National Institute of Standards & Technology

Certificate of Analysis

Standard Reference Material® 914b

Creatinine

This Standard Reference Material (SRM) is certified as a neat chemical material of known purity. It is intended to be used as a primary measurement standard for calibration of clinical measurement laboratory procedures to determine quantities of creatinine. A unit of SRM 914b consists of 10 g of high-purity crystalline creatinine.

Certified Creatinine Mass Fraction: 99.9 % ± 0.1 %

A NIST certified value is a value for which NIST has the highest confidence in its accuracy in that all known or suspected sources of bias have been investigated or taken into account [1]. The measurand is the mass fraction of creatinine (expressed as percent) [2] and the uncertainty is expressed as the 95 % confidence interval ($U_{95\%}$) [3,4]. Metrological traceability of the certified value is to the SI through practical realization of measurement units for specific amount of substance (mol/g) and mass fraction (%). The certified value was determined using a quantitative ^{1}H nuclear magnetic resonance spectroscopy (^{1}H-qNMR) primary ratio measurement procedure [5,6].

Expiration of Certification: The certification of **SRM 914b** is valid, within the measurement uncertainty specified, until **31 May 2028**, provided the SRM is handled and stored in accordance with the instructions given in this certificate (see "Instructions for Storage and Use"). The certification is nullified if the SRM is damaged, contaminated, or otherwise modified.

Maintenance of SRM Certification: NIST will monitor this SRM over the period of its certification. If substantive technical changes occur that affect the certification, NIST will notify the purchaser. Registration (see attached sheet or register online) will facilitate notification.

Overall direction and coordination of the technical activities were under the chairmanship of M.A. Nelson of the NIST Chemical Sciences Division.

Analytical measurements at NIST were performed by M.A. Nelson of the NIST Chemical Sciences Division and C. Salazar Arzate of Centro Nacional de Metrología (CENAM), México.

Statistical analysis was provided by B. Toman of the NIST Statistical Engineering Division.

Support aspects involved in the issuance of this SRM were coordinated through the NIST Office of Reference Materials.

Carlos A. Gonzalez, Chief
Chemical Sciences Division

Gaithersburg, MD 20899
Certificate Issue Date: 21 November 2018

Steven J. Choquette, Director
Office of Reference Materials

INSTRUCTIONS FOR STORAGE AND USE

Storage: The SRM should be stored in its original container, tightly closed and protected from moisture, heat, and direct light. Refrigeration is recommended (4 °C) for long term storage, though the material should be brought to room temperature (between 20 °C and 30 °C) before opening the container for each use. It should not be exposed to temperatures greater than 30 °C.

Use: SRM 914b stored as described above, should be used without preliminary drying. The minimum sample size is 5 mg.

SOURCE AND ANALYSIS

Source of Material: The SRM source material was obtained from a commercial supplier.

Analytical Approach and Heterogeneity assessment: Analyses for chemical identity, purity, and heterogeneity were performed by NIST using twenty-two units, selected at regular intervals across the entire production lot. A ^{1}H-qNMR primary ratio measurement procedure using an internal standard approach was implemented for the determination of creatinine mass fraction with metrological traceability to SI units. Calculation of the 95 % coverage interval was performed under the Bayesian paradigm using a hierarchical measurement model for the ^{1}H-qNMR procedure [7,8]. No trend in mass fraction of creatinine was observed with respect to filling order and there is no significant heterogeneity at the 95 % confidence level. Methanol impurity content was approximated via ^{1}H-qNMR as 0.004 %. Supporting and confirmatory measurements for assessment of impurity components were made via liquid chromatography with ultraviolet detection (LC-UV) and liquid chromatography with mass spectrometric detection (LC-MS). While no significant amount of structurally-related organic chemical impurity was determined with respect to the 95 % confidence interval, an insignificant relative amount of creatine was identified as an impurity via LC-MS.

REFERENCES

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[4] JCGM 101:2008; *Evaluation of Measurement Data – Supplement 1 to the Guide to Expression of Uncertainty in Measurement, Propagation of Distributions Using a Monte Carlo Method*; JCGM (2008); available at https://www.bipm.org/utils/common/documents/jcgm/JCGM_101_2008_E.pdf (accessed Nov 2018).

[5] Milton, M.J.; Quinn T.J.; *Primary methods for the measurement of amount of substance*; Metrologia, Vol. 38, pp 289−296 (2001).

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[8] Toman, B., Nelson, M.A.; Lippa, K.A.; *Chemical Purity Using Quantitative ^{1}H-nuclear Magnetic Resonance: A Hierarchical Bayesian Approach for Traceable Calibrations*; Metrologia, Vol. 53, pp 1193−1203 (2016).

Users of this SRM should ensure that the Certificate of Analysis in their possession is current. This can be accomplished by contacting the SRM Program: telephone (301) 975-2200; fax (301) 948-3730; e-mail srminfo@nist.gov; or via the Internet at https://www.nist.gov/srm.