COMPARISON OF EUROPEAN, US & JAPANESE PHARMACOPOEIA MONOGRAPHS FOR MEDICINAL GASES

Doc 152/18

Revision of Doc 152/11

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COMPARISON OF
EUROPEAN, US & JAPANESE PHARMACOPOEIA
MONOGRAPHS FOR MEDICINAL GASES

Prepared by WG-7 Medical and Breathing Gases

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Table of Contents

1 Introduction ............................................................................................................................ 1

2 Scope and purpose ................................................................................................................ 1

2.1 Scope ................................................................................................................................ 1

2.2 Purpose ............................................................................................................................... 2

3 Specifications and test methods .......................................................................................... 3

3.1 European Pharmacopoeia test requirements ................................................................. 4

4 Currency of information ....................................................................................................... 5

5 European Pharmacopoeia compared to United States Pharmacopoeia .............................. 5

5.1 Medical oxygen ................................................................................................................... 6

5.2 93% Oxygen ....................................................................................................................... 7

5.3 Nitrous oxide ...................................................................................................................... 8

5.4 Nitrogen ............................................................................................................................... 9

5.5 97% Nitrogen ..................................................................................................................... 10

5.6 Low oxygen nitrogen ........................................................................................................... 11

5.7 Carbon dioxide ................................................................................................................ 12

5.8 Medicinal air ..................................................................................................................... 13

5.9 Synthetic medicinal air ...................................................................................................... 14

5.10 Helium ............................................................................................................................ 15

5.11 Nitric oxide ..................................................................................................................... 16

5.12 Argon ................................................................................................................................. 17

5.13 Carbon monoxide ............................................................................................................ 18

5.14 Carbon monoxide intermix (5 per cent) in nitrogen ....................................................... 19

5.15 Methane ........................................................................................................................ 20

5.16 Methane intermix (2% per cent) in nitrogen .................................................................. 21

5.17 Acetylene intermix (1% per cent) in nitrogen ................................................................. 22


6.1 Oxygen ............................................................................................................................... 23

6.2 Nitrous oxide ................................................................................................................... 24

6.3 Carbon dioxide ............................................................................................................... 25

6.4 Nitrogen ........................................................................................................................... 26

Amendments from 152/11

<table>
<thead>
<tr>
<th>Section</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Editorial to align style with EIGA Style Manual</td>
</tr>
<tr>
<td>5.14</td>
<td>Minor changes to US Pharmacopoeia</td>
</tr>
<tr>
<td>5.15</td>
<td>Carbon monoxide intermix (5%) in nitrogen added</td>
</tr>
<tr>
<td>5.16</td>
<td>Methane added</td>
</tr>
<tr>
<td>5.17</td>
<td>Methane intermix (2%) in nitrogen added</td>
</tr>
<tr>
<td>6</td>
<td>Acetylene intermix (1%) in nitrogen added</td>
</tr>
<tr>
<td>6</td>
<td>Updates to Japanese Pharmacopoeia</td>
</tr>
</tbody>
</table>

Note: Technical changes from the previous edition are underlined
1 Introduction

There are three prime regional Pharmacopoeia organisations that are responsible for the preparation and publication of Pharmacopoeia monographs, covering the commonly used substances involved in the manufacture and supply of medicinal products.

The three organisations are:

- European Directorate for the Quality of Medicines (EDQM), who are responsible for the European Pharmacopoeia (Ph. Eur.) monographs
- United States Pharmacopeia Convention, who are responsible for the US Pharmacopoeia (USP)
- Ministry of Health and Welfare, who are responsible for the Japanese Pharmacopoeia (JP)

The three Pharmacopoeias have monographs for a number of medical / medicinal gases. These gases can be used either as active ingredients in medicinal products or excipients, used in the manufacture of medical gas mixtures, administered to patients. Alternatively, they can be used as pharmaceutical gases, used in the manufacture, storage or distribution of all medicinal products.

The purpose of these monographs is to specify for each gas:

- Minimum assay / purity for the product that is suitable for medicinal use;
- Maximum level of defined impurities, that could have an adverse effect on the patient; and
- Appropriate test methods for determining quality of the product.

This publication provides a comparison between the specifications and the test methods defined in each of the regional pharmacopoeia compendiums.

2 Scope and purpose

2.1 Scope

This publication covers the pharmacopoeia monographs for medicinal and pharmaceutical gases published by the:

- European Pharmacopoeia;
- United States Pharmacopeia; and
- Japanese Pharmacopoeia.

It includes the monographs for gases used in the manufacture and supply of medicinal products including:

- Medicinal gases, that are used as active ingredients in medical gases and gas mixtures supplied for patient use;
- Excipient gases, that are added to gas mixtures but have no pharmacological effects; and
- Pharmaceutical gases, that are specified in the manufacture, storage and distribution of medicinal products.

The comparison tables provide a comparison between the European and the United States Pharmacopoeia monographs for all of the specified gases.
A separate table is included to detail the monographs published by the Japanese Pharmacopoeia, where the monographs do not specify acceptance limits and only provide test criteria for compliance.

2.2 Purpose

To provide a cross reference between the three sets of published monographs to enable a comparison of the requirements for each method. This is intended to demonstrate compliance between monographs but should not be used as a detailed method of carrying out the relevant tests.

Where the testing to a specific monograph is required, the user should refer to the original document (and all supporting documents within the relevant pharmacopoeia) to ensure that the tests are carried out correctly.
3 Specifications and test methods

The most commonly used medicinal gases have been included in the Pharmacopoeia for many years but recently a number of new medical gases have been added.

The following table gives a reference for the different gases that have been covered by published monographs in the three Pharmacopoeias:

<table>
<thead>
<tr>
<th>Gases</th>
<th>European Pharmacopoeia</th>
<th>US Pharmacopoeia</th>
<th>Japanese Pharmacopoeia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical oxygen</td>
<td>0417</td>
<td>No reference no.</td>
<td>No reference no.</td>
</tr>
<tr>
<td>Oxygen 93%</td>
<td>2455</td>
<td>No reference no.</td>
<td>NS</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>0416</td>
<td>No reference no.</td>
<td>No reference no.</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>1247</td>
<td>No reference no.+</td>
<td>No reference no.</td>
</tr>
<tr>
<td>Nitrogen 97%</td>
<td>NS</td>
<td>No reference no.</td>
<td>NS</td>
</tr>
<tr>
<td>Low oxygen nitrogen</td>
<td>1685</td>
<td>No reference no.</td>
<td>NS</td>
</tr>
<tr>
<td>Carbon dioxide</td>
<td>0375</td>
<td>No reference no.</td>
<td>No reference no.</td>
</tr>
<tr>
<td>Medicinal air</td>
<td>1238</td>
<td>No reference no.</td>
<td>NS</td>
</tr>
<tr>
<td>Synthetic medicinal air</td>
<td>1684</td>
<td>See medicinal air</td>
<td>NS</td>
</tr>
<tr>
<td>Helium</td>
<td>2155</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Nitric oxide</td>
<td>1550</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Argon</td>
<td>2407</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>2408</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Carbon monoxide intermix (5 per cent) in nitrogen</td>
<td>2904</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Methane</td>
<td>2413</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Methane intermix (2 per cent) in nitrogen</td>
<td>2905</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Acetylene</td>
<td>IP</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Acetylene intermix (1 per cent) in nitrogen</td>
<td>2903</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

+ Nitrogen is covered in the National Formulary
NS: Not specified
IP: In preparation

Each monograph defines the specification of the medicinal gas, including the:

- Assay of the product;
- Maximum allowable impurity levels for those contaminants specified in the product;
- Approved analytical method for identifying the gas;
• Approved analytical method for determining the assay, and
• Approved analytical test method for determining each contaminant specified within the monograph.

The validated analytical methods described in the monographs are the official test methods upon which the specifications in the relevant Pharmacopoeia are based.

3.1 European Pharmacopoeia test requirements

For the European Pharmacopoeia, the test methods are verified against the protocols set out in the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, (ICH) guidelines for accuracy and precision, linearity and range and specificity. The results also need to conform to the requirements of repeatability and peak symmetry.

In addition to the specific medicinal gas monographs there are several general notices that apply to all monographs.

The following general test methods are particularly applicable to the analysis of medical gases:

<table>
<thead>
<tr>
<th>Test reference</th>
<th>Test method</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.6</td>
<td>Gas detector tubes</td>
</tr>
<tr>
<td>2.2.24</td>
<td>Absorption spectrophotometry, infrared</td>
</tr>
<tr>
<td>2.2.28</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td>2.2.46</td>
<td>Chromatographic separation techniques</td>
</tr>
<tr>
<td>2.5.24</td>
<td>Carbon dioxide in gases</td>
</tr>
<tr>
<td>2.5.25</td>
<td>Carbon monoxide in gases</td>
</tr>
<tr>
<td>2.5.26</td>
<td>Nitrogen monoxide and nitrogen dioxide in gases</td>
</tr>
<tr>
<td>2.5.27</td>
<td>Oxygen in gases</td>
</tr>
<tr>
<td>2.5.28</td>
<td>Water in gases</td>
</tr>
<tr>
<td>2.5.35</td>
<td>Nitrous oxide in gases</td>
</tr>
</tbody>
</table>

Alternative methods of analysis can be used for testing medical gases, after agreement with the competent authority, provided that the test methods have been validated in line with the ICH protocols to demonstrate that they are equivalent to the specified methods.

The European Pharmacopoeia monographs test methods specified for medical gases are divided into two main sections, production and tests.

The production methods are intended to be the methods used by the manufacturers. These methods are the basis for the release of the product at the manufacturer’s site for patient use. The methods specified in the production section of the monograph normally utilise the latest analytical instruments, that should be available to the manufacturers of the gases.

The test methods are intended to be the methods used by the end user to assure themselves that the medical gases are of the appropriate quality. For example, these could be used for routine testing by the Pharmacist at the hospital of the pipeline gases at the terminal outlets in the hospital. The test methods generally utilise detector tubes for the test method as it is unlikely that the end users would have all of the appropriate analytical instruments available to them for testing.

Where the hospital is the manufacturer, for example where they are producing medicinal air on site using an air compressor, the production test methods should be applied.

The United States and Japanese Pharmacopoeia monographs only specify one method for the analysis of the medical gas.
The Japanese Pharmacopoeia monographs only detail the test methods and do not give the values of the specification limits for the impurities in percentage terms or parts per million. The approved test methods include either gas chromatography, detector tubes or wet chemistry as the approved methods.

In all cases the test methods specified in the monographs should have been validated. For the European Pharmacopoeia, this work is normally undertaken by one of the national representative on the relevant Pharmacopoeia committee.

4 Currency of information

The versions of the relevant Pharmacopoeias used to provide the information for the comparison tables are:


As and when there are relevant changes to any of these monographs this publication shall be updated. However, where it is important that the latest information is available, the original Pharmacopoeia document should be referenced to ensure that there have been no revisions to the individual monograph.

5 European Pharmacopoeia compared to United States Pharmacopoeia

The following tables provide a comparison between the European and US Pharmacopoeia monographs for each of the specified medicinal or pharmaceutical gas.
### 5.1 Medical oxygen

<table>
<thead>
<tr>
<th>Monograph</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Oxygen</td>
<td>Oxygen</td>
</tr>
<tr>
<td>Reference</td>
<td>01/2010:0417</td>
<td>Not specified</td>
</tr>
<tr>
<td>Chemical formula</td>
<td>$O_2$</td>
<td>$O_2$</td>
</tr>
</tbody>
</table>

**Definition**

Oxygen contains not less than 99.5% V/V of oxygen. It is produced by a purification process followed by a cryodistillation of the ambient air.

Oxygen contains not less than 99.0% V/V of oxygen.

Note: Oxygen produced by the air-liquefaction is exempt from the requirements of carbon monoxide and carbon dioxide testing.

**Identification**

Complies with the assay

Complies with the assay

**Production**

**Assay**

- **Specification**: $\geq 99.5\%$ V/V oxygen
- $\geq 99.0\%$ V/V oxygen
- **Analytical method**: Paramagnetic analyser
- Paramagnetic analyser

**Impurities**

<table>
<thead>
<tr>
<th>Impurity</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO</td>
<td>$\leq 5$ ppm V/V</td>
<td>$\leq 0.001%$ V/V</td>
</tr>
<tr>
<td>Analytical method</td>
<td>Infrared analyser</td>
<td>Detector tube</td>
</tr>
<tr>
<td>CO$_2$</td>
<td>$\leq 300$ ppm V/V</td>
<td>$\leq 0.03%$ V/V</td>
</tr>
<tr>
<td>Analytical method</td>
<td>Infrared analyser</td>
<td>Detector tube</td>
</tr>
<tr>
<td>H$_2$O</td>
<td>$\leq 67$ ppm V/V</td>
<td>Not specified</td>
</tr>
<tr>
<td>Analytical method</td>
<td>Electrolytic hygrometer</td>
<td></td>
</tr>
</tbody>
</table>

**Tests**

- **CO**: $\leq 5$ ppm V/V
  - Analytical method: Detector tube
- **CO$_2$**: $\leq 300$ ppm V/V
  - Analytical method: Detector tube
- **H$_2$O**: $\leq 67$ ppm V/V
  - Analytical method: Detector tube

No tests section specified
## 5.2 93% Oxygen

### Oxygen 93

<table>
<thead>
<tr>
<th>Monograph</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Oxygen (93 per cent)</td>
<td>Oxygen 93 Percent</td>
</tr>
<tr>
<td>Reference</td>
<td>04/2011:2455</td>
<td>Not Specified</td>
</tr>
<tr>
<td>Chemical formula</td>
<td>$O_2$</td>
<td>$O_2$</td>
</tr>
</tbody>
</table>

**Definition**

Oxygen 93% contains between 90.0% V/V and 96% V/V of oxygen. Remainder mainly consists of argon and nitrogen. Monograph applies to oxygen 93% produced in single-stage concentrators by absorption purification of ambient air using zeolites. It does not apply to gas produced using individual concentrators for domiciliary use.

Oxygen 93 is oxygen produced from air by molecular sieve process. Contains not less than 90.0% V/V and not more than 96% oxygen V/V, the remainder consists of mostly argon and nitrogen.

### Identification

Complies with the assay

Complies with the assay

### Production

<table>
<thead>
<tr>
<th>Assay</th>
<th>Specification</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO</td>
<td>$90.0 % \leq O_2 \leq 96.0 %$ V/V oxygen</td>
<td>Paramagnetic analyser</td>
</tr>
<tr>
<td>CO$_2$</td>
<td>$90.0 % \leq O_2 \leq 96.0 %$ V/V oxygen</td>
<td>Paramagnetic analyser</td>
</tr>
</tbody>
</table>

### Impurities

<table>
<thead>
<tr>
<th>CO</th>
<th>Limit</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\leq 5$ ppm V/V</td>
<td>Infrared analyser</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Detector tube</td>
</tr>
<tr>
<td>CO$_2$</td>
<td>Limit</td>
<td>Analytical method</td>
</tr>
<tr>
<td></td>
<td>$\leq 300$ ppm V/V</td>
<td>Infrared analyser</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Detector tube</td>
</tr>
<tr>
<td>H$_2$O</td>
<td>Limit</td>
<td>Analytical method</td>
</tr>
<tr>
<td></td>
<td>$\leq 67$ ppm V/V</td>
<td>Electrolytic hygrometer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not specified</td>
</tr>
</tbody>
</table>

### Odour

Limit | Analytical method |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No odour</td>
</tr>
</tbody>
</table>

### NO/NO$_2$

Limit | Analytical method |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemiluminescence analyser</td>
</tr>
<tr>
<td></td>
<td>Not specified</td>
</tr>
</tbody>
</table>

### SO$_2$

Limit | Analytical method |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UV Fluorescence analyser</td>
</tr>
<tr>
<td></td>
<td>Not specified</td>
</tr>
</tbody>
</table>

### Oil

Limit | Analytical method |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\leq 0.1$ mg/m$^3$</td>
</tr>
<tr>
<td></td>
<td>Detector tube</td>
</tr>
</tbody>
</table>

### Tests

<table>
<thead>
<tr>
<th>CO</th>
<th>Limit</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\leq 5$ ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No specific tests section</td>
</tr>
<tr>
<td>CO$_2$</td>
<td>Limit</td>
<td>Analytical method</td>
</tr>
<tr>
<td></td>
<td>$\leq 300$ ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No specific tests section</td>
</tr>
<tr>
<td>H$_2$O</td>
<td>Limit</td>
<td>Analytical method</td>
</tr>
<tr>
<td></td>
<td>$\leq 67$ ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No specific tests section</td>
</tr>
<tr>
<td>NO/NO$_2$</td>
<td>Limit</td>
<td>Analytical method</td>
</tr>
<tr>
<td></td>
<td>$\leq 2$ ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No specific tests section</td>
</tr>
<tr>
<td>SO$_2$</td>
<td>Limit</td>
<td>Analytical method</td>
</tr>
<tr>
<td></td>
<td>$\leq 1$ ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No specific tests section</td>
</tr>
<tr>
<td>Oil</td>
<td>Limit</td>
<td>Analytical method</td>
</tr>
<tr>
<td></td>
<td>$\leq 0.1$ mg/m$^3$</td>
<td>Detector tube</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No specific tests section</td>
</tr>
</tbody>
</table>
### Nitrous oxide

<table>
<thead>
<tr>
<th>Monograph</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Nitrous oxide</td>
<td>Nitrous oxide</td>
</tr>
<tr>
<td>Reference</td>
<td>01/2008:0416</td>
<td>Not specified</td>
</tr>
<tr>
<td>Chemical Formula</td>
<td>N₂O</td>
<td>N₂O</td>
</tr>
</tbody>
</table>

**Definition**

- Contains not less than 98.0% V/V of nitrous oxide in the gaseous phase, when sampled at 15°C. Nitrous oxide is produced from ammonium nitrate by thermic decomposition.

- Nitrous oxide contains not less than 99.0% V/V of nitrous oxide.

**Identification**

- Complies with the assay.
- Place a glowing splinter of wood in the substance to be examined. The splinter bursts into flame.
- Introduce the substance to be examined into alkaline pyrogallol solution R. A brown colour does not develop.

**Production**

<table>
<thead>
<tr>
<th>Assay</th>
<th>Assay</th>
<th>Analytical method</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥ 98.0% V/V nitrous oxide Measured in gas phase at 15°C</td>
<td>Infrared analyser</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤ 1.0% air indicating</td>
<td>Gas chromatography</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 99.0% V/V of nitrous oxide</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Impurities**

<table>
<thead>
<tr>
<th>Impurity</th>
<th>Limit</th>
<th>Method</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CO</td>
<td>≤ 5 ppm V/V</td>
<td>Gas chromatography</td>
<td>Detector tube</td>
</tr>
<tr>
<td>CO₂</td>
<td>≤ 300 ppm V/V</td>
<td>Gas chromatography</td>
<td>Detector tube</td>
</tr>
<tr>
<td>NO/NO₂</td>
<td>≤ 2 ppm V/V in total in the gaseous and liquid phases</td>
<td>Chemiluminescence analyser</td>
<td>Detector tube</td>
</tr>
<tr>
<td>H₂O</td>
<td>≤ 67 ppm V/V</td>
<td>Electrolytic hygrometer</td>
<td>Detector tube</td>
</tr>
<tr>
<td>NH₃</td>
<td>Not specified</td>
<td></td>
<td>Detector tube</td>
</tr>
<tr>
<td>Halogen</td>
<td>Not specified</td>
<td></td>
<td>≤ 1 ppm</td>
</tr>
</tbody>
</table>

**Tests**

<table>
<thead>
<tr>
<th>Impurity</th>
<th>Limit</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO</td>
<td>≤ 5 ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td>CO₂</td>
<td>≤ 300 ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td>NO/NO₂</td>
<td>≤ 2 ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td>H₂O</td>
<td>≤ 67 ppm V/V</td>
<td>Detector tube</td>
</tr>
</tbody>
</table>

No specific tests section
### 5.4 Nitrogen

<table>
<thead>
<tr>
<th>Monograph</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Nitrogen</td>
<td>Nitrogen</td>
</tr>
<tr>
<td>Reference</td>
<td>01/2008:1247</td>
<td>7727-37-9</td>
</tr>
<tr>
<td>Chemical formula</td>
<td>$N_2$</td>
<td>$N_2$</td>
</tr>
<tr>
<td>Definition</td>
<td>Nitrogen contains not less than 99.5% V/V of nitrogen.</td>
<td>Nitrogen contains not less than 99.0%, by volume of nitrogen</td>
</tr>
<tr>
<td>Identification</td>
<td>Retention time of peak with gas chromatography or - Place a glowing splinter of wood in the substance to be examined. The splinter is extinguished. or - Test with magnesium turnings</td>
<td>Extinguishing of burning wood splinter in a nitrogen test tube.</td>
</tr>
</tbody>
</table>

### Production

<table>
<thead>
<tr>
<th>Assay</th>
<th>Assay</th>
<th>≥ 99.5% V/V nitrogen</th>
<th>≤ 1.0% oxygen indicates ≥ 99.0% V/V of nitrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Gas chromatography</td>
<td>Gas chromatography</td>
<td></td>
</tr>
</tbody>
</table>

### Impurities

<table>
<thead>
<tr>
<th>CO</th>
<th>Limit</th>
<th>≤ 5 ppm V/V</th>
<th>≤ 0.001 % V/V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Infrared analyser</td>
<td>Detector tube</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CO₂</th>
<th>Limit</th>
<th>≤ 300 ppm V/V</th>
<th>Not specified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Infrared analyser</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>O₂</th>
<th>Limit</th>
<th>≤ 50 ppm V/V</th>
<th>≤ 1.0 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Oxygen analyser with electrochemical cell</td>
<td>Determined in assay</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>H₂O</th>
<th>Limit</th>
<th>≤ 67 ppm V/V</th>
<th>Not specified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Electrolytic hygrometer</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Odour</th>
<th>Limit</th>
<th>Not specified</th>
<th>No odour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td></td>
<td>Organoleptic</td>
<td></td>
</tr>
</tbody>
</table>

### Tests

<table>
<thead>
<tr>
<th>CO</th>
<th>Limit</th>
<th>≤ 5 ppm V/V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Detector tube</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CO₂</th>
<th>Limit</th>
<th>≤ 300 ppm V/V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Detector tube</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>H₂O</th>
<th>Limit</th>
<th>≤ 67 ppm V/V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Detector tube</td>
<td>No specific tests section</td>
</tr>
</tbody>
</table>
### 5.5 97% Nitrogen

<table>
<thead>
<tr>
<th><strong>Nitrogen 97%</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monograph</strong></td>
</tr>
<tr>
<td><strong>Name</strong></td>
</tr>
<tr>
<td><strong>Reference</strong></td>
</tr>
<tr>
<td><strong>Chemical formula</strong></td>
</tr>
<tr>
<td><strong>Definition</strong></td>
</tr>
<tr>
<td><strong>Identification</strong></td>
</tr>
</tbody>
</table>

#### Production

<table>
<thead>
<tr>
<th><strong>Assay</strong></th>
<th><strong>Analytical method</strong></th>
<th><strong>Limit</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Assay</td>
<td></td>
<td>≤ 3.0% oxygen indicates ≥ 97.0% V/V of nitrogen</td>
</tr>
<tr>
<td>Analysis</td>
<td>Gas chromatography</td>
<td></td>
</tr>
</tbody>
</table>

#### Impurities

<table>
<thead>
<tr>
<th><strong>CO</strong></th>
<th><strong>Limit</strong></th>
<th><strong>Analytical method</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 0.001 % V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>CO$_2$</strong></td>
<td><strong>Limit</strong></td>
<td><strong>Analytical method</strong></td>
</tr>
<tr>
<td></td>
<td>≤ 0.03 % V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>SO$_2$</strong></td>
<td><strong>Limit</strong></td>
<td><strong>Analytical method</strong></td>
</tr>
<tr>
<td></td>
<td>≤ 5 ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>NO/NO$_2$</strong></td>
<td><strong>Limit</strong></td>
<td><strong>Analytical method</strong></td>
</tr>
<tr>
<td></td>
<td>≤ 2.5 ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>O$_2$</strong></td>
<td><strong>Limit</strong></td>
<td><strong>Analytical method</strong></td>
</tr>
<tr>
<td></td>
<td>≤ 3.0 % V/V</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td><strong>Odour</strong></td>
<td><strong>Limit</strong></td>
<td><strong>Analytical method</strong></td>
</tr>
<tr>
<td></td>
<td>No odour</td>
<td>Organoleptic</td>
</tr>
</tbody>
</table>

#### Tests

<table>
<thead>
<tr>
<th><strong>Limit</strong></th>
<th><strong>Analytical method</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No specific tests section</td>
</tr>
</tbody>
</table>
5.6 Low oxygen nitrogen

<table>
<thead>
<tr>
<th>Monograph</th>
<th>Ph. Eur.</th>
<th>USP No equivalent US Pharmacopoeia monograph</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Nitrogen low oxygen</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>01/2008:1685</td>
<td></td>
</tr>
<tr>
<td>Chemical formula</td>
<td>N₂</td>
<td></td>
</tr>
<tr>
<td><strong>Definition</strong></td>
<td>This monograph applies to nitrogen which is used for inerting finished medicinal products which are particularly sensitive to degradation by oxygen. Does not necessarily apply to nitrogen used in earlier production steps of pharmaceutical manufacturing.</td>
<td></td>
</tr>
<tr>
<td><strong>Identification</strong></td>
<td>Examine the chromatograms obtained in the test for impurities. or - Flame of burning wood splinter in a nitrogen test tube/test with magnesium turnings.</td>
<td></td>
</tr>
<tr>
<td><strong>Production</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assay</td>
<td>Assay</td>
<td>≥ 99.5% V/V nitrogen</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td>Impurities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O₂ Limit</td>
<td>≤ 5 ppm V/V</td>
<td>Oxygen analyser with electrochemical cell</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td></td>
</tr>
<tr>
<td>Total impurities Limit</td>
<td>≤ 0.5% V/V</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td></td>
</tr>
<tr>
<td>Tests</td>
<td>Limit</td>
<td>No test section specified</td>
</tr>
<tr>
<td></td>
<td>Limit</td>
<td></td>
</tr>
</tbody>
</table>
### 5.7 Carbon dioxide

<table>
<thead>
<tr>
<th>Carbon dioxide</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Name</strong></td>
<td>Carbon dioxide</td>
<td>Carbon dioxide</td>
</tr>
<tr>
<td><strong>Reference</strong></td>
<td>01/2008:0375</td>
<td>Not specified</td>
</tr>
<tr>
<td><strong>Chemical Formula</strong></td>
<td>CO₂</td>
<td>CO₂</td>
</tr>
<tr>
<td><strong>Definition</strong></td>
<td>Carbon dioxide contains not less than 99.5% V/V carbon dioxide in gaseous phase.</td>
<td>Carbon dioxide contains not less than 99.0%, by volume of carbon dioxide</td>
</tr>
<tr>
<td><strong>Identification</strong></td>
<td>Infrared absorption spectrophotometry or - glowing wood splinter extinguished or - test with magnesium turnings</td>
<td>Carbon dioxide detector tube</td>
</tr>
<tr>
<td><strong>Production</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Assay</strong></td>
<td>Assay</td>
<td>Assay</td>
</tr>
<tr>
<td></td>
<td>≥ 99.5% V/V carbon dioxide</td>
<td>≥ 99.0% V/V of carbon dioxide</td>
</tr>
<tr>
<td><strong>Analytical method</strong></td>
<td>Infrared analyser</td>
<td>Determined with volumetric gas absorption apparatus</td>
</tr>
<tr>
<td><strong>Impurities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CO</strong></td>
<td>Limit</td>
<td>≤ 5 ppm V/V</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td></td>
<td>Limit</td>
<td>≤ 0.001% V/V</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>NO/NO₂</strong></td>
<td>Limit</td>
<td>≤ 2 ppm V/V in total (in gas phase)</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Chemiluminescence analyser</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NO ≤ 2.5 ppm (in gas phase)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NO₂ ≤ 2.5 ppm (in liquid phase)</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>Total Sulfur</strong></td>
<td>Limit</td>
<td>≤ 1 ppm V/V</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>UV fluorescence analyser</td>
</tr>
<tr>
<td><strong>H₂O</strong></td>
<td>Limit</td>
<td>≤ 67 ppm V/V</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Electrolytic hygrometer</td>
</tr>
<tr>
<td></td>
<td>Limit</td>
<td>≤ 150 mg/m³</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>NH₃</strong></td>
<td>Limit</td>
<td>Not specified</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Not specified</td>
</tr>
<tr>
<td></td>
<td>Limit</td>
<td>≤ 0.0025 % V/V</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>H₂S</strong></td>
<td>Limit</td>
<td>Not specified</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Not specified</td>
</tr>
<tr>
<td></td>
<td>Limit</td>
<td>≤ 1 ppm</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>SO₂</strong></td>
<td>Limit</td>
<td>Not specified</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Not specified</td>
</tr>
<tr>
<td></td>
<td>Limit</td>
<td>≤ 5 ppm</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>Tests</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CO</strong></td>
<td>Limit</td>
<td>≤ 5 ppm V/V</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>SO₂</strong></td>
<td>Limit</td>
<td>≤ 2 ppm V/V</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>H₂S</strong></td>
<td>Limit</td>
<td>≤ 1 ppm V/V</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>NO/NO₂</strong></td>
<td>Limit</td>
<td>≤ 2 ppm V/V</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Detector tube</td>
</tr>
<tr>
<td><strong>H₂O</strong></td>
<td>Limit</td>
<td>≤ 67 ppm V/V</td>
</tr>
<tr>
<td></td>
<td>Analytical method</td>
<td>Detector tube</td>
</tr>
</tbody>
</table>
# Medicinal air

<table>
<thead>
<tr>
<th>Monograph</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Air, Medicinal</td>
<td>Medical air</td>
</tr>
<tr>
<td>Reference</td>
<td>01/2009:1238</td>
<td>Not specified</td>
</tr>
</tbody>
</table>

**Chemical formula**

<table>
<thead>
<tr>
<th>Name</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Identification**

<table>
<thead>
<tr>
<th>Name</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compressed ambient air containing not less than 20.4 % V/V and not more than 21.4 % V/V of oxygen.</td>
<td>Natural or synthetic mixture consisting largely of nitrogen and oxygen, containing not less than 19.5% and not more than 23.5% V/V of oxygen.</td>
<td></td>
</tr>
</tbody>
</table>

**Production**

<table>
<thead>
<tr>
<th>Assay</th>
<th>Analytical method</th>
<th>Paramagnetic analyser</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assay</td>
<td>20.4%V/V ≤ oxygen ≤ 21.4 % V/V</td>
<td>19.5% V/V ≤ oxygen ≤ 23.5% V/V</td>
</tr>
</tbody>
</table>

**Impurities**

<table>
<thead>
<tr>
<th>Name</th>
<th>Limit</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO</td>
<td>≤ 5 ppm V/V</td>
<td>Infrared analyser</td>
</tr>
<tr>
<td>CO₂</td>
<td>≤ 500 ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td>SO₂</td>
<td>≤ 1 ppm V/V</td>
<td>UV fluorescence analyser</td>
</tr>
<tr>
<td>NO/N₂</td>
<td>≤ 2 ppm V/V in total</td>
<td>Chemiluminescence analyser</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name</th>
<th>Limit</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oil</td>
<td>≤ 0.1 mg/m³</td>
<td>Detector tube when oil lubricated compressor is used</td>
</tr>
<tr>
<td>H₂O</td>
<td>≤ 67 ppm V/V</td>
<td>No condensate on mirror</td>
</tr>
</tbody>
</table>

**Tests**

<table>
<thead>
<tr>
<th>Name</th>
<th>Limit</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO</td>
<td>≤ 5 ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td>CO₂</td>
<td>≤ 500 ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td>SO₂</td>
<td>≤ 1 ppm V/V</td>
<td>Detector Tube</td>
</tr>
<tr>
<td>NO/N₂</td>
<td>≤ 2 ppm V/V</td>
<td>Detector Tube</td>
</tr>
<tr>
<td>Oil</td>
<td>≤ 0.1 mg/m³</td>
<td>Detector Tube</td>
</tr>
<tr>
<td>H₂O</td>
<td>≤ 67 ppm V/V</td>
<td>Detector Tube</td>
</tr>
</tbody>
</table>

* Not required for synthetic air if so labelled
### 5.9 Synthetic medicinal air

<table>
<thead>
<tr>
<th><strong>Monograph</strong></th>
<th><strong>Ph. Eur.</strong></th>
<th><strong>USP</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Name</strong></td>
<td>Air, Synthetic Medicinal</td>
<td>No equivalent US Pharmacopoeia monograph specified, but covered by medical air</td>
</tr>
<tr>
<td><strong>Reference</strong></td>
<td>01/2008:1684</td>
<td></td>
</tr>
<tr>
<td><strong>Chemical formula</strong></td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

**Definition**

Gas mixture of nitrogen (Ph. Eur) and oxygen (Ph.Eur) containing between 95.0 % to 105.0 % of the nominal value which is between 21.0 % V/V to 22.5 % V/V of oxygen.

**Identification**

Complies with the assay
- glowing wood splinter not extinguished
- oxygen content tested by passing sample through potassium hydroxide/sodium dithionite solution.

**Production**

**Assay**

Containing between 95.0% to 105.0% of the nominal value which is between 21.0 % V/V to 22.5 % V/V of oxygen.

**Analytical method**

Paramagnetic analyser

**Impurities**

**H₂O**

Limit ≤ 67 ppm V/V

**Analytical method**

Electrolytic hygrometer

**Tests**

**H₂O**

Limit ≤ 67 ppm V/V

**Analytical method**

Detector tube
5.10 Helium

<table>
<thead>
<tr>
<th>Helium</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monograph</strong></td>
<td><strong>Ph. Eur.</strong></td>
<td><strong>USP</strong></td>
</tr>
<tr>
<td><strong>Name</strong></td>
<td>Helium</td>
<td>Helium</td>
</tr>
<tr>
<td><strong>Reference</strong></td>
<td>01/2008:2155</td>
<td>Not specified</td>
</tr>
<tr>
<td><strong>Chemical formula</strong></td>
<td>He</td>
<td>He</td>
</tr>
<tr>
<td><strong>Definition</strong></td>
<td>Helium contains not less than 99.5 % V/V of helium. Applies to helium obtained by separation from natural gas supplies.</td>
<td>Helium contains not less than 99.0 % V/V of helium</td>
</tr>
<tr>
<td><strong>Identification</strong></td>
<td>Complies with the assay</td>
<td>The flame of a burning splinter of wood is extinguished. A small balloon filled with helium shows decided buoyancy</td>
</tr>
</tbody>
</table>

### Production

<table>
<thead>
<tr>
<th>Assay</th>
<th>Specification</th>
<th>≥ 99.5 % V/V helium,</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical Method</td>
<td>Gas chromatography</td>
<td>Gas chromatography</td>
</tr>
</tbody>
</table>

### Impurities

<table>
<thead>
<tr>
<th>CH₄</th>
<th>Limit</th>
<th>≤ 50 ppm V/V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Infrared analyser</td>
<td>Not specified</td>
</tr>
<tr>
<td>O₂</td>
<td>Limit</td>
<td>≤ 50 ppm V/V</td>
</tr>
<tr>
<td>Analytical method</td>
<td>Electrochemical cell</td>
<td>Not specified</td>
</tr>
<tr>
<td>H₂O</td>
<td>Limit</td>
<td>≤ 67 ppm V/V</td>
</tr>
<tr>
<td>Analytical method</td>
<td>Electrolytic hygrometer</td>
<td>Not specified</td>
</tr>
<tr>
<td>CO</td>
<td>Limit</td>
<td>Not specified</td>
</tr>
<tr>
<td>Analytical method</td>
<td>Not specified</td>
<td>Detector tube</td>
</tr>
<tr>
<td>Air</td>
<td>Limit</td>
<td>Not specified</td>
</tr>
<tr>
<td>Analytical method</td>
<td>Not specified</td>
<td>Determined in the assay</td>
</tr>
<tr>
<td>Odour</td>
<td>Limit</td>
<td>Not specified</td>
</tr>
<tr>
<td>Analytical method</td>
<td>Not specified</td>
<td>Organoleptic</td>
</tr>
</tbody>
</table>

### Tests

<table>
<thead>
<tr>
<th>Limit</th>
<th>No tests section specified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>No tests section specified</td>
</tr>
</tbody>
</table>
### 5.11 Nitric oxide

<table>
<thead>
<tr>
<th>Monograph</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Nitric oxide</td>
<td>No equivalent US Pharmacopoeia monograph specified</td>
</tr>
<tr>
<td>Reference</td>
<td>01/2008:1550</td>
<td></td>
</tr>
<tr>
<td>Chemical Formula</td>
<td>NO</td>
<td></td>
</tr>
</tbody>
</table>

**Definition**
Nitric oxide contains not less than 99.0% V/V of nitric oxide.

**Identification**
Examine by infrared spectrometry and compare with the reference spectrum.

### Production

**Assay**

<table>
<thead>
<tr>
<th>Specification</th>
<th>≥ 99.0 % V/V nitric oxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Determine content of nitric oxide by difference using the mass balance equation after determining the sum of the impurities described under production.</td>
</tr>
</tbody>
</table>

### Impurities

<table>
<thead>
<tr>
<th></th>
<th>Limit</th>
<th>Analytical Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO₂</td>
<td>≤ 3000 ppm V/V</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td>N₂</td>
<td>≤ 3000 ppm V/V</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td>NO₂</td>
<td>≤ 400 ppm V/V</td>
<td>UV spectrophotometry analyser</td>
</tr>
<tr>
<td>N₂O</td>
<td>≤ 3000 ppm V/V</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td>H₂O</td>
<td>≤ 100 ppm V/V</td>
<td>Electrolytic hygrometer</td>
</tr>
</tbody>
</table>

### Tests

<table>
<thead>
<tr>
<th>Limit</th>
<th>Analytical Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>No tests section specified</td>
<td></td>
</tr>
</tbody>
</table>
## 5.12 Argon

<table>
<thead>
<tr>
<th>Monograph</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Argon</td>
<td>No equivalent US Pharmacopoeia monograph specified</td>
</tr>
<tr>
<td>Reference</td>
<td>07/2010:2407</td>
<td></td>
</tr>
<tr>
<td>Chemical Formula</td>
<td>Ar</td>
<td></td>
</tr>
</tbody>
</table>

### Definition
Gas obtained by cryogenic fractional distillation of ambient air. Argon contains not less than 99.995% v/v of argon calculated by deduction of the sum of impurities found when performing the test for impurities and water content.

### Identification
- Gas chromatography;
- Verify that the gas is not oxygen using a paramagnetic analyser.

### Production

<table>
<thead>
<tr>
<th>Assay</th>
<th>Specification</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥ 99.995 % V/V argon</td>
<td>Gas chromatography</td>
</tr>
</tbody>
</table>

### Impurities

<table>
<thead>
<tr>
<th>Impurities</th>
<th>Limit</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td>O₂</td>
<td>≤ 5 ppm V/V</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td>H₂O</td>
<td>≤ 10 ppm V/V</td>
<td>Electrolytic hygrometer</td>
</tr>
</tbody>
</table>

### Tests

<table>
<thead>
<tr>
<th>Limit</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td>No tests section specified</td>
<td></td>
</tr>
</tbody>
</table>
5.13 Carbon monoxide

<table>
<thead>
<tr>
<th>Carbon monoxide</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Carbon monoxide</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>01/2011:2408 corrected 7.2</td>
<td></td>
</tr>
<tr>
<td>Chemical Formula</td>
<td>CO</td>
<td></td>
</tr>
<tr>
<td>Definition</td>
<td>Gas obtained by steam reforming (catalytic oxidation) of hydrocarbons. Carbon monoxide contains not less than 99.5% V/V of carbon monoxide.</td>
<td></td>
</tr>
<tr>
<td>Identification</td>
<td>Infrared absorption spectrophotometry or it complies with the limits of the assay.</td>
<td></td>
</tr>
</tbody>
</table>

### Production

<table>
<thead>
<tr>
<th>Assay</th>
<th>Specification</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \geq 99.5 % \text{ V/V carbon monoxide} )</td>
<td>Infrared analyser</td>
</tr>
</tbody>
</table>

### Impurities

<table>
<thead>
<tr>
<th>Impurities</th>
<th>Limit</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO₂</td>
<td>( \leq 300 \text{ ppm V/V} )</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td>CH₄</td>
<td>( \leq 100 \text{ ppm V/V} )</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td>H₂</td>
<td>( \leq 300 \text{ ppm V/V} )</td>
<td>Gas chromatography</td>
</tr>
</tbody>
</table>

### Nickel tetracarbonyl / Iron pentacarbonyl

<table>
<thead>
<tr>
<th>Limit</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not detectable</td>
</tr>
</tbody>
</table>

### H₂O

<table>
<thead>
<tr>
<th>Limit</th>
<th>Analytical Method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Electrolytic Hygrometer</td>
</tr>
</tbody>
</table>

### Tests

<table>
<thead>
<tr>
<th>Limit</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No tests section specified</td>
</tr>
</tbody>
</table>
### Carbon monoxide intermix (5 per cent) in nitrogen

<table>
<thead>
<tr>
<th>Monograph</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Carbon monoxide intermix (5% in nitrogen)</td>
<td>No equivalent US Pharmacopoeia monograph specified</td>
</tr>
<tr>
<td>Reference</td>
<td>01/2018:2904</td>
<td></td>
</tr>
<tr>
<td>Chemical formula</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Definition</td>
<td>Mixture containing 5% carbon monoxide (2408) in Nitrogen, low-oxygen (1685)</td>
<td></td>
</tr>
<tr>
<td>Identification</td>
<td>Carry out tests - A and C or - B and C A - Infrared absorption spectrophotometry B - Complies with limits of assay C - Gas chromatography</td>
<td></td>
</tr>
<tr>
<td>Production</td>
<td>Assay 95.0 per cent to 105.0 per cent of the nominal value of carbon monoxide (CO) in nitrogen (N2). NOTE This can be considered as containing between 4.75 % and 5.25% carbon monoxide</td>
<td></td>
</tr>
<tr>
<td>Analytical method</td>
<td>Infrared analyser</td>
<td></td>
</tr>
<tr>
<td>Impurities</td>
<td>H₂O Limit</td>
<td>≤ 10 ppm V/V</td>
</tr>
<tr>
<td>Analytical method</td>
<td>Electrolytic hygrometer</td>
<td></td>
</tr>
<tr>
<td>Tests</td>
<td>Limit</td>
<td>No tests section specified</td>
</tr>
<tr>
<td>Analytical method</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## 5.15 Methane

<table>
<thead>
<tr>
<th><strong>Methane</strong></th>
<th><strong>Ph. Eur.</strong></th>
<th><strong>USP</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monograph</strong></td>
<td></td>
<td>No equivalent US Pharmacopoeia monograph specified</td>
</tr>
<tr>
<td><strong>Name</strong></td>
<td>Methane</td>
<td></td>
</tr>
<tr>
<td><strong>Reference</strong></td>
<td>01/2015:2413</td>
<td></td>
</tr>
<tr>
<td><strong>Chemical Formula</strong></td>
<td>CH₄</td>
<td></td>
</tr>
<tr>
<td><strong>Definition</strong></td>
<td>This monograph applies to methane obtained from natural gas and intended for medicinal use. Methane contains not less than 99.5% V/V of methane.</td>
<td></td>
</tr>
<tr>
<td><strong>Identification</strong></td>
<td>Gas chromatography obtained in the assay</td>
<td></td>
</tr>
</tbody>
</table>

### Production

<table>
<thead>
<tr>
<th><strong>Assay</strong></th>
<th><strong>Specification</strong></th>
<th><strong>Analytical method</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assay</strong></td>
<td>≥ 99.5 % V/V methane</td>
<td>Gas chromatography Using molecular sieve column</td>
</tr>
</tbody>
</table>

### Impurities

<table>
<thead>
<tr>
<th><strong>N₂</strong></th>
<th><strong>Limit</strong></th>
<th><strong>Analytical method</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Limit</strong></td>
<td>≤ 500 ppm V/V</td>
<td>Gas chromatography</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>C₂-C₄ Hydrocarbons</strong></th>
<th><strong>Limit</strong></th>
<th><strong>Analytical method</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Limit</strong></td>
<td>≤ 100 ppm V/V</td>
<td>Gas chromatography</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>H₂O</strong></th>
<th><strong>Limit</strong></th>
<th><strong>Analytical Method</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Limit</strong></td>
<td>≤ 10 ppm V/V</td>
<td>Electrolytic Hygrometer</td>
</tr>
</tbody>
</table>

### Tests

<table>
<thead>
<tr>
<th><strong>Limit</strong></th>
<th><strong>Analytical method</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No tests section specified</strong></td>
<td></td>
</tr>
</tbody>
</table>
### Methane intermix (2% per cent) in nitrogen

<table>
<thead>
<tr>
<th>Monograph</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Methane intermix (2%) in nitrogen</td>
<td>No equivalent US Pharmacopoeia monograph specified</td>
</tr>
<tr>
<td>Reference</td>
<td>01/2018:2905</td>
<td></td>
</tr>
<tr>
<td>Chemical formula</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Definition</td>
<td>Mixture containing 2% methane (2413) in nitrogen, low-oxygen (1685)</td>
<td></td>
</tr>
<tr>
<td>Identification</td>
<td>Carry out tests A or B</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A -</td>
<td>Complies with limits of assay</td>
</tr>
<tr>
<td></td>
<td>B -</td>
<td>Gas chromatography</td>
</tr>
</tbody>
</table>

#### Production

<table>
<thead>
<tr>
<th>Assay</th>
<th>95.0 per cent to 105.0 per cent of the nominal value of methane (CH4) in nitrogen (N2). NOTE This can be considered as containing between 1.9 % and 2.1% methane</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Gas chromatography</td>
</tr>
</tbody>
</table>

#### Impurities

<table>
<thead>
<tr>
<th>H₂O Limit</th>
<th>≤ 10 ppm V/V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Electrolytic hygrometer</td>
</tr>
</tbody>
</table>

#### Tests

<table>
<thead>
<tr>
<th>Limit</th>
<th>No tests section specified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>-</td>
</tr>
</tbody>
</table>
### Acetylene intermix (1 per cent) in nitrogen

<table>
<thead>
<tr>
<th>Monograph</th>
<th>Ph. Eur.</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Acetylene intermix (1% in nitrogen)</td>
<td>No equivalent US Pharmacopoeia monograph specified</td>
</tr>
<tr>
<td>Reference</td>
<td>01/2018:2903</td>
<td></td>
</tr>
<tr>
<td>Chemical formula</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

#### Definition
- Mixture containing 1% Acetylene in Nitrogen, low-oxygen (1685).
- The acetylene used in the manufacturing process is limited to acetylene produced by hydrolysis of calcium carbide.
- The method of storage of the acetylene is limited to cylinders filled with a porous mass and using acetone as a solvent.
- Prior to using the gas in the manufacturing process, the acetylene must be passed through an activated charcoal filter.

#### Identification
- Carry out tests - A or B
  - A - Complies with limits of assay
  - B - Gas chromatography

#### Production

<table>
<thead>
<tr>
<th>Assay</th>
<th>95.0 per cent to 105.0 per cent of the nominal value of acetylene (C2H2) in nitrogen (N2).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytical method</td>
<td>Gas chromatography</td>
</tr>
</tbody>
</table>

#### Impurities

<table>
<thead>
<tr>
<th>Substance</th>
<th>Limit</th>
<th>Analytical method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetone</td>
<td>≤ 5 ppm V/V</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td>AsH3</td>
<td>≤ 0.25 ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td>PH3</td>
<td>≤ 0.2 ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td>H2S</td>
<td>≤ 0.2 ppm V/V</td>
<td>Detector tube</td>
</tr>
<tr>
<td>H2O</td>
<td>≤ 10 ppm V/V</td>
<td>Electrolytic hygrometer</td>
</tr>
</tbody>
</table>

#### Tests
- No tests section specified

6.1 Oxygen

<table>
<thead>
<tr>
<th>Oxygen</th>
</tr>
</thead>
</table>
| Monograph | JP16  
| Name | Oxygen  
| Chemical Formula | O\textsubscript{2}  
| Definition | Oxygen is oxygen produced by the air liquefaction separation method. It contains not less than 99.5 v/v% of oxygen.  
| Description | Oxygen is a colourless gas under atmospheric pressure, and is odourless.  
| Identification | The retention time of principal peak obtained from oxygen is the same as that of the peak obtained from oxygen by gas chromatography.  

### Purity

| Nitrogen | Limit | The peak area of nitrogen in the oxygen is not larger than that of the control sample.  
| Analytical Method | Gas chromatography  

### Assay

| Specification | ≥ 99.5% vol of O\textsubscript{2}.  
| Analytical method | Volumetric gas absorption apparatus  

## Nitrous oxide

<table>
<thead>
<tr>
<th><strong>Monograph</strong></th>
<th>JP16</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Name</strong></td>
<td>Nitrous oxide</td>
</tr>
<tr>
<td><strong>Chemical Formula</strong></td>
<td>N₂O</td>
</tr>
<tr>
<td><strong>Definition</strong></td>
<td>Nitrous oxide contains not less than 97 vol% of nitrous oxide</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Nitrous oxide is a colourless gas at room temperature and at atmospheric pressure, and is odourless.</td>
</tr>
</tbody>
</table>
| **Identification** | 1. A glowing splinter of wood held in nitrous oxide: it bursts into flame immediately.  
2. The retention time of the main peak from nitrous oxide coincides with that of nitrous oxide by gas chromatography. |

### Purity

<table>
<thead>
<tr>
<th><strong>Acidity or alkalinity</strong></th>
<th>Limit</th>
<th>Colour of the test solution is not deeper than the reference solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analytical method</strong></td>
<td>Pass through acidified methyl red and bromothymol blue test solution in a Nessler tube. Compare colour against control solution</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Reducing Substances</strong></th>
<th>Limit</th>
<th>The colour is the same as the control solution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analytical method</strong></td>
<td>Pass through potassium permanganate solution in a Nessler tube. Compare colour against control solution</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Oxidising Substances</strong></th>
<th>Limit</th>
<th>The colour is the same as the control solution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analytical method</strong></td>
<td>Pass through potassium iodide-starch solution in a Nessler tube. Compare colour against control solution</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Chloride</strong></th>
<th>Limit</th>
<th>Turbidity produced does not exceed that produced in the control solution (can be calculated by the method)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analytical method</strong></td>
<td>Pass through silver nitrate solution in a Nessler tube. Compare turbidity against control solution</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>CO₂</strong></th>
<th>Limit</th>
<th>Turbidity produced does not exceed that produced in the control solution (can be calculated by the method)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analytical method</strong></td>
<td>Pass through barium hydroxide in a Nessler tube. Compare turbidity against control solution of barium hydroxide containing sodium hydrogen carbonate</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>CO</strong></th>
<th>Limit</th>
<th>No peak observed at the same retention time as that for carbon monoxide.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analytical method</strong></td>
<td>Gas chromatography</td>
<td></td>
</tr>
</tbody>
</table>

### Assay

<table>
<thead>
<tr>
<th><strong>Specification</strong></th>
<th>≥ 97.0 vol% of nitrous oxide</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analytical Method</strong></td>
<td>Gas chromatography</td>
</tr>
</tbody>
</table>
### 6.3 Carbon dioxide

<table>
<thead>
<tr>
<th>Carbon dioxide</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monograph</strong></td>
</tr>
<tr>
<td><strong>Name</strong></td>
</tr>
<tr>
<td><strong>Chemical Formula</strong></td>
</tr>
<tr>
<td><strong>Definition</strong></td>
</tr>
<tr>
<td><strong>Description</strong></td>
</tr>
</tbody>
</table>
| **Identification**             | 1. Put 100mL of carbon dioxide through a carbon dioxide measuring detector tube: the detector tube is changed to a stipulated colour tone by each detector tube, provided that the detector tube with an upper limit of measurement of not less than 10% is used.  
                                  | 2. Pass carbon dioxide into calcium hydroxide and a white precipitate is produced. Add acetic acid to the precipitate and it dissolves with effervescence. |

### Purity

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acidity</strong></td>
<td>Limit</td>
</tr>
<tr>
<td><strong>Analytical method</strong></td>
<td>The test solution is not more coloured than the control solution.</td>
</tr>
<tr>
<td></td>
<td>Pass through water in a Nessler tube and add methyl orange detector. Compare colour against control solution.</td>
</tr>
<tr>
<td><strong>Reducing Substances</strong></td>
<td>Limit</td>
</tr>
<tr>
<td><strong>Analytical method</strong></td>
<td>The turbidity is the same as the control solution.</td>
</tr>
<tr>
<td></td>
<td>Pass through silver nitrate solution in a Nessler tube. Compare turbidity against control solution.</td>
</tr>
<tr>
<td><strong>CO</strong></td>
<td>Limit</td>
</tr>
<tr>
<td><strong>Analytical method</strong></td>
<td>The concentration of carbon monoxide is less than 15 ppm according to each detector tube.</td>
</tr>
<tr>
<td></td>
<td>Carbon monoxide measuring detector tube</td>
</tr>
</tbody>
</table>

### Assay

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Specification</strong></td>
<td>≥ 99.5 vol% of carbon dioxide.</td>
</tr>
<tr>
<td><strong>Analytical method</strong></td>
<td>Volumetric gas absorption apparatus</td>
</tr>
</tbody>
</table>

* Reducing substances includes test for phosphine (PH₃) hydrogen sulphide (H₂S) and reducing organic substances.
### Nitrogen

<table>
<thead>
<tr>
<th><strong>Monograph</strong></th>
<th>JP16</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Name</strong></td>
<td>Nitrogen</td>
</tr>
<tr>
<td><strong>Chemical Formula</strong></td>
<td>N\textsubscript{2}</td>
</tr>
<tr>
<td><strong>Definition</strong></td>
<td>Nitrogen is the nitrogen produced by the air liquefaction separation method. It contains not less than 99.5 vol% of nitrogen.</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>Nitrogen is a colourless gas at room temperature and under atmospheric pressure, and is odourless.</td>
</tr>
<tr>
<td><strong>Identification</strong></td>
<td>The principal peak obtained from nitrogen has the same retention time with the peak from nitrogen by gas chromatography.</td>
</tr>
<tr>
<td><strong>Purity</strong></td>
<td></td>
</tr>
<tr>
<td>O\textsubscript{2} Limit</td>
<td>The peak area of oxygen obtained from nitrogen in the assay is not larger than 1/2 times that obtained from the standard gas mixture.</td>
</tr>
<tr>
<td>Analytical method</td>
<td>Gas chromatography</td>
</tr>
<tr>
<td><strong>Assay</strong></td>
<td></td>
</tr>
<tr>
<td>Specification</td>
<td>( \geq 99.5 \text{ vol}% ) of nitrogen.</td>
</tr>
<tr>
<td>Analytical method</td>
<td>Gas chromatography</td>
</tr>
</tbody>
</table>