

**Reference Material Institute for Clinical Chemistry Standards (ReCCS)****Certified reference material for dialysate measurement****JCCRM 300-16****Certificate of Analysis****■ Applicability**

This certified reference material (CRM) is applied for calibration of instrument for dialysate measurement (pH, pCO<sub>2</sub>, HCO<sub>3</sub><sup>-</sup>, Na, K and Cl) described here, and has an acetic acid component and a citric acid component. [1],[2]

**■ Instructions for Use**

This CRM is a liquid product sealed in a glass ampoule to maintain constant partial pressure of CO<sub>2</sub> gas and pH. To obtain the prescribed certified values, measurements of this material must be taken after equilibrating gases and liquids in the ampoule at a constant temperature range of 23°C to 28°C. The instructions for use to do so are shown below.

- (1) Ensure the room temperature is between 23°C to 28°C.

If there is a dialysate mode on the measuring device, set the device to that mode, and prepare for measurement.

- (2) Remove only the number of ampoules required for measurement of this certified reference material from the refrigerator, and stand them at room temperature for two hours or more<sup>\*1</sup> to equalize the temperatures inside the ampoules and the room. Do not use vial stands made of styrofoam or other insulation materials as they are difficult to bring to room temperature.

It is also possible to remove the ampoules from the refrigerator and place them at room temperature the previous day or two days prior to measurement.

Note 1: After placing the refrigerated ampoules in a water bath of 23°C to 28°C for more than 16 minutes, measurements are possible via the following operations of (3) onwards.

- (3) Holding the tip of the ampoule, which has reached room temperature, shake it quickly horizontally 20 to 30 times for 10 seconds so as to suck in bubbles. By repeating the mixing operation once more after about one minute, you will completely equilibrate the gases and liquids in the ampoule. Holding the ampoule upright, lightly flick the tip with your fingertip so the liquid falls to the bottom.

- (4) Keeping the ampoule upright, turn the red dot above the notch on the ampoule towards you, and slowly insert the supplied ampoule opener<sup>\*2</sup> from the top section. **Fold the opener so it pushes into the opposite side.**

Note 2: The ampoule opener can be used repeatedly. For the second time onwards, the previously cut top section of the ampoule will come out from the opener when the opener is inserted into the ampoule. Exercise caution removing it, and use the opener repeatedly by the same procedure as stated above.

- (5) Prioritizing pH, pCO<sub>2</sub> and HCO<sub>3</sub><sup>-</sup> that are easily changed by air contact, take measurement<sup>\*3</sup> immediately within 30 seconds of opening.

If sampling for the measurement device is by aspiration method, quickly insert the device's aspiration part, such as a needle, down to the lower layer, aspirate the liquid, and take measurement.

If it is by injection method, extract as sufficient an amount as possible from the lower layer of the ampoule using a syringe, and inject it into the device. For devices that measure only electrolytes, take measurements according to the device's operating manual by extracting in a sample cup or similar.

Note 3: Because CO<sub>2</sub> gas rapidly flies off on opening the ampoule, for measurement of pH, pCO<sub>2</sub> and HCO<sub>3</sub><sup>-</sup>, sampling from one ampoule is done only once.

● **Warning**

**This CRM is intended for IN-VITRO diagnostic use only.**

■ **General instructions for use**

- (1) This CRM is a liquid product sealed in a glass ampoule. To open a glass ampoule, use an attached ampoule opener for your safety.
- (2) Such safety procedures should include the wearing of protective gloves. Take care to avoid cuts and projectile glass fragments that enter eyes. Take care that no material is lost from the ampoule and that no glass falls into the ampoule.
- (3) This CRM does not contain preservatives and is not sterilized with  $\gamma$ -rays. Therefore, any remaining reference material in the vial where a portion had previously been used should not be reused.  
You should remember the expiration date, and materials of over expiration date should not be used.
- (4) This CRM described was confirmed to be used for calibration of a pCO<sub>2</sub> electrode which is composed of a platinum electrode and a CO<sub>2</sub> permeable membrane.

■ **Storage method and expiration date**

This CRM should be stored in a refrigerator (2 °C~8°C).

Expiration date : September 30 , 2019

\*The material should not be stored near the cold air outlet in the refrigerator to avoid frozen.

[Measurable items & set]

**JCCRM 300A-16M acetic acid component Medium level (2/ampoule )**

: Na, K, Cl , pH, pCO<sub>2</sub>, HCO<sub>3</sub><sup>-</sup>

**JCCRM 300A-16H acetic acid component High level ( 1/ampoule)**

: Na, K, Cl

**JCCRM 300C-16M citric acid component Medium level (2/ampoule)**

: Na, K, Cl, pH, pCO<sub>2</sub>, HCO<sub>3</sub><sup>-</sup>

**JCCRM 300C-16H citric acid component High level (1/ampoule )**

: Na, K, Cl

Each ampoule contains 3 ml/ampoule, total 6 ampoules.

■ **Certified value and expanded uncertainty**

Certified values and expanded uncertainties<sup>1)</sup> of the acetic acid component and the citric acid component are shown in Table 1 and Table 2, respectively:

**Table 1 Acetic acid component: JCCRM 300A-16**  
(Measured at 37°C for pH, pCO<sub>2</sub>, and HCO<sub>3</sub><sup>-</sup>. Measured at 25°C for Na, K and Cl)

Type	JCCRM 300A-16M (Medium concentration)		JCCRM 300A-16H (High concentration)		Unit
	Certified value	Expanded uncertainty	Certified value	Expanded uncertainty	
<b>pH</b>	7.26	0.04	-	-	— (37°C)
<b>pCO<sub>2</sub></b>	67.1	1.6	-	-	mmHg(37°C)
	8.9	0.2	-	-	kPa(37°C)
<b>HCO<sub>3</sub><sup>-</sup></b>	28.5	0.7	-	-	mmol/L(37°C)
<b>Na</b>	140.0	0.5	160.0	0.6	mmol/L
<b>K</b>	1.96	0.01	3.97	0.02	mmol/L
<b>Cl</b>	109.6	0.5	131.7	0.5	mmol/L

**Table 2 Citric acid component: JCCRM 300C-16**  
 (Measured at 37°C for HCO<sub>3</sub><sup>-</sup>. Measured at 25°C for Na, K and Cl)

Type	JCCRM 300C-16M (Medium concentration)		JCCRM 300C-16H (High concentration)		Unit
	Certified value	Expanded uncertainty	Certified value	Expanded uncertainty	
<b>pH</b>	7.60	0.04	-	-	— (37°C)
<b>PCO<sub>2</sub></b>	34.3	1.0			mmHg(37°C)
	4.6	0.1			kPa(37°C)
<b>HCO<sub>3</sub></b>	32.5	1.0			mmol/L (37)
<b>Na</b>	139.6	0.6	159.2	0.7	mmol/L
<b>K</b>	1.96	0.01	3.96	0.02	mmol/L
<b>Cl</b>	111.5	0.5	133.3	0.5	mmol/L

- 1) Expanded uncertainty indicated as comprehensive expanded uncertainty (95% confidence level, coverage factor  $k=2$ ) according to ISO guidelines (GUM: Guide to the Expression of Uncertainty in Measurement) [3] which combined measurement uncertainty, and standard uncertainty of both homogeneity and storage stability.

**Date of certificate : August 5 , 2019**

**■Preparation of this material**

This CRM for dialysate measurement was prepared by referencing to theoretical values [1][4][5] of the reagent composition for an acetic acid system dialysate and a citric acid system dialysate, which are commonly used in routine medical treatment. The reference material prepared in accordance with Table 3 was dispensed up to full of a 3 ml ampoule.

**■Measurement method**

With regards to pH, pCO<sub>2</sub>, HCO<sub>3</sub><sup>-</sup>, Na, K and Cl, the certified values of these reference materials for dialysate measurement described here were measured according to the following methods at the Reference Material Institute for Clinical Chemistry Standards (ReCCS). (Measured by Hirohito Umemoto, Hideo Saito and Kei Inoue)

(1) pH

After a pH electrode, which is a glass electrode with an internal liquid of saturated KCl, was calibrated at 37°C, using NIST SRM 186g (consisting of 186-I-g and 186-II-g), the pH of this reference material for dialysate measurement described here was measured [6]

(2) pCO<sub>2</sub>

The blood gas analyzer for CO<sub>2</sub> was calibrated by standard tonometry [7] where standard CO<sub>2</sub> gas (nitrogen diluted grade 1: 4.033% and 8.569%: JCSS certification) was used and the pCO<sub>2</sub> of this reference material for dialysate measurement described here was measured (reference 2).

(3) HCO<sub>3</sub><sup>-</sup>

The certified value for HCO<sub>3</sub><sup>-</sup> of JCCRM 300A (acetic acid system medium concentration) was obtained by the Henderson-Hasselbalch formula (reference 4) using measured pH and pCO<sub>2</sub>. The HCO<sub>3</sub><sup>-</sup> value obtained by the Siggaard-Andersen chart was compared with the phosphoenolpyruvate carboxylase- malate dehydrogenase method (PEPC-MD method) [9]. The two should be within ±1 mM. The HCO<sub>3</sub><sup>-</sup> measurement value obtained by the PEPC-MD method was determined as the certified value for JCCRM 300C (citric acid system medium concentration).

(4) Na, K, Cl

Na and K were measured by flame photometry [1] Cl was measured by Coulometric Titration. [2] Calibration of Na and K was conducted using a standard solution prepared from NIST SRM919b and NIST SRM918b, respectively.

■ **Certification Committee**

Analysis of measurement results of this CRM and determination of certified values were carried out by the certification committee (Chair : Katsuhiko Kuwa ; National Institute of Advanced Industrial Science and Technology)

■ **References**

- [1]RinsyoKagaku 45:140-165,2016.  
[2]RinsyoKagaku 46:60-63,2017.  
[3] Evaluation of measurement data - Guide to the expression of uncertainty in measurement, ISO/IEC Guide 98-3 (JCGM 100:2008).  
[4]Information ; Dialysate for artificial Kidney, Kindaly 2E, 3E, 4E  
[5 ]Information; Dialysate for artificial Kidney, Carboster • P  
[6]Approved IFCC methods. Reference method (1986) for pH measurement in blood. Clin Chim Acta165:97-109,1987.  
[7]IFCC Method (1988) for tonometry of blood : Reference materials for  $P_{CO_2}$  and  $P_{O_2}$ . J Clin Chem Clin Biochem 27:403-408,1989.  
[8]Ole Siggaard-Andersen : The acid-base status of the blood, Munksgaard, Copenhagen, 1976.  
[9]Forrester RL, Wataji LJ, Silverman DA, Pierre KJ: Enzymatic method for determination of  $CO_2$  in serum. Clin Chem 22:243-245,1976.

Provider of JCCM 300-16

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Reference Material Institute for Clinical Chemistry Standards (ReCCS):  
General Incorporated Association

ReCCS has been certified as a reference material certification laboratory (ISO Guide 34)  
and a reference measurement laboratory for clinical tests (ISO 16195 and ISO/IEC  
17025)

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