Macedonian pharmaceutical bulletin, **70** (2) 47 - 55 (2024)
ISSN: 1857-8969
DOI: 10.33320/maced.pharm.bull.2024.70.02.007
Professional paper

Medical oxygen: quality assurance and quality control practices for safe and effective application

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Received: January 2025; Accepted: February 2025

Abstract

Medicinal oxygen (MOX) is an essential medicine listed on the World Health Organization's (WHO's) List of Essential Medicines for acutely ill individuals and for people with chronic diseases resulting in hypoxemia. Safe administration of MOX implies that internationally recognized quality standards are followed from production to final use at the medical facilities. The aim of this article is to present an overview of some of the most important quality assurance practices for production, storage and transportation of MOX to medical facilities as well as to patients, and the pharmacopeial requirements for the quality of this medicinal product.

Strict regulations and requirements are set by the European Pharmacopoeia (Ph. Eur) and by the United States Pharmacopoeia (USP), organizations that specify MOX purity in order to meet highest healthcare standards and to ensure that patients receive high quality product free of harmful impurities.

Key words: medicinal oxygen, quality assurance, quality control, healthcare safety

Introduction

Medicinal gases are gases or mixtures of gases with known concentrations and purity intended for direct use in humans or animals for therapeutic purposes (Carnero and Gomez, 2019). They can be used as active ingredients in medicinal products, as excipients in the production of medicinal gas mixtures, or as pharmaceutical gases used in the manufacture, storage, or distribution of all medicinal products (EIGA 152/23, 2023). One of the most commonly administered medicinal gases is oxygen (O2), an essential medicine included in the WHO Model List of Essential Medicines (EML) since 1979 and an essential medicine in the first WHO Model List of Essential Medicines for Children (EMLc, 2007) (Bakare et al., 2020). Oxygen therapy is among the most commonly used medicinal treatments for acutely ill patients (Mart et al., 2022). It is also necessary for newborns, children with respiratory illnesses, vulnerable groups such as elderly and pregnant women as well as for surgery and trauma patients. It has been the critical component of the medicinal treatment during the COVID-19 pandemic (Bhat et al., 2023; WHO, 2023).

The sources of O_2 for low- and middle-income countries settings include bulk-stored liquid oxygen (LOX) produced by large air separation units (ASUs) in a process based on cryogenic fractional distillation and oxygen concentrators that use technologies like pressure swing adsorption (PSA) and vacuum swing adsorption (VSA) (Bhat et al., 2023; USAID MTaPS, 2023). These techniques are expensive and require intensive maintenance. In recent years, more economical methods have been developed such as Integrated Energy Systems

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(IES) and Ion Transport Membranes (ITM), which can produce large volumes of high purity O_2 (> 99.5%) at low costs (Bhat et al., 2023; Kadam et al., 2021). Regardless the production technique used, MOX must be sourced from approved suppliers, meet defined quality standards and be used appropriately under the oversight of qualified healthcare professionals to ensure that the product supplied to healthcare facilities is safe and effective (WHO, 2023).

Quality assurance (QA) is an aspect of quality management focused on providing confidence that quality requirements will be continuously fulfilled. It gives suppliers a means of ensuring that their products consistently meet specified quality requirements and helps consumers trust that the products supplied will measure up to quality parameters (ISO, 2015). The purpose of QA in MOX production, storage, and delivery is to ensure that the product used by the patient is safe, effective and it meets specified quality standards (WHO, 2023). Therefore, the aim of this article is to provide an overview of some of the most important QA practices as well as quality control (QC) requirements applied through the entire life cycle of MOX, from the time it leaves the production unit up to the point of patient use, in order to achieve highest product quality and patient safety.

MO production methods, transport and storage requirements and delivery to the patient

Production methods

MOX is commercially manufactured in large volumes by fractional distillation of liquid air (cryogenic separation) and oxygen concentrators, devices that pass air through molecular sieves of zeolite (Westwood and Rieley, 2015). The selection of suitable production source (and storage method depends) on several factors, the most important in the medicinal field being the supply chain and the amount of O_2 needed at the treatment facility (WHO, 2019).

The cryogenic separation is a technology/process for obtaining high purity LOX at large production rates (approximately 5000 tons per day) (Bhat et al., 2023; Jha and Gaur, 2022). It takes place in so called Air Separation Units (ASUs) that can produce not only O_2, but also nitrogen and argon with different grades of purity, at cryogenic temperatures lower than -150 ºC. Air is first filtered to remove impurities and then cooled to - 200 ºC. Carbon dioxide freezes at -79 ºC and is discarded at this point, but oxygen only liquefies at -183 ºC. At -200 ºC, the liquid air (now free of carbon dioxide) is passed into the bottom of a fractioning column, which is warmer at the bottom (-185 ºC) than it is at the top (-195 ºC). Liquefied nitrogen (nitrogen liquefies at -195 ºC) boils, returns to its gaseous form, and exits via the top of the column leaving LOX and argon. These gases have similar boiling points and, therefore, another fractioning is required in order to produce pure O_2. LOX produced in an ASU account for up to 99% purity, thereby making it particularly suitable for medicinal use (Bhat et al., 2023; USAID MTaPS, 2023).

Oxygen concentrators (OC) are devices for extracting O_2 from atmospheric air. They range in size from small portable units to large ones capable of supplying entire hospitals. The process of O_2 production is based on different technologies such as VSA, membrane gas separation, and PSA and produces oxygen that is up to 96% pure. When the O_2 they produce is used for medicinal applications, it must contain no less than 90% and no more than 96%, and this product is referred to as Oxygen 93 on pharmacopoeia monographs (EIGA 152/18). OC are useful in the community where lower flows of 2-4 L/minute O_2 are required. However, modern OC units can achieve flows as high as 10 L/minute. The main drawback is the fact that its output could be insufficient to meet MOX demand during the busiest hospital hours, even at maximum flow (Paul et al., 2020).

Storage and transportation

After production, MOX can be transported in its liquid and gaseous states, with each form requiring varying degrees of supportive infrastructure. Liquid MOX is the best way of storing large volumes of O_2 (Blakeman and Branson, 2013). One-liter liquid O_2 provides approximately 860 L of gaseous O_2, making this the most efficient system of transportation and storage (Blakeman & and Branson, 2013; Hardavela et al., 2019). Hospitals typically rely on large liquid MOX supplies as their primary source (Jain and Sharma, 2022). Liquid MOX can be moved great distances using “ISOtainers” on ships, trains, or trailer trucks, or it can be transported in purpose-built tanker trucks if road conditions allow for safe passage. In cases when the manufacturer is transporting its own product, the wholesaler or distributor will be responsible for maintaining the integrity of the product (USAID MTaPS, 2023).

The use of liquid MOX at a healthcare facility requires on-site storage. When this product is delivered in certified tankers to the facility (the end-user), it is transferred to cryogenic tanks, which supply it to the piped system of the healthcare facility by self-vaporization. This process is needed to move MOX to the patients. Strict quality requirements must be fulfilled before distribution.

Delivery to the patient

The delivery to the patient is the final stage in the lifecycle of MOX. Delivery interface products are typically single-use, and thus facilities do not need to consider their longer-term maintenance. However, they need to ensure that all medical devices are registered in the country and that stock is appropriately managed within the facility, typically by the pharmacy.

Quality systems framework for MOX

Quality systems framework for MOX covers with the application of the principles of Good Manufacturing

Practice (GMP), Quality Assurance (QA), and Quality Control (QC) and are governed by strict regulatory standards (USAID MTaPS, 2023).

Regulatory requirements for MOX

Most countries have a National Regulatory Agency (NRA) and/or a registration process for medicines whereby local laws and regulations must be followed. However, many NRAs do not have a clear framework for the regulation of medicinal gases, including MOX, which would typically cover:

- Quality control of oxygen as a medicine along the entire supply chain;
- Certification of manufacturers for compliance with GMP;
- Enforcement of MOX distributors and suppliers' compliance with a quality management system, including good distribution practices (GDP) and the application of vigilance principles;
- Provision of tools for the application and assessment of QA compliance for medicinal gases.

When a NRA does not possess a quality framework for MOX, stringent standards and existing guidelines from well-established regulatory agencies should be accepted and implemented.

Good Manufacturing Practices (GMPs) and MOX – GMPs describe the minimum standard that a medicines manufacturer must meet in their production processes. In order to verify the compliance with the GMP, regulatory authorities can perform various inspections at the manufacturer's site. The main aim of the GMPs is continued safe production of medicines, including the medicinal gases. There are number of documents regarding the application of GMPs in the production of medicinal gases, including MOX. The European Commission's (EC) GMP recognizes differences between the manufacture of medicinal gases and that of more traditional pharmaceutical products. The manufacture and handling of medicinal gases in hospital (such as with PSA or VSA) falls outside the scope of the WHO's and EC's GMP guidance documents. Nevertheless, relevant GMP principles should be applied to the facility-level manufacture and distribution of MOX. As with any medicine, the manufacturing process for MOX must be clearly defined, validated, and systematically reviewed to ensure that it can consistently produce high quality oxygen.

Application of GMP principles to the production of MOX within a hospital should consider the following: personnel; premises and equipment; source-specific requirements (including on site production); transportation and storage; documentation and record keeping; quality control; complaints and recalls; and self-auditing (WHO, 2022; EudraLex, 2011; EIGA, "DOC 99/15/Part 1, 2015).

Quality control of MOX and overview of pharmacopeial requirements and methods of analysis

The production process for O_2 is complex, involving both specialized medical equipment and industrial enterprises. It takes place in a controlled environment with clean, filtered air and extremely precise management of the process. Air quality, temperature and humidity are closely monitored parameters. This clean environment is the first essential step to ensure the O_2 produced is as safe as possible.

Quality control of MOX is a very important task. MOX is very often supplied to medical institutions mainly in reusable containers and cylinders, both in gaseous and liquid form. Since the containers are used for filling repeatedly, there is a high probability of MOX quality deterioration in a particular vessel used in a hospital, and not in the entire batch of oxygen (Galeeva et al., 2024).

Depending on the source and production method, MOX may have different O_2 content. As per the requirements of the International Pharmacopoeia, European Pharmacopoeia, or US Pharmacopoeia, oxygen for medicinal use, obtained by the method of cryogenic distillation of air, must contain at least 99.5%. Oxygen concentrators must provide a continuous supply of pure and concentrated oxygen at a low flow rate, with a content of at least 82%. In addition to the requirements for quantitative oxygen content for MOX as per the monograph: Oxygen (not less than 99.5% *v/v* oxygen) and Oxygen 93 (not less than 90.0-96.0 % *v/v* oxygen), there are also requirements for the impurities content, such as carbon monoxide (less than 0.0005%), carbon dioxide (less than 0.0100%), water (less than 0.0067%) (Ph. Eur 11.5; USP40, NF35, 2024).

Each monograph in the relevant Pharmacopoeias, defines the specification of MOX, including the:

- Assay of the product;
- Maximum allowable impurity levels for those contaminants specified in the product;
- Approved analytical method for identification of the gas;
- Approved analytical method for assay determination;
- Approved analytical test method for determination of each contaminant specified within the monograph.

Test methods provided in the Ph. Eur monographs, must be verified against the protocols set in the ICH Guidelines for accuracy, precision, linearity and range, and specificity. The results need to conform to the requirements of repeatability and peak symmetry. Different alternative methods validated according to the requirements of the ICH guidelines that demonstrate equivalency to the compendial methods can also be used (EIGA 152/23, 2023).

The methods used for QC of MOX (O_2 content and impurities content) are specially designed for gas analysis and have certain advantages and disadvantages. Regardless the method used, the accuracy of the results is highly dependent on the experience of the operator and the quality of reagents and utensils (Galeeva et al., 2024).

Table 1 provides a comparison between Ph. Eur and US Pharmacopoeia monographs for MOX (Oxygen, not less than 99.5% *v/v* oxygen). As it can be seen, the specified test methods fall into two categories, tests intended for the manufacturer and tests intended for the end (final user). As it can be seen from Table 1, USP specifies only one test method for the analysis of MOX. Unlike Ph. Eur monograph which specifies the tests that should be performed at the manufacturers as well as at the end user, USP specifies only the test methods intended for the manufacturer (EIGA 152/23, 2023).

The Pharmacopoeia test methods for MOX analysis, due to their unique nature, their principle and some of their characteristics, are presented in Table 2.

To control the content of impurities, besides the IR analyzers, qualitative reactions which are performed using gas detection tubes, simple and effective method for measuring the concentration of specific gases. They consist of a sealed glass tube filled with a reagent that reacts with the target gas, causing a color change that is proportional to the gas concentration (EIGA 152/23; Kawamura, 2021). There are two main types of gas detector tubes. Monolayer tubes contain a single reagent for detecting one impurity, while multilayer tubes contain multiple reagents to detect multiple substances. During operation, a known volume of the gas is passed through the tube using a pump. The reagents react with the target gas, causing a visible color change. The length or intensity of this color change is measured against a graduated scale to determine the impurity's concentration. Although convenient, they lack the precision of more advanced techniques (EDQM, 2022).

Table 1. Ph. Eur and US Pharmacopoeia monograph comparison for MOX Oxygen, not less than 99.5% *v/v* oxygen)

	Oxygen		
	Monograph*	Ph. Eur	USP
	Name	Oxygen	Oxygen
	Reference	01/2010:0417	Not specified
	Chemical formula	O_2	O_2
	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 air liquefaction is exempt from the requirements of carbon monoxide and carbon dioxide
	Identification	Complies with the assay	Complies with the assay
Tests intended for the manufacturer			
Assay	Specification	≥ 99.5% *v/v* oxygen	≥ 99.0% *v/v* oxygen
	Analytical method	Paramagnetic analyzer	Paramagnetic analyzer
Impurities			
CO	Limit	≤ 5 ppm *v/v*	≤ 0.001% *v/v*
	Analytical method	Infrared analyzer	Detector tube
CO_2	Limit	≤ 300 ppm *v/v*	≤ 0.03% *v/v*
	Analytical method	Infrared analyzer	Detector tube
H_2O	Limit	≤ 67 ppm *v/v*	Not specified
	Analytical method	Electrolytic hygrometer	
Test intended for the end user			
CO	Limit	≤ 5 ppm *v/v*	Not specified
	Analytical method	Infrared analyzer	
CO_2	Limit	≤ 300 ppm *v/v*	
	Analytical method	Infrared analyzer	
H_2O	Limit	≤ 67 ppm *v/v*	
	Analytical method	Detector tube	

*Ph. Eur 11.5 (2023); USP40 NF35 (2017)

Table 2. General test methods for the analysis of medicinal oxygen (MOX)

Specification parameter	Test method	Principle
Oxygen content	Paramagnetic analyzer	Principle: Use of the paramagnetic properties of O_2 molecules which are drawn by the magnetic field into the area of greatest field strength (Jasek et al., 2022); Sophisticated and sensitive technique Must be performed by the manufacturer
Impurities content		
CO	Absorption spectrophotometry, infrared	Principle: Gases can absorb the energy of specific wavelengths of infrared light; the amount of radiation absorbed at these wavelengths is directly proportional to the concentration of CO in the sample; Interferences are removed by a filter fitted in the apparatus; Must be performed by the manufacturer
CO_2	Absorption spectrophotometry, infrared	Principle: The same as for *CO*; Some analyzers utilize a reference cell that contains a known amount of CO_2 for comparison, while others employ electronic systems; Interferences are removed by a filter Must be performed by the manufacturer of MOX
Water content	Electrolytic hygrometer	Principle: electrolysis The devices utilize a cell coated with a thin film of P_2O_5, which absorbs water from the gas under measurement. When an electrical potential is applied to the electrodes and incorporated in the measurement cell, the water vapor absorbed by the P_2O_5 is dissociated into hydrogen and oxygen molecules, generating a current; The resulting current is a measure of the sample's moisture content. The amount of current required to dissociate the water is proportional to the number of water molecules in the gas sample (Korotchenkov, 2019); Must be performed by the manufacturer

Table 3. United nations (UN) transport product classification for oxygen

Oxygen, compressed gas	Oxygen, cryogenic liquid
Product name: oxygen, compressed	Product name: oxygen, refrigerated liquid
Safety conditions: oxidizing substance, non-flammable gas	Safety conditions: oxidizer, non-flammable gas
UN ID Number: UN1072	UN ID Number: UN1073
Risk identification/hazard class: 2.2	Risk identification/hazard class: 2.2

The use of gas analyzers based on the paramagnetic effect of oxygen or IR absorption allows one to accurately determine the analyzed components. However, their use requires several sensors for each component to be determined separately, and does not allow detection of other possible undeclared components in oxygen as well as unspecified impurities (Galeeva et al., 2024).

Storage - Oxygen (Oxygen, not less than 99.5% *v/v* oxygen) should be stored in a vacuum-insulated bulk storage tank made of stainless steel that is cleaned for MOX service and equipped with unique connection fittings to avoid cross contamination while filling. Tanks must be positioned outside, at a safe minimum distance from nearby buildings, services, or identified hazards, in accordance with the national guidelines. Stored O_2 is always at pressure. Thus, pressures must always be reduced through pressure regulation devices for safe distribution and/or administration to patients.

Shelf life - Oxygen, as a stable element, has been recognized to have a long shelf life; therefore, unless stability-testing indicates otherwise, it has no expiry (US FDA, 2017; Health Canada, 2021). However, cylinder valves will require inspection at set intervals, and it is recommended that the date of last inspection be affixed to cylinders and bulk tanks (USAID MTaPS, 2023).

Application of QA along the entire MOX supply chain

QA practices along the entire MOX supply chain play a vital role in ensuring safety.

QA practices at the health facility level are shared by many cadres of the workforce; however, to verify and accept medicines such as oxygen, that responsibility should be assigned to a specific role, for example, to the head pharmacist, and/or the quality unit (QU), which is responsible for QA of in-facility medicinal products. In the case of MOX, the facility's biomedical engineer could play a key role in establishing and managing QA practices. Each facility may have a different structure regarding roles and responsibilities for managing QA related to the size and the number of employees. The objectives of establishing robust QA practices for MOX (in addition to the existing regulations) are:

- Creating, implementing, maintaining, and monitoring a quality system, including documenting operations and procedures using standard operating procedures (SOPs), and work instructions, which should be strictly followed;
- Ensuring that the appropriate and functioning equipment is in place and that it is available to the QC personnel for approval (or rejection) of any medical products, accessories, and ancillary materials, either incoming or produced in-house;
- Approving or rejecting all procedures or specifications of any manufacturer that could negatively influence on the identity, quality, and purity of the medicine;
- Conducting internal audits, with all relevant staff, where applicable. (US Code of Federal Regulations, 2023; EudraLex, 2011).

Qualified personnel are critical factor for the safe production, safe storage and transportation as well as for the end use by the patient.

In that manner, the entire personnel must be adequately and regularly trained in QA practices as they relate to MOX as well as in other critically important aspects of O_2, including safety requirements and potential hazards to both patients and personnel (USAID MTaPS, 2023). Also, all personnel should be assessed for competencies regarding MOX, its application and risks, and their roles and responsibilities (EudraLex, 2011).

Understanding and proper training for the following general topics is required:

- Oxygen safety (safe handling, risks and hazards, PPE requirements, emergency contact; quality system principles);
- Quality requirements for MOX.
- Additionally, for personnel working in specific areas of the supply chain, the following topics are to be covered in training:
- Health care workers: clinical guidelines and emergency contacts for MOX issues;
- Oxygen generator plant operations: daily site-check, power-supply assurance, start up, automatic and manual shutdown, safety checks, PPM, troubleshooting, and repair;
- Pipeline distribution network: system and safety checks, secondary supply, and alarms;
- Cylinders: properties, risks, management, safety checks and cleaning, and safe handling for loading, unloading, and transport;
- Transport: qualified drivers for vehicle operators, maintenance and upkeep of vehicles, transport of dangerous goods, and GDP of medical products.

Facilities supporting any production, storage, distribution, and delivery of MOX must have dedicated and designated work areas, accessible only by authorized personnel, which are to be always kept organized and clean (USAID, MTaPS, 2023).

QA practices for cylinder filling and inspection

O_2 cylinders are refillable containers, available in international standard capacity/pressure and dimensions. All cylinders must have a serial number (SN) and all pertinent information related to their production and intended service hard-stamped onto their shoulder, as per ISO 13769: Gas cylinders—Stamp marking (ISO 13796, 2018). The valve connection point on the filling manifold (ramp) must be intended for oxygen use. Another practice for QA during cylinder filling is purging of the cylinder beforehand. This can be achieved by using a vacuum pump (a small compressor) or by establishing a fill-purge protocol. Lastly, there must be enough space for the filling and management of cylinders. Appropriate areas (space) are required to store cylinders safely according to their categories: empty, full, cylinders prepared for deliveries, faulty/rejected cylinders, etc. Color-coded cylinder paint should be maintained to facilitate ease of sorting and minimize any potential cross-contamination. Repainting of the white shoulders should be carried out as soon as a

cylinder's identity is no longer apparent. Additionally, hydrostatic (pressure) testing must take place for each cylinder every 10 years.

Another important aspect of QA is cylinder identification. Only cylinders rated for and dedicated to MOX service should be accepted at health facilities and filled by hospital cylinder filling stations. These cylinders are typically easily identifiable by their coloring, which may vary depending on geography and, equally important, by the valves that are used. Proper valves are required for both filling station connection points and for accessory sets for regulation and conditioning before oxygen can be delivered to patients. Cylinder filling involves working with high-purity oxygen at high pressure. Therefore, cylinder valves always must be opened slowly to ensure that gas is not released too quickly. Another often overlooked safety risk is the potential for the cylinders themselves to inflict bodily harm. Large cylinders have a tare weight of approximately 70 kg; if they fall on personnel or a patient, they can cause severe trauma. Thus, the handling and management of cylinders is an important activity for QA, including safety. After filling, a mild, oil-free soap solution should be applied to the valves to check for leaks, which are indicated by bubbling. Depending on the facility's quality management plan, at least one cylinder from each batch should be tested by a quality controller. All cylinder filling details (production batch, cylinder ID, etc.) must be documented and sustained to ensure traceability (USAID MTaPS, 2023).

QA practices for transportation and storage

Vehicles transporting O_2, as well as vessels filled with O_2, must be properly classified, certified, labelled, and identified; they must bear a symbol indicating that they contain an oxidizer (Table 3).

Bulk Liquid Oxygen - Road conditions must allow safe passage of fully loaded LOX tanker trucks. Transfilling, or shifting LOX from one tank to another, will happen at multiple points along the LOX supply chain—for example, from point of manufacture to a LOX tanker truck, then to a bulk LOX storage point, back onto a LOX tanker truck, and finally to one or more facility LOX storage vessels. And so, while many transfer points need to be managed, all transfers upstream of the final on-site fill, from a QA perspective, will be reflected in one Certificate of Analysis (CoA), which will be handed over upon delivery of bulk LOX at the health facility. Quality practices are required for the final transfer of LOX to the facility storage vessel(s), a responsibility of the LOX supplier. In addition to the safety points listed above:

- The transport tanker should be pressurized slightly higher than the recipient vessel(s) and a non-return valve should be located downstream of the transfer pump. Both features serve to ensure that no oxygen back-flows from the on-site storage vessel into the tanker truck;
- A CoA for the LOX in the tanker should be handed over from the driver to the quality unit (QU) representative. A formal acceptance process must take place prior to transfilling the facility storage vessel(s). This document is essential for recordkeeping;
- No vehicles should block the entrance or exit of the LOX tanker truck;
- Only authorized persons should be allowed near the tanker truck; to avoid oxygen enrichment, personnel involved in the process should not stand near oxygen vents;
- Transfilling should not take place over, under, or through anything;
- The operator responsible for transfilling must wear appropriate clothing.

Quality control along the MOX supply chain

QC is an activity complementary to QA and consists of testing the production process as well as batch testing of products. QC aims to indicate whether a medical product meets Pharmacopoeia specification or in-house standards at a specific point in time. This point-in-time data also provides information on how the quality systems functions, and a positive outcome supports the QA practices.

The requirements in the Pharmacopoeia monographs are mandatory. However, this does not imply that a MOX manufacturer must perform all the monograph tests when assessing compliance with the specified standards before release. The manufacturer should obtain assurance for the products quality using data derived from validation studies of the manufacturing process. Also, with the agreement of the responsible authority, alternative analytical procedures may be used for control purposes. The results obtained from product's quality control are recorded on batch-specific CoA before the product's release. Personnel involved in QC must be independent from those involved in production of MOX.

Production of MOX is continuous in nature, and testing of the product therefore will not come from a sample of a clearly identifiable batch. A framework for defining a batch can be found in ICH's Continuous Manufacturing of Drug Substances and Drug Products; Q13. This batch definition will determine the frequency with which to test and document (USAID, MTaPS, 2023).

Product Release - the QU has the authority to approve or reject all products. Any product with test results that do not conform to specifications will need to be investigated. QC will flag these results to QU, and the procedure indicated in the facility risk management plan will be followed. For any product from an external supplier/distributor, agreements should be in place with the health facility QU regarding the supplier's/distributor's quality system. Additionally, any delivery must come with a CoA reflecting the batch to be offloaded. The QU again has the authority to release the batch, either by accepting or rejecting it. To maintain the required level of quality, it is also important to examine all returned medicinal gases (Health Canada, 2018).

Conclusion

The production, management and the QC of MOX must follow global and country-specific quality standards to ensure its safety. From production to storage and transportation, each phase must be strictly controlled, such as keeping the production environment clean, regularly maintaining equipment, and routinely checking gas cylinders. Post-production steps, such as cylinder filling and inspection, are designed to maintain these standards, ensuring that every batch meets the stringent requirements set by the Ph. Eur and GMP. Methods of analysis described in the Pharmacopeial monographs reflect the technical precision required to produce a product that consistently meets high-quality benchmarks. By maintaining rigorous standards, the healthcare industry can continue to depend on MOX as a fundamental tool in saving lives and improving patient outcomes.

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Резиме

Медицински кислород: обезбедување и контрола на квалитет за безбедна и ефикасна употреба

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Клучни зборови: медицински кислород, контрола на квалитет, обезбедување квалитет, безбедност на здравствениот систем

Медицинскиот кислород е неопходен лек што припаѓа на модел листата на есенцијални лекови предложена од Светската Здравствена Организација за третман на акутно болни пациенти и пациенти со хронични болести како последица на хипоксемија. Безбедната примена на медицинскиот кислород подразбира придржување и примена на интернационално прифатени стандарди за квалитет, почнувајќи од процесите на производство па сè до неговата примена во медицинските установи. Целта на овој труд е да направи преглед на најзначајните аспекти за обезбедување квалитет, што треба да се задоволат почнувајќи од процесот на производство, чување и дистрибуција до медицинските установи, како и испораката до пациентите. Строги критериуми и барања се поставени од страна на Европската Фармакопеја (Ph. Eur) и Американската Фармакопеја (USP) што ја специфицираат чистотата на медицинскиот кислород со цел да се задоволат највисоките здравствени стандарди.