

Conseil national de recherches Canada

## **Certificate of Analysis**

**Certified Reference Material** 

# ETOH-1

Certified Reference Material of high purity ethanol

ETOH-1 is a certified reference material (CRM) designed for ethanol measurements where accuracy is critical, such as the assessment of ethanol purity destined for use in hand sanitizers or for verification of ethanol solutions used in the evaluation of alcohol breath testing devices. It also contains acetaldehyde at a level just under the 10 ppm limit in ethanol for use in hand sanitizers in Canada [1], based on limits set by the British, European, and US pharmacopeia, and therefore would be suitable for method validation and quality control to support the analysis of acetaldehyde in ethanol. Certified values for the mass fraction and mass concentration of ethanol in ETOH-1 have been established, as listed in Table 1. Information values for the mass fraction and mass concentration of an acetaldehyde impurity in ETOH-1 are provided in Table 2.

The certified values for high purity ethanol are based on results from data generated at the National Research Council of Canada (NRC). Quantitative nuclear magnetic resonance spectroscopy (<sup>1</sup>H-qNMR) with internal calibration was employed for value assignment of ethanol in ETOH-1. The expanded uncertainty (*U*) for all values is equal to  $U = ku_c$ , where  $u_c$  is the combined standard uncertainty calculated according to the JCGM Guide [2] and *k* is the coverage factor of two (k = 2, 95 % confidence interval). It is intended that the *U* for certified values accounts for every aspect that reasonably contributes to their uncertainties.

Substance	Molecular formula	Mass fraction g/g	Mass concentration g/mL	
ethanol (a)	C <sub>2</sub> H <sub>6</sub> O	$0.9968 \pm 0.0052$	0.7845 ± 0.0090	

Table 1: C	Certified values	and expanded	uncertainties for	r ETOH-1	(k = 2, 9)	95 % CI)
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H<sub>3</sub>C \_ OH

ethanol CAS registry number: 64-17-5 InChI Key: LFQSCWFLJHTTHZ-UHFFFA0YSA-N Molecular formula:  $C_2H_6O$ Molar mass: 46.0684 ± 0.0026 g/mol



## Table 2: Information values for ETOH-1

Substance	Molecular formula	Mass fraction µg/g	Mass concentration µg/mL	
acetaldehyde (b)	C <sub>2</sub> H <sub>4</sub> O	8.32	6.55	

## Coding

The coding refers to the instrument method used for value assignment.

- a Internal standard quantitative nuclear magnetic resonance spectroscopy (<sup>1</sup>H-qNMR)
- **b** Headspace gas chromatography tandem mass spectrometry (HS-GC-MS/MS) combined with standard addition calibration

### **Certified values**

Certified values are considered to be those for which the NRC has the highest confidence in accuracy and that all known and suspected sources of bias have been taken into account and are reflected in the stated expanded uncertainties. Certified values are the best estimate of the true value and uncertainty (Table 1).

### Information values

Information values are those for which insufficient data are available to provide a comprehensive estimate of uncertainty (Table 2).

### Intended use

Distributed in 1 mL units, this certified reference material is primarily intended for use in method development and in the calibration of instrumentation for the quantitative analysis of ethanol.

### Storage

It is recommended that the material be stored in a controlled cold temperature environment such as a refrigerator at approximately +4 °C or below.

### Instructions for use

Prior to opening, each ampule should be allowed to warm to room temperature and the contents should be thoroughly mixed. The ampule should be opened at the pre-scored mark immediately prior to use. Ethanol is a highly volatile compound, therefore precautionary measures to avoid evaporation of ETOH-1 should be taken. Please note that the volume of the material is not certified; only the concentration is certified. Therefore, the entire contents of the ampule should not be diluted to volume. Once opened, the contents of the ampule should be transferred to an amber glass vial, tightly sealed, and stored in the dark at +4 °C or below.

The mass concentration values reported were calculated from the mass fraction values using a density of 0.787  $\pm$  0.008 g/mL (*k* = 2, 95 % confidence interval) at 21 °C determined at the NRC on the actual CRM. However, note that the density of ethanol changes by 0.11 % per degree Celsius (in the interval of 10 to 30 °C; decreasing density with increasing temperature).



## Preparation of material

The material was acquired from a commercial supplier and was used as received. The ethanol was dispensed in 1 mL aliquots in clean amber glass ampules. The ampules were immediately flame-sealed in a controlled environment at 40 % relative humidity.

## Stability

The transportation stability of ethanol in ETOH-1 was assessed using <sup>1</sup>H-qNMR at four- and twelve-week time points after exposure to +50 °C. No significant degradation was observed during this period. The long-term stability of ethanol in ETOH-1 at +4 °C was assessed after two and a half years using <sup>1</sup>H-qNMR and compared to the certified value. No significant difference in the measured mass fraction was observed over this period. Therefore, the uncertainty components for transportation and long-term stability were set to zero.

## Homogeneity

The material is expected to have a high degree of homogeneity as it is a liquid of high purity. Nevertheless, the homogeneity was tested at the NRC using <sup>1</sup>H-qNMR. Results from a representative number of ampules across the fill series were evaluated using the DerSimonian-Laird (DSL) random effects model [3]. The between-unit variability was determined to be negligible for ethanol in ETOH-1, therefore, the material is deemed to be homogeneous.

## Uncertainty

Included in the combined uncertainty estimate ( $u_c$ ) are uncertainties in the batch characterization ( $u_{char}$ ), uncertainties related to possible between-unit variation ( $u_{hom}$ ), and uncertainties related to stability ( $u_{stability}$ ). Expressed as standard uncertainties, these components are listed in Table 3.

Substance	<i>U<sub>k=2</sub></i>	u <sub>c</sub>	u <sub>char</sub>	u <sub>hom</sub>	U <sub>stability</sub>
	g/g	g/g	g/g	g/g	g/g
ethanol	0.0052	0.0026	0.0026	0.0000	0.0000

Table 3: Uncertainty components of the certified value for ETOH-1

## Metrological traceability

Results presented in this certificate are traceable to the SI through gravimetrically prepared standards of NIST SRM 84L potassium hydrogen phthalate employed as an internal standard for <sup>1</sup>H-qNMR. As such, ETOH-1 serves as a suitable reference material for laboratory quality assurance programs, as outlined in ISO/IEC 17025.

## Quality Management System (ISO 17034, ISO/IEC 17025)

This material was produced in compliance with the NRC Metrology Quality Management System, which conforms to the requirements of ISO 17034 and ISO/IEC 17025. The Metrology Quality Management System supporting the NRC Calibration and Measurement Capabilities, as listed in the *Bureau international des poids et mesures* (BIPM) Key Comparison Database (<u>http://kcdb.bipm.org/</u>), has been reviewed and approved under the authority of the Inter-American Metrology System (SIM), and found to be in compliance with the expectations of the *Comité international des poids et mesures* (CIPM) Mutual Recognition Arrangement. The SIM approval is available upon request.



## Updates

Users should ensure that the certificate they have is current. Our website at <u>www.nrc.gc.ca/crm</u> will contain any new information.

### References

- Government of Canada. (2020, May 9). Interim guidance for producing ethanol for use in alcoholbased hand sanitizers. Retrieved from <u>https://www.canada.ca/en/health-canada/services/drugshealth-products/disinfectants/covid-19/interim-guide-ethanol-hand-sanitizers.html</u>. Accessed: 04 December 2020.
- [2] Evaluation of measurement data: Guide to the expression of uncertainty in measurement. JCGM 100:2008. <u>https://www.bipm.org/en/publications/guides/gum.html</u>.
- [3] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials (1986), 7: 177-188. https://doi.org/10.1016/0197-2456(86)90046-2

#### Cited by

A list of scientific publications citing ETOH-1 can be found at <u>doi.org/10.4224/crm.2020.etoh-1</u>.

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### ETOH-1

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This Certificate is only valid if the corresponding material was obtained directly from NRC or an Authorized Reseller.

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