



PS-22—2020

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POSITION STATEMENT

CONFORMING WITH USP/NF MONOGRAPHS FOR MEDICAL GASES

Question

How does the medical gas industry conform with the United States Pharmacopeia/National Formulary (USP/NF) monographs for medical gases?

Answer for the air separation process

Validated air liquefaction plants produce medical gases that meet or exceed the compendial requirements, see CGA P-8.2, *Guideline for Validation of Air Separation Unit and Cargo Transport Unit Filling for Medical Oxygen and Medical Nitrogen* [1]. The incoming air is prepurified and then segregated into its component gases by liquefaction. The thermodynamic properties of the component gases govern this process. No chemical reactions occur within the cryogenic air separation column.

- **Oxygen USP**—The most common test method used to identify and assay oxygen USP is a method validated paramagnetic oxygen analyzer. This test method ensures that the identity, strength, quality, and purity of oxygen USP meets or exceeds the monograph requirements. In addition, the identity of oxygen USP produced by the air liquefaction process is ensured through process validation, dedicated piping, and product specific CGA connections.
- **Nitrogen NF**—The most common test method used to determine nitrogen NF is to subtract the oxygen content. The most common test method used to determine oxygen content is a method validated electrochemical trace oxygen analyzer. The identity of nitrogen NF produced by the air liquefaction process is ensured through process validation, dedicated piping, and product specific CGA connections. This treatment in conjunction with carbon monoxide analysis and odor testing ensures that the identity, strength, quality, and purity of nitrogen NF meets or exceeds the monograph requirements.

Validation of the analyzers, make valves, isolation circuits, piping, storage vessels, and fill zone ensures that the identity, strength, quality, and purity of the product meets or exceeds the monograph requirements.

Answer for the cylinder filling process

Bulk product received from a validated process into a product specific storage vessel with unique CGA fill connections ensures the incoming product identity in the storage vessel. Cylinder fill process validation and in-process controls including product specific piping and transfilling equipment ensures the identification of the product throughout the filling process.

- **Oxygen USP**—The most common test method used to identify and assay oxygen USP is a method validated paramagnetic oxygen analyzer. This test method ensures that the identity, strength, quality, and purity of oxygen USP meets or exceeds the monograph requirements.
- **Nitrogen NF**—The most common method used to determine nitrogen NF assay is to subtract the oxygen content. The most common test method used to determine oxygen content is a method validated paramagnetic oxygen analyzer or an electrochemical trace oxygen analyzer. These test methods in conjunction with carbon monoxide analysis and odor testing ensures that the identity, strength, quality, and purity of nitrogen NF meets or exceeds the monograph requirements.

- Nitrous oxide USP, carbon dioxide USP, helium USP—Perform the compendial methods or validated alternative methods to ensure the identity, strength, quality, and purity of the product meets or exceeds the monograph requirements.

NOTE—The compendial identity test for nitrous oxide, which uses pyrogallol to determine the absence of oxygen, cannot be performed because the reagent is unavailable. Suitable alternatives include the use of a paramagnetic oxygen analyzer, gas chromatograph, or other appropriate method.

Process validation, analytical methods, documented procedures, and training ensures that the identity, strength, quality and purity of product meets or exceeds monograph requirements.

Answer for reference standards

Reference standards are required for the accurate calibration of analytical equipment. Testing product lots utilizing the source gas as a reference standard is not an acceptable practice. CGA recommends using reference gas standards in appropriate ranges that are traceable to a recognized standard, e.g., National Institute of Standards and Technology (NIST). These standards must be accompanied by a certificate of analysis (COA) documenting at a minimum the actual test results, the analytical accuracy, a unique identifier for traceability, and a statement of traceability to the recognized standard.

Reference

Unless otherwise specified, the latest edition shall apply.

[1] CGA P-8.2, *Guideline for Validation of Air Separation Unit and Cargo Transport Unit Filling for Medical Oxygen and Medical Nitrogen*, Compressed Gas Association, Inc. www.cganet.com

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Medical Gases Committee

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