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**STANDARD FOR THE
MANUFACTURER
OF CALIBRATION
GAS STANDARDS
USED TO ANALYZE
MEDICAL AND FOOD
GASES**

Documents

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Work Item 23-003
Medical Gases Committee

NOTE—No technical information has been changed from the 2018 edition. This reaffirmed edition may include minor editorial changes.

NOTE—Appendix A (Normative) is a requirement.

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1 Introduction

This publication establishes the minimum requirements for the manufacture, analysis, and qualification of calibration gas standards used to qualify gases regulated by the U.S. Food and Drug Administration (FDA) or Health Canada (HC). The intent of this publication is to ensure consistent manufacture of calibration gas standards.

For the purpose of this publication, the term manufacturer shall mean calibration gas manufacturer unless it is preceded by a specific qualifier, e.g., equipment manufacturer.

2 Scope

This publication applies to the manufacture, analysis, and qualification of primary gas standards used to calibrate analytical equipment used to verify the concentration of standards. It also applies to the manufacture and analysis of certified gas standards used to calibrate analytical instruments used to test FDA or HC regulated gases.

This publication does not apply to the manufacture of calibration gas standards classified as medical devices.

3 Definitions

For the purpose of this publication, the following definitions apply.

3.1 Publication terminology

3.1.1 Shall

Indicates that the procedure is mandatory. It is used wherever the criterion for conformance to specific recommendations allows no deviation.

3.1.2 Should

Indicates that a procedure is recommended.

3.1.3 May

Indicate that the procedure is optional.

3.1.4 Will

Is used only to indicate the future, not a degree of requirement.

3.1.5 Can

Indicates a possibility or ability.

3.2 Technical definitions

3.2.1 Accuracy

Degree of conformity of a measured or calculated quantity to its actual (true) value.

3.2.2 Absolute

Degree of variance independent of comparison to a reported value.

NOTE—For example, if the reported concentration of a gas standard is $5\% \pm 2\%$ absolute, the actual concentration lies in the range of 3% to 7%.

3.2.3 Relative

Degree of variance dependent on comparison to a reported value.

NOTE—For example, if the reported concentration of a gas standard is $5\% \pm 2\%$ relative, the actual concentration lies in the range of 4.9% to 5.1%, which is $5\% \pm (2\% \text{ of } 5\%)$ or $5\% \pm 0.1\%$ absolute.

3.2.4 Calibration

Comparison of a measurement standard or instrument of known accuracy and precision with a measurement standard or instrument of unknown accuracy and precision.

NOTE—Used to detect, correlate, report, and eliminate by adjustment any variation in the accuracy and precision of the unknown item.

3.2.5 Calibration standard

Material of a known value to which other materials are compared.

3.2.6 Calibration gas standard

Gases that have been analyzed and certified to appropriate levels of accuracy using standards that are traceable to a national standards organization and are used to calibrate gas analysis equipment.

3.2.7 Certified standard

Calibration gas standard analytically qualified against a primary standard.

3.2.8 Evacuation

Process of removing residual product by mechanical means, creating a negative atmospheric pressure.

3.2.9 Nationally recognized standards

3.2.9.1 NIST Standard Reference Materials® (SRM)

Certified reference materials supplied by the National Institute of Standards and Technology (NIST).

3.2.9.2 NIST Traceable Reference Materials™ (NTRM)

Materials that are manufactured and distributed by specialty gas companies in accordance with NIST technical specifications.

3.2.10 VSL primary reference materials (PRMs)

Certified reference materials supplied by the Van Swinden Laboratory (VSL).

3.2.11 Partial pressure

Pressure exerted by a single component in a mixture of gases.

3.2.12 Performance check

Periodic verification of calibration where no adjustments are intended.

3.2.13 Precision

The closeness of agreement between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions.

3.2.14 Primary standard

Calibration gas standard manufactured to the highest metrological qualities using gravimetric methods.

3.2.15 Purge

Process where gas is added and vented to dilute residual gas(es) in a container prior to evacuation.

3.2.16 Tolerance

Permissible deviation from the reported value.

3.2.17 Uncertainty

Estimated amount by which an observed or calculated value may differ from the true value.

3.2.18 User

Consumer of the gas standard(s).

4 Raw materials

4.1 Component raw materials

4.1.1 Quality of incoming gases

The quality of the source materials shall be appropriate for the intended use. The manufacturer shall establish specifications for the receipt of raw materials. Impurities of interest shall be identified and quantified either through receipt of certificate of analysis (COA) or by analysis of incoming raw material. In some cases further purification of the source material could be required by the manufacturer in order to meet the following specifications.

When manufacturing standards used for testing medical or food gases that are listed in the current *United States Pharmacopeia* and *National Formulary (USP–NF)* or the *Food Chemicals Codex (FCC)*, the source gases shall meet the following specifications:

- oxygen—total impurities shall be less than or equal to 0.01%, therefore the assay by difference shall be greater than or equal to 99.99% oxygen;
- nitrogen—total impurities shall be less than or equal to 0.01%, therefore the assay by difference shall be greater than or equal to 99.99% nitrogen;
- helium—total impurities shall be less than or equal to 0.01%, therefore the assay by difference shall be greater than or equal to 99.99% helium;
- nitrous oxide—total impurities shall be less than or equal to 0.01%, therefore the assay by difference shall be greater than or equal to 99.99% nitrous oxide; and
- carbon dioxide—total impurities shall be less than or equal to 0.01%, therefore the assay by difference shall be greater than or equal to 99.99% carbon dioxide [1].¹

When air is a component in a standard, the air component shall be manufactured by the standard manufacturer using oxygen and nitrogen source gases meeting the previous specifications. When air is identified as the balance gas, the oxygen concentration shall be 19.5% to 23.5% and the balance nitrogen.

4.1.2 Qualification of source gas supplier

The source gas supplier should have a documented quality system in place to ensure consistency in manufacturing the source materials. The standard gas manufacturer is responsible for qualifying the supplier.

4.2 Cylinders and valves

4.2.1 Cylinder selection

Cylinders shall be selected based on their material of construction. The cylinder material of construction shall be chemically compatible for its intended use, e.g., carbon monoxide at ppm levels in aluminum.

4.2.2 Valve selection

Standard cylinder valve outlet connections suitable for gas cylinders are provided in CGA V-1, *Standard for Compressed Gas Cylinder Valve Outlet and Inlet Connections* [2]. The method for selecting the proper cylinder valve outlet connections for gas mixtures is provided in CGA V-7, *Standard Method of Determining Cylinder Valve Outlet Connections for Industrial Gas Mixtures* [3]. The valve material(s) of construction selected shall be chemically compatible for the intended use.

4.2.3 Cylinder preparation

The manufacturer shall have established procedures for cylinder preparation.

¹ References are shown by bracketed numbers and are listed in order of appearance in the reference section.