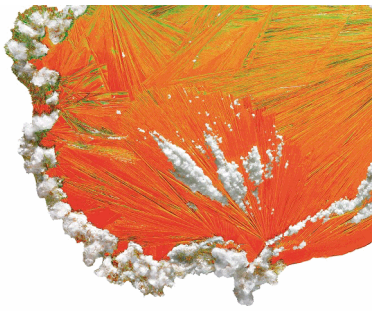


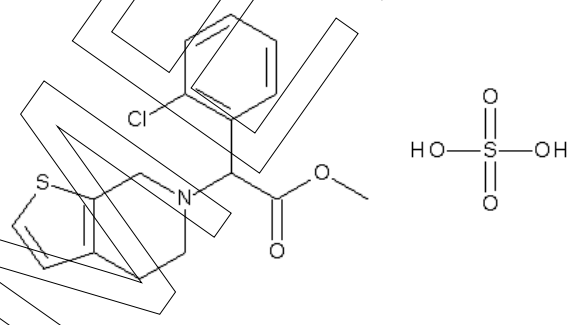
Certificate of Analysis

Characterisation methods are accredited according to ISO 17025

Reference Material

Product name

Methyl
(2RS)-(2-Chlorophenyl)[4,7-dihydrothieno[2,3-c]pyridin-6(5H)
-yl]acetate Hydrogen Sulfate



Product code MM0455.13	**Lot number** W1017689
CAS number not listed	**Appearance** light beige solid
Molecular weight 419.90	**Melting point** 207 °C
Molecular formula $C_{16}H_{16}ClNO_2S \quad H_2SO_4$	**Long-term storage** 2 to 8 °C, dark

Assay[1] "as is"	Uncertainty[2] U
98.1 %	**0.4 %**

Intended Use: Use for identification and quantification. The assay is verified by a second testing method.

Date of shipment: **02 Sep 2019**

Producer confirms that this reference material (RM) meets the specification detailed on this Certificate of Analysis for **two years** from the date of shipment, provided the substance is stored under the recommended conditions unopened in the original container.

Release by:	**Date of Release:**		
Dr. Sabine Schröder	Luckenwalde, 05 Aug 2019		Product Release

[1] Calibration and verification were carried out using standards traceable to SI-units. The value is expressed on an "as is" basis.

[2] The uncertainty "U" is the expanded uncertainty of the testing method for the assigned value estimated in accordance with the Guide to the Expression of Uncertainty in Measurement (GUM). It corresponds to a level of confidence of about 95%. Coverage factor k =2.

Product information

This RM is intended for laboratory use only and is not suitable for human or animal consumption.
This RM conforms to the characteristics of a primary standard as described in the ICH Guidelines. The values quoted in this Certificate of Analysis are the producer's best estimate of the true values within the stated uncertainties and based on the techniques described in this Certificate of Analysis. The characterisation of this material was undertaken in accordance with the requirements of ISO/IEC 17025. The identity is verified by data from international scientific literature.

Storage and handling

Before usage of the RM, it should be allowed to warm to room temperature. No drying is required, as assigned values are already corrected for the content of water and other volatile materials.

Reference Material quality is controlled by regularly performed quality control tests (retests).

Further content

Assigned value

Purity

Identity

Revision table

Assigned value

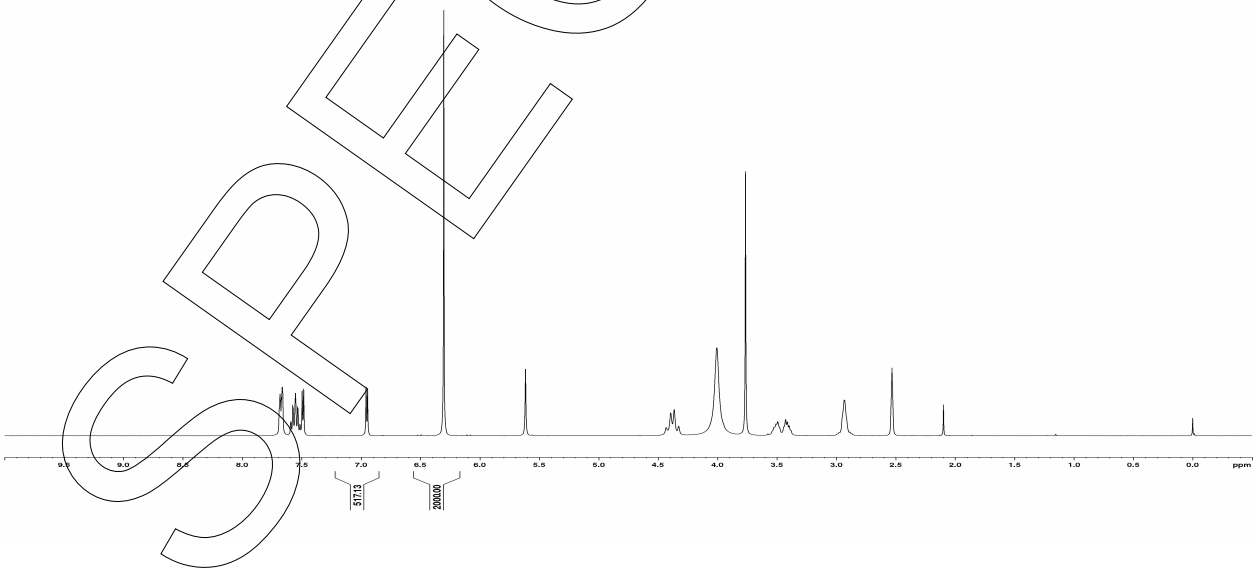
Assay "as is": **98.09 %; U = 0.42 %**

The assay "as is" is assessed by quantitative NMR spectroscopy and is equivalent to the assay based on the not-anhydrous and not-dried substance. The assay is verified by 100% method (mass balance).
The verified result lies inside our acceptance criteria, i.e. less than 1.0 % difference to assay assigning technique.

For quantitative applications, use the assay as a calculation value on the "as is basis". The uncertainty of the assay can be used for estimation/calculation of measurement uncertainty.

Method 1: Value assigning technique - quantitative NMR spectroscopy	
Conditions	400 MHz, DMSO-d_6 / D_2O
Internal standard	Maleic acid (certified reference material), signal 6.2 - 6.6 ppm, 2 H
Results (mass fraction, **n = 6**)	98.09 %; U = 0.42 %

Quantitative NMR spectrum



Method 2: Value verifying technique - 100% method	
100% method (mass balance) with chromatographic purity by HPLC	
Result	97.39 %

The calculation of the 100% method follows the formula:

$$\text{Assay (\%)} = (100\ \% - \text{volatile contents (\%)}) \quad * \quad \frac{\text{Purity (\%)}}{100\ \%}$$

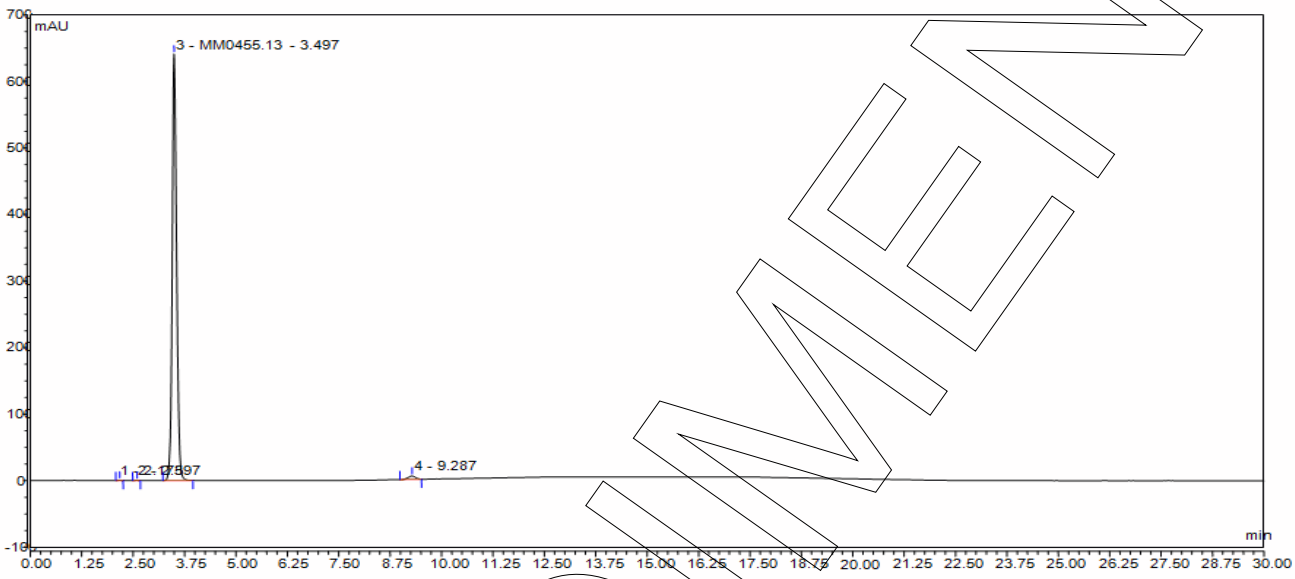
Volatile contents are considered as absolute contributions and purity is considered as relative contribution.
Inorganic residues are excluded by additional tests.

Purity

Purity by High Performance Liquid Chromatography (HPLC)

HPLC Conditions:	
Column	LiChrospher 60 RP-select B; 5 µm, 125 x 4.0 mm
Column temperature	40 °C
Detector	DAD, 215 nm
Injector	Auto 2 µl; 0.252 mg/ml in Acetonitrile/Water 50/50 (v/v)
Flow rate	1.0 ml/min
Phase A	Water, 0.1 % H_3PO_4
Phase B	Acetonitrile, 0.1 % H_3PO_4
Gradient program	0-5 min A/B 60/40 5-10 min A/B to 50/50 10-15 min A/B 50/50 15-20 min A/B to 60/40 20-30 min A/B 60/40 (v/v)

HPLC chromatogram and peak table



Area percent report - sorted by signal				
Pk #	**Retention time**	**Area**	**Area %**	
1	2.173	0.046	0.06	
2	2.597	0.033	0.04	
3	3.497	79.886	98.56	
4	9.287	1.088	1.34	
Totals		**81.053**	**100.00**	

The content of the analyte was determined as ratio of the peak area of the analyte and the cumulative areas of the purities, added up to 100 %. System peaks were ignored in calculation.

Result (n = 3)	98.55 %; U = 0.19 %

Volatile content

Water content	
Method	Karl Fischer titration
Result (n = 3)	0.41 %*; SD = 0.01 %

*not accredited testing method

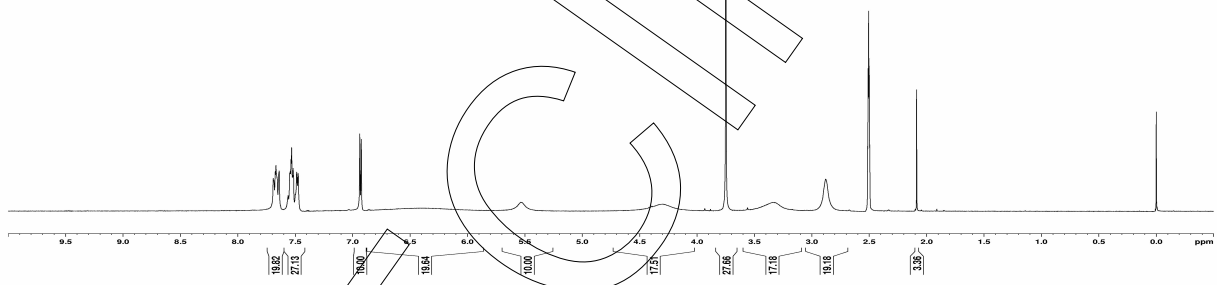
Residual solvents	
Method	^{1}H-NMR
Result (n = 1)	Sum: 0.77 %* 0.77 % Acetone

*not accredited testing method

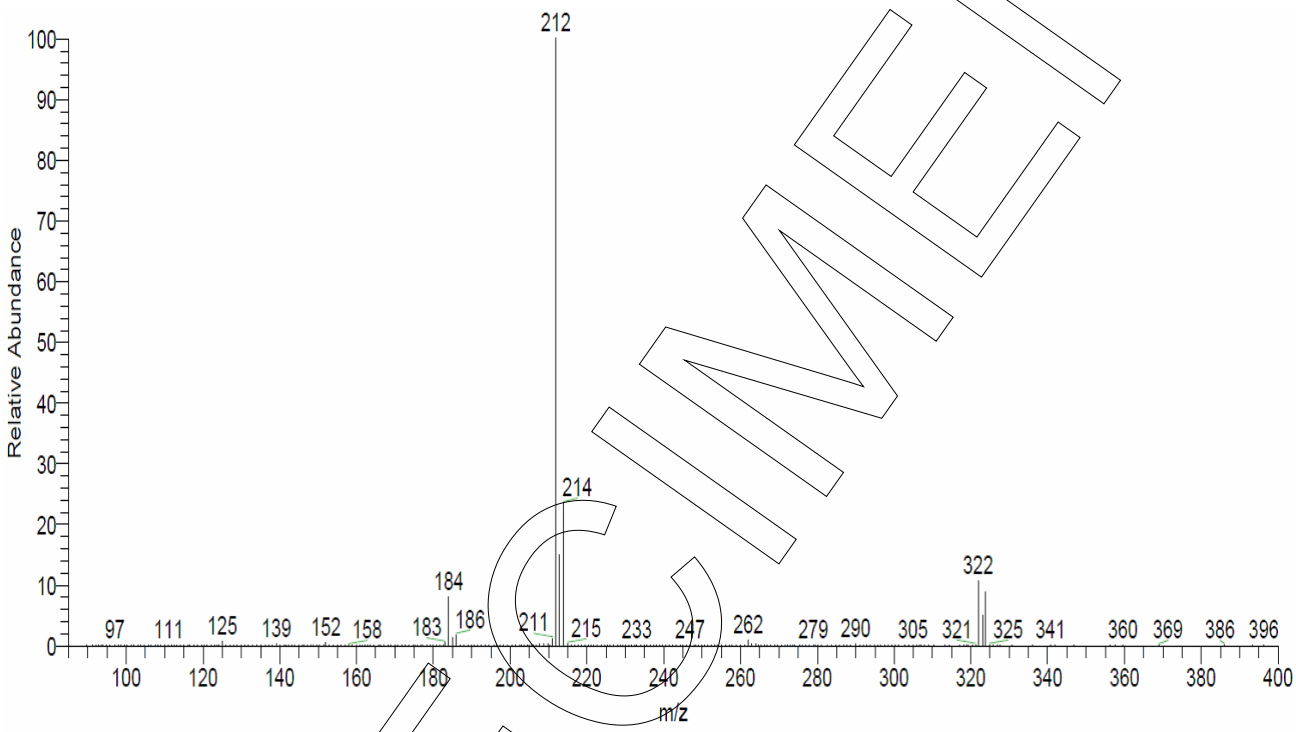
Identity

The identity is assessed by ISO/IEC 17025 accredited testing methods.

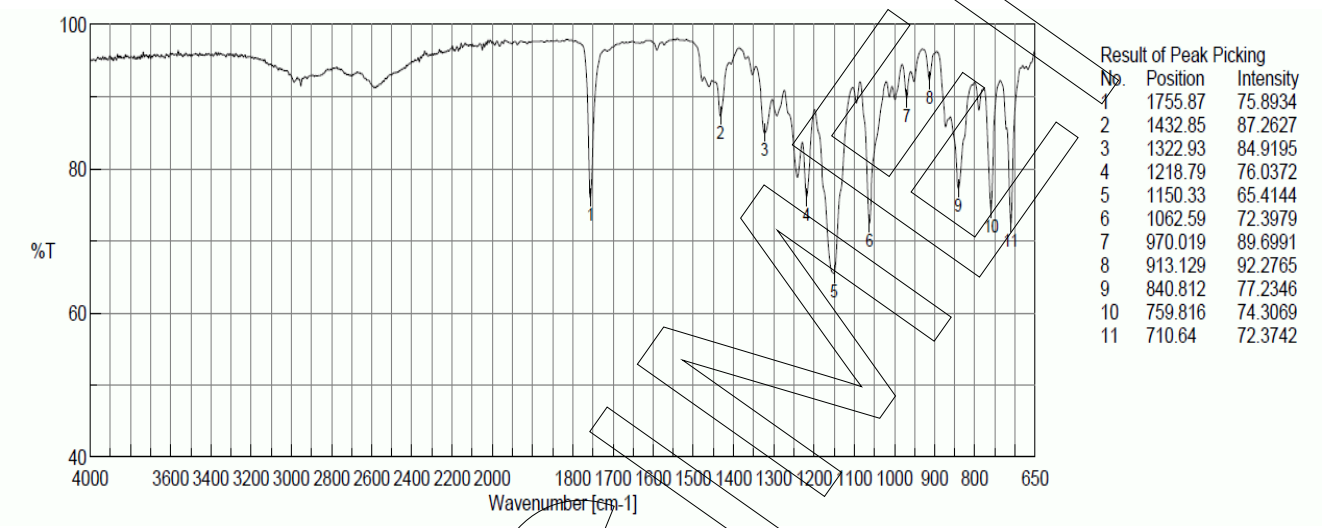
Method	Conditions	Result
^{1}H-NMR	400 MHz, DMSO-d_6	Structure confirmed



Method	Conditions	Result
MS	4.5 kV ESI; vaporization temperature: 200 °C	Structure confirmed



Method	Conditions	Result
IR	Attenuated Total Reflection Fourier Transform Infrared (ATR-FTIR) Spectroscopy	Structure confirmed



Revision table

Revision	Date	Reason for revision
00	05 Aug 2019	Release of the Certificate of Analysis - initial version

Product warranties for the RM are set out in the terms and conditions of purchase.