

Certified Reference Material

Reference material certificate

Bruker quantitative PQ (qPQ) Certified Reference Material

TraceCERT®
Traceable Certified Reference Materials

Product no.:	42350
Lot no.:	BCCL0964
Description of CRM:	1,3,5-Trimethoxybenzene (TMXB) and 1,2,4,5-Tetrachloro-3-nitrobenzene (TCNB) in DMSO-d ₆ (solution)
Expiry date:	FEB 2028
Storage:	15-25°C; storage under Argon
Chemical formula:	C ₉ H ₁₂ O ₃ (TMXB); C ₆ HCl ₄ NO ₂ (TCNB)
Molecular mass:	168.19 g/mol (TMXB); 260.89 g/mol (TCNB)

Constituent	Certified value ± Expanded uncertainty, $U_{CRM}=k \cdot u_{CRM}$ ($k=2$) ^{[1][2]}
1,2,4,5-Tetrachloro-3-nitrobenzene	23.53 mg/g ± 0.15 mg/g
1,3,5-Trimethoxybenzene	5.00 mg/g ± 0.03 mg/g

Metrological traceability:	Traceable to the SI through an unbroken chain of comparisons via NIST PS1 (Benzoic acid) ^[3] Details see "Certification process details" on page 2.
Measurement method:	The certified value is established by high-resolution quantitative NMR measurements (qNMR) in accordance with ISO/IEC 17025. ^[4]
Intended use:	Use this certified reference material (CRM) as standard for quantitative ¹ H-NMR measurements.
Minimum sample size:	There is no recommended minimum sample size. The substance is liquid at room-temperature and therefore homogeneous under these conditions. Potential inhomogeneity is covered by the expanded measurement uncertainty.
Instructions for handling and correct use:	The CRM should be stored in the original ampule and protected from light. Shake well before opening. Do not flush the NMR tube with inert gas.
Health and safety information:	Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.
Accreditation:	Sigma-Aldrich Production GmbH is accredited by the Swiss Accreditation Service SAS as reference material producer under no. SRMS 0001 in accordance with international standard ISO 17034.
Certificate issue date:	23 MAY 2024



ISO 17034
SRMS 0001

Dr. A. Rück – CRM Operations

Dr. P. Zell – Approving Officer



Packaging:

Brown glass ampule

Starting material details:

Potential raw materials are checked for suitability in terms of purity. Only materials of highest available purity are accepted. 2D-NMR (H-H COSY) measurements are applied to guarantee that no impurities underlie the peak of interest. Detection limit usually is below 0.1 %.

Compatibility of candidate substance with solvent and internal qNMR reference is checked (t=0 and t=24 h comparison).

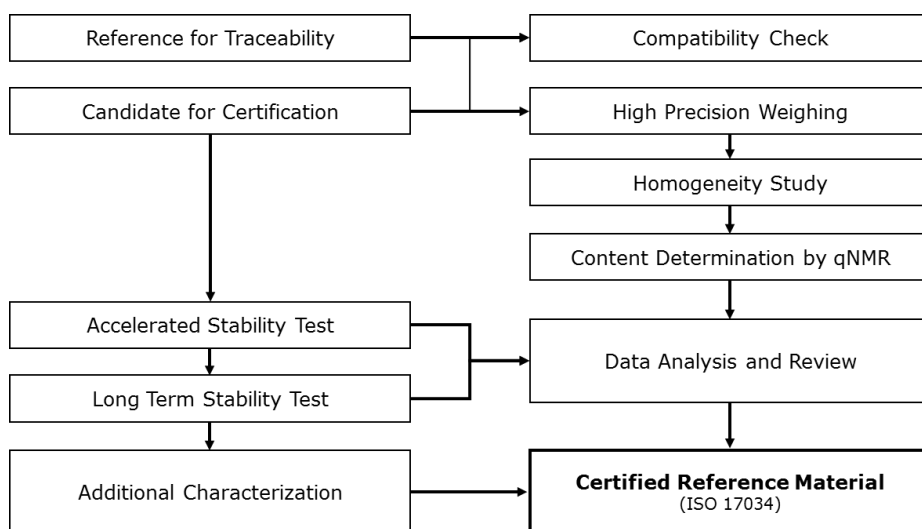
Certification process details:

In order to guarantee highest reliability of this *TraceCERT* CRM a multi-component approach was applied whereby the certified value is determined by high-resolution quantitative NMR measurements (qNMR on a 600 MHz NMR spectrometer).^[4] The whole workflow follows the ISO 17034 guidelines. The certificate is designed in accordance with ISO Guide 31.

The certified values are confirmed by extended analytical data. These data are not covered by the scope of accreditation but determined following best practices in analytical measurements.

The high precision weighing steps are performed in accordance with ISO/IEC 17025^[4] using ultra-micro balances certified by DKD and calibrated with OIML Class E2 weights.

Absolute content determination by qNMR is performed using 5-10 separate samples of the candidate substance which are each spiked with an adequate amount of internal reference and then immediately dissolved in deuterated solvent. In most cases 16-32 scans are recorded for every sample with a ¹H relaxation time of d1= 115 seconds. Quantification of the candidate content is directly calculated from the ¹H-NMR peak areas and the initial mass of the candidate and reference substance. After ANOVA the resulting standard deviation is included into the uncertainty calculation of the certified value. Extensive stability and homogeneity tests are considered for certification.^[8]

**Homogeneity assessment:**

Homogeneity of the material is tested by qNMR measurements using 5-10 subsamples. Data have been evaluated by analysis of variance (ANOVA).

Stability assessment:

An accelerated stability test is performed with samples which are stored above the recommended storage temperature. The material is tested by qNMR double determination at appropriate time intervals, e.g. 3 months.

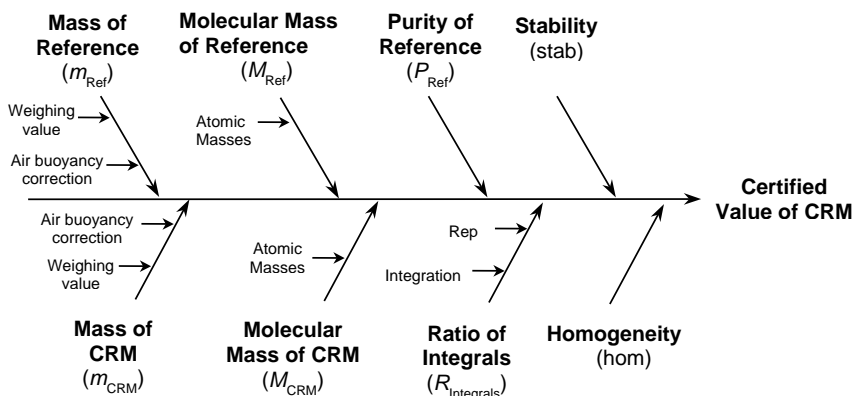
The long-term stability test is performed with samples which are stored at the recommended storage temperature and applying qNMR double determination at appropriate time intervals.

Uncertainty evaluation:

The uncertainty contributions are illustrated by the following cause-effect diagram.

Typical relative contributions are:

$u(P_{\text{Ref}})$	< 0.05 %
$u(m_{\text{Ref}})$	< 0.05 %
$u(m_{\text{CRM}})$	< 0.05 %
$u(M_{\text{Ref}})$	< 0.003 %
$u(M_{\text{CRM}})$	< 0.003 %
$u(R_{\text{Integrals}})$	< 0.15 %
u_{hom}	< 0.15 %
u_{stab}	< 0.25 %



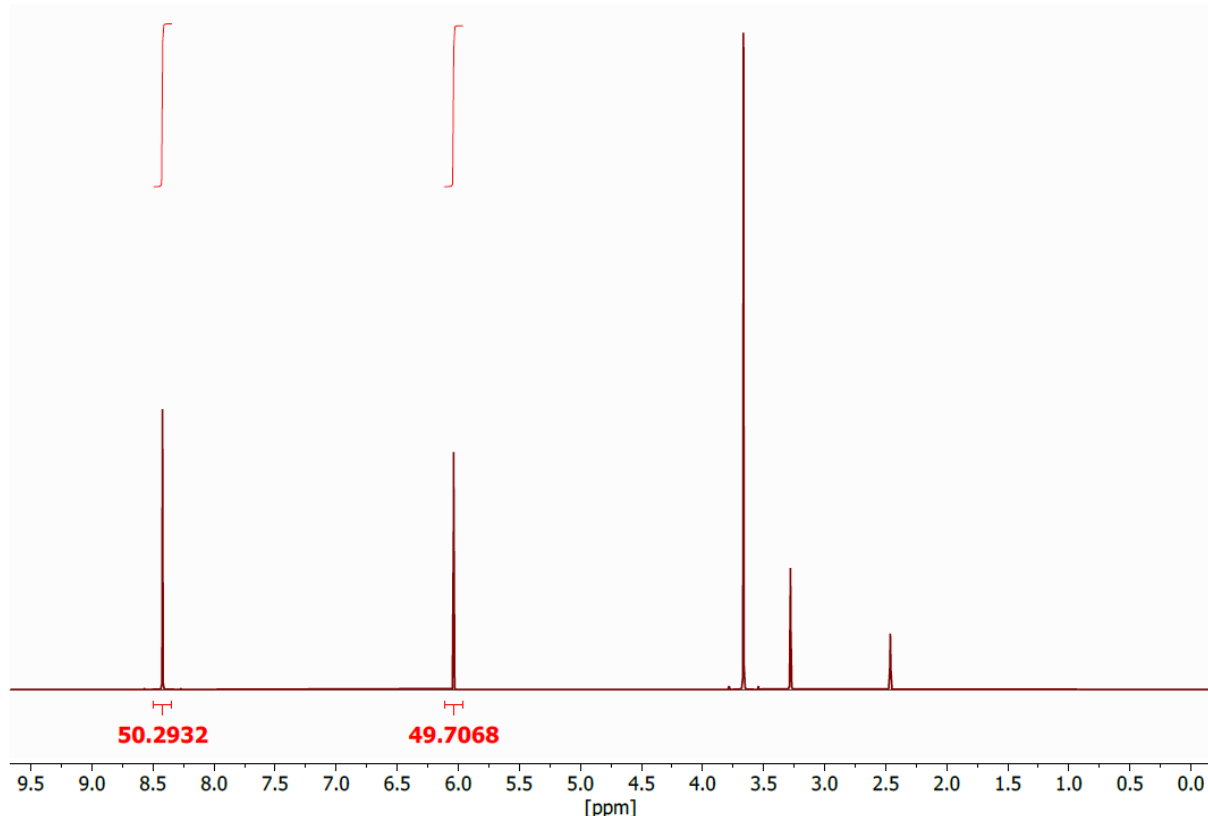
The combined standard uncertainty is calculated by combination of the standard uncertainties of the input estimates according to Eurachem/CITAC Guide "Quantifying Uncertainty in Analytical Measurement" and ISO 17034.^[2]

Expanded uncertainty is then calculated to a confidence level of 95 %, typically by multiplying with a coverage factor of $k=2$.

Indicative values:

T_1 relaxation times (in DMSO- d_6)	Peak at 8.5 ppm: 18 s Peak at 6.1 ppm: 3.7 s Peak at 3.7 ppm: 1.5 s These times may vary depending on the experimental conditions. Therefore it is recommended to check the T_1 delay prior to the qNMR experiment.
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¹H-NMR Spectrum (600 MHz, 1,2,4,5-Tetrachloro-3-nitrobenzene and 1,3,5-Trimethoxybenzene in DMSO-d₆)



References:

- [1] ISO Guide 35:2017, "Reference materials - Guidance for characterization and assessment of homogeneity and stability"
- [2] Eurachem/CITAC Guide, 3rd Ed. (2012), "Quantifying uncertainty in analytical measurement"
- [3] Eurachem/CITAC Guide, 2nd Ed. (2019), "Metrological traceability in chemical measurement"
- [4] The accredited testing laboratory STS 0490 performs the measurements and weighing steps for the certification of this CRM under ISO/IEC 17025:2017, "General requirements for the competence of testing and calibration laboratories"
- [5] ISO 17034:2016, "General requirements for the competence of reference material producers"
- [6] Weber M, Hellriegel C, Rueck A, Sauermoser R, Wuethrich J, Accred. Qual. Assur. 18 (2013) 91-98
- [7] ISO Guide 31:2015, "Reference materials - Contents of certificates, labels and accompanying documentation"
- [8] Weber M, Hellriegel C, Rueck A, Wuethrich J, Jenks P, JPBA 93 (2014) 102-110

Certificate of analysis revision history:

Certificate version	Date	Reason for version
01	23 MAY 2024	Initial version

Disclaimer:

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