

Certified Reference Material

Reference material certificate

Extractables and Leachables Screening Standard for LC

TraceCERT®
 Traceable Certified Reference Materials

Product no.: 95636
Lot no.: BCCL4865
Description of CRM: Extractables and Leachables Screening Standard, 21 components in Acetonitrile
Expiry date: JUL 2028
Storage: Store at -20°C ± 5°C
Density at 20°C: 782.3 kg m⁻³ ± 0.4 kg m⁻³ (k = 2)

Constituent	Certified values at 20°C and expanded uncertainties, $U = k \cdot u$ (k = 2) ^{[1][2]}									
Pentaerythritol tetrakis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate)	63.9	mg kg ⁻¹	±	3.7	mg kg ⁻¹	50.0	mg L ⁻¹	±	2.9	mg L ⁻¹
Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate	63.9	mg kg ⁻¹	±	3.8	mg kg ⁻¹	50.0	mg L ⁻¹	±	3.0	mg L ⁻¹
Drometrizole	63.9	mg kg ⁻¹	±	5.0	mg kg ⁻¹	50.0	mg L ⁻¹	±	3.9	mg L ⁻¹
ε-Caprolactam	63.9	mg kg ⁻¹	±	4.5	mg kg ⁻¹	50.0	mg L ⁻¹	±	3.5	mg L ⁻¹
Dibenzylamine	57.1	mg kg ⁻¹	±	4.9	mg kg ⁻¹	44.6	mg L ⁻¹	±	3.9	mg L ⁻¹
Benzoic acid	63.8	mg kg ⁻¹	±	4.4	mg kg ⁻¹	49.9	mg L ⁻¹	±	3.4	mg L ⁻¹
2-Mercaptobenzothiazole	63.8	mg kg ⁻¹	±	4.0	mg kg ⁻¹	49.9	mg L ⁻¹	±	3.1	mg L ⁻¹
Bisphenol A	63.9	mg kg ⁻¹	±	3.2	mg kg ⁻¹	50.0	mg L ⁻¹	±	2.5	mg L ⁻¹
2-Ethylhexanoic acid	63.9	mg kg ⁻¹	±	3.6	mg kg ⁻¹	50.0	mg L ⁻¹	±	2.8	mg L ⁻¹
Bis(4-chlorophenyl) sulfone	63.9	mg kg ⁻¹	±	3.3	mg kg ⁻¹	50.0	mg L ⁻¹	±	2.6	mg L ⁻¹
3,5-Di-tert-butyl-4-hydroxybenzyl alcohol	63.9	mg kg ⁻¹	±	3.4	mg kg ⁻¹	50.0	mg L ⁻¹	±	2.7	mg L ⁻¹
Butylhydroxytoluene (BHT)	63.9	mg kg ⁻¹	±	4.0	mg kg ⁻¹	50.0	mg L ⁻¹	±	3.1	mg L ⁻¹
1,3-Di-tert-butylbenzene	63.9	mg kg ⁻¹	±	5.6	mg kg ⁻¹	50.0	mg L ⁻¹	±	4.4	mg L ⁻¹
Oleamide (certified value is non-stereo specific)	63.9	mg kg ⁻¹	±	7.9	mg kg ⁻¹	50.0	mg L ⁻¹	±	6.2	mg L ⁻¹
Bis(2-ethylhexyl) phthalate	63.9	mg kg ⁻¹	±	4.2	mg kg ⁻¹	50.0	mg L ⁻¹	±	3.3	mg L ⁻¹
Stearic acid	63.9	mg kg ⁻¹	±	4.1	mg kg ⁻¹	50.0	mg L ⁻¹	±	3.2	mg L ⁻¹
cis-13-Docosenoamide	63.9	mg kg ⁻¹	±	7.4	mg kg ⁻¹	50.0	mg L ⁻¹	±	5.8	mg L ⁻¹
Tris(3,5-di-tert-butyl-4-hydroxybenzyl) isocyanurate	63.9	mg kg ⁻¹	±	3.8	mg kg ⁻¹	50.0	mg L ⁻¹	±	3.0	mg L ⁻¹
Tris(2,4-di-tert-butylphenyl)phosphate	63.9	mg kg ⁻¹	±	3.4	mg kg ⁻¹	50.0	mg L ⁻¹	±	2.7	mg L ⁻¹
2,4-Di-tert-butylphenol	63.9	mg kg ⁻¹	±	4.4	mg kg ⁻¹	50.0	mg L ⁻¹	±	3.5	mg L ⁻¹
Palmitic acid	63.9	mg kg ⁻¹	±	5.0	mg kg ⁻¹	50.0	mg L ⁻¹	±	3.9	mg L ⁻¹

Certificate issue date: November 11, 2024



ISO 17034
SRMS 0001

Dr. P. Zell – Approving Officer
(Quality Assurance)



Accreditation:	Sigma-Aldrich Production GmbH is accredited by the Swiss Accreditation Service SAS as registered reference material producer under no. SRMS 0001 in accordance with international standard ISO 17034 ^[5] .
Metrological traceability:	Traceable to NIST SRM. Details see "Certification process details". ^[3]
Measurement method:	The certified value is established by weighing of well characterized starting materials in accordance with ISO/IEC 17025 ^[4] .
Intended use:	Use this certified reference material (CRM) as a calibrant for Extractables and Leachables testing in various plastic compounds.
Instructions for handling and correct use:	Shake well and allow to warm to room temperature before opening the ampule. Open a new ampule for each measurement series.
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.
Packaging:	Amber glass ampule
Accreditation:	Sigma-Aldrich Production GmbH is accredited by the Swiss Accreditation Service SAS as registered reference material producer under no. SRMS 0001 in accordance with international standard ISO 17034 ^[5] .

Certification process details:

To guarantee top reliability of the values for this *TraceCERT*[®] certified reference material, well-established procedures were followed. The values have to agree in the range of their uncertainties, but the value from the gravimetric preparation (except Dibenzylamine) has been chosen as certified value:

1. Gravimetric preparation using well-characterized materials is a practical realization of concentration units, through conversion of mass to amount of substance.^[6] If the purity of the materials is demonstrated and if contamination and loss of material is strictly prevented this approach allows highest accuracy. The certified value of *TraceCERT*[®] reference materials is based on this approach and directly traceable to the SI unit kilogram. Therefore, comprehensively characterized materials are used. All balances are certified by DKD and calibrated with OIML Class E2 (up to 12 kg) and F2 (up to 64 kg) weights.
2. The starting material is measured against a certified reference material which is traceable to SRM[®] from NIST followed by gravimetric preparation using balances calibrated with SI-traceable weights. Consequently, the value calculated by this unbroken chain of comparisons is traceable to the reference to which the starting material is compared. Due to the nature of qNMR measurements, different analytes can be characterized using the same SRM[®] from NIST (see table „Details on starting material“ on page 3-4).
3. The mix in its final packaged form is measured by different LC methods to underpin the gravimetric values.
4. Double IDMS measurements for certified mass fraction of Dibenzylamine.
5. Density measurement is performed in accordance with ISO/IEC 17025.^[4]
6. The certificate is designed in accordance with ISO 33401.^[7]

Homogeneity assessment:	Due to the nature of the production process, a homogeneous solution derives. Nevertheless, homogeneity is assessed by LC measurements and a homogeneity contribution is included into the calculation of content uncertainty of this CRM.
Stability assessment:	A stability study is performed with samples which are stored at different temperatures. The material is tested by LC after certain time intervals and a stability component included in the overall uncertainty.

All sample and reference solutions are mixed with an internal standard solution according to "Guidelines for achieving high accuracy in IDMS"^[8] to give matching signal ratios. When available isotopologues of the corresponding compound are used, for all other compounds 3-amino-9-ethylcarbazole serves as internal standard. The mixtures are prepared gravimetrically. The analysis of the sample is bracketed by the reference and repeated several times to minimize instrumental variations. The repeatability is included in the combined measurement uncertainty. The set of compounds is analyzed by one LC method. The Method is used for all UV absorbing compounds (1, 2, 3, 7, 8, 10, 11, 12, 13, 15, 18, 19, 20) and for all compounds detectable by mass spectrometry (4, 5, 6, 9, 14, 16, 17, 21). Both methods originate from BPOG guide^[9] and were optimized and validated for this set of compounds.

Method (A):

Column: Supelco Ascentis Express C18, 100 x 2.1 mm, 2.0 μ m and Supelco Ascentis Express C18 5 x 3 mm, 2.0 μ m (pre-column).

Temperature: 50 °C.

Mobile Phase: 0.01 % Acetic Acid/water (A), Methanol (B)

Flow Rate: 0.5 ml/min

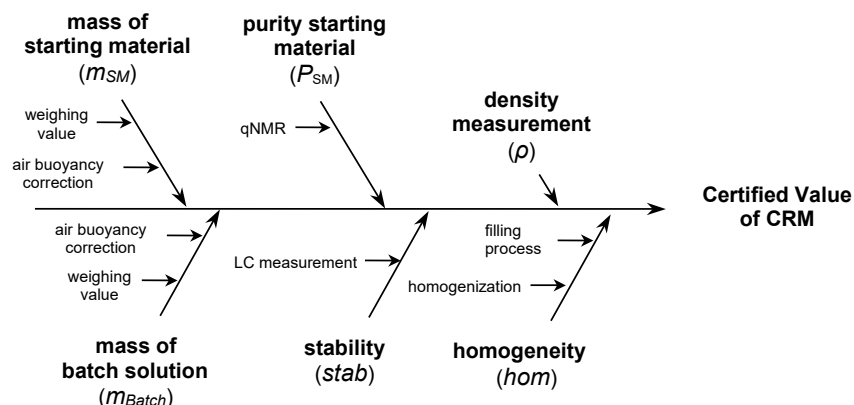
Gradient: 0.00 min (95 % A), 0.30 min (95 % A), 6.8 min (2 % A), 11.50 min (2 % A), 12.00 min (2 % A, Flow: 0.8 ml/min), 14.70 min (2 % A, Flow: 0.8 ml/min), 14.80 min (2 % A), 15.00 min (95 % A), 15.90 min (95 % A), 16.20 min (95 % A, Flow: 0.75 ml/min), 18.00 min (95 % A, Flow: 0.75 ml/min), 18.10 min (95 % A), 18.50 min (95 % A)

Postcolumn Addition: 1 mM Ammonium acetate and 0.1 % Acetic acid in Water (Time Range: 7.85 min to 11.52 min, Rate: 60 μ L/min)

Injection Vol.: 1.8 μ L.

Uncertainty evaluation:

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



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

Details on starting materials:

#	Compound	CAS Number	Method	Traceability
1	Pentaerythritol tetrakis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate)	6683-19-8	Mass balance	SI unit kg by mass balance
2	Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate	2082-79-3	qNMR	NIST PS1 (Benzoic acid)
3	Drometrizole	2440-22-4	qNMR	NIST PS1 (Benzoic acid)
4	ϵ -Caprolactam	105-60-2	qNMR	NIST PS1 (Benzoic acid)
5	Dibenzylamine	103-49-1	LC/MS	NIST PS1 (Benzoic acid)
6	Benzoic acid	65-85-0	qNMR	NIST PS1 (Benzoic acid)
7	2-Mercaptobenzothiazole	149-30-4	qNMR	NIST PS1 (Benzoic acid)
8	Bisphenol A	80-05-7	qNMR	NIST SRM 84I (KHP)
9	2-Ethylhexanoic acid	149-57-5	Mass balance	SI unit kg by mass balance
10	Bis(4-chlorophenyl) sulfone	80-07-9	qNMR	NIST PS1 (Benzoic acid)
11	3,5-Di-tert-butyl-4-hydroxybenzyl alcohol	88-26-6	qNMR	NIST PS1 (Benzoic acid)

12	Butylhydroxytoluene (BHT)	128-37-0	qNMR	NIST PS1 (Benzoic acid)
13	1,3-Di-tert-butylbenzene	1014-60-4	qNMR	NIST PS1 (Benzoic acid)
14	Oleamide	301-02-0	qNMR	NIST PS1 (Benzoic acid)
15	Bis(2-ethylhexyl) phthalate	117-81-7	qNMR	NIST SRM 84I (KHP)
16	Stearic acid	57-11-4	qNMR	NIST PS1 (Benzoic acid)
17	cis-13-Docosenoamide	112-84-5	qNMR	NIST PS1 (Benzoic acid)
18	Tris(3,5-di-tert-butyl-4-hydroxybenzyl) isocyanurate	27676-62-6	qNMR	NIST PS1 (Benzoic acid)
19	Tris(2,4-di-tert-butylphenyl)phosphate	95906-11-9	qNMR	NIST PS1 (Benzoic acid)
20	2,4-Di-tert-butylphenol	96-76-4	qNMR	NIST PS1 (Benzoic acid)
21	Palmitic acid	57-10-3	qNMR	NIST PS1 (Benzoic acid)

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" ISO
- [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] 17034:2016, "General requirements for the competence of reference material producers"
- [6] Reichmuth, A., Wunderli, S., Weber, M., Meyer, V. R. (2004), "The uncertainty of weighing data obtained with electronic analytical balances", Microchimica Acta 148: 133-141.
- [7] ISO 33401:2024, "Reference materials - Contents of certificates, labels and accompanying documentation"
- [8] Sargent, M., Harrington, C., Harte, R. (eds.), "Guidelines for achieving high accuracy in IDMS", LGC (RSC), Cambridge, 2002.
- [9] McAuley, G., Derby, S. (eds.), "Biophorum Operations Group (BPOG) – Best practice guide for evaluating leachables risk from polymeric single-use systems used in biopharmaceutical manufacturing" (<https://www.biophorum.com/download/3325/>), 2017.

Certificate of analysis revision history:

Certificate version	Date	Reason for version
01	November 11, 2024	Initial version

The most recent version of the Certificate is available online (www.sigmaaldrich.com).

Disclaimer:

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