World Health Organization

MEDICINAL OXYGEN

(OXYGENIUM MEDICINALIS)

Draft proposal for revision in *The International Pharmacopoeia*

(July 2021)

DRAFT FOR COMMENTS

Please send any comments you may have on this draft working document to **Dr Herbert Schmidt**, Technical Officer, Norms and Standards for Pharmaceuticals, Technical Standards and Specifications (schmidth@who.int), with a copy to Ms Sinead Jones (jonessi@who.int) by **10 September 2021**.

Our working documents are sent out electronically and they will also be placed on the WHO Medicines website (https://www.who.int/teams/health-product-and-policy-standards/standards-and-specifications/pharmaceuticals/current-projects) for comments under the "*Working documents in public consultation*" link. If you wish to receive our draft guidelines, please send your e-mail address to jonessi@who.int and your name will be added to our electronic mailing list.

SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/20.867:

MEDICINAL OXYGEN

(OXYGENIUM MEDICINALIS)

Description	Date
Revision drafted following internal discussions.	December 2020
Draft proposal sent out for public consultation.	December 2020 - February 2021
Revision 1 drafted following the review of comments received during the first public consultation.	April 2021
Discussion at the Consultation on Screening Technologies, Laboratory Tools and Pharmacopoeias Specifications for Medicines.	May 2021
Feedback on revision 1 sought from colleagues within WHO.	June 2021
Feedback on revision 1 sought from Experts attending the Consultation on Screening Technologies, Laboratory Tools and Pharmacopoeias Specifications for Medicines in May 2021.	June 2021
Revision 2 drafted following the review of comments received on revision 1.	July 2021
Revision 2 discussed at a virtual meeting with a group of Experts.	July 2021
Revision 2 discussed at a virtual meeting with a group of clinical experts (including respiratory therapists, anaesthesiologist and paediatricians)	July 2021
Draft revision 2 sent out for public consultation.	July – September 2021
Presentation at the 56th meeting of the Expert Committee on Specifications for Pharmaceutical Preparations.	TBD

Further follow-up action as required.	

[Note from the Secretariat. *It is intended to revise the monograph on Oxygen in* The International Pharmacopoeia:

- *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 and concentrators, 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% pure oxygen, referred to in the draft revision as "Oxygen 99%"; and*
- *to define quality requirements for these products.*

Following discussions of the comments received during the public consultation of the draft proposal for revision and during subsequent meetings, a second revision of the draft proposal is presented for comments. The Secretariat sincerely thanks all reviewers for their valuable comments and invites all interested parties to also review the updated version of the working document.

All comments submitted using the dedicated comment form sheet and received by the above deadline will be considered in the preparation of the final version of the revision.

The form sheet for comments can be found here.

Note that the draft proposal for revision shall replace the existing monograph on Oxygen.]

MEDICINAL OXYGEN
(OXYGENIUM MEDICINALIS)

O_2

Relative molecular mass. 32.00

Chemical name. Oxygen; CAS Reg. No. 7782-44-7.

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 concentrators for home care or bedside use[1].

Definition. Medicinal oxygen is Oxygen 93% or Oxygen 99%. It is applied in combination with ambient or compressed air of a suitable quality or in pure form depending on the clinical medical necessity. *[**Note from the Secretariat**. The Secretariat is aware of discussions regarding the use of oxygen produced of ambient air by **double** stage pressure/vacuum swing adsorption (PSA/VSA) oxygen-generating plants for respiratory care. We will follow the discussions and amend the monograph, when necessary.]*

[1] Specifications for concentrators for home care or bedside use can be found in: WHO-UNICEF technical specifications and guidance for oxygen therapy devices. Geneva: World Health Organization and the United Nations Children's Fund (UNICEF), 2019 (WHO medical device technical series), (https://www.who.int/medical_devices/publications/tech_specs_oxygen_therapy_devices/en/), accessed 3 December 2020.

OXYGEN 93%

Requirements

Definition. Oxygen 93% contains not less than 90.0% and not more than 96.0% (v/v) of O_2, the remainder mainly consisting of argon and nitrogen.

Production. Oxygen 93% is produced of ambient air by pressure/vacuum swing adsorption (PSA/VSA) oxygen-generating plants. During production, the oxygen content is continuously monitored by a paramagnetic analyser. 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 10 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 10 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).

Assay. Determine the percentage content of Oxygen (O_2) using a paramagnetic analyser which measures electronically the molecule's interaction with magnetic fields.

Impurities

A. CO_2, carbon dioxide.

B. CO, carbon monoxide.

OXYGEN 99%

Requirements

Definition. Oxygen 99% contains not less than 99.0% (v/v) of O_2.

Production. Oxygen 99% is produced of ambient air by cryogenic distillation.

The production method is validated to demonstrate that Oxygen 99% complies with the following limits: carbon dioxide: maximum 300 ppm (v/v), carbon monoxide: maximum 10 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.

Assay. Determine the percentage content of Oxygen (O_2) using a paramagnetic analyser which measures electronically the molecule's interaction with magnetic fields.

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