Chemical Metrology Division
Applied Sciences Group
Health Sciences Authority
1 Science Park Road, #01-05/06,
The Capricorn, Singapore Science Park II,
Singapore 117528
Tel: 65 6775 1605 Fax: 65 6775 1398
Website: www.hsa.gov.sg
Email: HSA_CML@hsa.gov.sg

Ref. No.: CML-HRM-1029A/03
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Certificate of Analysis

CERTIFIED REFERENCE MATERIAL
HRM-1029A

N-Nitrosodimethylamine (NDMA) in Methanol

Batch Number
STY-0163-001

Description
A unit of the certified reference material (CRM) consists of about 1 mL of N-nitrosodimethylamine (NDMA) in methanol in an amber glass ampoule.

The CRM was certified with reference to the requirements set out in ISO/IEC 17025:2017 [1], ISO 17034:2016 [2] and ISO Guide 35:2017 [3].

Certified Mass Fraction Value
A certified value is a value for which a laboratory has the highest confidence in its accuracy, in that all known or suspected sources of biases have been investigated and accounted for. The certified mass fraction value for NDMA in methanol was determined by gas chromatography-isotope dilution tandem mass spectrometry (GC-IDMS/MS).

Certified Mass Fraction Value: 119.9 ± 4.8 mg/kg

The final result is expressed as the certified value ± the expanded uncertainty.

The uncertainty listed with the certified value is an expanded uncertainty about the mean, with coverage factor 2 (approximately 95 % confidence). The certified value has an associated measurement uncertainty attributed to uncertainty contribution from characterisation of the material (u_{char}), uncertainty in the homogeneity of the material (u_{bb}) and uncertainty in the stability of the material (u_{stab}). The u_{char} was evaluated by combining uncertainties from method precision, weighing, the concentration of calibration solution (which included the purity of the standard), biases using different ion pairs, bias using different instruments [i.e. GC-MS/MS vs liquid chromatography-tandem mass spectrometry (LC-MS/MS)] and method recovery, in accordance with ISO/IEC Guide 98-3:2008 [4].

Homogeneity

Homogeneity testing on NDMA in methanol was performed on ten ampoules with two sub-samples taken from each ampoule using GC-IDMS/MS. The sample size taken for homogeneity testing was approximately 0.45 g (approximately 0.5 mL). No significant differences in the between and within-bottle variances were found using one-way ANOVA at 95 % confidence level [3]. Thus, the material was regarded to be sufficiently homogeneous. The u_{bb} was evaluated from the uncertainty due to between-bottle inhomogeneity.

Stability

The long-term stability of NDMA in methanol at storage temperature (18 °C to 25 °C) was evaluated on four occasions over a period of up to 3 months after preparation. The results showed that NDMA in methanol was stable over the study period. The u_{stab} was evaluated from the standard error of the slope.

Validity of Certified Mass Fraction Value

The certified mass fraction value is valid within the specified measurement uncertainty until **23 Feb 2026**, provided that the reference material is subjected to the same handling and storage conditions as stated in this Certificate of Analysis (COA).

The CRM will be continuously monitored during the validity period to determine if any substantive change to the certified value has occurred. If necessary, its user will be advised or an updated COA may be issued when the property value of the CRM is found to have changed.

Analytical Methods

The certified mass fraction of NDMA in methanol was determined by exact-matching GC-IDMS/MS. A reference material of neat NDMA obtained from a commercial source, which was purity assessed in-house *via* quantitative proton nuclear magnetic resonance (qNMR) approach [with the use of a CRM of acesulfame potassium (HRM-1012A) from Health Sciences Authority (HSA) as the internal standard] was used as calibration standard. Isotope-labelled $^{13}C_2$,D_6-NDMA from Cambridge Isotope Laboratories Inc. was used as the internal standard.

The calibration blends were prepared gravimetrically by mixing appropriate amount of calibration standard solutions and internal standard solutions. The sample blends were gravimetrically prepared by mixing at least 0.46 g of sample and internal standard solutions. Quality control blends were also prepared and analysed concurrently. The sample blends and quality control blends were vortexed and diluted with methanol prior to analysis. Each sample and quality control blends were bracketed with a series of calibration blends and analysed five times.

Metrological Traceability

The certified mass fraction value is traceable to the International System of Units (SI) through the use of acesulfame potassium CRM from HSA.

Intended Use

The CRM is intended for use as a calibrant for the determination of NDMA.

Instructions for Use

Prior to use, the ampoule should be inverted at least twice. Gentle pressure should be applied on the neck of the ampoule to ensure it breaks with a clean snap. **Always wear gloves and googles when breaking off the top of the ampoule. Exercise precaution as the edges may be sharp.** The CRM should be used without delay after opening to avoid concentration changes due to evaporation. The certified value applies only to aliquots removed at 18 °C to 25 °C. The certified value is not valid for ampoules which have been stored after opening, even if resealed. The minimum sample size for

each use should be about 0.45 g (approximately 0.5 mL).

Storage

The CRM should be stored at room temperature (18 °C to 25 °C) in a dry and cool area in its original sealed ampoule. Exposure to light should be avoided.

Safety Precautions for Users

This CRM contains methanol. Treat the material as hazardous substance. Use appropriate work practices when handling to avoid skin or eye contact, ingestion or inhalation of solvent. See Safety Data Sheet.

Further Information

Please direct all enquiries regarding this reference material to the contact above.

References

[1] ISO/IEC 17025:2017 General requirements for the competence of testing and calibration laboratories.
[2] ISO 17034:2016 General requirements for the competence of reference material producers.
[3] ISO Guide 35:2017 Reference materials – Guidance for characterisation and assessment for homogeneity and stability.
[4] ISO/IEC Guide 98-3:2008 Uncertainty of measurement – Part 3: Guide to the expression of uncertainty in measurement (GUM:1995).

Certificate Revision Records

Certificate of Analysis CML-HRM-1029A/02 replaces Certificate CML-HRM-1029A/01 issued on 23 Feb 2022.

Certificate of Analysis CML-HRM-1029A/03 replaces Certificate CML-HRM-1029A/02 issued on 7 Feb 2023.

Note

HSA does not assume any liability with respect to any loss caused by improper use and/or storage of the reference material by the customer.

Dr Teo Tang Lin
Division Director
Chemical Metrology Laboratory
Chemical Metrology Division