MEDICINAL OXYGEN
(OXYGENIUM MEDICINALIS)

Draft proposal for revision in The International Pharmacopoeia
(October 2021)

INTERIM VERSION FOR SUBMISSION TO EXPERT COMMITTEE
ON SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS

This document is placed on the WHO Medicines website (https://www.who.int/teams/health-product-and-policy-standards/standards-and-specifications/pharmaceuticals/current-projects). Contact information: Dr Herbert Schmidt, Technical Officer, Norms and Standards for Pharmaceuticals, Technical Standards and Specifications (schmidt@who.int), with a copy to Ms Sinead Jones (jonessi@who.int).

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### SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/20.867:

**MEDICINAL OXYGEN**

(OXYGENIUM MEDICINALIS)

<table>
<thead>
<tr>
<th>Description</th>
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<tr>
<td>Revision drafted following internal discussions.</td>
<td>December 2020</td>
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<tr>
<td>Draft proposal sent out for public consultation.</td>
<td>December 2020 - February 2021</td>
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<tr>
<td>Revision 1 drafted following the review of comments received during the first public consultation.</td>
<td>April 2021</td>
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<tr>
<td>Discussion at the Consultation on Screening Technologies, Laboratory Tools and Pharmacopoeias Specifications for Medicines.</td>
<td>May 2021</td>
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<tr>
<td>Feedback on revision 1 sought from colleagues within WHO.</td>
<td>June 2021</td>
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<tr>
<td>Feedback on revision 1 sought from Experts attending the Consultation on Screening Technologies, Laboratory Tools and Pharmacopoeias Specifications for Medicines in May 2021.</td>
<td>June 2021</td>
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<tr>
<td>Revision 2 drafted following the review of comments received on revision 1.</td>
<td>July 2021</td>
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<td>Revision 2 discussed at a virtual meeting with a group of Experts.</td>
<td>July 2021</td>
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<tr>
<td>Revision 2 discussed at a virtual meeting with a group of clinical experts (including respiratory therapists, anaesthesiologist and paediatricians).</td>
<td>July 2021</td>
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<tr>
<td>Draft revision 2 sent out for public consultation.</td>
<td>July – September 2021</td>
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<tr>
<td>Revision 3 drafted based on the comments received during the public consultation.</td>
<td>September 2021</td>
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<tr>
<td>Discussion at the Follow-Up Consultation on Screening Technologies, Laboratory Tools and Pharmacopeial Specifications for Medicines. Agreement on an interim version (Rev 4) of the monograph.</td>
<td>29 September 2021</td>
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</table>
[Note from the Secretariat. With the revision of the monograph on Oxygen, it is intended:

- to clarify that WHO Member States, considering options for increasing the supply of medicinal oxygen to treat COVID-19 and other patients, can safely apply oxygen generated by:
  - Oxygen Generation Plants, which use Pressure Swing Adsorption (PSA) or Vacuum Swing Adsorption (VSA) technologies to generate 90 to 96% pure oxygen, referred to in the draft revision as “Oxygen 93%”; and/or
  - Air Separation Units, which use cryogenic technology to generate 99.5% pure oxygen, referred to in the draft revision as “Oxygen 99.5%”, and
- to define quality requirements for these two products.

The monograph is being revised following the Procedure for the elaboration, revision and omission of monographs and other texts for The International Pharmacopoeia (WHO Technical Report Series, no. 1025, Annex 1). Draft versions of the monograph were sent out for public consultation twice and the comments received were discussed and included, if appropriate.

The monograph was lastly discussed at the Follow-Up Consultation on Screening Technologies, Laboratory Tools and Pharmacopeial Specifications for Medicines (29 September 2021). The Experts reviewed the comments received during the second public consultation and agreed upon an interim version of the monograph, which will be submitted to the next meeting of the Expert Committee on Specifications for Pharmaceutical Preparations. The Experts recommended that the interim version shall be submitted to the Committee for possible adoption.

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1 Interim guidance Technical specifications for Pressure Swing Adsorption (PSA) Oxygen Plants
Note that the draft proposal for revision shall replace the existing monograph on Oxygen.

For more information on oxygen, please visit the following websites:

- Oxygen health topic page.
MEDICINAL OXYGEN
(OXYGENIUM MEDICINALIS)

Molecular formula. O₂

Relative molecular mass. 32.00


Description. A colourless gas.

Category. Gas for inhalation.

Additional information. Oxygen is mentioned in the current *WHO Model list of essential medicines* (EML) and in the *EML for Children*.

This monograph does not apply to gas produced using portable concentrators for home care or bedside use².

Definition. Medicinal oxygen is Oxygen 93% or Oxygen 99.5%. It is applied in combination with ambient or compressed air of a suitable quality or in pure form, depending on the clinical medical necessity.

OXYGEN 93%

Requirements

Definition. Oxygen 93% contains not less than 90.0% and not more than 96.0% (v/v) of O₂, the remainder mainly consisting of argon and nitrogen.

Production. Oxygen 93% is produced from ambient air by pressure swing adsorption (PSA) or vacuum swing adsorption (VSA). During production, the oxygen content is continuously

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monitored. The production method is validated to demonstrate that Oxygen 93% complies
with the following limits: carbon dioxide: maximum 300 ppm (v/v); carbon monoxide:
maximum 5 ppm (v/v); nitrogen monoxide and nitrogen dioxide: maximum 2 ppm (v/v) in total;
sulfur dioxide: maximum 1 ppm (v/v); oil: maximum 0.1 mg/m$^3$; water: maximum 67 ppm (v/v)
and that viable and non-viable particulates are eliminated or minimized and adequately
controlled in the product.

Identity test. Carry out the test as described under “Assay”. The sample gas complies with
the limit. The paramagnetic signal exhibited confirms the presence of oxygen.

Carbon monoxide. Determine the content using a carbon monoxide detector tube according
to the manufacturer’s instruction. Pass the required volume of the test gas through the tube and
read the value corresponding to the length of the coloured layer or the intensity of the colour
on the graduated scale; not more than 5 ppm (v/v).

Carbon dioxide. Determine the content using a carbon dioxide detector tube according to the
manufacturer’s instruction. Pass the required volume of the test gas through the tube and read
the value corresponding to the length of the coloured layer or the intensity of the colour on the
graduated scale; not more than 300 ppm (v/v).

Water. Determine the content using a water vapour detector tube according to the
manufacturer’s instruction; not more than 67 ppm (v/v).

Assay. Determine the percentage content of Oxygen (O$_2$) using a paramagnetic analyser which
electronically measures the molecule's interaction with magnetic fields.

Impurities

A. CO$_2$, carbon dioxide;
B. CO, carbon monoxide;
C. Water.
OXYGEN 99.5%

Requirements

Definition. Oxygen 99.5% contains not less than 99.5% (v/v) of \( \text{O}_2 \).

Production. Oxygen 99.5% is produced from ambient air by cryogenic distillation.

The production method is validated to demonstrate that Oxygen 99.5% complies with the following limits: carbon dioxide: maximum 300 ppm (v/v), carbon monoxide: maximum 5 ppm (v/v), water: maximum 67 ppm (v/v).

Identity test. Carry out the test as described under “Assay”. The sample gas complies with the limit. The paramagnetic signal exhibited confirms the presence of oxygen.

Water. Not more than 67 ppm (v/v) determine by water vapor detector tube or electrolytic hygrometer.

Assay. Determine the percentage content of Oxygen (\( \text{O}_2 \)) using a paramagnetic analyser which electronically measures the molecule's interaction with magnetic fields.

Impurities

A. Water.

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