National Institute of Standards & Technology

Certificate of Analysis

Standard Reference Material® 1401

Trace Metals in Frozen Human Blood

This Standard Reference Material (SRM) is intended primarily for use in the validation of analytical methods for measuring the concentrations of trace metals in human blood as well as for quality assurance and proficiency testing with respect to such methods. A unit of SRM 1401 consists of four vials of frozen human blood, two vials each of two different concentration levels. Each vial contains nominally 1.6 mL of human whole blood.

The development of SRM 1401 was a collaboration between the National Institute of Standards and Technology (NIST), the Centers for Disease Control and Prevention (CDC), National Centers for Environmental Health, Division of Laboratory Sciences (Atlanta, GA) and LGC (Teddington, Middlesex, UK).

Certified Mass Concentration Values: Certified mass concentration values for four elements in Level 1 and four elements in Level 2 of SRM 1401 are listed in Table 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 certified values in this material are the weighted means [2–4] of the individual sets of measurements made by NIST and collaborating laboratories. The associated expanded uncertainties include between-laboratory and within-laboratory components of uncertainty and are provided at the 95 % level of confidence [5]. The measurands are elements listed in Table 1. Metrological traceability is to the SI derived units for mass concentration (expressed as micrograms per liter).

Information Values: Information values for the mass concentration of nickel and blood density are provided in Table 2. An information value is considered to be of interest to the SRM user, but insufficient information is available to assess the uncertainty associated with the value, or only a limited number of analyses were performed [1]. Information values cannot be used to establish metrological traceability.

Expiration of Certification: The certification of **SRM 1401** is valid, within the measurement uncertainty specified, until **01 December 2024**, provided the SRM is handled and stored in accordance with the instructions given in this certificate (see "Instructions for Handling, 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 before the expiration of this certificate, NIST will notify the purchaser. Registration (see attached sheet or register online) will facilitate notification.

Coordination of the technical measurements leading to the certification of this SRM was performed by S.E. Long and L.L. Yu of the NIST Chemical Sciences Division. Coordination of collaborative production and measurement of the SRM at CDC was performed by C.D. Ward and K.L. Caldwell of the Inorganic and Radiation Analytical Toxicology Branch, Division of Laboratory Sciences, National Center for Environmental Health (Atlanta, GA).

Analytical measurements were performed by S.J. Christopher, B.L. Kassim, S.E. Long, and L.L. Yu of the NIST Chemical Sciences Division; J. Castro Georgi, Y.L. Sommer, and M. Franklin of the CDC Inorganic and Radiation Analytical Toxicology Branch, Division of Laboratory Sciences, National Center for Environmental Health; M. Wermers of Mayo Clinic (Rochester, MN); and S. Hill of LGC.

Statistical consultation for this SRM was provided by C. Hagwood of the NIST Statistical Engineering Division.

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Certificate Issue Date: 02 August 2017

Steven J. Choquette, Director
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Support aspects involved with the issuance of this SRM were coordinated through the NIST Office of Reference Materials.

Partial support for the development of this SRM was provided by the CDC, National Centers for Environmental Health, Division of Laboratory Sciences under the direction of R.L. Jones and K.L. Caldwell of the Inorganic and Radiation Analytical Toxicology Branch.

NOTICE AND WARNING TO USERS

SRM 1401 IS INTENDED FOR RESEARCH USE. THIS IS A HUMAN SOURCE MATERIAL. HANDLE PRODUCT AS A BIOHAZARDOUS MATERIAL CAPABLE OF TRANSMITTING INFECTIOUS DISEASE. The supplier has reported that each donor unit of blood used in the preparation of this product was tested by FDA-licensed tests and found to be negative for human immunodeficiency virus (HIV), HIV-1 antigen, hepatitis B surface antigen, and hepatitis C. However, no known test method can offer complete assurance that hepatitis B virus, hepatitis C virus, HIV, or other infectious agents are absent from this material. Accordingly, this human blood-based product should be handled at the Biosafety Level 2 or higher as recommended for any POTENTIALLY INFECTIOUS HUMAN SERUM OR BLOOD SPECIMEN in the Centers for Disease Control and Prevention/National Institutes of Health (NIH) Manual [6]. This SRM was developed after an appropriate human subjects research determination by NIST.

INSTRUCTIONS FOR HANDLING, STORAGE, AND USE

The blood is shipped frozen (on dry ice) and, upon receipt, must be stored frozen until ready for use. The SRM should be kept in its original vials and stored at or below –60 °C. The certification does not apply to contents of previously opened material as the stability of the analytes has not been investigated under such conditions. SRM 1401 should be thawed at room temperature. The material should be used or discarded within 4 h of removal from the suggested storage temperature. Each vial of the SRM should be homogenized by gently inverting the vial several times before a test portion is removed. A minimum test portion of 0.5 mL should be used for the values provided in this certificate to be valid.

PREPARATION AND ANALYSIS[(1)]

SRM 1401 was prepared from "off-the-shelf" whole blood, collected from donors with no age or gender requirements. Blood bags from a commercial vendor were combined in two pre-cleaned 5 L high density polyethylene (HDPE) bottles to form the pools for SRM 1401, Level 1 and SRM 1401, Level 2. The mass concentrations of Cr, Co, Mo, and Ni were adjusted to the target levels by spiking with appropriate volumes of 20 mg/mL single element standard solutions prepared from SRM 3112a *Chromium (Cr) Standard Solution*, SRM 3113 *Cobalt (Co) Standard Solution*, SRM 3134 *Molybdenum (Mo) Standard Solution*, and SRM 3136 *Nickel (Ni) Standard Solution*, respectively. The contents were then homogenized with a magnetic stirrer for 24 h prior to dispensing into individual pre-screened polypropylene cryovials.

Analytical determinations for certification of this SRM were performed at NIST, CDC, Mayo Clinic, and LGC using methods listed in Tables 1 and 2.

Homogeneity: Measurements for homogeneity assessment were made at CDC and at NIST using the inductively coupled plasma mass spectrometry (ICP-MS) methods listed in Table 1. The SRM was determined to be homogeneous based on the statistical analysis of between-vial variances.

Value Assignment: Certified mass concentration values for trace elements are the weighted means of results from NIST and collaborating laboratories, found by leveraging a linear, Gaussian random effects statistical model [2,3] and the methods of maximum likelihood estimation [4,7] or the DerSimonian-Laird procedure [2,8]. Maximum likelihood estimation was utilized when degrees of freedom were readily available, otherwise the DerSimonian-Laird procedure was used. The estimation procedures are supplemented by the parametric bootstrap [9] for uncertainty propagation. The associated uncertainty is expressed as an expanded uncertainty, U. The expanded uncertainty is calculated as $U = ku_c$, where u_c is intended to represent, at the level of one standard deviation, the combined effect of between-laboratory, within-laboratory, and inhomogeneity components of uncertainty. The coverage factor, k, corresponds to approximately 95 % confidence for each analyte.

[(1)]Certain commercial equipment, instruments or materials are identified in this certificate to adequately specify the experimental procedure. Such identification does not imply recommendation or endorsement by the National Institute of Standards and Technology, nor does it imply that the materials or equipment identified are necessarily the best available for the purpose.

Table 1. Certified Mass Concentration Values for SRM 1401

	Level 1		Level 2	
	Mass Concentration (µg/L)	Coverage Factor, *k*	Mass Concentration (µg/L)	Coverage Factor, *k*
Chromium (Cr)[a,b,c,d]	2.89 ± 0.13	1.96	10.71 ± 0.35	1.96
Cobalt (Co)[a,b,e,f]	3.12 ± 0.18	1.96	11.11 ± 0.31	1.96
Manganese (Mn)[a,b,e]	11.51 ± 1.14	1.96	11.81 ± 0.70	1.96
Molybdenum (Mo)[a,e]	8.20 ± 0.97	1.96	9.75 ± 0.23	1.97

[a] ICP-MS at the Mayo Clinic
[b] ICP-MS at CDC
[c] Isotope dilution ICP-MS at NIST
[d] Isotope dilution ICP-MS at LGC
[e] ICP-MS at NIST
[f] ICP-MS at LGC

Table 2. Information Values for SRM 1401

	Level 1	Level 2	Units
Nickel (Ni)[a]	1.9	9.7	µg/L
Blood density (21.1 °C)[b]	1.054	1.050	g/mL

[a] ICP-MS at the Mayo Clinic
[b] Oscillation frequency density meter at NIST

REFERENCES

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[8] DerSimonian, R.; Laird, N.; *Meta-Analysis in Clinical Trials;* Controlled Clin. Trials, Vol. 7, pp. 177–188 (1986).

[9] Efron, B.; Tibshirani, R.J.; *An Introduction to the Bootstrap*; New York: Chapman & Hall (1993).

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 http://www.nist.gov/srm.