National Institute of Standards & Technology

Certificate of Analysis

Standard Reference Material® 1598a

Inorganic Constituents in Animal Serum

This Standard Reference Material (SRM) is a serum sample derived from a mixture of serum from healthy bovine and porcine animals collected under strict protocols designed to preserve the original composition and to minimize contamination [1]. The SRM is intended primarily for use in calibrating instrumentation and evaluating the accuracy of analytical methods for selected elements in blood serum, plasma, and similar biological fluids. A unit of SRM 1598a consists of two capped polyethylene vials, each containing 5 mL to 6 mL of frozen serum.

Certified Concentration Values: Certified values for concentrations for elements are provided in Table 1. The certified values are based on results from either a primary analytical technique carried out at NIST, or the combined results from two or more chemically independent analytical techniques obtained at NIST and collaborating expert laboratories [2]. 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 accounted for by NIST.

Reference Concentration Values: Reference values for concentrations for additional elements are provided in Table 2. Reference values are non-certified values that are the best estimate of the true value. However, the values do not meet the NIST criteria for certification and are provided with associated uncertainties that may reflect only measurement precision, may not include all sources of uncertainty, or may reflect a lack of sufficient statistical agreement among multiple analytical methods [2].

Information Concentration Values: Information values for concentrations for elements are provided in Table 3. An information value is considered to be a value that will be of interest and use to the SRM user, but for which insufficient information is available to assess adequately the uncertainty associated with the value, or a value derived from a limited number of analyses [2]. Information values cannot be used to establish metrological traceability.

Expiration of Certification: The certification of **SRM 1598a** is valid, within the measurement uncertainty specified, until **01 October 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 investigations and technical measurements leading to the certification of this material was under the leadership of R. Zeisler of the NIST Chemical Sciences Division.

Collection and preparation of SRM 1598a were performed by C. Veillon, N. Bryden, D. Hill, and K. Patterson of the USDA Beltsville Agricultural Research Center.

Consultation on the statistical design of the experimental work and evaluation of the data were provided by S.D. Leigh of the NIST Statistical Engineering Division.

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

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Steven J. Choquette
Office of Reference Materials

INSTRUCTIONS FOR HANDLING, STORAGE, AND USE

Handling: This material is derived from a mixture of serum from healthy bovine and porcine animals. These animals have been inspected by an USDA Veterinary Medical Officer and have not shown signs of infectious, contagious, and/or communicable disease. Normal caution and care should be exercised during its handling and use. The users should be aware of sources of contamination, and handling in an at least Class 100 clean air environment is recommended.

Storage: The material should be stored in its original container at −70 °C or below. SRM 1598a should not be exposed to intense sources of radiation, including ultraviolet lamps or sunlight.

Use: After thawing, prior to removal of sub-samples for analysis, the contents of the vials should be mixed. The concentrations of constituents in SRM 1598a are reported on a volume basis to better serve the clinical users. The density of the serum was determined at 1.0274 g/mL with an expanded uncertainty of 0.0006 g/mL (coverage factor $k = 2$). The latter must be considered when determinations are carried out on a gravimetric basis.

PREPARATION AND ANALYSIS

Sample Collection and Preparation: The procedures and protocols established for the 1985 collection of the previously issued SRM 1598 *Bovine Serum* were adhered to reference 3. The blood was obtained directly from an incision of the carotid artery and was collected in clean polyethylene pails. It was then immediately (before clotting) distributed to clean polyethylene bottles for further preparation in the USDA clean room facility. After clotting, purified serum was obtained by centrifugation. Individual animal serum samples had been obtained during the period of 02 July 2003 to 10 July 2003. These samples were kept at 4 °C. The serum was then pooled and 5 mL aliquots were dispensed into pre-cleaned polypropylene tubes, which were capped and frozen at –80 °C; the vials have been kept in frozen storage since 14 July 2003.

Homogeneity Assessment: The homogeneity of SRM 1598a was assessed by analyzing samples of approximately 1 mL from six vials selected from the beginning and the end of the bottling period and six samples from one vial from the middle of the bottling sequence. Selenium was determined as an indicator for homogeneity by isotope dilution gas chromatography − mass spectrometry (ID GC-MS). There was no statistically significant difference in concentration values among the samples; the standard deviation of the twelve results was 0.9 % relative. During the course of the analytical characterizations sample sizes down to 0.2 mL were used. No evidence of material inhomogeneity was found for these determinations. The recommended minimum sample size is 0.2 mL.

Analytical Approach: NIST values for cadmium and nickel were obtained with ID ICP-MS, all other elements were determined with at least one method carried out at NIST: instrumental neutron activation analysis (INAA), neutron activation analysis with pre-concentration of selected elements on Chelex 100 columns (PNAA), and inductively coupled plasma mass spectrometry (ICP-MS). The measurements were complemented by collaborating scientists from research and clinical laboratories using graphite furnace atomic absorption spectrometry (GF-AAS), ID GC-MS, ICP-MS, ICP atomic emission (ICP-AES), INAA, and neutron activation analysis with radiochemical separations (RNAA).

Certified Values: Certified values are derived from the NIST analytical results and the results of the collaborators. The "bound on bias" consensus method was used for combining results from individual laboratories [4]. The uncertainty listed with each value is an expanded uncertainty, with coverage factor 2 (approximately 95 % confidence). The reporting follows the ISO/JCGM Guides [5]. The measurands are the total concentration values for the elements in Table 1. The certified values are metrologically traceable to the derived SI unit for mass concentration (expressed as micrograms per liter).

For each element, there is a NIST result with an uncertainty that is complete in terms of coverage of recognized sources of uncertainties. Except for the elements measured by IDMS, these results are combined with results from collaborating laboratories with similarly complete uncertainties, and in certain cases several results without complete uncertainties. The uncertainties of the latter results were augmented for probable bias on the basis of the differences among the results obtained by different methods [4].

Table 1. Certified Concentrations for Elements

Elements	Concentration (µg/L)	Elements	Concentration (µg/L)
Cadmium (Cd)[a]	0.048 ± 0.004	Nickel (Ni)[a]	0.94 ± 0.18
Cobalt (Co)[c,d,g]	1.24 ± 0.07	Rubidium (Rb)[c,f,d]	274 ± 19
Cesium (Cs)[c,d,g]	0.64 ± 0.10	Antimony (Sb)[c,f,d,g]	1.00 ± 0.15
Copper (Cu)[f,h,e,g]	1580 ± 90	Selenium (Se)[c,f,b,d,g]	134.4 ± 5.8
Iron (Fe)[c,f,d,e]	1680 ± 60	Vanadium (V)[f,h,g,i]	1.88 ± 0.11
Manganese (Mn)[f,g,i]	1.78 ± 0.33	Zinc (Zn)[c,f,d,e,g]	880 ± 24

[a] ID ICP-MS at NIST
[b] ID GC-MS at collaborating laboratories
[c] INAA at NIST
[d] INAA at collaborating laboratories
[e] ICP-AES at collaborating laboratories
[f] ICP-MS at NIST
[g] ICP-MS at collaborating laboratories
[h] PNAA at NIST
[i] RNAA at collaborating laboratories

Reference Values: Reference values are based on results from one method carried out in several laboratories or from two or more analytical methods without NIST results. The measurands are the references values listed in Table 2 as determined by methods indicated below. Metrological traceability is to the derived SI unit for mass concentration (expressed as micrograms per liter or milligrams per liter). The methods of combining the results by different methods from different laboratories were applied as above. These results do not fulfill the criteria for certification since they lack a full estimate of method bias or results from NIST methods are not available. The reporting follows the ISO/JCGM Guides [5]. Aluminum is included as reference value because none of the techniques reported results on the control material SRM 1598 that agreed with the certified values. Chromium is provided as reference value because two out of sixteen determinations carried out at NIST resulted in values >> 1 µg/L, probably due to contamination whose source could have been in the investigated vials. Mercury showed poor agreement among techniques.

Table 2. Reference Values for Concentrations of Selected Elements

Elements	Concentration (µg/L)	Elements	Concentration (mg/L)
Aluminum (Al)[e,g]	2.3 ± 0.6	Calcium (Ca)[b,c]	96 ± 7
Chromium (Cr)[a,f,d,g]	0.33 ± 0.08		
Mercury (Hg)[a,d]	0.32 ± 0.19		
Molybdenum (Mo)[d]	5.5 ± 1.0		

[a] INAA at NIST
[b] INAA at collaborating laboratories
[c] ICP-AES at collaborating laboratories
[d] ICP-MS at collaborating laboratories
[e] PNAA at NIST
[f] RNAA at NIST
[g] GFAAS at collaborating laboratories

Information Values: Information values are based on results from one method performed at a collaborating laboratory.

Table 3. Information Values for Elements

Elements	Concentration (µg/L)	Elements	Concentration (mg/L)
Arsenic (As)[(a)]	0.3	Potassium (K)[(c)]	265
Thallium (Tl)[(b)]	0.033	Sodium (Na)[(c)]	3200
		Phosphorous (P)[(c)]	140
		Sulfur (S)[(c)]	940

[(a)] RNAA at collaborating laboratory
[(b)] ICP-MS at collaborating laboratory
[(c)] ICP-AES at collaborating laboratory

SUPPLEMENTAL INFORMATION

Density: The density was determined at NIST with a pycnometer in test portions from six vials. A value of 1.0274 ± 0.0006 g/mL was determined. This value was confirmed using an electronic digital density meter (PAAR Model DMA 35; measured value, 1.027 g/mL).

REFERENCES

[1] Veillon C; Lewis, S.A.; Patterson, K.Y.; Wolf, W.R.; Harnly J.M.; Versieck J.; Vanballenberghe, L.; Cornelis, R.; Ohaver, T.C.; *Characterization of a Bovine Serum Reference Material for Major Elements, Minor Elements, and Trace Elements*; Anal. Chem. 57, pp. 2106–2109 (1985).

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Certificate Revision History: 10 January 2017 (Change of expiration date; editorial changes); 25 August 2008 (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 http://www.nist.gov/srm.

APPENDIX: ANALYSTS

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