National Institute of Standards & Technology

Certificate of Analysis

Standard Reference Material® 955c

Toxic Metals in Caprine Blood

This Standard Reference Material (SRM) is intended primarily for use in evaluating methods for determining elements and mercury species in whole blood and similar matrices. This SRM can also be used for quality assurance when assigning values to in-house control materials. A unit of SRM 955c consists of four vials of frozen caprine blood at four concentration levels: a base level (Level 1) and three progressively elevated levels (Levels 2 – 4) that contain endogenous lead and spiked inorganic arsenic, cadmium, ethylmercury, inorganic mercury, and methylmercury. Each vial contains approximately 2 mL of whole blood.

Certified Values: Certified values for selected elements (Levels 1 – 4) in SRM 955c are provided 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 for cadmium, lead and total mercury are based on the mean results from a single NIST primary method. Confirmatory results were obtained from collaborating laboratories. For arsenic (Levels 2, 3 and 4) the certified values are the weighted mean of NIST and collaborating laboratory data computed using the DerSimonian-Laird procedure [2]. For selenium (Level 1), the certified value is the weighted mean of measurements from two independent methods performed at NIST, computed using the DerSimonian-Laird procedure [2]. The uncertainties associated with each certified value are expressed as expanded uncertainties with a confidence level of approximately 95 % [3].

Reference Values: Reference values for manganese (Level 1) and mercury species (Levels 2, 3, and 4) in SRM 955c are provided in Table 2. A reference value is a noncertified value that is the best estimate of the true value based on available data [1]. These values do not meet NIST criteria for certification [1] and are provided with associated uncertainties that may reflect only measurement reproducibility, may not include all sources of uncertainty, or may reflect a lack of sufficient statistical agreement among multiple analytical methods. For manganese (Level 1), the reference value is the weighted mean of measurements from two independent methods performed at NIST, computed using the DerSimonian-Laird procedure [2]. The reference values for ethylmercury (Levels 2, 3 and 4), inorganic mercury (Levels 2 and 4) and methyl mercury (Levels 2 and 4) are the weighted mean of multiple NIST and collaborating laboratory data sets computed using the DerSimonian-Laird procedure [2]. The reference values for inorganic mercury (Level 3) and methylmercury (Level 3) are based on the mean results from a single NIST primary method (NIST data set 1). The uncertainty associated with each reference value is expressed as an expanded uncertainty with a confidence level of approximately 95 % [3].

Information Values: Information values for arsenic and uranium (Level 1) are provided in Table 3. A NIST information value is a value that may be of interest to the SRM user, but insufficient information is available to assess the uncertainty associated with the value [1]. Information values cannot be used to establish metrological traceability.

Expiration of Certification: The certification of **SRM 955c** is valid, within the measurement uncertainty specified, until **01 December 2028**, provided the SRM is handled in accordance with 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 Certification: NIST will monitor this SRM over the period of its certification. If substantive technical changes occur that affect the certification before expiration, NIST will notify the purchaser. Registration (see attached sheet or register online) will facilitate notification.

Overall direction and coordination of measurements leading to the certification of this material were performed by K.E. Murphy NIST Chemical Sciences Division and G.C. Turk, formerly of NIST.

Carlos A. Gonzalez, Chief
Chemical Sciences Division

Gaithersburg, MD 20899
Certificate Issue Date: 12 February 2020
Certificate Revision History on Last Page

Steven J. Choquette, Director
Office of Reference Materials

Analytical measurements at NIST were performed by D.P. Berry, C.E. Bryan, W.C. Davis, S.E. Long, J.L. Molloy, K.E. Murphy, R.L. Paul, T.W. Vetter, L.J. Wood, and L.L. Yu of the NIST Chemical Sciences Division.

Partial financial support for the development of this SRM was provided by the Centers for Disease Control and Prevention (CDC) under the direction of project officer R.L. Jones of the CDC National Center for Environmental Health, Division of Laboratory Sciences (Atlanta, GA).

Experimental design and statistical analysis of the data were provided by W.F. Guthrie and C.R. Hagwood of the NIST Statistical Engineering Division.

Collection, preparation, and homogeneity assessment for lead, cadmium, and mercury were performed by P.J. Parsons, C. Geraghty, C.D. Palmer, and M.E. Lewis, Jr. of the Division of Environmental Health Sciences, Laboratory of Inorganic and Nuclear Chemistry, Wadsworth Center, New York State Department of Health (NYSDOH; Albany, NY).

Additional data for lead, cadmium, mercury, and arsenic were provided by P.J. Parsons from reference laboratories participating in the NYSDOH proficiency testing (PT) program for blood lead and trace elements. Additional data for ethylmercury, inorganic mercury, and methylmercury were provided by S.Q. Abad, P. Rodríguez-González and J.I.G. Alonso at the University of Oviedo, Spain.

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

NOTICE AND WARNING TO USERS[(1)]

SRM 955c IS INTENDED FOR RESEARCH USE. This SRM is derived from whole caprine (goat) blood collected at NYSDOH's Wadsworth Center according to a protocol approved by the Center's Institutional Animal Care and Use Committee. The Wadsworth Center is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International, has an approved Animal Welfare Assurance (#A3183-01) with the Public Health Service, and is registered as a Class R Research Facility (#21-R-0124) with the United States Department of Agriculture. The Wadsworth Center affirms that the donor animals were sourced in the United States.

INSTRUCTIONS FOR STORAGE AND USE

Storage: The blood is shipped frozen (on dry ice) and, upon receipt, must be stored frozen at or below –20 °C until ready for use. The SRM should be kept in its original vials and stored in the box and aluminized bag in which they are supplied. Frost-free freezers should not be used because of temperature fluctuations.

Use: Before use, a frozen sample should be allowed to thaw at room temperature. The sample should be mixed by gently rocking or mildly swirling (not shaking) the vial to remix any water that may have separated on freezing. Shaking will cause bubbles to form at the top of the sample. Do not use if clotted. The contents of a vial may be thawed, a sample withdrawn, and the contents refrozen. Because of possible evaporative losses, it is advised that the contents of a vial not be used if less than one-third of the original blood volume remains. For the certified concentration to be applicable to an analytical determination, a minimum sample of 200 µL must be used.

SOURCE, PREPARATION, AND ANALYSIS

Source: The source of blood for this SRM was goats that had been dosed with gelatin capsules containing lead acetate at the Wadsworth Center's Griffin Laboratory (Guilderland, NY) according to a standard protocol established for blood lead proficiency testing purposes [4]. Each unit of blood was collected into a sterile blood bag containing dipotassium ethylene diamine tetraacetic acid (EDTA) at a concentration of 1.5 mg/mL as an anticoagulant.

Preparation: At the Wadsworth Center, individual blood units were analyzed for lead by graphite furnace atomic absorption spectrometry (GFAAS) [5], filtered through cheesecloth, and then blended under Class 100 clean room conditions into a single pool at the desired lead concentration. This procedure was repeated to produce four pools at different lead concentrations. Levels 2, 3 and 4 were further supplemented with inorganic arsenic, cadmium, and mercury as ethylmercury, inorganic mercury, and methylmercury. Blood (2 mL) was dispensed into 3.8 mL high-density polyethylene vials, which were capped and stored at –80 °C. The fill sequence was preserved. The frozen pools were shipped overnight to NIST on dry ice.

[(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.

Homogeneity Assessment: To test for homogeneity, 4 vials to 12 vials per level and method were selected based on a randomized sampling plan. Lead, cadmium, and mercury (total) in the four levels were measured in duplicate 200 µL portions by inductively coupled plasma mass spectrometry (ICP-MS) [6,7]. GFAAS was used to measure lead in Levels 2, 3, and 4 in duplicate 50 µL portions [5,6]. A LECO AMA 254 mercury analyzer was used to measure mercury (total) in duplicate 40 mg portions in Level 3. Arsenic was measured in Levels 1 and 3 in duplicate 1 g portions by ICP-MS and in Levels 2 and 4 in duplicate 1 g portions by radiochemical neutron activation analysis (RNAA). Manganese and selenium were measured in duplicate 1 g portions by ICP-MS. Based on statistical analysis of the analytical results by NIST, an allowance for potential uncertainty from material heterogeneity was added for arsenic in Level 4, cadmium in Levels 1 and 2, lead in Level 1, and mercury (total) in Levels 1, 2, 3 and 4. Because mercury (total) was found to exhibit heterogeneity, an allowance for material heterogeneity was added for ethylmercury, inorganic mercury, and methylmercury.

Determination of Arsenic (Levels 1, 2, 3 and 4) at NIST: Arsenic was measured using RNAA [8]. For Levels 1 and 3, the entire content of each of six vials was analyzed. For Levels 2 and 4, duplicate 1 g portions from four vials were analyzed. Test portions were transferred to polyethylene bags and freeze dried prior to irradiation. Samples and standards were irradiated in the NIST reactor pneumatic tube irradiation facility for 3 h at 20 MW reactor power, which provided a thermal neutron fluence rate of 1.0×10^{14} $cm^{-2}s^{-1}$. Irradiated samples were allowed to decay 4 days after which they were transferred to a beaker containing 1 mg/g As and 1 mL of a tracer solution containing <1 µCi ^{77}As. Samples were leached from the encapsulation bags with 1:1 (mass fraction) HNO_3, evaporated, and then wet-ashed with HNO_3 and $HClO_4$. Digests were dissolved in 4.5 mol/L sulfuric acid, then arsenic was reduced to As^{3+} by addition of KI and ascorbic acid, and extracted with 0.025 mol/L zinc diethyldithiocarbamate in chloroform. Count rates of ^{76}As and ^{77}As were determined by gamma-ray spectroscopy.

Additionally, arsenic was measured by standard additions using two different ICP-MS approaches: quadrupole ICP-MS operated in collision cell mode (Level 1 and Level 3) and sector field ICP-MS (Level 1) operated in high resolution mode. Duplicate 1 g portions from eight vials of each level were spiked with an arsenic standard or dummy solution and ruthenium and rhodium internal standards prior to digestion with nitric acid and peroxide in a focused microwave system. Samples were diluted in 1 % volume fraction butanol in water prior to analysis by ICP-MS in kinetic energy discrimination mode using 8 % mole fraction H_2 in balance (92 %) mole fraction He as the collision gas. Samples measured using Sector Field ICP-MS were diluted with water and introduced into the ICP-MS via a micro-peristaltic pump into a low-flow (100 µL/min) micro-concentric nebulizer fitted to a membrane desolvation system. Measurements were made at nominally 10,000 mass resolution.

Due to a considerable lack of statistical agreement among methods for the measurement of arsenic in Level 1, an information value is assigned which is an approximate upper bound based on collaborating laboratory data (described below).

Determination of Cadmium at NIST (Levels 1, 2, 3 and 4): Cadmium was measured using ID-ICP-MS [9]. For Level 1, eleven test portions were analyzed with sample sizes ranging from the entire content of each vial (1.8 g) to the combined content of two vials (3.6 g). For Levels 2 and 3, the entire content of each of six to eight vials was analyzed. For Level 4, single 1 g portions from eight vials were analyzed. Isotopically enriched ^{111}Cd was added to the test portions prior to digestion with nitric acid in a high-pressure microwave system. Samples were subjected to anion exchange chromatography prior to analysis to reduce spectral and non-spectral interference.

Determination of Lead at NIST (Levels 1, 2, 3 and 4): Lead was measured using ID-ICP-MS [7,10]. Single portions from nine vials at each concentration level, selected based on a randomized sampling plan, were analyzed. For Level 1, the entire content of each vial was analyzed. For Levels 2 through 4, 1 g portions were analyzed. Isotopically enriched ^{206}Pb was added to the test portions prior to digestion with nitric acid in a high-pressure microwave system. For Level 1, test portions were additionally wet-ashed with 0.7 g of perchloric acid. The residue was redissolved in 2 % volume fraction nitric acid prior to measurement.

Determination of Mercury (Total) at NIST (Levels 1, 2, 3 and 4): Mercury (total) was measured using ID-ICP-MS with cold-vapor mercury generation using tin [II] chloride reductant [11]. For Level 1, single 1 g portions from five vials were analyzed. For Levels 2, 3 and 4, duplicate 0.2 g – 0.4 g portions from five to eight vials were analyzed. Isotopically enriched ^{201}Hg was added to the test portions prior to digestion with nitric acid in a high-pressure microwave system. Following digestion, samples were diluted with quartz-distilled water. Samples were allowed to degas overnight at 4 °C, prior to further dilution and measurement.

Collaborating Laboratory Data for Arsenic, Cadmium, Lead and Mercury (total) in Levels 1, 2, 3 and 4: Blind samples of SRM 955c were distributed for analysis in addition to regularly scheduled proficiency testing samples as part of a special education event conducted by NYSDOH. Samples were analyzed in the same manner as routine

patient specimens. A subset of the reported data, composed of results from a group of experienced reference laboratories as specified by NYSDOH, was used either to confirm NIST results (lead, cadmium, and total mercury) or combined with NIST results (arsenic) to report values for Levels 1 through 4. For arsenic, the equally weighted mean of the reference laboratory data was combined with the NIST values.

Determination of Ethylmercury, Inorganic Mercury, and Methylmercury:
NIST Data Set 1 (Levels 2, 3 and 4): Ethylmercury, inorganic mercury, and methylmercury were measured using triple-spike speciated isotope dilution gas chromatography (GC) ICP-MS [12]. Single 0.5 g – 1.0 g portions from six vials were analyzed. Isotopically enriched $CH_3{}^{202}Hg$, $C_2H_5{}^{201}Hg$, and ^{198}Hg were added to test portions prior to extraction with 25 % (mass fraction) tetramethylammonium hydroxide (TMAH) in water using a focused microwave system. Samples were buffered at pH 5, derivatized with 20 % (mass fraction) sodium tetrapropylborate in water, back-extracted into hexane, and subjected to clean up on solid-phase extraction cartridges packed with 5 % (mass fraction) water-deactivated alumina. Collected fractions were concentrated to 0.2 mL and analyzed by GC/ICP-MS. The stability of the mercury species was confirmed by performing additional analyses over a multi-year period. For ethylmercury, data from each of these studies were combined using the DerSimonion-Laird procedure [2] prior to deriving the consensus value.

NIST Data Set 2 (Level 3): Inorganic mercury and methylmercury were measured using single spike isotope dilution; ethylmercury was measured using matrix-matched external calibration. Inorganic mercury was extracted by acidification with hydrochloric acid at room temperature for ten minutes after which 0.25 % (mass fraction) potassium permanganate solution was added, and measurements performed using cold-vapor mercury generation with ICP-MS. Methylmercury was extracted with 25 % (mass fraction) TMAH using a focused microwave system, buffered at pH 5 and derivatized by ethylation. Prior to the TMAH extraction of ethylmercury, a trimethlytin internal standard was added and samples were derivatized with sodium tetrapropylborate. Methylmercury and ethylmercury samples were back extracted into hexane and subjected to clean up on solid-phase extraction cartridges packed with 5 % (mass fraction) water-deactivated alumina. Collected fractions were concentrated to 0.2 mL and analyzed by GC/ICP-MS.

NIST Data Set 3 (Level 3): Triple-spike isotope dilution measurements employing capillary gas chromatography (GC) and ICP-MS operated with a dynamic reaction cell were performed by NIST staff at the CDC, Atlanta, GA and used either to confirm NIST data set 1 results (inorganic mercury and methylmercury) or combined with the other three data sets (ethylmercury) to report values for Level 3. Different-sourced enriched species-specific isotopes from NIST data set 1 were used. Mercury species were solubilized by combining with 25 % mass fraction TMAH and placing the samples into a convection oven at 80 °C for 18 h. Samples were buffered at pH 5 and derivatized by adding sodium tetrapropylborate. Samples were introduced into the GC *via* a twin fiber-based solid phase micro-extraction (SPME) system.

Collaborating Laboratory Data (Levels 2, 3, and 4): Triple-spike speciated isotope dilution GC/ICP-MS measurements using different-sourced enriched species-specific isotopes from NIST data set 1 and performed by an expert laboratory at the University of Oviedo, Spain [13], were used either to confirm NIST Data Set 1 results (inorganic mercury and methylmercury) or combined with the other three data sets (ethylmercury) to report values for Level 3. Mercury species were solubilized by adding 25 % mass fraction TMAH and processing in a focused microwave oven. Samples were buffered at pH 4, derivatized with sodium tetrapropylborate and extracted into hexane. The organic layer was cleaned up using homemade Florisil columns. Samples were concentrated to 10 µL and analyzed by GC/ICP-MS.

A lack of sufficient statistical agreement among data sets was observed for ethylmercury (Levels 2, 3, and 4) and inorganic mercury (Levels 2 and 4). Furthermore, a lack of statistical agreement between the total mercury measurement and the computed sum of species value was observed for Level 2. As a result, the mercury species are listed as reference values.

Determination of Manganese at NIST (Level 1): Manganese was measured by standard additions using two different ICP-MS approaches: quadrupole ICP-MS operated in reaction mode using hydrogen as the reaction gas, and Sector Field ICP-MS operated in the high resolution mode (nominal 10,000 mass resolution). For samples analyzed by quadrupole ICP-MS, duplicate 1 g portions from eight vials were digested with nitric acid in a high-pressure microwave system after which rhodium internal standard was added and the samples gravimetrically diluted. From each diluted digest, two accurately weighed subsamples were prepared by adding a known amount of manganese standard to one sub-sample and a dummy solution to the second subsample.

For samples analyzed by Sector Field ICP-MS, duplicate 1 g portions from three vials were prepared as listed above. In addition, portions from six additional vials were prepared as follows. One g portions from the six vials were added to digestion vessels along with a scandium internal standard. A second set of 1 g portions from the same six vials were added to additional digestion vessels along with a scandium internal standard and a manganese standard solution.

Samples were digested with nitric acid and hydrogen peroxide in a high-pressure microwave system and diluted quantitatively prior to analysis.

Determination of Selenium at NIST (Level 1): Selenium was quantified using two approaches: standard additions with measurement by ICP-MS operated in reaction mode using hydrogen as the reaction gas; and isotope dilution analysis with measurement by Sector Field ICP-MS operated in the high-resolution mode (nominal 10,000 mass resolution). For standard additions approach, duplicate 1 g portions from eight vials were digested with nitric acid in a high-pressure microwave system after which a rhodium internal standard was added and the samples gravimetrically diluted. From each diluted digest, two accurately weighed subsamples were prepared by adding a known amount of selenium standard to one sub-sample and a dummy solution to the second subsample.

For isotope dilution analysis approach, single 0.75 g portions from eight vials were analyzed. Isotopically enriched ^{77}Se was added to the test portions prior to digestion with nitric acid in a high-pressure microwave system.

Determination of Uranium at NIST (Level 1): Uranium was measured by standard additions using sector field ICP-MS operated in the high-resolution mode (nominal 10000 mass resolution). Portions, 0.6 g from each of the six vials, were added to digestion vessels along with ruthenium and rhodium internal standards. A second set of 0.6 g portions from the same six vials was added to additional digestion vessels along with the ruthenium and rhodium internal standards and a uranium standard solution. Samples were digested with nitric acid and hydrogen peroxide in a high-pressure microwave system and diluted quantitatively with water prior to analysis. Samples were introduced into the ICP-MS via a micro-peristaltic pump into a low-flow (100 µL/min) micro-concentric nebulizer fitted to a membrane desolvation system.

Density at 22 ºC: Densities were determined at NIST using a semi-micro gravimetric method [14] and are provided to allow conversions between results expressed as mass concentrations and mass fractions. The density values are 1.05182 g/mL ± 0.00091 g/mL for Level 1, 1.05277 g/mL ± 0.00058 g/mL for Level 2, 1.05292 g/mL ± 0.00069 g/mL for Level 3, and 1.05265 g/mL ± 0.00065 g/mL for Level 4. The uncertainty in each value is given as an expanded uncertainty, $U = ku_c$, where u_c is the combined standard uncertainty calculated according to the ISO Guide [3] and $k = 2$ is a coverage factor used to obtain an approximate level of confidence of 95 %.

Table 1. Certified Values[a] for SRM 955c Caprine Blood

Constituent	Units	Mass Concentration	*k*
		Level 1	
Cadmium (Cd)	µg/L	0.0317 ± 0.0062	2.17
Lead (Pb)	µg/dL	0.424 ± 0.011	2.02
Mercury (Hg)(Total)	µg/L	0.017 ± 0.011	2.00
Selenium (Se)	µg/L	278.7 ± 2.4	1.96
		Level 2	
Arsenic (As)	µg/L	21.66 ± 0.73	1.97
Cadmium (Cd)	µg/L	2.16 ± 0.22	2.19
Lead (Pb)	µg/dL	13.950 ± 0.080	2.00
Mercury (Hg)(Total)	µg/L	5.42 ± 0.66	2.16
		Level 3	
Arsenic (As)	µg/L	52.7 ± 1.1	1.97
Cadmium (Cd)	µg/L	5.201 ± 0.038	2.00
Lead (Pb)	µg/dL	27.76 ± 0.16	2.00
Mercury (Hg)(Total)	µg/L	17.8 ± 1.6	2.54
		Level 4	
Arsenic (As)	µg/L	78.8 ± 4.9	1.85
Cadmium (Cd)	µg/L	10.26 ± 0.11	2.00
Lead (Pb)	µg/dL	45.53 ± 0.27	2.00
Mercury (Hg)(Total)	µg/L	35.4 ± 2.0	2.11

[a] The uncertainty in each certified value is given as an expanded uncertainty, $U = ku_c$, where u_c is the combined standard uncertainty calculated according to the ISO Guide [3] and k is a coverage factor used to obtain an approximate level of confidence of 95 %. The value of u_c is intended to represent, at the level of one standard deviation, the combined effect of uncertainty components associated with random measurement error, systematic sources of measurement error, and material heterogeneity, where applicable. With the exception of arsenic in Level 4, the value of k is determined from Student's t distribution with ν_{eff} effective degrees of freedom. For the arsenic in Level 4, the value of k was obtained by back-calculation from an expanded uncertainty obtained using the DerSimonian-Laird procedure [2] with a parametric bootstrap uncertainty assessment [15]. If needed for further propagation of uncertainty, standard uncertainties for each analyte should be obtained by dividing the expanded uncertainty by the associated value of k. Except for arsenic in Level 4, the effective degrees of freedom for the combined standard uncertainty can be obtained by finding the degrees of freedom for the Student's t distribution that give the listed value of k at the 95% confidence level. For arsenic in Level 4, the effective degrees of freedom can be taken to be infinite. The measurands are the certified concentrations of the constituents listed in Table 1. Metrological traceability is to the SI derived unit for mass concentration (expressed as micrograms per deciliter or micrograms per liter).

Table 2. Reference Values[a] for SRM 955c Caprine Blood

Constituent	Units	Mass Concentration		*k*
		Level 1		
Manganese (Mn)	µg/L	17.0	± 1.6	1.96
		Level 2		
Ethylmercury (as Hg)	µg/L	1.84	± 0.81	1.96
Inorganic Mercury (as Hg)	µg/L	2.33	± 0.61	1.96
Methylmercury (as Hg)	µg/L	1.82	± 0.14	1.99
		Level 3		
Ethylmercury (as Hg)	µg/L	4.42	± 0.78	1.96
Inorganic Mercury (as Hg)	µg/L	9.0	± 1.3	2.47
Methylmercury (as Hg)	µg/L	4.5	± 1.0	2.50
		Level 4		
Ethylmercury (as Hg)	µg/L	9.4	± 3.9	1.96
Inorganic Mercury (as Hg)	µg/L	18.4	± 5.2	1.96
Methylmercury (as Hg)	µg/L	7.70	± 0.37	1.96

[a] The uncertainty in each reference value is given as an expanded uncertainty, $U = ku_c$, where u_c is the combined standard uncertainty calculated according to the ISO Guide [3] and k is a coverage factor used to obtain an approximate level of confidence of 95 %. The value of u_c is intended to represent, at the level of one standard deviation, the combined effect of uncertainty components associated with random measurement error, known systematic sources of measurement error, and material heterogeneity. The value of k is determined from Student's t distribution with ν_{eff} effective degrees of freedom. The measurands are the reference concentrations of the constituents listed in Table 2 as determined by the methods stated above. Metrological traceability is to the SI derived unit for mass concentration (expressed as micrograms per deciliter or micrograms per liter).

Table 3. Information Values for SRM 955c Caprine Blood

Constituent	Units	Mass Concentration
	Level 1	
Arsenic (As)	µg/L	< 5
Uranium (U)	µg/L	0.02

REFERENCES

[1] May, W.; Parris, R.; Beck II, C.; Fassett, J.; Greenberg, R.; Guenther, F.; Kramer, G.; Wise, S.; Gills, T.; Colbert, J.; Gettings, R.; MacDonald, B.; *Definition of Terms and Modes Used at NIST for Value-Assignment of Reference Materials for Chemical Measurements*; NIST Special Publication 260-136 (2000); available at https://www.nist.gov/srm/upload/SP260-136.PDF (accessed Feb 2020).

[2] DerSimonian R, Laird N. Meta-analysis in clinical trials. Controlled Clinical Trials 1986; 7:177-188.

[3] JCGM 100:2008; *Evaluation of Measurement Data — Guide to the Expression of Uncertainty in Measurement* (GUM 1995 with Minor Corrections); Joint Committee for Guides in Metrology (2008); available at https://www.bipm.org/utils/common/documents/jcgm/JCGM_100_2008_E.pdf (accessed Feb 2020); see also Taylor, B.N.; Kuyatt, C.E.; *Guidelines for Evaluating and Expressing the Uncertainty of NIST Measurement Results*; NIST Technical Note 1297; U.S. Government Printing Office: Washington, DC (1994); available at http://www.nist.gov/pml/pubs/tn1297/index.cfm (accessed Feb 2020).

[4] Parsons, P.J.; Reilly, A.A.; Esernio-Jenssen, D.; Werk, L.N.; Mofenson, H.C.; Stanton, N.V.; Matte, T.D.; *Evaluation of Blood Lead Proficiency Testing: Comparison of Open and Blind Paradigms*; Clin. Chem., Vol. 47 (2), pp. 322–330 (2001).

[5] Parsons, P.J.; Slavin, W.; *A Rapid Zeeman Graphite-Furnace Atomic-Absorption Spectrometric Method for the Determination of Lead in Blood*; Spectrochim. Acta B, Vol. 48, pp. 925–939 (1993).

[6] Palmer, C.D.; Lewis Jr., M.E.; Geraghty, C.; Barbosa Jr., F.; Parsons, P.J.; *Determination of Lead, Cadmium and Mercury in Blood for Assessment of Environmental and Occupational Exposures: A Comparison Between Inductively Coupled Plasma-Mass Spectrometry and Atomic Absorption Spectrometry*; Spectrochimi Acta B, Vol. 61, pp. 980–990 (2006).

[7] Murphy, K.E.; Vetter, T.; Turk, G.C.; Palmer, C.D.; Lewis Jr., M.E.; Geraghty, C.M.; Parsons, P.J.; Guthrie, W.; *Comparison of Clinical Methods with Isotope Dilution ICP-MS for the New Standard Reference Material 955c Lead in Caprine Blood*; J. Anal. At. Spectrom., Vol. 24, pp. 1170–1178 (2009).

[8] Paul, R.L.; Davis, W.C.; Yu, L.L.; Murphy, K.E.; Guthrie, W.F.; Leber, D.D.; Bryan, C.E.; Vetter, T.W.; Shakirova, G.; Mitchell, G.; Kyle, D.J.; Jarrett, J.M.; Caldwell, K.L.; Jones, R. L.; Eckdahl, S.; Wermers, M.; Maras, M.; Palmer, C.D.; Verostek, M.F.; Geraghty, C.M.; Steuerwald, A.J.; Parsons, P.J.; *Certification of Total Arsenic in Blood and Urine Standard Reference Materials by Radiochemical Neutron Activation Analysis and Inductively Coupled Plasma-Mass Spectrometry*; J. Radioanal. Nucl. Chem., Vol. 299, pp. 1555–1563 (2014).

[9] Murphy, K.E.; Long, S.E.; Vocke, R.D.; *On The Certification of Cadmium at Trace and Ultra-Trace Levels in Standard Reference Materials Using ID ICP-MS*; Anal. Bioanal. Chem., Vol. 387, pp. 2453–2461 (2007).

[10] Murphy, K.E.; Paulsen, P.J.; *The Determination of Lead in Blood Using Isotope Dilution Inductively Coupled Plasma Mass Spectrometry*; Fresenius J. Anal. Chem., Vol. 352, pp. 203−208 (1995).

[11] Christopher, S.J.; Long, S.E.; Rearick, M.S.; Fassett, J.D.; *Development of Isotope Dilution Cold Vapor Inductively Coupled Plasma Mass Spectrometry and Its Application to the Certification of Mercury in NIST Standard Reference Materials*; Anal. Chem., Vol. 73, pp. 2190−2199 (2001).

[12] Davis, W.C.; Long, S.E.; *Measurements of Methylmercury, Ethylmercury, and Inorganic Mercury Species in a Whole Blood Standard Reference Material: SRM 955c-Toxic Elements in Caprine Blood*; J. Anal. At. Spectrom., Vol. 26, pp. 431–436 (2011).

[13] Abad, S. A.; Rodríguez-González, P.; Davis, W.C.; García Alonso, J.I.; *Development of a Common Procedure for the Determination of Methylmercury, Ethylmercury, and Inorganic Mercury in Human Whole Blood, Hair, and Urine by Triple Spike Species-Specific Isotope Dilution Mass Spectrometry;* Anal. Chem., Vol 89, pp 6731–6739 (2017).

[14] Sniegoski L.T.; Moody J.R.; *Determination of Serum and Blood Densities*; Anal. Chem., Vol. 51, pp. 1577−1578 (1979).

[15] Coskun, A.; Ceyhan, E.; Inal, T.C.; Serteser, M.; Unsal, I.; *The Comparison of Parametric and Nonparametric Bootstrap Methods for Reference Interval Computation in Small Sample Size Groups;* Accred. Qual Assur, Vol. 18, pp. 51–60 (2013).

Certificate Revision History: 12 February 2020 (Change of arsenic, cadmium and total mercury reference values to certified values in Level 2 and Level 4; change of arsenic reference value to information value in Level 1; change of ethylmercury, inorganic mercury, and methylmercury certified values to reference values for Level 3; addition of certified selenium value, reference manganese value and uranium information value in Level 1; addition of ethylmercury, inorganic mercury, and methylmercury as reference values for Levels 2 and 4; change of expiration date; editorial changes) **27 January 2016** (Editorial changes); **28 July 2010** (Change of cadmium and total mercury information values to certified values in Level 1 and Level 3; change of cadmium and total mercury information values to reference values in Level 2 and Level 4; addition of arsenic reference values in Levels 1 through 4; change of information density values to reference values in Levels 1 through 4; addition of ethylmercury, inorganic mercury, and methylmercury certified values in Level 3; change of SRM name to *Toxic Metals in Caprine Blood*; change of expiration date; editorial changes); **05 February 2007** (Original certificate date).

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.