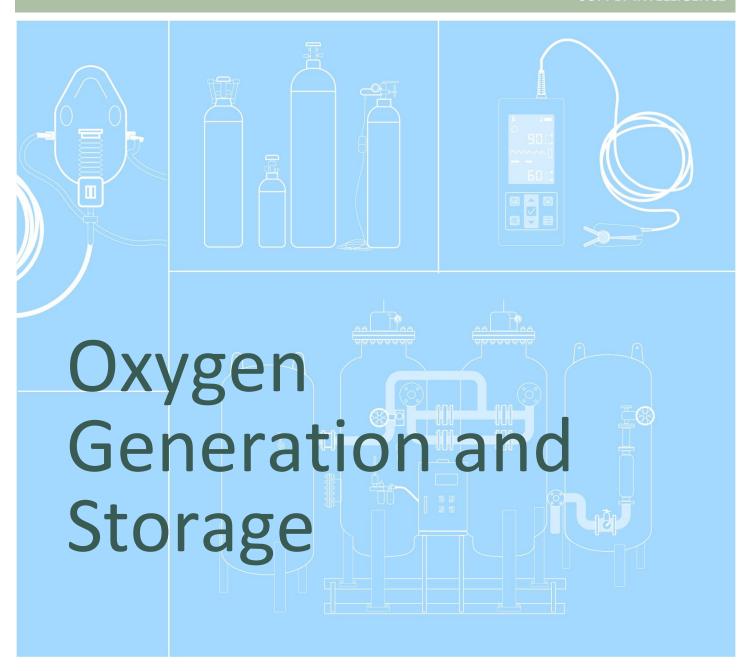
SUPPLY INTELLIGENCE



July 2021

Acknowledgments

This brief series is based on research funded by the Bill & Melinda Gates Foundation. The findings and conclusions contained within are those of the authors and do not necessarily reflect positions or policies of the Bill & Melinda Gates Foundation.

The brief series was developed by PATH and Clinton Health Access Initiative (CHAI) as part of the COVID-19 Respiratory Care Response Coordination project—a partnership between PATH, CHAI, and the Every Breath Counts coalition to support country decision-makers in the development and execution of a comprehensive respiratory care plan to meet the demands of COVID-19. The project is also pursuing strategies to help prioritize and improve access to oxygen therapy and other essential equipment involved in respiratory care as an integral part of health systems strengthening, beyond the pandemic response. For information: oxygen@path.org.

The brief series was written by PATH staff Scott Knackstedt, Alex Rothkopf, Stassney Obregon, and Alec Wollen, with support from CHAI staff Jason Houdek, Martha Gartley, and Tayo Olaleye. The authors would like to thank the following individuals for their insightful feedback, including Lisa Smith, Andy Gouws, Evan Spark-DePass, Elena Pantjushenko, Carrie Hemminger, and Conner House.

i

Table of contents

Introduction	
Air separation unit	3
Technical overview	3
Key specifications	3
Regulatory considerations	3
Infrastructure requirements	4
Supply/shipping	4
Dependencies for use	4
Maintenance	5
Cost	5
COVID-19 considerations	5
Pressure/vacuum swing adsorption plant	6
Technical overview	
Key specifications	6
Regulatory considerations	
Infrastructure requirements	
Supply/shipping	7
Dependencies for use	
Maintenance	8
Cost	8
COVID-19 considerations	8
Vacuum-insulated evaporator system	9
Technical overview	
Key specifications	g
Regulatory considerations	
Infrastructure requirements	
Supply/shipping	10
Dependencies for use	
Maintenance	
Cost	11
COVID-19 considerations	11
Oxygen concentrators	
Technical overview	
Key specifications	
Regulatory considerations	
Infrastructure requirements	
Supply/shipping	
Dependencies for use	
Maintenance	
Cost	
COVID-19 considerations	
Oxygen cylinders	15
Technical overview	
Key specifications	
Regulatory considerations	
Infrastructure requirements	

Supply/shipping	
Dependencies for use	
Maintenance	
Cost	
COVID-19 considerations	17
Oxygen therapy accessories	18
Technical overview	18
Key specifications	18
Regulatory considerations	18
Infrastructure requirements	
Supply/shipping	
Maintenance	
Cost	
Additional information	20
COVID-19 considerations	20
Oxygen therapy interfaces	21
Technical overview	
Key specifications	21
Regulatory considerations	22
Infrastructure requirements	22
Supply/shipping	22
Maintenance	22
Cost	22
COVID-19 considerations	

Abbreviations

ASME American Society of Mechanical Engineers

ASU air separation unit

CE European certification

DISS Diameter Index Safety System

FDA Food and Drug Administration

Hz hertz

ISO International Organization for Standardization

kPa kilopascals

kWh kilowatt hours

LOX liquid oxygen

LPM liters per minute

NFPA National Fire Protection Association

Nm³ normal cubic meters

PSA pressure swing adsorption

psi pounds per square inch

V volt

VIE vacuum-insulated evaporator

VSA vacuum swing adsorption

WHO World Health Organization

Unit conversion

Kilopascal (kPa)	Unit of pressure, defined as one thousand times the unit of force of 1 Newton	1 kPa = 0.145 psi = 0.0099
	uniformly distributed over an area of 1 square meter	atmosphere = 0.01 bar
Atmosphere	Unit of pressure, defined as the pressure exerted by 760 millimeters of mercury	1 atmosphere = 101.3 kPa =
	at 0 °C and standard gravity	14.7 psi = 1.013 bar
Pounds per square inch	Unit of pressure, defined as the force exerted on an object expressed in pounds	1 psi = 6.89 kPa = 0.070
(psi)	of force per square inch of area	atmosphere = 0.069 bar
Pounds per square inch	Unit of pressure, relative to the ambient or atmospheric pressure	psig = absolute pressure –
gauge (psig)		atmospheric pressure
Liters per minute (LPM)	Unit of volume flow rate	1 LPM = 0.06 Nm ³ /h
Normal cubic meters per	Unit of volume flow rate, where 'normal' refers to being measured at standard	1 Nm ³ /h = 16.7 LPM
hour (Nm³/h)	temperature and pressure (101.325 kPa, 0°C)	

Introduction

Medical oxygen has for too long been an afterthought among the competing priorities of global health. It is a World Health Organization (WHO) essential medicine and necessary treatment for acute and chronic conditions alike, but inequitable access, production shortages, logistical failures, and a host of additional circumstances have inhibited the widespread adoption and consistent provision of this lifesaving resource. The SARS-CoV-2/COVID-19 pandemic has given added salience to the importance of medical oxygen and made stark the seriousness that a lack of access creates. As governments and health systems come to terms with the harsh realities that the pandemic has laid bare, and the resulting political capital and social engagement is mustered, there is a robust opportunity to make inroads against this inequity and help ensure that patients the world over can again breathe easy—in more ways than one.

This supply intelligence brief series, Oxygen Generation and Storage, is intended to be a concise primer for decision-makers who govern, lead, support, or manage health systems and their associated facilities. Providing an overview of the key elements that define each technology—as well as key considerations related to COVID-19—it can establish a starting point for understanding the solutions available to meet a health system's need for medical oxygen and its delivery. It should serve alongside a broader suite of planning and analytical requirements necessary for the implementation of medical oxygen solutions. As interest from governments, international organizations, and other stakeholders have coalesced behind this issue, the opportunity is ripe for those decision-makers to act and to do so with the judgment, responsibility, and respect befitting the patients that have for too long suffered without this necessary commodity.

SUPPLEMENTAL RESOURCES

World Health Organization (WHO). *Technical Specifications for Oxygen Concentrators*. Geneva: WHO; 2015. http://apps.who.int/iris/bitstream/handle/10665/199326/9789241509886_eng.pdf?sequence=1.

World Health Organization (WHO), United Nations Children's Fund (UNICEF). WHO-UNICEF Technical Specifications and Guidance for Oxygen Therapy Devices. Geneva: WHO; 2019. https://apps.who.int/iris/handle/10665/329874.

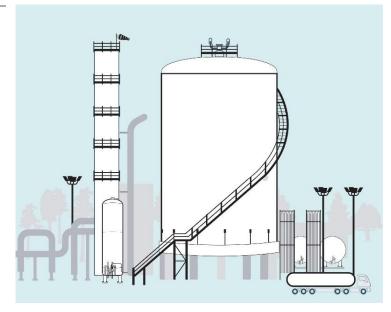
World Health Organization (WHO). Chapter 3: Technical specifications for oxygen therapy and monitoring devices. In: *Priority Medical Devices List for the COVID-19 Response and Associated Technical Specifications*. Geneva: WHO; 2020. https://www.who.int/medical_devices/priority/Chapter_3_20167_WHO_Priority_medical_devices_list_for_COVID_19 response 3.pdf?ua=1.

PATH, Clinton Health Access Initiative. *Respiratory Care Equipment Market Report*. Seattle: PATH; 2020. https://www.path.org/resources/respiratory-care-equipment-market-report/.

Air separation unit

Technical overview

A cryogenic air separation unit (ASU) is a plant that utilizes the distinct properties between the primary components of air to produce highly purified oxygen, nitrogen, and sometimes other gases, such as argon. The ASU technology uses a process referred to as cryogenic fractional distillation, where the components of the air are separated by compressing the gas until it liquefies at extremely low temperatures (-173°C to -193°C), then selectively distilling the components at their various boiling temperatures. As it is a very energy-intensive process, ASU technology is generally reserved for medium- to large-scale production. An ASU can be designed for the required product purity and delivery pressures. Skilled technicians are required on-site at all hours to ensure smooth operation of the plant.



Key specifications

An ASU can produce 100 to over 5,000 tons of oxygen per day at purity levels of 95% to 99.5% or higher. The process of air separation consists of the following main steps:

- Filtration, to remove dust and other impurities.
- Compression, where the air is compressed between 72 to 144 psig and water is condensed out in inter-stage coolers.
- Removal of contaminants, using a molecular sieve bed, which is constantly regenerated to remove any remaining water vapor, hydrocarbons, and carbon dioxide, which would freeze and plug the cryogenic equipment.
- *Heat exchange*, where the air is passed through integrated heat exchangers and cooled against product and waste cryogenic streams to produce liquefied air enriched in oxygen and nitrogen. This happens in separate low- and high-pressure distillation columns using refrigeration.
- Product compression, where oxygen is compressed to a prescribed settled pressure.
- Storage, where the liquid oxygen produced from the ASU is stored in cryogenic insulated storage tanks.

The construction of an ASU plant varies depending on the production capacity, purity, and pressure requirements for the application and may influence the materials used in its construction. For oxygen, carbon steel is commonly preferred due to cost and its effectiveness at the extreme temperatures endured during ASU operation.

Regulatory considerations

If the product is intended for medical application, an ASU must be certified for medical oxygen production and all liquid oxygen (LOX) storage tanks must be certified both at the site of the ASU and at the medical facility. Analytical equipment using high-purity oxygen analyzers are used in the ASU production process to ensure that the oxygen produced by the ASU is of

medical-grade quality and complies with European and US pharmacopeia directives. A quality system or testing validation process of the product is carried out on a regular basis to ensure the oxygen produced complies with the international medical gas standards. Refrigerants used to facilitate the low temperatures necessary for an ASU plant, such as hydrochlorofluorocarbons and some halocarbons, may need to be regulated by local authorities. An evaluation of local environmental regulations and guidelines may be required, and pressure vessels may need to be built to comply with local codes.

Infrastructure requirements

Two key infrastructure requirements for ASU technology include electricity and cooling water:

- *Electricity:* An ASU relies on large amounts of energy (either from electricity or other fuel sources) to maintain the cryogenic temperatures necessary for the process. For example, a 1,200-metric ton per day ASU uses over 16 megawatts of power when operating and will require a local utility company to install a dedicated power supply.
- *Cooling water:* An evaporative cooling water system (either open or closed) is required to cool the compressors and process air during the production process.

Supply/shipping

For the plant: Depending on the size and location of the facility, the duration—from the onset of the project to the first delivery of oxygen—can exceed 18 to 24 months. In addition to the mechanical equipment supplied by a manufacturer of ASU facilities, plant construction may depend on the services of multiple contractors, including excavation, concrete installation, piping installation, electrical and instrument installation, column assembly and aluminum welding, and oxygen cleaning and lube oil flushing, among others, and any one service may depend on the successful completion of another. Additionally, construction can be delayed during wet seasons in certain geographies, sometimes in excess of 45 days per year. Thorough project planning in close collaboration with the manufacturing partner will help optimize construction timelines.

For the oxygen generated: Given the scale of production, energy requirements, and associated risks, liquid oxygen is always produced off-site. In order to use liquid oxygen for medical application, there are additional equipment needs for transport, storage, and use. Different network supply and distribution options are used by different companies. The structure of a company's network can determine how quickly a supplier can respond to orders and how costly shipping is. Any liquid oxygen provider's anticipated lead-times will have to be factored in when planning for refill frequency to ensure continuity of supply.

If demands are larger, consideration should be given to installing a vacuum-insulated evaporator (VIE) tank at the health facility, sized according to refill frequency, and an evaporator, sized to meet demand. If demands are smaller, or for back-up considerations, high-pressure gas cylinders are used. There is also the option of liquid cylinders, which have built-in vaporizers and connect to a distribution manifold. However, given the potential usable volume, they are rarely the most efficient option. All storage vessels must be certified for use with medical oxygen. For delivery, cryogenic tanker trucks are used for liquid oxygen and must be certified for medical use. Trucks transporting oxygen cylinders should comply with safety protocols for transporting compressed gases.

Dependencies for use

Related equipment needed with an ASU are static vacuum-insulated storage vessels for the storage of LOX, a vaporizer at the site of production, a high-pressure gaseous cylinder filling plant to fill cylinders, and trucks to transport LOX and cylinders. For delivery purposes, cryogenic trucks and storage vessels must be validated for use with medical oxygen and cryogenic vacuum-insulated storage vessels must be present at or adjacent to the medical facility.

Maintenance

Major maintenance requires the plant be taken offline for hours to days, and supply chains must plan accordingly to accommodate the gap in production. Key requirements for appropriate maintenance of ASU technology include:

- Labor: Well-trained operators (typically 3 operators operating 3 shifts of 8 hours each) and technical maintenance support staff (operation managers, millwrights, and instrument technicians) are required to operate and maintain the production facilities 24/7.
- Liquid oxygen transport: LOX is a hazardous good and countries typically have specific regulations in place to guide its safe transportation. LOX intended for large medical facilities is usually transported by specialized road tankers to be decanted into a cryogenic vacuum-insulated storage tank located at the medical facility. For large industrial gas users, gaseous oxygen may be supplied via pipeline directly to the point of use.
- *Cylinder filling:* Depending on the facility, LOX can be vaporized into a gas and filled into cylinders using high-pressure compressors, or via a cryogenic pump and vaporizer, and transported in cylinder trucks or a flatbed truck modified for the safe transport of high-pressure gas cylinders.

Cost

The capital cost for an ASU plant is significant, and there are critical factors to consider. The first is plant size; determining the requisite size may be informed by demand and its anticipated growth rate. If demand growth is 8%, for example, plant size should allow for an initial loading of 50% capacity to enable it to reach full capacity in approximately 9.5 years. The second critical factor to consider is the distance to the user base, as transportation costs will affect the cost of the product and, ultimately, the return on investment of the ASU plant. Third, the cost of power will determine whether a more efficient plant should be built at the expense of a higher capital outlay. On average, 75% of a 200-metric ton per day ASU plant's total lifetime costs are energy costs. When taken together, capital costs can range from approximately US\$25 million for a 200-metric ton per day plant to US\$125 million for a 3,000 ton per day plant.

From a gas supplier's perspective, a high level of capital investment is common for an ASU due to the equipment requirements to support the production facilities. To ensure optimized plant operation, the gas supplier will enter into long-term contracts with medical facilities as well as large industrial gas users who will pay for service on a monthly, quarterly, or another period of frequency as determined by the contract. Accompanying infrastructure—including cryogenic vacuum-insulated storage tanks, generators, appliances, cylinder filling plant, trucks, and offices—will also require notable capital outlay. In order for the plant to achieve cost-effective production, its capacity utilization must be optimized. For the gas supplier, key operating costs include electricity, labor, and maintenance.

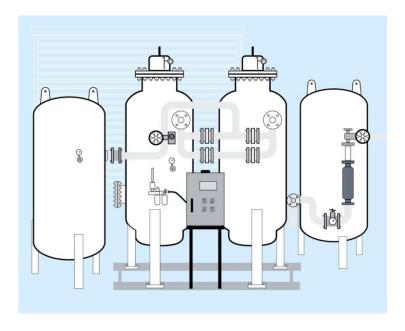
COVID-19 considerations

In the context of a global pandemic like COVID-19, additional considerations should be raised. Liquid oxygen offers the most affordable cost-per-liter pathway to deliver oxygen to facilities with high demand and is suitable for large referral hospitals with high patient loads related to COVID-19 or acute respiratory distress syndrome. This cost benefit is realized when facilities are located close to an existing liquid oxygen production plant or bulk storage hub, depending on the distribution model. However, although an ASU can affordably provide a large supply of oxygen, the time required to build and begin production will take longer than other generation modalities available, and construction is resource intensive. (For additional considerations, see Vacuum-insulated evaporator system section.)

Pressure/vacuum swing adsorption plant

Technical overview

Oxygen can be generated by using pressure swing adsorption (PSA) technology, which concentrates oxygen from ambient air. In this process, the air is dried, and impurities, such as carbon dioxide, hydroc/arbons, and water, are removed. The air passes into pressure adsorption vessels fitted with interconnecting valves that house zeolite material—a porous mineral containing aluminum and silicon compounds—that preferentially adsorbs nitrogen while allowing oxygen to pass through. Once the zeolite is saturated and the oxygen collected, the pressure in each adsorption vessel is reduced (swinging from high to low), and the nitrogen is released to allow more air to be treated to produce oxygen using the same zeolite. An on-site PSA plant can supply highpressure oxygen throughout a hospital via a central pipeline system or cylinders filled at the plant.



Vacuum swing adsorption (VSA) technology also uses a

zeolite sieve for separating the oxygen and nitrogen, but plants utilize a vacuum blower instead of an air compressor and a smaller number of adsorption vessels and valves. These systems are more energy-efficient, have lower operating costs, and can operate at higher altitudes without a reduction in performance, but typically have a higher upfront capital cost than a comparable PSA plant. They also produce oxygen at a much lower pressure than a PSA plant and often require an additional high-pressure oxygen compressor to boost pressure to meet needs of health facility piping networks. When selecting either a PSA or VSA system, irrespective of the technology, it is most important that the tender includes robust technical and performance requirements based on the intended use case and location.

Key specifications

PSA and VSA plants can vary in size and capacity, but basic specifications include oxygen production purity at 93% ±3% and continuous output pressure of 50 to 55 pounds per square inch gauge (psig) (US NFPA 99: Health Care Facilities Code) or 400 to 500 kilopascals (kPa) (ISO; piping only). They are designed for a minimum life span of 10 years and should be capable of supplying the specified oxygen concentration continuously in ambient temperatures from 10°C to 40°C, relative humidity from 15% to 95%, and elevation from 0 to at least 2,000 meters. A PSA/VSA plant should include audible and visual alarms in the event of power failure, system failure, or when oxygen concentration falls below 90% purity. For a conventional PSA plant, the nominal flow rate ranges from 8 to 2,500 liters per minute (LPM) (0.5 to 150 normal cubic meters per hour [Nm³/h]) at 50 psi. VSA plants can achieve nominal flow rates of 52 to 3,155 Nm³/h at 5 psig (34.5 kPa).

Regulatory considerations

PSA and VSA plants should have European certification (CE marking) or other stringent regulatory authority approval. Relevant guidelines include ISO 7396-1 and/or US/European Union pharmacopeia compliance standards for oxygen at 93% production purity. Registration with local health authorities may be necessary if distributing cylinders outside the facility.

Infrastructure requirements

PSA/VSA plants all require electricity and sufficient ambient air flow. For electricity, a continuous and reliable source of power, ideally 230V single-phase (for VSA and valve operations) and 380V–400V three-phase power at 50 Hz (for PSA and compressor/dryer operations), is necessary. Although there can be notable variation, a conventional PSA plant requires approximately 1.2 kilowatt hours (kWh) per Nm³ produced at 65 psig, depending on system efficiency and oxygen service pressure. For a VSA plant, approximately 0.39 kWh per Nm³ of total flow at 2.7 psig is necessary, depending on system efficiency. Energy consumption will increase for higher service pressures and if cylinder filling is required.

For operational requirements, certain environmental conditions must be met, such as air conditioning, roofing, and a proper ventilation system to ensure clean air intake for breathing; also, the designated area must not have flammable products present. The equipment generates substantial amounts of heat and requires adequate air conditioning for cooling. A PSA plant, if skid-mounted, should be in a well-ventilated housing, for security and protection from adverse weather conditions.

To note, PSA/VSA plants are also commonly configured with medical oxygen piping. Hospital pipeline systems typically supply oxygen at higher pressure to equipment such as anesthesia machines and ventilators. These systems eliminate the need for transporting heavy cylinders between hospital wards and should be composed of type L copper tubing and brazed copper fittings. A backup supply (e.g., cylinders) is required to maintain oxygen flow in case of a power outage or mechanical failure. In lieu of piping, some hospitals will instead use a compressor and fill cylinders for local use.

Supply/shipping

Depending on size, customization, and supplier's capacity, production lead times range from 2 to 24 weeks. In addition, depending on the port of origin and final destination, 2 to 12 weeks of shipping lead time is required. Installation requires complex logistics to ship multiple containers from the port of entry to the final destination, and the time required to develop the installation site must be considered (and can be done in parallel). Systems may be assembled on-site or are available preassembled on a skid or shipping container installation. Furthermore, considerations should be made the routine maintenance and repairs, which will require a supply of spare parts. In many settings, a stockpile of manufacturer-recommended spare parts is advised to ensure interruptions remain short.

Dependencies for use

Depending on manufacturer recommendations, a compressed air surge tank and/or oxygen receiver tank, an air compressor, and a filter/drier for the air compressor may be required. In that event, it is common for PSA/VSA manufacturers to provide recommended models or specifications with additional equipment as a package. For piping, flowmeters and regulators are necessary. Other related equipment could include a high-pressure oxygen compressor, in the event that the PSA/VSA plant will be used for cylinder filling.

Maintenance

For *preventive* (scheduled) maintenance, a buyer/owner can contract with the manufacturer for maintenance that requires highly trained technicians and engineers. This can include cleaning or replacing filters, draining water or oil traps, replacing lubricants, and calibrating pressure and oxygen sensors. The plant operating environment should be maintained with correct ventilation and cooling. Although common, such a maintenance agreement may not always be feasible, and in such an instance, buyers should evaluate whether there are trained technicians or qualified third parties available to service the system.

For *corrective* maintenance, it may be necessary to rebuild a valve assembly or compressor in the event of failure. Additionally, sieve beds must be recharged periodically if there is a reduction in performance in the oxygen generating capacity or purity.

Cost

The investment costs for a PSA or VSA plant depends on size, functionality, equipment, whether accessories (or other products) are purchased, and whether the product is containerized (which would require lower plant housing costs). Generally, PSA plants require a lower capital expenditure than VSA plants, which command a 10% to 20% premium in upfront costs, and may require a compressor to feed a piped system. The improved efficiency of VSA plants, however, could allow for notably lower operating costs that balance the upfront costs quickly. As a reference, for a large hospital (greater than 1,000 beds) in east Africa requiring a total oxygen capacity of 4,114 kg per day of 93% purity, a PSA plant solution is estimated to cost US\$800,000 with anticipated monthly operating expenditures of US\$1,900 to cover electricity, service, and maintenance. A VSA plant for the same hospital, daily volume, and purity is estimated at approximately US\$880,000 with anticipated monthly operating expenditures of US\$1,000. For smaller health facilities (150 to 200 beds), a plant with suitable production volumes will be closer to US\$100,000 to US\$110,000. Prices may vary significantly depending on manufacturer, production volume, purity level, and other factors. In general, a CE mark or other stringent regulatory approval on a plant will add approximately 5% to the price of a new unit. It is important to research local production demands and thoroughly understand the operating requirements and associated costs of the equipment under consideration.

COVID-19 considerations

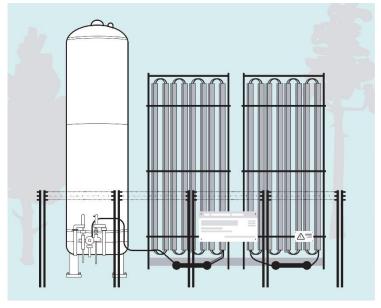
In the context of a global pandemic like COVID-19, additional considerations should be raised, including:

- PSA and VSA plants can be scaled depending on production volume needs. Smaller plants can be skid-mounted and
 delivered to health facilities for on-site production. Large, permanent systems can be built farther afield and oxygen
 from the facility can be stored in cylinders and delivered via cylinder trucks. Further, PSA and VSA plants can be
 configured for dual use when the plant is co-located at a health facility with directly piped oxygen supply along with a
 booster compressor to fill and distribute oxygen cylinders to other, nearby health facilities.
- Smaller, on-site plants are largely self-sufficient and do not require constant technician involvement, but qualified staff presence is necessary to prevent problematic outcomes.
- On-site PSA/VSA systems should ensure infection control practices are relevant to the piping system that delivers the oxygen from the plant to the patient rooms.

Vacuum-insulated evaporator system

Technical overview

A cryogenic liquid oxygen storage tank is an insulated vessel consisting of a carbon steel outer shell and a stainless-steel inner vessel, with an insulating vacuum space between the layers to minimize heat ingress. Oxygen liquifies at -183°C at one atmosphere of pressure and is generally stored at pressures closer to 23 atmospheres. Together with vaporizers, valves, piping, and a pressure control and pressure relief system, the tank constitutes a vacuuminsulated evaporator (VIE), which can supply a central oxygen piping system in a medical facility and is often leased from the medical gas supplier. Oxygen enters the piping system after passive evaporation in the vaporizer, and therefore does not require a source of power. VIEs can be configured to fill cylinders, too, without electricity. Transporting oxygen to these tanks and storing it as a liquid takes less space and is less expensive than moving and



storing it as a gas under high pressure, as one liter of liquid oxygen produces 861 liters of gaseous oxygen. Although liquid oxygen is economical for facilities that use large quantities, the bulk liquid to fill the tanks is produced at a cryogenic air separation unit (ASU) and requires a specialized bulk road tanker for transport from ASU to VIE. Careful handling is required due to the possibility of accidentally rupturing the pressurized tank, which could lead to safety risks such as cold burns and a source of ignition for fires.

Key specifications

Key requirements for properly operating VIEs include:

- A cryogenic liquid oxygen tank which can be installed in a vertical or horizontal position.
- Capacity typically ranges from 500 to 25,000 liters of liquid oxygen storage for health facility use. Larger capacity units can be custom built as needed.
- The maximum allowable working pressure ranges from 1 to 37 atmospheres.
- Hold time (time between filling and the unit venting to atmosphere) for the tank ranges from 10 to 150 days, based on the manufacturer specifications and the ambient conditions.
- Flow capacities between 150 and 20,000 liters per minute, based on the vaporizer design and specification.
- Different approved fill adaptors are used for filling liquid oxygen VIEs and liquid nitrogen VIEs to prevent inadvertent cross filling.

Regulatory considerations

It is advisable to confirm with a supplier that VIEs under consideration adhere to ASME Boiler and Pressure Vessel Certification standards and ensure pressure vessel certification, as well as ISO 21029 requirements addressing the design, fabrication, inspection, and testing of VIEs. Quality management protocols should adhere to ISO 9001/2000 to ensure consistency and applicable regulatory requirements. VIEs must also comply to the following regulatory requirements:

- ISO 20421-1 for Cryogenic vessels Large transportable vacuum-insulated vessels Part 1: Design, fabrication, inspection, and testing
- ISO 21009-1 for Cryogenic vessels Static vacuum-insulated vessels Part 1: Design, fabrication, inspection, and tests
- ISO 21010 for Cryogenic vessels Gas/materials compatibility
- ISO 21013-1 for Cryogenic vessels Pressure-relief accessories for cryogenic service Part 1: Reclosable pressure relief valves
- ISO 23208 for Cryogenic vessels Cleanliness for cryogenic service

Infrastructure requirements

While a VIE itself does not require electricity to operate, its filling pumps, monitoring systems, alarms, and other safety features do. VIE and support infrastructure must be placed in a secure, fenced, well-ventilated area that is free of overhead powerlines and other potential sources of ignition, such as diesel generators. Parking and smoking must be strictly prohibited. The fenced area must be fitted with safety signage prescribed by international safety directives. The tank must be accessible by large cryogenic bulk road tankers for refills. A central pipeline distribution system with vaporizers is required, along with ancillary shut-off valves, pressure-reducing and safety valves, and pressure flow regulators. If an ambient vaporizer is used, it must have adequate airflow to absorb sufficient heat and prevent icing, although an electrically heated vaporizer is available for colder climates. The vaporizer must also be sized correctly to meet the maximum flow rate required by the medical facility. A second vaporizer is normally installed to enable continuous operation on 8-hour cycles, to minimize the build-up of ice.

Supply/shipping

For the VIE: Prefabricated vacuum-insulated tanks and vaporizers can be ordered from a manufacturer and, depending on geography, may be delivered in approximately 1 month. Preparing the site, including excavation, leveling, concrete pouring, or other activity required for the location of the VIE, should be addressed in advance. Installation, both of the VIE system and its associated piping, may take 5 to 7 days depending on the unit, site proximity, and availability of technicians. Typically, a large gas manufacturer and supplier have a range of different sizes of VIEs that can be deployed to medical health facilities, thereby reducing VIE manufacturing lead times. If sufficient infrastructure is available, the lead time from order placement to delivery for a VIE is 3 to 6 months, but for urgent applications, VIEs can be installed and be operational within 4 weeks to the medical facility. Transportation lead times depend on distance, road conditions, and availability of suitable trucks such as flatbeds.

For the oxygen generated: The liquid oxygen that is stored in a VIE is produced commercially in a continuous process from an ASU. A VIE can also be used by a bulk oxygen company as intermediate storage (e.g., when importing liquid oxygen into the country). After vaporizing the liquid oxygen, a booster compressor can be used to fill cylinders for local distribution to hospitals. Some VIEs can provide liquid-to-gas cylinder filling without the need for a compressor. Further, VIEs installed in a standard shipping container frame can be used as mobile sources of oxygen supply for field hospitals (these are commonly known as "ISO-tanks"). Shipments of liquid oxygen by cryogenic road tankers must comply with local transportation regulations of the country, and different network options are used by companies to optimize delivery. The structure of a company's network can determine how quickly a supplier can respond to orders.

Dependencies for use

The following accessories are needed for VIE operation at a hospital:

- Vaporizer to convert liquid oxygen to gaseous oxygen.
- Piping to deliver gaseous oxygen to/through a facility.
- VIE configured to fill cylinders directly where cylinder filling is required.
- Pressure controls and pressure relief systems for safe use and operation.
- System and operation alarms.

Maintenance

VIE maintenance requires highly trained technicians or engineers. Because VIEs are leased to medical facilities and are maintained by the gas supplier, technicians and engineers for maintenance are provided as part of a gas supply contract.

Preventive (scheduled) tasks include but are not limited to cleaning grease and oil from metallic components with an appropriate cleaning solvent (such as trichloroethylene), maintaining the VIE in good operating condition, and regularly inspecting key system components. VIE inspection and maintenance tasks (which depend on the original equipment manufacturer and local regulations) generally are recommended as follows: valves and fittings must be checked quarterly for leaks and other malfunctions, level and pressure gauges must be inspected annually, relief valves to verify proper settings must be checked every two years, and the VIE bursting discs (if fitted) should be replaced every two years.

For *corrective* maintenance, plumbing must return to ambient temperature before any repair work is performed. The VIEs must be vented or drained as specified before replacing any component(s) exposed to pressure or to cryogenic liquid.

Cost

Depending on a VIE's size, installation with all required infrastructure (e.g., pipes, vaporizer, housing, and shady location) can cost from US\$10,000 to US\$100,000. Typically, facilities will enter into a leasing agreement with a service provider. Cost to lease and provide maintenance/operational service can be up to 40% of the VIE cost on an annual basis. Thus, a US\$100,000 VIE will merit a monthly payment of US\$3,330. Additional costs to install delivery technology such as pipes for transfer into hospitals or a cylinder-filling plant may need to be considered. In addition to procurement and transportation cost for liquid oxygen storage tank, operating costs include maintenance and labor.

COVID-19 considerations

In the context of a global pandemic like COVID-19, additional considerations should be raised, including:

- Liquid oxygen offers the most affordable cost-per-liter pathway to deliver oxygen to facilities with high demand and is suitable for large referral hospitals with high patient loads related to COVID-19 or acute respiratory distress syndrome. This cost benefit is realized when facilities are located close to a liquid oxygen production plant or bulk storage hub, depending on the distribution model.
- High demand for liquid oxygen delivery and subsequent increased frequency for VIE refills require logistics
 considerations to ensure uninterrupted service. In addition, when meeting or exceeding peak demand—as may occur
 during the pandemic—vaporizers that convert oxygen from a liquid to gaseous state may require additional monitoring.
 Higher flow volumes, particularly in humid environments, will cause ice build-up on the vaporizer (which can be
 mitigated by increasing the size, twinning, de-icing with water, or heating).

Oxygen concentrators

Technical overview

An oxygen concentrator is a medical device that draws in ambient air and passes it through molecular sieve beds to remove nitrogen, thereby concentrating room oxygen to therapeutic levels for safe delivery to patients. Concentrators can provide a sustainable source of medical oxygen across many levels of health systems at facilities that have reliable electricity.

Key specifications

Oxygen concentrators deliver a continuous flow of oxygen (typically between 90% and 96% concentration) and usually have one built-in-flowmeter (sometimes two) to control the flow of oxygen supplied in liters per minute (LPM). The typical maximum output flow rate ranges from 3 to 12 LPM but can exceed 20 LPM in some units. Oxygen concentrator output pressures range between 30 and 135 kilopascals (kPa). These pressures and flow rates may be insufficient for use with certain equipment, so it is recommended to check the oxygen requirements of accessories to ensure compatibility.



- Audio alarms must be included to alert users of oxygen concentrations below 82%, no flow of oxygen, power supply
 failure, low battery, overheating, and high or low system pressure. Alarms are also indicators that maintenance is
 needed.
- Oxygen concentrator manuals must be provided and shall include information on how to troubleshoot common issues with the device.
- The recommended weight of a lightweight oxygen concentrator is less than 27 kilograms.
- Oxygen concentrators should make no more than 50 A-weighted decibels of noise when being used.
- Oxygen concentrators should have a power consumption of less than 70 watts per LPM.

Review the specifications and technical requirements as listed in the <u>WHO-UNICEF Technical Specifications and Guidance for Oxygen Therapy Devices</u> for oxygen concentrators as well as the <u>WHO Technical Specifications for Oxygen Concentrators</u>.

Regulatory considerations

Oxygen concentrators must be approved by a national regulatory authority of the country of use, and/or any stringent regulatory authority (such as the United States Food and Drug Administration [FDA] or European certification [CE mark]) depending on the country's regulatory requirements. They must also comply with the latest ISO 80601-2-69 or its equivalent.

Infrastructure requirements

To ensure the safety and functionality of an oxygen concentrator, it must have an electrical plug that is compatible with the power outlets of its designated location with an alternating current power format. Furthermore, a concentrator must be

configured to match in-country power supply. The two most common configurations are 120 volt (V)/60 hertz (Hz) and 220 V/50 Hz. However, there are enough alternate variations that warrant exploration for each procurement.

Back-up power sources, such as generators or uninterruptible power supply, can help provide oxygen during power outages. Power conditioning devices like voltage stabilizers and surge suppressors can help protect the electronics to extend the life of the unit. Oxygen concentrator power requirements can vary from 300 to 600 watts, and these must be accommodated. Deployment of a concentrator will require trained clinical providers and maintenance technicians.

Supply/shipping

The production lead time of oxygen concentrators ranges from 1 to 2 weeks but may take up to 8 weeks or more during high demand. Five to 10 LPM concentrators typically measure 35 to 55 cm wide, 25 to 40 cm deep, and 50 to 70 cm high. They are usually packaged in individual boxes and weigh 15 to 30 kg, with 10 LPM models being heavier and larger than most 5 LPM models. Shipping lead time varies depending on the port of origin and destination, typically between 2 and 12 weeks.

Dependencies for use

To ensure the effectiveness of an oxygen concentrator, it requires a variety of accessories, such as oxygen adaptors, oxygen delivery tubing, an oxygen delivery interface (e.g., nasal prongs, nasal catheter), a flowmeter stand with mounted flowmeters, and a bubble humidifier. An external, hand-held oxygen analyzer must be available for any facility with a concentrator. The cost for an oxygen analyzer might be a deterrent, but they should be made available for all trained technicians.

Maintenance

Maintenance for oxygen concentrators is divided into preventive (scheduled) and corrective:

- Under *preventive* maintenance, buyers are recommended to schedule a maintenance appointment with a trained technician at least once per year or every 5,000 operating hours. A trained technician will check oxygen concentration with an oxygen analyzer, check the pressure with a pressure gauge, replace filters as necessary, and check output pressure and flow rate (bubble test). Regular cleaning and decontamination should be performed. Gross particle filters should be removed, washed, and dried weekly or more often in a dusty environment.
- Under *corrective* maintenance, buyers will have to adjust or replace device components over time, typically as the result of a device failure or reduction in performance. Commonly replaced components include but are not limited to a compressor, circuit board, internal tubing, sensors, sieve beds, valves, and a ventilation fan.

With proper maintenance and repair, oxygen concentrators can have a lifetime of at least seven years.

Cost

The investment for an oxygen concentrator varies across device models, including the output capacity, manufacturers, and locations. Costs range from US\$400 to US\$2,000 per concentrator, and approximately US\$80 to US\$400 for analyzers. Operating costs include electricity, repairs, and maintenance, which will vary by geography, availability of replacement parts, and the on-site technician's skill levels, respectively. Oxygen concentrators have a minimal cost for initial on-site set-up and installation per unit, but buyers need to consider spare-part supply for maintenance and ongoing power costs.

COVID-19 considerations

In the context of a global pandemic like COVID-19, additional considerations should be raised, including:

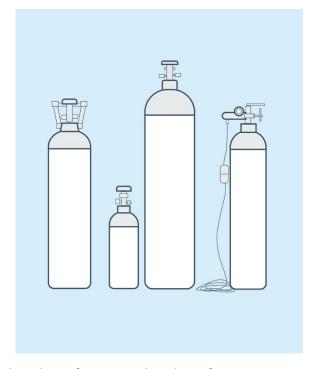
- Only concentrators with the requisite pressure specifications can be used to support ventilation. Most ventilators require a 50-psi gas supply, and some have a built-in air compressor. Ensure that concentrators used in combination with mechanical ventilation meet this threshold.
- Due to higher usage during the pandemic, the concentrator's filters should be cleaned more frequently to reduce the risk of contamination.
- Concurrent usage of pulse oximeters is recommended. Other related equipment, such as anesthesia machines, bubble continuous positive airway pressure, and nebulizers, are optional and may require greater pressure than that provided by the available concentrator.
- During the COVID-19 pandemic, production/shipping delays vary by manufacturers.

Oxygen cylinders

Technical overview

Cylinders are durable and refillable containers that hold compressed gases, such as oxygen, in a high-pressure (between 725 and 2,900 psig), non-liquid state. Portable cylinders range in size from approximately 50 to 1,000 liters (L) of compressed gas, while larger stationary tanks can store up to about 10,000L of compressed gas. Gas used to fill cylinders can be produced in multiple ways, including pressure swing adsorption (PSA), vacuum swing adsorption (VSA), or cryogenic distillation at an air separation unit (ASU).

Oxygen cylinders are graded according to liquid capacity (by liter) and fill pressure (kPa) and are color-coded to specify the contents (typically black with white shoulder per ISO standards; some geographies denote medical oxygen cylinders in green or blue). They should be transported to health facilities with their valve head protected by a steel cover or a carrying handle. A regulator and flowmeter assembly is used to access the oxygen supply, whether direct or to other medical devices. Oxygen cylinders may be the primary oxygen source or serve as a back-up supply for health facilities with another primary source for oxygen. Review the



specifications and technical requirements as listed in the <u>WHO-UNICEF Technical Specifications and Guidance for Oxygen</u> <u>Therapy Devices</u>.

Key specifications

- Oxygen cylinders that store compressed oxygen are typically constructed of steel or an aluminum alloy.
- Standard cylinder sizes under ISO international standard are size AZ, C, D, E, F, G, H, and J, and United States (US) sizes are M2 to M265.
- Cylinders must be used with a pressure regulator in order to release oxygen at the correct working pressure.
- Standard (bullnose or pin-index) or integral valves are compatible to use with oxygen cylinders. If a standard valve is selected, it must comply with international ISO and US standards, which are ISO 407/BS 850/CGA 870 valve, CGA 540 valve, or % inch BSP (F) Bullnose BS 341 valve.
- If the cylinder employs an integral valve, a manometer and flow regulator (400 kilopascals nominal outlet pressure) are already affixed to some but not all cylinder heads, and typically have a 6 millimeter (mm) barbed fitting, and BS Schrader outlet. Available sizes for integral valves under ISO are ZA, CD, ZD, HX, ZX, and US sizes in the M coding system. The nominal pressure for an integral valve cylinder ranges from 23,000 to 30,000 kPa (3,336 to 4,351 psi) depending on the cylinder capacity, and a standard valve cylinder nominal pressure is 13,700 kPa (1,987 psi).

Regulatory considerations

Oxygen cylinders are required to provide proof of regulatory compliance and risk classifications per product. They must have the correct labels at all times and need to be color-coded accordingly. Transport and storage regulations for oxygen cylinders vary depending on the cylinder's current capacity status (e.g., empty, partially filled, or full) and require hydrostatic pressure testing every five years. Oxygen cylinders must comply with international standards and with the Globally Harmonized System of Classification and Labeling of Chemicals regulations on hazardous goods, flammable, explosive, and compressed gas (usually black, red, orange, and green diamonds, respectively). Local fire codes may also dictate requirements for storage and handling of oxygen cylinders, such as ventilation, separation from flammables or ignition sources, and protection against tipping.

Infrastructure requirements

Oxygen cylinders require no electricity to be functional. They can provide oxygen to patients in two primary ways:

- **Directly within patient care areas:** Cylinders can be placed at or close to the patient and need to be accompanied with pressure regulators, associated gauges, and flowmeters.
- Piped into a health facility via a distribution manifold system: Distribution manifolds supplying piped systems are permanent installations of copper piping (typically type L) with brazed copper fittings. Manifolds have pressure regulation built into the header of both banks to ensure that pressure entering the system will be adequate to reach the bedside terminal unit. These piped systems need only a flowmeter with the appropriate connection fitting at the wall outlet (also known as bedside or terminal unit).

The health facility will need to have a system for organizing filled, partially filled, and empty cylinders regardless of system so that they may be replaced rapidly in case of emergency.

Supply/shipping

Transport of cylinders: Cylinders are usually transported via flatbed trucks, but the mode of transportation can vary within different companies. Trucks should include placards or appropriate signage with hazard statements, signal words, and pictograms in accordance with local regulations for the transport of flammable compressed gas (see *Regulatory considerations* above). Companies also use different distribution networks, which can influence a supplier's response time from hours to days and their logistical costs. Depending on local supply conditions, health facilities may contract delivery for cylinder refills or transport to and from supply depots themselves or via third party logistics services.

Supply of cylinders to a health facility: In normal conditions where there are only moderate fluctuations in demand (unlike pandemic situations), cylinder delivery can be prompt as suppliers draw from their reserve inventory.

Purchasing new cylinders from a manufacturer: When medical demand exceeds available inventory, suppliers may procure additional cylinders and, in medical emergencies, recall cylinders from industrial customers. Increased demand may lead to bottlenecks in either production or raw materialⁱ access, contributing to substantial delays. Shipping lead time varies depending on the port of origin and destination, which typically requires 2 to 12 weeks.

¹ The primary raw materials for cylinders are aluminum (aluminum alloy 6061) and steel. Aluminum is used to manufacture a range of cylinder sizes, but larger cylinders may also be manufactured from steel. Stainless steel is used almost exclusively for liquid oxygen storage (such as vacuum-insulated evaporator).

Dependencies for use

Oxygen cylinders require a variety of accessories to ensure effectiveness. At an operational level, cylinders will need the following accessories to be functional: cylinder-holding carts or trolleys; keys (or spanners/wrenches) to open valves; pressure regulators; tubing adapters for use with pressure regulators and/or integral valve with all common international standard fittings; flowmeter; non-heated bubble humidifier; and common and frequently used spare parts such as sealing set, maintenance kit, regulating unit (knobs), adapters, and connectors.

Upon delivery of the oxygen to a patient, oxygen cylinders will require nasal cannulae, masks, tubing, nasal catheter or high-flow nasal cannulae, pulse oximeter, heated humidifier, blender, and continuous positive airway pressure machines. If cylinders are attached to a manifold system, a flowmeter is needed at the bedside terminal.

Maintenance

With proper maintenance and repair, a cylinder lifespan is around 20 to 25 years; valves and flowmeters last approximately 7 to 10 years. Preventive (scheduled) maintenance for oxygen cylinders consists of conducting a visual evaluation and a function check prior to use to ensure sufficient pressure. These tasks should be performed daily. In addition, valves and regulators require periodic checks for functionality. Planned maintenance with regular cleaning and functionality checks should be performed by a certified service provider for compressed medical gases, and cylinders themselves should include hydrostatic pressure testing every five years. For safety purposes, broken or defective cylinders should be replaced immediately.

Cost

Cost of cylinders from a manufacturer: The price of a "J" or equivalent-sized cylinder (6,800-L nominal content/oxygen capacity) can range from US\$54 to US\$229, with a median of US\$71, from a manufacturer. However, in situations of high demand, such as the COVID-19 pandemic, prices can increase substantially or fluctuate rapidly with global demand.

Cost of leasing from a medical oxygen provider: Medical oxygen providers generally take on the responsibility of cylinder procurement, filling, and maintenance as part of a leasing agreement with the health facility or health system. The lessee will put up collateral to the provider against the risk of damage to or loss of a cylinder tank. Thus, an initial deposit is typically paid prior to a monthly rental fee, which is approximately US\$25 per cylinder (in addition to deposit) but can vary widely depending on the service provider. Costs of necessary accessories, such as regulators, are also born by the lessee.

Cost of cylinder filling: Filling fees for standard "J" cylinders, 6.8 cubic meters of gas, can vary broadly due to differences in production costs, with a spread of roughly US\$23 to US\$112 depending on geography. Transport, inspection, and maintenance costs are often bundled with the refill cost."

COVID-19 considerations

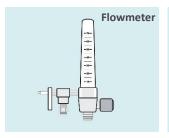
In the context of a global pandemic like COVID-19, additional considerations should be raised. For example, to reduce the spread of COVID-19 through surface contamination, cylinders and associated accessories should be cleaned regularly. This cleaning should take place in a "decontamination zone" before leaving any area of known contamination. If there is any suspected contaminated contact to the cylinder, decontaminate it immediately.

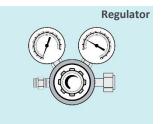
[&]quot;This information comes from: Davies M, Onwuzoo A, Mednick S. Fighting for breath: How the medical oxygen industry is failing African hospitals. *The Guardian*. August 10, 2020. https://www.theguardian.com/global-development/2020/aug/10/fighting-for-breath-how-the-medical-oxygen-industry-is-failing-african-hospitals.

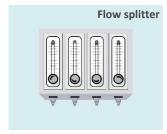
Oxygen therapy accessories

Technical overview

Oxygen therapy accessories are devices that help regulate the delivery of oxygen from sources, such as central lines, cylinders, or concentrators, to patients. These products include various types of flowmeters (i.e., Thorpe tube flowmeters, click-style dial flowmeters, Bourdon tube gauges); pressure-reducing valves (or regulators); and flow splitters. These devices ensure safe delivery of oxygen to the patient and reduce costs through the proper management of oxygen volumes delivered.







Key specifications

Key specifications for oxygen therapy accessories are as follows:

- Pressure-reducing valve or regulator: When fully closed, it
 must have a minimum flow rate of zero liters per minute.
- *Input connection*: There should be either a Diameter Index Safety System (DISS) threaded fitting or a 6mm barbed fitting for the inlet port.
- Cylinder valves: There are three common types of fitting: pin-index, bullnose, and integral.
- Thorpe tube flowmeters: These should have a clear, readable, and graduated column made of a shatter-resistant
 medically certified polymer. The needle valve and body of the Thorpe tube flowmeter should be made from aluminum
 or brass and must be calibrated to between 345 and 380 kilopascals (kPa) inlet gauge pressure. Flowmeters must be
 compatible with in-situ terminal units, and product selection decisions should take the required specifications into
 account. Terminal units have different connection styles, including DISS, Ohmeda, Chemetron, AFNOR,
 Oxequip/Medstar, Schrader, and Puritan-Bennett.

Regulatory considerations

Oxygen therapy accessories are required to provide proof of regulatory compliance and risk classifications per product under the following United States (US), European Union (EU), and Japan regulations:

- 21CFR part 820 (US).
- 21CFR part 868.2320 (US) Uncompensated Thorpe tube flowmeter.
- 21CFR part 868.2340 (US) Compensated Thorpe tube flowmeter.
- Regulation (EU) 2017/745.
- MHLW Ordinance No. 169 (Japan).
- 37132000 Flowmeter (Japan), oxygen therapy.

Oxygen therapy accessories must comply with the following international standards:

- ISO 13485 regulatory requirements of medical devices Quality management systems requirement for regulatory purposes.
- ISO 14971 for the application of risk management to medical devices.

Compliance with the latest available version is recommended, and devices must be rated and cleaned for service as part of regular maintenance at or equivalent to the standards set by the Compressed Gas Association's guidance CGA-4.1 for the cleaning of equipment for oxygen service.

Review the specifications and technical requirements as listed in the <u>WHO-UNICEF Technical Specifications and Guidance for</u> Oxygen Therapy Devices for these oxygen accessories.

Infrastructure requirements

Oxygen therapy accessories require no electricity. All devices are passive, operating via the flow of medical gases. Accessories can be connected to piped or cylinder oxygen supplies. Flowmeter stands can also be used with oxygen concentrators. Note that a pressure regulator must always be connected with cylinders before using a Thorpe tube flowmeter.

Supply/shipping

Production and shipping lead times for oxygen therapy accessories vary and depend on multiple factors, including the port of origin and destination. During peak demand or stockouts, delays of up to 12 weeks could be expected. Placing bulk orders in advance can reduce the probability of stockouts. See the <u>Respiratory Care Equipment Market Report</u> for additional information.

Maintenance

Maintenance for oxygen therapy accessories can be preventive (scheduled) or corrective:

Preventive maintenance involves the following elements:

- Accessories must be used according to the rated pressure of the flowmeter.
- Flowmeters must be regularly checked and cleaned, and prior to cleaning, the device must be disconnected.
- A flowmeter's exterior surface must be clean and sanitized according to the manufacturer's prevention and control protocol.
- The use of lubricants is prohibited, as they are flammable.

Corrective maintenance involves the following elements:

- Use of any defective device must stop immediately.
- Faulty devices are not recommended for repair, but instead should be promptly replaced.

Cost

The cost of oxygen therapy accessories varies according to the selection of products, the number of units procured (discounts may be available for volume purchases), manufacturers, and locations. Furthermore, desired technical performance

specifications, from percent accuracy (flowmeters) and pressure rating (valves and regulators), broaden the spread of anticipated costs for the accessory in question. Anticipated ranges for the accessories may include iii:

- Thorpe tube flowmeter, US\$20 to US\$140.
- Click-style dial flowmeter, US\$57 to US\$150.
- Bourdon tube gauge, US\$65 to US\$200.
- Pressure-reducing valve (or regulator), US\$30 to US\$280.
- Flow splitter, US\$113 to US\$220

Additional information

Flowmeters should be connected to humidifiers when delivering oxygen to patients via nasal cannulae and catheters at a higher flow rate (greater than two liters per minute).

COVID-19 considerations

In the context of a global pandemic like COVID-19, additional considerations should be raised, including:

- Accessories in patient environments should undergo regular surface decontamination.
- Production and shipping lead times should account for potential delays.

iii For the click-style flowmeter and the pressure-reducing valve/regulator, the range can be predicated on accuracy specifications and pressure rating, respectively. Sources for the anticipated ranges cited include Grainger, Medical Gas Installers, Broward A&C Medical Supply, 4MD Medical, and Medex Supply.

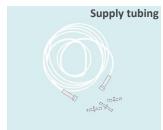
Oxygen therapy interfaces

Technical overview

Oxygen therapy interfaces are specialized, single-use products involved in respiratory disease management. These products enable health care professionals to administer supplementary oxygen to patients so that appropriate oxygen levels in the blood are maintained. Consumable products include nasal cannulae (prongs), nasal catheters or nasopharyngeal catheters, masks for non-invasive oxygen therapy (i.e., non-ventilator use), supply tubing, bubble humidifiers, and an assortment of connectors and adapters.







Key specifications

Key requirements for oxygen therapy interfaces noted above are:

- Nasal cannulae: Must be fitted with prongs and available in multiple sizes, including preterm, neonatal, pediatric, and adult.
- Supply tubing:
 - Different lengths of supply tubes should be available.
 - Single-use tubing is typically made from flexible clear or colored transparent polyvinyl chloride and should be kinkor crush-resistant to prevent permanent deformation if bent. Reinforced elastomeric or rigid tubing may be used in reusable applications and is typically capable of withstanding higher pressures.
 - For tubing, products also need to comply with US Food and Drug Administration (FDA) Title 21/USP VI, be certified
 for medical use, and 60 Shore A (ASTMD-2240).
 - Tubing wall thickness must be between 1.58 and 2.38 millimeters (mm) (1/16 and 3/32 inches). Internal diameter must range from 3 to 5 mm (1/8 to 3/16 inches) and must be compatible with standard 6-mm barbed (ribbed and tapered) fitting.
 - For a nasal catheter, sizing is presented in units of French gauge, which is equivalent to three times the tubing diameter in millimeters.
 - Masks should be available in both pediatric and adult sizes. The World Health Organization recommends a supply of 30 non-invasive masks per ventilator to be available.
- Bubble humidifier: Must have a flow rate capacity of up to 15 liters per minute, with a pressure relief safety valve of less than or equal to 14 kilopascals (kPa) or two pounds per square inch gauge (psig). It must also be paired with a Diameter Index Safety System (DISS) inlet connector for easy connection to flowmeter, and a barbed outlet connector for easy connection to tubing. A bubble humidifier works best at a water temperature of at least 30°C.

iv This information comes from: World Health Organization (WHO). Chapter 4: Technical specifications for invasive and non-invasive ventilators. In: Priority Medical Devices List for the COVID-19 Response and Associated Technical Specifications. Geneva: WHO; 2020. https://www.who.int/medical_devices/priority/Chapter_4_20167_WHO_Priority_medical_devices_list_for_COVID_19_response_4.pdf?ua=1.

• Barbed conical outlet adapter: To ensure safety, a barbed conical oxygen-specific outlet adapter must be used for connection to the DISS oxygen outlet port. DISS outlets differ in size depending on the type of medical gas used.

Review the specifications and technical requirements as listed in the <u>WHO-UNICEF Technical Specifications and Guidance for Oxygen Therapy Devices</u> for oxygen therapy interfaces.

Regulatory considerations

Oxygen therapy interfaces are required to provide proof of regulatory compliance and risk classifications per product, including the registration, clearance, and approval of each. This compliance should be appropriate per the risk classification of the given product. Oxygen therapy interfaces must comply with the following standards:

- ISO standards for biomedical equipment.
- ISO 13485 for medical devices and quality management regulatory requirements.
- ISO 14971 for application of risk management to medical devices.
- ISO 10993-1 for part 1 of the evaluation and testing within a risk management process.

Infrastructure requirements

Oxygen therapy interfaces have no infrastructure requirements.

Supply/shipping

Production and shipping lead times for oxygen therapy interfaces vary and depend on multiple factors, including the port of origin and destination. Placing bulk orders can help avoid stockouts.

Maintenance

Oxygen therapy interface products are single-use and, therefore, require no maintenance. If any interface product breaks, it is not repairable. Consumables such as (but not limited to) nasal cannulae, nasal catheters, and masks must be disposed of after a single use to prevent contamination. Some bubble humidifiers can be reused if properly decontaminated before use with another patient. Water inside a bubble humidifier must be replaced daily while in use, and the bottle must be decontaminated between uses.^v

Cost

Oxygen therapy interfaces are generally low-cost, with pricing varying based on the selection of products, the number of orders, manufacturers, and location. Indicative price ranges for the accessories are as follows^{vi}:

^v This information comes from: World Health Organization (WHO), United Nations Children's Fund (UNICEF). WHO-UNICEF Technical Specifications and Guidance for Oxygen Therapy Devices. Geneva: WHO; 2019. https://apps.who.int/iris/bitstream/handle/10665/329874/9789241516914-eng.pdf?ua=1.

vi Sources for the ranges cited include Grainger, UNICEF, 911 Emergency Supply, United Health Supply, Medex Supply.

- Nasal cannulae, US\$0.34 to US\$3.25.
- Nasal catheters or nasopharyngeal catheters, US\$3.49 to US\$4.80.
- Masks for non-invasive oxygen therapy, US\$0.89 to US\$2.95.
- Oxygen supply tubing, US\$0.55 to US\$3.95.
- Bubble humidifiers, US\$3.95 to US\$127.00.
- Barbed conical adapters, US\$24.00 to US\$50.00.

COVID-19 considerations

In the context of a global pandemic like COVID-19, additional considerations should be flagged, including:

- Surface decontamination should be practiced when handling or disposing of used consumables.
- Production and shipping lead time should account for potential delays.

