



SHORT COMMUNICATION

Medical oxygen: Sources and regulatory guidelines

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) revealed that it shares traits with the coronavirus family and belongs to the *Coronaviridae* family. SARS-CoV-2 and the bat coronavirus variant BatCov RaTG13 share $95 \pm 1\%$ of their genetic makeup, which is the closest similarity as well as the SARS-CoV sequence and these genome sequences, are 79 ± 1 identical. India is the second-most populous country in the world battled for the optimal use of medical infrastructures alongside several other nations fought for their daily needs. Life or death for the patient depends on the prompt provision of medicinal oxygen. During all these COVID times, need for oxygen increases day by day and the production of oxygen boosts up to 9400 metric tons per day. This review article focuses on the different sources of oxygen being used currently. Furthermore, the regulatory framework of compressed medical gases especially oxygen are also discussed with the objective to understand the regulatory requirements.

KEY WORDS: Coronavirus disease 19, Medical oxygen, Regulatory guidelines, Severe acute respiratory syndrome coronavirus 2

INTRODUCTION

The World Health Organization (WHO) has attributed this disease as “2019-nCoV” or “2019 novel coronavirus” or Coronavirus disease 19 “(COVID-19).”^[1] Globally, 6,532,705 deaths from COVID-19, including 617,597,680 confirmed cases, have been reported by the WHO till October 7, 2022.^[2] The coronavirus disease is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus (COVID-19). The current pneumonia outbreak started in early December 2019 near Wuhan City, Hubei Province, China. On March 11, 2020, the WHO proclaimed this illness to be a pandemic due to its rapid spread. Brazil, India, and the United States are the leading nations with the highest world population of confirmed cases.

The bioinformatics investigation of SARS-CoV-2 revealed that it shares traits with the coronavirus family. It is a member of the beta-coronavirus 2B lineage. Five patients with SARS-CoV-2 infection had their whole genomes sequenced early in the Wuhan pneumococcal pandemic.

The SARS-CoV-2 sequence and these genome sequences are 79.5% identical. The closest similarity between SARS-CoV-2 and the bat SARS-like coronavirus strain BatCov RaTG13 is a 96% identity. These studies suggest that RaTG13 (a bat coronavirus) may have served as the ancestor of SARS-CoV-2 and that this coronavirus may have spontaneously evolved from it. Positive sense single-stranded RNA is present in SARS-CoV-2. Spike, membrane, nucleocapsid, and envelope are different types of proteins that are protected within the viral structure and are recognized by their particular functions. Some coronaviruses also generate a hemagglutinin-esterase protein that is connected to the envelope.^[3]

Along with several other countries India is the second most populous country who battled for the best possible use for medical infrastructures including hospital beds, medical oxygen, and others. In parallel to its industrial usage,

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oxygen is employed in medicine for several treatments, including the delivery of generic medications, first aid, and emergency procedures. Life or death for the patient depends on the prompt provision of medicinal oxygen.^[4] The continual supply of medical oxygen is always given priority to hospitals above others. High-flow nasal oxygen has been demonstrated to be a secure and efficient treatment for COVID-19 patients outside of an intensive care unit. According to the WHO, 15% of COVID-19 patients have breathing problems and need medicinal oxygen. Even a ventilator is necessary for certain seriously unwell people. The production and supply of medicinal oxygen were clearly revealed as a significant limitation in the health-care systems by COVID-19.^[5]

During the first wave, consumption of oxygen peaked at 3100 metric tons per day, and by May 6, 2021, it had increased to 8900 metric tons during the second wave. As of May 6, 2021, the production was boosted to 9400 metric [Figure 1] tons to meet this demand. In an attempt to ensure that hospital demand could be satisfied, the Indian government diverted practically all industrial oxygen for medical purposes. Medical oxygen is governed by Section 3(b) (i) of the Drugs and Cosmetics Act of 1940, and the central government has the authority to control its production and distribution. The Drug Controller General of India grants licenses for the production of medical oxygen. The ownership, filling, and transportation of compressed oxygen in cylinders are governed by the Gas Cylinder Rules of 2004. Medical oxygen demonstrates harmful effects when used in doses above what the body needs, much like any other medicine. It frequently happens in uncontrolled or unmonitored environments, leading to hyperoxia and oxygen toxicity symptoms. It frequently happens in unstructured or unrestricted environments, leading to hyperoxia and oxygen toxicity consequences.^[6]

The significance of receiving the best oxygen therapy cannot be compromised. This review is explaining the various aspects of medical oxygen such as sources, usage, and supervision. In addition to this, the regulatory framework related to medical oxygen is also undertaken to understand the regulatory requirements. This review will provide a comprehensive understanding related to medical oxygen for making them easy to availability by ensuring all regulatory aspects specifically in pandemic-like conditions such as COVID-19.

OXYGEN SOURCES

The delivery of medical oxygen in healthcare is known as oxygen therapy or supplemental oxygen. Medical oxygen is produced by an oil-free compressor, is at least 82% pure oxygen, and is contamination-free. Patients should only be delivered medical-grade oxygen of the highest standard. Oxygen systems must include an oxygen source, its production, and storage. Oxygen-generating facilities,

liquid oxygen (LOX) in bulk storage tanks, and oxygen concentrators are all common oxygen sources.^[5] The most common type of oxygen storage used in health-care facilities is a cylinder. The amount of oxygen required at the treatment facility, as well as the availability of maintenance services and replacement components, as well as the infrastructure, costs, capacity, and supply chain for locally produced medical gases, all have an impact on the choice of oxygen source.^[5] In general, followings are the main source of oxygen production.

CRYOGENIC DISTILLATION/LOX PLANT

Carl Wilhelm Scheele, a Swedish pharmacist, discovered oxygen in 1771-72. He heated several nitrates, including mercury oxide (HgO), to create oxygen gas. Since it was the only gas known to support combustion at the time, Scheele termed the gas “fire air.”^[7] Cryogenic liquefaction and fractional distillation of air are used in the large-scale commercial production of oxygen. Von Linde and Hampson employed this method effectively for the 1st time in 1895. Low temperatures are associated with the term “cryogenic,” while “distillation” refers to the process of separating components from a mixture using those components’ boiling points. As a result, only the components in cryogenic distillations with very low boiling points are selectively distilled at low temperatures.^[8]

Steps in cryogenic distillation of Air^[9,10]: Here are a few steps involved in the cryogenic distillation of air which includes:

1. Pre-treatment, compressing, and cooling of incoming air
2. Removal of carbon dioxide
3. Heat transfer to bring air feed to cryogenic temperature
4. Distillation of air.

In this method, the air is first pre-treated to get rid of any major contaminants such as carbon dioxide and heavy hydrocarbons. The pre-treated air is, then, directed through a multi-stage compressor to the cooling plant, where water vapor is condensed and removed. After that, the residual carbon dioxide, water vapor, and hydrocarbons are captured by a molecular sieve absorber comprised of zeolite and silica gel-type absorbents.

The air is, now, introduced to the fractional distillation chambers, where it is divided into three main parts: nitrogen, oxygen, and argon. Cryogenic air separation units are needed before distillation to turn the gaseous component into liquid form since the distillation process relies on the fundamental idea that boiling a liquid separates its components. The variations in the boiling temperatures of each gas make this process possible.^[11]

The air stream enters the high-pressure fractionating chambers after becoming partially liquid and partially gas.

The separation process starts as the air rises. At the bottom of the column, oxygen begins to liquefy, while nitrogen and argon climb to the top of the column as vapors. This cooled liquefied carbon dioxide-free air is routed through the warmer (-183°C) bottom of the fractionating column. LOX is produced when nitrogen boils at -195°C and exits the column. This oxygen is then further purified to remove argon. The quality of this liquefied oxygen is currently 99.5%. This oxygen is a 99.5% pure, light blue liquid that has been chilled to -183°C . For storage and transportation, specialized cryogenic tanks are required. Large bulk LOX tanks that are periodically loaded by a vehicle from a manufacturer can be installed in medical facilities. The LOX tank uses self-vaporization to supply a centrally piped system across the medical facility without the need for electricity.^[8] Despite being a cost-effective option in some circumstances, the usage of LOX depends on external supply chain mechanisms and requires a little more caution when it comes to shipping and storage due to the dangers connected with greater pressures. Depends on the capacity, oxygen plant may be classify into small-capacity LOX plant (production range 20 l/h to 60 l/h), medium capacity LOX plant (production range 80 l/h to 170 l/h), and large-capacity LOX plant (production range 200l/h to 500l/h).^[12]

PRESSURE SWING ADSORPTION (PSA) PLANT

The basic principle of PSA is the idea that when air is passed through a vessel at high pressure with an adsorbent bed of zeolite (hydrated aluminium silicates) that attracts nitrogen more strongly than oxygen, some or all of the nitrogen will get absorbed by the adsorbent bed and the gas exiting the vessel will be richer in oxygen. Oxygen gets separated easily by this process and is stored in buffer tanks. To produce oxygen, these towers alternately absorb nitrogen, extract oxygen from the air, and regenerate by releasing the adsorbed nitrogen back into the atmosphere.

According to the Indian Pharmacopeia 2010 recommendations, the oxygen created using this process has a consistent purity of $93 \pm 3\%$. Deliveries of oxygen are made to the piped system at a pressure of 4 bar. However, PSA plants do not produce as much oxygen as cryogenic plant, though it has gained popularity due to the simple extraction process to meet the high demands of oxygen in an emergency. The output capacity of PSA plants is measured in cubic meters per hour (m^3/h) of oxygen, where $1 \text{ m}^3 = 1000 \text{ L}$ of oxygen. PSA plants require a continuous power source to continuously produce oxygen.^[8,11]

It is recommended to keep cylinders on hand as a safety net and need a continual, reliable power source with voltage regulation. The Indian government ordered the installation of 162 PSA plants during the initial COVID-19 outbreak. It increased the overall demand to 1594 PSA plants for

medical use in May 2021. Before the oxygen enters the storage tank, a computerized analyzer checks its purity.^[8]

VACUUM PSA (VPSA) PLANT

This is an affordable way of oxygen production. This technique has primarily been utilized in the mining, chemical, and steel industries. In the current situation, VPSA plants can be constructed in remote locations to address the imbalance in oxygen supply and demand. A cyclic swing between overpressure and vacuum takes place in a VPSA plant. Pressure is balanced between the manufacturing and regeneration processes to limit energy use.^[11]

Each adsorber undergoes a cyclic process, consisting of

- Adsorption (O_2 production)
- Desorption (evacuation)
- Re-pressurization (pressure build-up).^[13,14]

DEPLOYABLE OXYGEN CONCENTRATION SYSTEM (DOCS)

Portable oxygen generation technique using molecular sieve technology is presented here. Especially in times of pandemics relief, this method is largely used in the aerospace and defense industries. DOCS functions by adsorbing nitrogen and water from filtered air. The produced gas has increased oxygen at flow rates ranging from 30 to 500 L/min, depending on the size of the unit. Up to 93% of oxygen can be delivered using this device (90–96%).^[11]

OXYGEN CONCENTRATORS

An electrically driven, self-contained medical equipment called an oxygen concentrator is used to concentrate oxygen from outside air. An oxygen concentrator can continuously provide a source of 95.5% concentrated oxygen by drawing air from the atmosphere, removing the nitrogen.^[7] Concentrators use PSA technology to concentrate oxygen to more than 90% purity using zeolite adsorption from ambient air.^[8] The method involves taking atmosphere air, compressing it, filtering out the nitrogen, and then releasing oxygen. The main drawbacks of its use are caused by sieve malfunctions or water vapors that interfere with nitrogen absorption. Although smaller oxygen concentrator units are not the preferred oxygen delivery method for patients who are dying, they can be utilized as a portable device for patients who require long-term oxygen therapy at home or in emergency situations. Depending on whether low-flow or high-flow oxygen concentrators are used, this device can deliver 0.5–15 L of oxygen per minute.^[11] The

two common flow modes on concentrators are pulse and steady flow. The device measures the patient's inspiratory effort in pulse-free mode and provides oxygen when the patient inhales. Pulse flow devices are usually compact and lightweight, making them perfect for ambulatory patients with low oxygen needs. However, they are not compatible with other ventilation systems such as continuous positive airways pressure machine or bi-level positive airway pressure.^[8]

Commercially, oxygen concentrators are used to produce oxygen on a large scale utilizing a variety of technologies, including membrane technology or pressure swing absorption.^[11] It requires a constant flow of voltage-stabilized electricity. For ambulatory patients, smaller battery-powered portable devices are available. Concentrators are equipped with safety alarms that can recognize low oxygen levels, no flow, power supply problems, and extreme temperatures. The zeolite sieve should undergo routine maintenance to ensure that it is operating properly it may also need to be replaced every 25,000 h.^[8] Concentrators can simultaneously serve many patients with a steady supply of oxygen when combined with a flow meter stand for splitting flow. Concentrators can deliver an affordable and secure source of oxygen.^[7]

OXYGEN CYLINDERS

A patient is given oxygen through a surgical mask placed over a nasal cannula from an oxygen cylinder. Oxygen cylinders come in a variety of capacities, and the one picked depends on the patient's condition. Compressed gas form of oxygen produced at industrial cryogenic or PSA plants is pumped into high-pressure cylinders.^[5] They can be utilized in a variety of locations, including homes, hospitals, and ambulances, and are available for simple storage and transportation. These cylinders can be used for all oxygen requirements, including high-pressure supplies, and in locations with erratic or intermittent power supplies. Steel alloys are commonly used to construct cylinders.

Lightweight aluminium cylinders are magnetic resonance imaging compatible. The oxygen flow is managed by the valve at the top of the cylinder, and the pressure gauge shows oxygen content. Name, chemical symbol, diamond-shaped hazard warning, tare weight, volume, manufacturer name, safety instructions, and emergency contact information are among the information displayed on labels on the cylinder's shoulder. Oxygen cylinders are either white as ISO coding and green in color for US coding. There are typically two types of valves used to link the cylinders: Pin index valves and bull-nose valves. They are available in a range of sizes and storage capacities and have the following codes: B, D, E, G, and J. when filled, all cylinder sizes are at 200 bar of pressure. The normal filling pressure, however, is 137 bar or 2000 psi approx.^[8]

Storage and transport: The storage and transportation of oxygen cylinders must be as per the following guidelines.

- Store medical gas cylinders separately from industrial and other non-medical cylinders, fuel, oil, grease, alcohol based hand cleaner, etc., in a well-ventilated area that is clean and dry, preferably inside
- Smoking should not be permitted in the vicinity where cylinders are used or stored
- Do not store or use cylinders near naked flames, sources of ignition, or combustible materials
- Ensure the oxygen cylinders are stored in a safe and secure area where they cannot fall over and cause injury. Commonly, this is within a secure cage or chained to the wall
- Medical gas cylinders should not be stored in the same area that is being used to dry equipment
- Clearly identify the storage areas with appropriate signage
- Ensure separation of full and empty cylinders
- Oxygen is a non-flammable gas, but strongly supports combustion
- Located in a compartment separated from the driver
- Adequately restrained
- Check for leaking, and have their valves closed.^[15]

PRECAUTIONS DURING USAGE OF OXYGEN SOURCES

1. Oxygen gas cylinders should be stored at standard room temperature
2. Always use pure water to hydrate oxygen before usage
3. Never use poor-quality water such as tap water, boiled water, or purified RO water
4. Masks and nasal cannulae should be cleaned and checked by the attendee for any leaks
5. Attendees who use oxygen concentrators should follow the manufacturer's instructions for proper cleaning as needed
6. A clean, well-ventilated space should be chosen for the oxygen concentrator's placement
7. Oxygen filters need to be cleaned properly on occasion
8. Avoid using any kind of tobacco, including wood, cigarettes, or sticks, while near an oxygen concentrator
9. Attendees can check the patient's nostrils for any black pigmentation, and if even the smallest spot is seen, they should immediately call the doctor for additional treatment
10. Avoid using steroids irrationally or without a prescription.
11. Post signage that read "Oxygen in use" in prominent locations
12. Never put the tank or device close to an open flame (such as a lighted candle, match, or stove in use). Keep the oxygen tank at a minimum distance of six feet
13. If not in use, always switch off your oxygen
14. Inspect your oxygen tank's oxygen levels regularly. Both the active tank and the backup tank are incorporated here

15. The oxygen backup tank needs to be kept in a secure location that is safe and well-ventilated, laying flat (or upright and secured)
16. Avoid using items with a petroleum base while using oxygen. The use of alcohol-containing goods (such as skin care products) is not recommended.^[16]

REGULATORY/ADMINISTRATIVE STRATEGY OF COMPRESSED MEDICAL GASES (OXYGEN)

The compressed medical gases are subject to all portions of 21 code of federal regulation (CFR) Part 211 unless specifically exempted by the rules (for example, per 21 CFR Part 211.196, lot or control numbers are not necessary on CMG distribution records) or exempted by the Policy on Medical Gas CGMPs Unless a technique or method directly breaches a specific portion of 21 CFR Part 211, CGMP regulations do not apply to practices and procedures that differ from those outlined in the medical gas guidance. When the district office determines that the organization is not functioning in a state of control and exhibits major deviations according to the following list, and the organization's management is unwilling or unable to take required corrective actions in a timely manner.^[17]

Significant breaches that could cause regulatory or administrative action

1. Adopting test procedures that have not been examined against recognized test standards (Laboratory System)
2. False or invalid labeling, an mistaken description of the product's contents, or insufficient usage instructions (Packaging and labeling system; quality system)
3. Insufficient cylinder refill checks and procedures, in particular failing to carry out those intended to remove or detect residual gases or other pollutants in the cylinders (most important both before and after commercial usage) (Production system, materials system, and laboratory system)
4. Failure to conduct tests to ensure that filling apparatus or containers following repairs, cleaning, refurbishment, extended storage, or exposure to conditions that adversely affect the containers or apparatus remain acceptable for medical use
5. Failure to check at least one cylinder for both identity and strength throughout each unbroken filling sequence, provided the same tools, personnel, and bulk lot are being utilized. Failure to verify entangled tons of a single compressed medical gas for identification and strength
6. Failure to utilize other control methods to avoid contamination and mix-ups, or to undertake operations in clearly defined areas (Production System; Facilities and Equipment System)
7. If there are no written instructions for the test's processes, do not follow them
8. According to the manufacturer's instructions, the testing apparatus was not properly calibrated
9. Inadequate label control (Quality system; packaging; and labeling system)
10. Failure to test completed product quantities or bulk gases (Laboratory system; materials system; and production system).

Medical gas CGMP guidelines

Medical gas CGMP Guidelines divided into four parts:

Periodic report

In accordance with 21 CFR Parts 314.80(c)(2), periodic adverse drug experience reports, and 314.81(b)(2), annual report, the agency currently does not compel companies producing authorized medical gases to file the periodic reports. Please be aware that companies producing designated medical gases must still adhere to all other regulatory standards for ADE(Adverse drug reporting) and field alert reports (FARs) reporting (please these include CPGM 7353.001 "Post Marketing Adverse Drug Experience Inspections" and CPGM 7356.021 "Drug Quality Reporting System Reports and FARs").

Stability studies, component reconciliation, expiry dating, and yield determination

It is not necessary to conduct stability tests (21 CFR Part 211.166) unless a company labels a gas with an expiration date.

Component reconciliation is generally not appropriate for medicinal gases (21 CFR Part 211.184[c]), and it should not be flagged as a potential infraction without prior CDER approval.

No action will be taken if a company opts not to insert expiry dating (21 CFR Part 211.137) on the label. An expiration date must be backed by data (stability studies), which itself is subject to inspection during a site inspection, if a company labels a gas with one. A Form FDA 483 should not omit an expiration date unless CDER has previously provided its consent.

Without the previous consent of the CDER, yield determinations (21 CFR Part 211.103) should not be referenced as a potential infringement in the fabrication of medicinal gas.^[17]

Oxygen concentrators

Medical devices regulated as devices under 21 CFR Part 820 generally include oxygen concentrators, which are meant to supply a continuous flow of concentrated oxygen primarily to hospital supply systems. Since they

are neither ASUs. Cylinders that will be utilized later on can be filled using oxygen concentrators. The oxygen concentrator are considered medical gas manufacturing apparatus applicable to all drug production CGMPs if a company utilizes it (them) to fill standardized cylinders for later sale.

Validation of the air separation unit

For the purpose of validating medical gas ASU automation and computer controls, CDER considers “current industry standards” to be largely compatible with CGMP criteria. The greatest representation of the pertinent current industry standards is provided by CGA guide P-8.2. Guidelines for air separation unit validation and transport tanker loading of oxygen USP and nitrogen NF this paper should be read by investigators before they inspect an ASU.^[17]

Labeling

Follow IOM guidelines, such as 5.2.3.3–Non Reportable Observations, and seek advice from CDER’s Office of Unlicensed Drugs and Labeling Compliance (see Part VI) for any potential misbranding breaches.

CMG Cylinder Colors: According to labeling guidelines, there are different colors of cylinder which are listed in Tables 1 and 2.

Single gases: Followings are the colors of single gas

Table 1: Container color of different single gases

Color	Gas
Green	Oxygen USP
Gray	Carbon dioxide USP
Blue	Nitrous oxide USP
Brown	Helium USP
Black	Nitrogen NF

Mixtures: Followings are the container colors of mixture gas

Table 2: Container color of different mixture of gases

Color	Gas
Gray and green	Carbon dioxide USP and oxygen USP
Brown and green	Helium USP and oxygen USP
Yellow	Medical Air (mixtures of NF nitrogen and USP oxygen containing 19.5% to 23.5% oxygen)
Green and black	NF nitrogen/USP oxygen mixtures other than those containing 19.5% to 23.5% oxygen

OXYGEN TRANSFILLER FIRM TESTING REQUIREMENTS

Many firms are in business to supply Oxygen, USP to patients in need of supplemental oxygen, either as cylinders of compressed oxygen or as LOX for the patient’s home vessel. Our primary interest during an inspection of these firms is to establish that the oxygen provided to the patients meets the identity and strength specifications for Oxygen, USP.

Compressed oxygen cylinder testing requirements, USP

Screening one cylinder out of each manifold filling cycle for identity and strength will enough to satisfy the testing requirements if the company fills high-pressure cylinders in accordance with CGMP because each cylinder serves as a sample of the complete filling sequence.

One cylinder out of each continuous filling cycle should be tested if the company fills one cylinder at a period, provided the same staff, tools, and bulk are utilized. A single, uninterrupted filling sequence without any stops or shut-downs is referred to as an uninterrupted filling sequence.

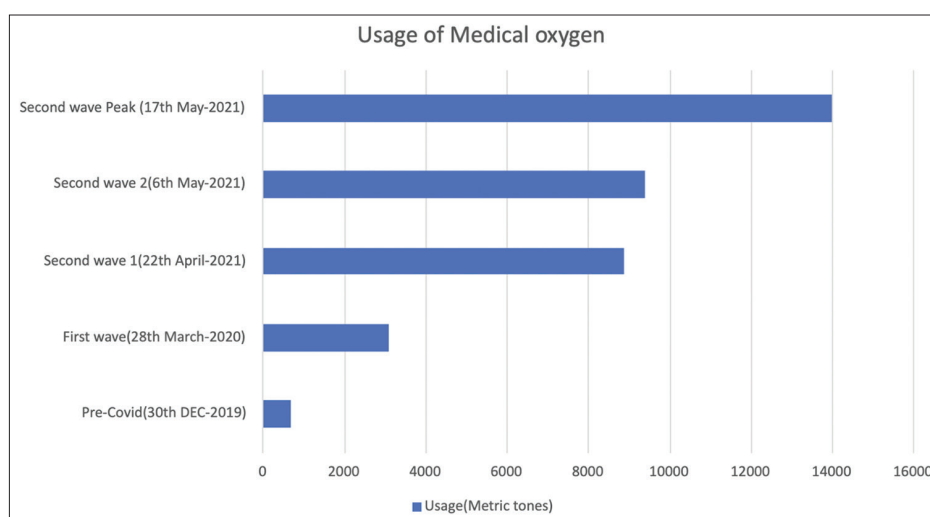


Figure 1: Indicates the rise in consumption of oxygen sources during COVID-19^[6]

Cryogenic home LOX vessel testing requirements

When the company receives notice that the oxygen level has reached a specific level, the cryogenic storage vessels are either periodically filled or filled immediately. The company will either fill the patient's container from a cryogenic vessel installed on their delivery device or exchange the empty vessel for a full one (a process known in the industry as "milk canning").

The researcher must decide whether testing of the LOX is necessary and who will do the testing. Is the company required to test the receiving LOX or the components of the cryogenic home vessel for identity and strength, for instance.

Incoming LOX testing in organizations filling cryogenic home vessels

If a business fills cryogenic home containers with LOX using either a permanently installed vessel or a portable vessel, such as a vertical gas liquid, gas pack, and portable liquid container.

- No testing is necessary as far as the receiving organization obtains a valid certificate of analysis for each container and records that the testing has been seen. This includes seeing the testing for each vessel's identity and strength.
- The company can rely on a genuine COA for the strength determination if the screening is not seen, but it should conduct an identity test on every cryogenic tank it receives or that the supplier fills.
- Full USP testing would be necessary if a company did not observe the testing or receive a legitimate COA.

Before any cryogenic vessels, along with any cryogenic home vessels, are filled, an identification and strength test taken straight from the storage reservoir after every oxygen supply should be carried out if the company owns or rents the tank.

- The VMVs are used only for delivering oxygen.
- The storage tank-filled VMVs have not been totally emptied or taken out of operation.

The evaluation of cryogenic home vessels

Who retains control or ownership of the cryogenic storage vessels is the most crucial factor in their filling. CGMPs mandate thorough testing of each vessel if there is a chance that a contaminant or an alien gas could be admitted into the cryogenic home vessel. According to industry standards, the company that owns the cryogenic storage vessels must conduct the filling and cannot permit any other company to fill these vessels.

Combined bulk oxygen testing requirements

Combination of the material occurs when a fresh large shipment of a component is placed in a large storage

tank with the remaining pieces of a previously acquired, examined, and approved component lot.

For CGMP recordkeeping purposes, the source of the new bulk shipment is regarded as the single origin of the fresh combined batch or lot, and the new combined large batch or lot is given a new lot number. The mixed lot cannot be used unless it gets permission to.

LOX testing filled into big cryogenic vessels

Each huge cryogenic vessel that is filled by one company, which is then given to another company that fills cryogenic home vessels for patients either on-site or at their homes, must be tested before being released. Cryogenic containers always include a residual, therefore mixing happens anytime a fresh product is added to the vessel.

Testing the LOX that will be used to fill high-pressure cylinders

Before being utilized to fill each and every cryogenic vessels combined LOX must first pass a full USP specification test when high-pressure cylinders as well as other cryogenic containers are loaded from a storage tank. This test must be performed promptly after each delivery. You could subject these things to testing:

- a. Sample collected straight from the storage reservoir
- b. A cylinder from the initial manifold filling cycle (this is the most typical approach).

CONCLUSION

Many locations with low resources have insufficient oxygen supplies and delivery methods. Access and distribution considerations must be given to each supply alternative. The core of the overall strategy for managing the COVID-19 epidemic is the ability to increase capacity to give oxygen therapy at all desired locations. Life or death for the patient depends on the prompt provision to ensure the availability of medicinal oxygen. The surge strategy can be framed and put into action with the support of quick recommendations made by regulatory authority, including product requirements and supply for any upcoming pandemic.

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