Chemical Metrology Division
Applied Sciences Group
Health Sciences Authority
1 Science Park Road, #01-05/06,
The Capricorn, Singapore Science Park II,
Singapore 117528
Tel: 65 6775 1605 Fax: 65 6775 1398
Website: www.hsa.gov.sg
Email: HSA_CML@hsa.gov.sg

Ref. No.: CML-HRM-J3004A/09
Date of Issue: 15 Apr 2025

Certificate of Analysis

CERTIFIED REFERENCE MATERIAL
HRM-3004A

Albumin and Creatinine in Human Urine

Batch Number
STY-0018-053
STY-0018-054

Foreword
A unit of the certified reference material (CRM) HRM-3004A consists of two vials of frozen human urine sample with different albumin and creatinine concentration levels. Each vial contains 2 ml of frozen human urine. The urine materials appear as a light yellow or yellow liquid after thawing.

The CRM was produced with reference to the requirements set out in ISO/IEC 17025:2017 [1], ISO 17034:2016 [2] and ISO Guide 35:2017 [3].

Certified Concentration Values
The certified concentration values for albumin and creatinine in HRM-3004A are provided in Table 1 and Table 2, respectively.

The certified values for albumin with the unit of mg/L in Table 1 were calculated from the concentration value of µg/g, the measured urine density at 23 °C (1.0068 g/ml and 1.0167 g/ml for STY-0018-053 and STY-0018-054, respectively). The certified values for creatinine with the unit of mmol/L in Table 2 were calculated from the concentration value of mg/kg, the measured urine density at 23 °C, and the relative molecular mass of creatinine (113.12 g/mol).

Table 1. Certified Values of Albumin in HRM-3004A

	STY-0018-053	STY-0018-054
Analyte	**(mg/L)**	**(mg/L)**
Albumin	40.1 ± 2.4	226 ± 11

Table 2. Certified Values of Creatinine in HRM-3004A

	STY-0018-053	STY-0018-054
Analyte	**(mmol/L)**	**(mmol/L)**
Creatinine	3.567 ± 0.093	10.82 ± 0.37

Each certified value is the mean of measurements of at least six samples taken from a minimum of three vials. The certified concentration values for HRM-3004A were determined using isotope dilution mass spectrometry (IDMS). A four-point calibration curve was used in the measurements.

The associated measurement uncertainty of each certified value was evaluated in accordance with ISO/IEC Guide 98-3:2008 [4]. The expanded uncertainty (coverage factor of 2) corresponded to a level of confidence of about 95%.

Validity

The certified values of HRM-3004A are valid within the specified measurement uncertainty until **15 Apr 2027**. The validity of HRM-3004A will be extended if it is tested to be sufficiently stable for continuous use. The certified values of HRM-3004A are invalid when the urine material has deteriorated or is mishandled.

Source of Materials

The urine materials were prepared by Solomon Park Research Laboratories (Kirkland, WA, USA).

Commutability

Commutability studies of albumin and creatinine in HRM-3004A were conducted by analysing 25 to 30 patient urine samples and the CRM by both liquid chromatography-isotope dilution tandem mass spectrometric (LC-IDMS/MS) method and routine methods (immunoturbidimetric method for albumin and Jaffe and enzymatic methods for creatinine) using various clinical analysers, namely Roche Cobas c702, Roche Cobas c311, Siemens Atellica Solution CH, Beckman AU5800, and Abbott Architect ci16200. The results demonstrated satisfactory commutability of albumin and creatinine in HRM-3004A for these clinical analysers, which suggested that HRM-3004A is commutable for these clinical analysers.

Homogeneity

Homogeneity testing on albumin and creatinine was performed on two subsamples taken from eleven vials using a Roche Cobas C501 chemistry analyzer. The sample size taken for homogeneity testing was 6 µL for albumin and 10 µL for creatinine. No significant differences in the between and within-vial variances were found using *F*-test (ANOVA) at 95 % confidence level. The u_{bb} was evaluated from the uncertainty due to between-vial inhomogeneity.

Stability

The stability of albumin and creatinine in HRM-3004A stored at a temperature of below – 60 °C was evaluated on at least three occasions over a period of up to three months. The results showed that the analytes were stable when stored at below – 60 °C over the study period [3]. The u_{stab} was evaluated from the standard error of the slope.

Analytical Methods

For the determination of albumin, a fully validated LC-IDMS/MS method was used [5]. The method involved spiking with isotope-labeled albumin, proteolysis of albumin using trypsin, separation using an Agilent Zorbax Eclipse Plus C18 column, followed by tandem mass spectrometric measurement of the signature peptides of albumin.

For the determination of creatinine, a fully validated LC-IDMS/MS method modified from previously published method [6] was used. The method involved spiking with isotope-labeled creatinine, separation using an Agilent Zorbax SB-Aq column, followed by tandem mass spectrometric measurement.

Metrological Traceability

The certified concentration values are traceable to the International System of Units (SI) through the use of albumin CRM 6202a from the National Metrology Institute of Japan (NMIJ), and creatinine

CRM (SRM 914a) from the National Institute of Standards and Technology (NIST).

Intended Use

HRM-3004A is a secondary measurement standard and is intended for use in the validation of methods or as quality control material for the determination of albumin and creatinine in human urine. Users may refer to ISO 33403:2024 [7] for the recommended statistical treatment of the certified reference value and the associated uncertainty of the CRM as control materials.

Warning and Safety Precautions for Users

HRM-3004A is intended for in-vitro use only and shall be handled as a biohazardous material with the potential of transmitting infectious disease. Hence, this material shall be handled using biosafety level 2 (or higher) practices, equipment, and facility [8].

Instructions for Use

HRM-3004A should be treated the same as patient specimens. Accordingly, these materials should be handled and disposed according to associated regional, national and local legislation and regulations for any potentially infectious human specimen.

Prior to use, the CRM should be thawed at room temperature (between 18 ^{o}C to 25 ^{o}C), then analysed immediately. The materials should be mixed well by gentle swirling before withdrawing any aliquots. The certified values may not be valid for re-thawed and opened bottles as the stability of both albumin and creatinine subjected to such conditions has not been investigated.

The recommended minimum sample size of HRM-3004A is 6 µL for albumin and 10 µL for creatinine. The certified values may not be valid if smaller amounts are taken.

Transport and Storage

The CRM is transported in frozen state (in dry ice). Upon receipt, it should be stored at below – 60 ^{o}C. The CRM should not be exposed to sunlight or ultraviolet radiation. Storage of the thawed material at room temperature or in the refrigerator may result in changes in the certified values.

Further Information

Please direct all enquiries regarding this CRM to the contact in this Certificate.

References

[1] ISO/IEC 17025:2017 General requirements for the competence of testing and calibration laboratories.
[2] ISO 17034:2016 General requirements for the competence of reference material producers.
[3] ISO Guide 35:2017 Reference materials – Guidance for characterisation and assessment for homogeneity and stability.
[4] ISO/IEC Guide 98-3:2008 Uncertainty of measurement – Part 3: Guide to the expression of uncertainty in measurement (GUM: 1995).
[5] Chen, Y. Z.; Liu, H.; Loh, T. P.; Liu, Q.; Teo, T. L.; Lee, T. K.; Sethi, S. K.; Clim. Chem. Lab. Med., 2021, 59(4), 711-720.
[6] Dodder, N. G.; Tai, S.; Sniegoski, L. T.; Zhang, N. F.; Welch, M. J.; Clin. Chem., 2007, 53, 1694-1699.
[7] ISO 33403:2024 Reference materials – Requirements and recommendations for use.
[8] U.S Department of Health and Human Services; Biosafety in Microbiological and Biomedical Laboratories, 5th ed.; HHS Publication No. (CDC) 21-1112.

Certificate Revision Records

Certificate Ref. No.	Date of issue	Reason for issuance
CML-HRM-3004A/01	06 Feb 2018	Issuance of first certificate
CML-HRM-3004A/02	12 Nov 2018	Extension of expiry date
CML-HRM-3004A/03	30 Jan 2019	Extension of expiry date
CML-HRM-3004A/04	06 Jan 2020	Extension of expiry date
CML-HRM-3004A/05	20 Jan 2021	Extension of expiry date
CML-HRM-3004A/06	24 Jan 2022	Extension of expiry date
CML-HRM-3004A/07	25 May 2023	Extension of expiry date
CML-HRM-3004A/08	18 Nov 2024	Addition of information on commutability
CML-HRM-3004A/09	15 Apr 2025	Extension of expiry date

Note

HSA does not assume any liability with respect to any loss caused by improper use and/or storage of the CRM by the customer.

Dr Teo Tang Lin
Division Director
Chemical Metrology Laboratory
Chemical Metrology Division