetonitrile	1 mL/ampul	ea.

Custom Reference Standards

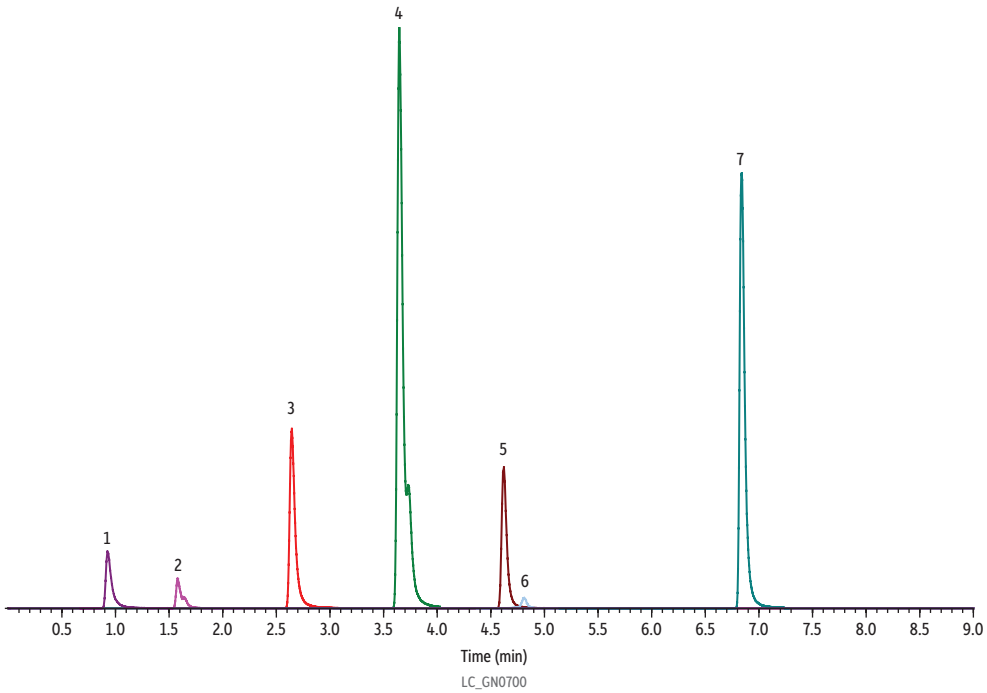
Do you need specific compounds to meet your method requirements?

Visit **www.restek.com/standards** and start a request today!

See Chromatographic Results of our Nitrosamine CRM Ampul

Our Nitrosamine 7 Standard achieved excellent chromatographic performance when analyzed by both LC-MS and GC-MS, as shown in Figure 1 and Figure 2, below. Though peak splitting is commonly reported in nitrosamine testing, very minimal peak slitting was observed with our standard. Good separations were achieved for both the LC and GC analysis, while maintaining fast run times of under 9 min and 8 min, respectively.

Figure 1: LC-MS Analysis of Nitrosamine 7 Standard on Raptor C18



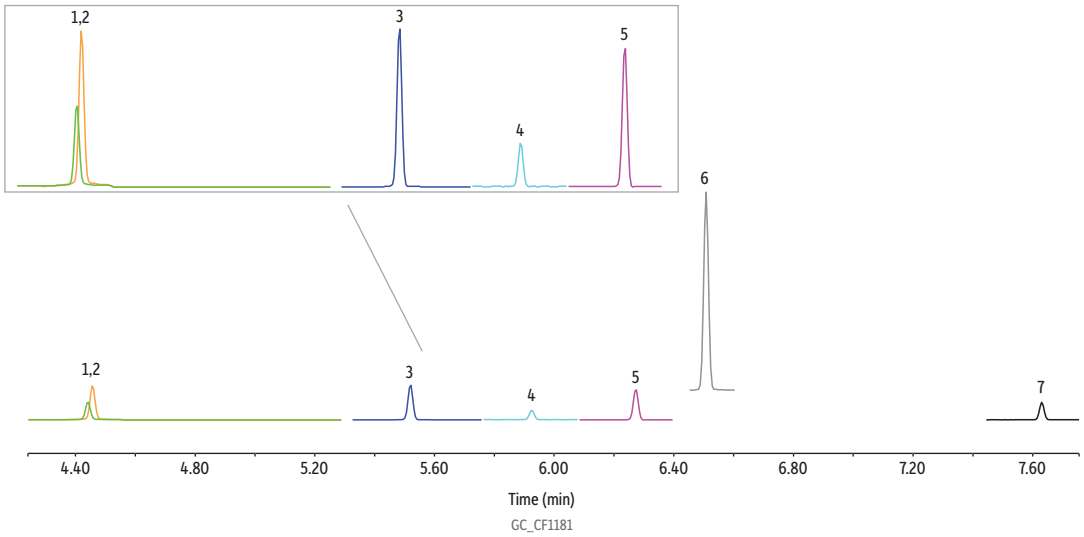
Peaks	t_R (min)	Precursor Ion	Product Ion
1. *N*-Nitrosodimethylamine (NDMA)	0.93	75.1	58.0
2. *N*-Nitroso-*N*-methyl-4-aminobutyric acid (NMBA)	1.58	147.0	117.1
3. *N*-Nitrosodiethylamine (NDEA)	2.65	103.1	75.0
4. *N*-Nitrosoethylisopropylamine (NEIPA)	3.66	117.1	75.0
5. *N*-Nitrosodiisopropylamine (NDIPA)	4.61	131.2	43.1
6. *N*-Nitrosomethylphenylamine (NMPA)	4.82	137.0	65.9
7. *N*-Nitrosodibutylamine (NDBA)	6.84	159.1	57.0

Column Raptor C18 (cat.# 9304A12)
Dimensions: 100 mm x 2.1 mm ID
Particle Size: 2.7 µm
Pore Size: 90 Å
Temp.: 40 °C
Standard/Sample Nitrosamines 7 Standard (cat.# 36025)
Diluent: Water
Conc.: 100 ng/mL
Inj. Vol.: 5 µL
Mobile Phase
A: Water, 0.1% formic acid
B: Methanol, 0.1% formic acid

Time (min)	Flow (mL/min)	%A	%B
0.00	0.4	95	5
9.00	0.4	5	95
9.01	0.4	95	5
11.00	0.4	95	5

Max Pressure: 340 bar
Detector SCIEX 4500 MS/MS
Ion Source: APCI
Ion Mode: APCI+
Mode: Scheduled MRM
Instrument Shimadzu Nexera X2
Sample Preparation A 100 ng/mL stock was prepared by adding 1 µL of Nitrosamines 7 Standard to 999 µL of water in 2 mL, screw-thread amber vials (cat.# 21143) and capped with 9 mm, short-cap, screw-vial closures (cat.# 24498).

Figure 2: GC-MS Analysis of Nitrosamine 7 Standard on Rxi-5Sil MS



Peaks	t_R (min)	Conc. (ng/mL)	Precursor Ion	Product Ion	Collision Energy	Confirmation Precursor Ion	Confirmation Product Ion	Confirmation Collision Energy
1. *N*-Nitrosodimethylamine-d6 (NDMA-d6)	2.28	100	80	30	12	80	46	14
2. *N*-Nitrosodimethylamine (NDMA)	2.30	100	74	42	18	74	43	18
3. *N*-Nitrosodiethylamine (NDEA)	3.30	100	102	29	8	102	44	10
4. *N*--Ethyl-N-nitroso-2-propanamine (NEIPA)	3.70	100	116	42	24	116	99	4
5. *N*-Nitrosodiisopropylamine (NDIPA)	4.04	100	130	42	8	130	88	4
6. *N*-Methyl-N-nitrosoaniline (NMPA)	4.34	100	106	51	28	106	51	28
7. *N*--Nitrosodi-*n*-butylamine (NDBA)	5.36	100	116	74	6	116	99	6

Column	Rxi-5Sil MS, 30 m, 0.25 mm ID, 0.25 µm (cat.# 13623)
Standard/Sample	Nitrosamines 7 Standard (cat.# 36025) *N*-Nitrosodimethyl-d6-amine standard (cat.# 36026)
Diluent:	ACN
Conc.:	100 ng/mL
Injection	
Inj. Vol.:	1 µL split (split ratio 10:1)
Liner:	Topaz, Precision inlet liner, 4.0 mm x 6.3 x 78.5 (cat.# 23305)
Inj. Temp.:	280 °C
Oven	
Oven Temp.:	35 °C (hold 1 min) to 320 °C at 30 °C/min (hold 1.5 min)
Carrier Gas	He, constant flow
Flow Rate:	1.2 mL/min
Detector	TSQ9000
Transfer Line Temp.:	280 °C
Source Temp.:	325 °C
Tune Type:	PFTBA
Ionization Mode:	EI
Instrument	Thermo Trace GC
Sample Preparation	Standards were diluted to final concentration of 100 ppb with ACN. The sample was mixed in a 2 mL, short-cap, screw-thread vial (cat.# 21143) and capped with a short-cap, screw-vial closure (cat.# 24495).
Notes	*N*-Nitroso-*N*-methyl-4-aminobutyric acid (NMBA) was not observed during the GC-MS/MS run.

Interested in Speeding Up and Simplifying Method Development?

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- Optimize existing methods accurately and reliably.
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www.restek.com/chromablography/a-nitrosamines-crm-and-method-development-utilizing-resteks-pro-ezlc

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LC Products for Nitrosamines Analysis

Raptor C18 Column

- A traditional end-capped C18 ideal for general-purpose use in reversed-phase chromatography.
- Wide pH range (2–8) provides excellent data quality for many applications, matrices, and compounds.
- Offers the highest hydrophobic retention of any Raptor phase.
- Part of Restek's Raptor LC column line featuring 1.8, 2.7, and 5 µm SPP core-shell silica.

Catalog No.	Product Name	Units
9304A12	Raptor C18, 2.7 µm, 100 x 2.1 mm HPLC Column	ea.

Vials and Caps

Catalog No.	Product Name	Units
21143	Short-Cap Vial with Grad Marking Spot, 9-425 Screw-Thread, 2.0 mL, 9 mm, 12 x 32 (vial only), Amber	1000-pk.
24498	Short Screw Caps, Polypropylene, Screw-Thread, PTFE/Silicone/PTFE Septa, Blue, Preassembled, 2.0 mL, 9 mm	1000-pk.

Additional GC Products for Nitrosamines Analysis

LPGC Rxi-624 Sil MS column

- Low-bleed, high-thermal stability column—maximum temperatures up to 300–320 °C.
- Inert—excellent peak shape for a wide range of compounds.
- Selective—G43 phase highly selective for volatile organics, terpenes, and residual solvents, great choice for USP<467>.
- Manufactured for column-to-column reproducibility—well suited for validated methods.
- Temperature range: -20 °C to 320 °C.

Catalog No.	Product Name	Units
13868	Rxi-624Sil MS GC Capillary Column, 30 m, 0.25 mm ID, 1.40 µm	ea.

Topaz Precision Inlet Liner

Topaz GC inlet liners feature revolutionary technology and inertness to deliver you the next level of True Blue Performance:

- Deactivation—unbelievably low breakdown for accurate and precise low-level GC analyses.
- Reproducibility—unbeatable manufacturing controls and QC testing for superior reliability across compound classes.
- Productivity—unparalleled cleanliness for maximized GC uptime and lab throughput.
- 100% Satisfaction—if a liner doesn't perform to your expectations, we will replace it or credit your account.

Patented

Catalog No.	Product Name	Units
23305	Topaz, Precision Inlet Liner, 4.0 mm x 6.3 x 78.5, for Agilent GCs, w/Quartz Wool, Premium Deactivation	5-pk.

Vials and Caps

Catalog No.	Product Name	Units
21142	Short-Cap Vial with Grad Marking Spot, 9-425 Screw-Thread, 2.0 mL, 9 mm, 12 x 32 (vial only), Amber	100-pk.
23841	Short Screw Caps, Polypropylene, Ribbed, Screw-Thread, PTFE/Silicone Lined for Agilent 7693A, Blue, Preassembled, 2.0 mL, 9mm	100-pk.

Testing for residual solvents?

Browse our selection of certified residual solvent reference standards by visiting **www.restek.com**; then search for *Residual Solvent Standards* with *Products* selected in the dropdown menu.

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