National Institute of Advanced Industrial Science and Technology

National Metrology Institute of Japan

Reference Material Certificate

NMIJ CRM 6003-a

No. +++

Progesterone

This certified reference material (CRM) is produced in accordance with the NMIJ's management system is in compliance with ISO 17034 and ISO/IEC 17025. This CRM is intended for use in the calibration of analytical instruments and validation of analytical techniques.

Certified Value

The certified value of this CRM is given in the table below. The uncertainty of the certified value is the expanded uncertainty obtained by multiplying the combined standard uncertainty by a coverage factor (k) of 2, and it is the half-width of an interval estimated to have a level of confidence of approximately 95 %.

Substance	CAS No.	Certified value, Mass fraction (kg/kg)	Expanded uncertainty, Mass fraction (kg/kg)
Progesterone (4-pregnene-3,20-dione)	57-83-0	0.993	0.005

Analysis

The certified value of this CRM was the weighted mean of purities (in mass fraction) determined by the mass balance approach, the freezing point depression method and the nuclear magnetic resonance (NMR) method. In the mass balance approach, impurities were analyzed using a high-performance liquid chromatography with an ultraviolet absorption detector (HPLC/UV), a high-performance liquid chromatography with a corona-charged aerosol detector (HPLC/CAD), Karl–Fischer titration (KF), a head space–gas chromatography with mass spectrometer (HS-GC/MS), and a thermogravimetry (TG). In purity assay by the freezing point depression method, a continuous scan method with a differential scanning calorimeter (DSC) was used. The combined standard uncertainty was estimated by the combination of standard uncertainties due to purity determinations by the mass balance approach, by the freezing point depression method and by the NMR method, differences between the methods, homogeneity and stability.

Metrological Traceability

Organic impurities were determined with HPLC/UV, HPLC/CAD, and HS-GC/MS by using the standard solutions prepared by the gravimetric blending method by NMIJ. The water content was determined by the coulometry with KF Ignition residue was determined with TG calibrated with weight. By the freezing point depression method, amount of substance fraction of progesterone was assayed using a DSC calibrated with NMIJ CRM 5401-a (cyclohexane) and NIST SRM 2232 (indium), and the amount of substance fraction was converted into mass fraction with a molecular weight of progesterone and mean molecular weight of impurities. The mass fraction of progesterone was determined with NMR by using benzoic acid, whose purity was assayed with NMR, as an internal standard. The certified value is traceable to the International System of Units (SI).

Mutual Recognition Arrangement under Metre Convention

The certified value of this CRM is recognized for international equivalence based on the Mutual Recognition Arrangement under the Metre Convention (CIPM MRA). The calibration measurement capability (capabilities) (CMC) of NMIJ related to this CRM is registered in the Key Comparison Database (KCDB) (see https://www.bipm.org/kcdb/) of the International Bureau of Weights and Measures (BIPM).

Expiration of Certification

This certificate is valid for one year from the date of shipment, provided that this CRM is stored in accordance with the instructions given in this certificate.

Description of the material

This CRM is in the form of a white powder at room temperature. 300 mg of this CRM was bottled in an amber glass vial and kept in an aluminum-laminated bag.

Instructions for Storage

This CRM should be stored at a temperature of 2 °C to 8 °C, and protected from light.

Instructions for Use

This CRM is for laboratory use only. The vial of this CRM should be allowed to warm to room temperature before use. This CRM should be used promptly once a vial is opened. Considering the homogeneity, a minimum sample mass of 20 mg should be used for each measurement and sample preparation.

Precautions for Handling

Wear personal protective equipment such as safety glasses, safety mask, and safety gloves in handling. Refer to the safety data sheet (SDS) on this CRM before use.

Preparation

This CRM was purified and subdivided by Wako Pure Chemical Industries, Ltd. This CRM was prepared by purifying a commercial high-purity reagent. 300 mg of purified progesterone is bottled in an amber glass vial in argon atmosphere.

Technical Information

The mass fraction of 4-pregnen-20α-ol-3-one, water, and ethanol were 1.56 g/kg, 0.16 g/kg and 0.41 g/kg, respectively at the time of certification time.

NMIJ Analysts

The technical manager for this CRM is KATO K., the production manager is YAMAZAKI T., and the analysts are YAMAZAKI T., SHIMIZU Y., KITAMAKI Y., SAITO T., OHTE Y., BAO X. and NAKAMURA S.

Information

If substantive technical changes occur that affect the certification before the expiration of this certificate, NMIJ will notify the registered customers. Customer registration on the NMIJ Website (given below) will facilitate notification. Technical reports regarding this CRM can be obtained from the contact details given below.

Reproduction of Certificate

In reproducing this certificate, it should be clearly indicated that the document is a copy.

April 1, 2020

ISHIMURA Kazuhiko
President
National Institute of Advanced Industrial Science and Technology

If you have any questions about this CRM, please contact:
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Revision history	
April 1, 2015:	"Metrology Management Center" was renamed to "Center for Quality Management of Metrology."
January 6, 2016:	The description in "Expiration of Certification" was changed to "one year after the date of shipment."
	In order to add uncertainty of the stability, the description of uncertainty of the certified value was changed to 0.005 kg/kg from 0.003 kg/kg.
	The description on Mutual Recognition Arrangement was added.