

# Standard Reference Material<sup>®</sup> 1401 Trace Metals in Frozen Human Blood **CERTIFICATE OF ANALYSIS**

**Purpose:** The certified values delivered by this Standard Reference Material (SRM) are 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.

**Description:** 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.

**Certified 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 International System of Units (SI) derived units for mass concentration (expressed as micrograms per liter).

Table 1. Certified	Mass Concentration	Values for SRM 1401
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	Level 1		Level 2	
	Mass Concentration (µg/L)	Coverage Factor, <i>k</i>	Mass Concentration (µg/L)	Coverage Factor, k
Chromium (Cr) <sup>(a,b,c,d)</sup>	$2.89 \pm 0.13$	1.96	$10.71 \ \pm \ 0.35$	1.96
Cobalt (Co) <sup>(a,b,e,f)</sup>	$3.12 \pm 0.18$	1.96	$11.11 \pm 0.31$	1.96
Manganese (Mn) <sup>(a,b,e)</sup>	$11.51 \pm 1.14$	1.96	$11.81 \pm 0.70$	1.96
Molybdenum (Mo) <sup>(a,e)</sup>	$8.20 \ \pm \ 0.97$	1.96	$9.75 ~\pm~ 0.23$	1.97

(a) ICP-MS at the Mayo Clinic

(b) ICP-MS at CDC

(c) Isotope dilution ICP-MS at NIST

<sup>(d)</sup> Isotope dilution ICP-MS at LGC

(e) ICP-MS at NIST

(f) ICP-MS at LGC

Additional information: Additional information is provided in Appendices A and B.

**Period of Validity:** The certified values delivered by **SRM 1401** are valid within the measurement uncertainty specified until **01 August 2034**. The certified values are nullified if the material is stored or used improperly, damaged, contaminated, or otherwise modified.

**Maintenance of Certified Values:** NIST will monitor this SRM over the period of its validity. If substantive technical changes occur that affect the certification, NIST will issue an amended certificate through the NIST SRM website (https://www.nist.gov/srm) and notify registered users. SRM users can register online from a link available on the NIST SRM website or fill out the user registration form that is supplied with the SRM. Registration will facilitate notification. Before making use of any of the values delivered by this material, users should verify they have the most recent version of this documentation, available through the NIST SRM website (https://www.nist.gov/srm).

Carlos A. Gonzalez, Chief Chemical Sciences Division Certificate Revision History on Page 2 Steven J. Choquette, Director Office of Reference Materials **Safety:** SRM 1401 IS INTENDED FOR RESEARCH USE. This is a human-source material. SRM 1401 is a Biosafety Level 2 material and should be handled according to applicable federal, state, and/or local regulations and according to policies and procedures of recipient's organization. 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. This SRM was developed after an appropriate human subjects research determination by NIST.

**Storage:** 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.

**Use:** 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.

#### REFERENCES

- Beauchamp, C.R.; Camara, J.E.; Carney, J.; Choquette, S.J.; Cole, K.D.; DeRose, P.C.; Duewer, D.L.; Epstein, M.S.; Kline, M.C.; Lippa, K.A.; Lucon, E.; Molloy, J.; Nelson, M.A.; Phinney, K.W.; Polakoski, M.; Possolo, A.; Sander, L.C.; Schiel, J.E.; Sharpless, K.E.; Toman, B.; Winchester, M.R.; Windover, D.; *Metrological Tools for the Reference Materials and Reference Instruments of the NIST Material Measurement Laboratory*; NIST Special Publication (NIST SP) 260-136, 2021 edition; National Institute of Standards and Technology, Gaithersburg, MD (2021); available at https://nvlpubs.nist.gov/nistpubs/SpecialPublications/NIST.SP.260-136-2021.pdf (accessed Sep 2024).
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Certain commercial equipment, instruments, or materials may be identified in this Certificate of Analysis 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.

Users of this SRM should ensure that the Certificate of Analysis in their possession is current. This can be accomplished by contacting the Office of Reference Materials 100 Bureau Drive, Stop 2300, Gaithersburg, MD 20899-2300; telephone (301) 975-2200; e-mail srminfo@nist.gov; or the Internet at https://www.nist.gov/srm.

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## **APPENDIX A**

**Values of Potential Interest to Users:** Values of potential interest to users for the mass concentration of nickel and blood density are provided in Table A1. A value of potential interest to users 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]. Values of potential interest to users cannot be used to establish metrological traceability.

Table A1. Values of Potential Interest to Users for SRM 1401

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

<sup>(a)</sup> ICP-MS at the Mayo Clinic

<sup>(b)</sup> Oscillation frequency density meter at NIST

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## **APPENDIX B**

**Preparation and Analysis:** 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 A1.

**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 [4,6] or the DerSimonian-Laird procedure [2,7]. 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 [8] 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.

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