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Overview of regulatory requirements for medical gases and pharmaceutical gases

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Abstract
Generally medical gases are administered or supplied directly to the patients. They should be monitored as required by the respective regulatory authorities of every country or via a central line which runs through the entire hospital. They should be manufactured and transferred with the highest quality possible as per standards and limits decided by the different regulatory authorities. For the manufacturing of the medical gases manufacturer needs to issue license (or regulatory approval) hence they justify about maintaining quality of the gases as standard/limitation regarding quality decided by the drug regulatory authorities.
Pharmaceutical gases is defined as gaseous material that are manufactured for the use in pharmaceutical industries and laboratories and used in Process/Quality Control and R&D for hydrogenation process, reactors, analytical instruments etc. They are needed to handle under the standards with which they are governed are strictly controlled by a nation's pharmacological oversight agency.

Keywords: medical gas, pharmaceutical gas, regulatory requirements, regulatory authorities standard for gases, healthcare facilities, quality of gases, safety

Introduction
Medical and pharmaceutical gases are fluids manufactured specifically for the medical, pharmaceutical manufacturing and biotechnology industries. They are frequently used to synthesize, sterilize and insulate process or product which contributes to human health.
A medical gas a medicinal product (pharmaceutical) used for treating or preventing disease and for life support of human beings. The use of medical gases should be subject to prescription by a clinician.
Due to the fact that all medical gases are considered drugs which are only available by prescription, the standards with which they are governed are strictly controlled by a nation's pharmacological oversight agency.
The Four Tenets of Medical Gas System Safety:

Continuity
The gas supplies must always be available

Adequacy
The correct flow and pressure must always be delivered

Identity
The correct gas should always be administered

Quality
Gases must be safe and pure

Medical Gases [1, 2]
"A medical gas is defined as one that is manufactured, packaged, and intended for administration to a patient in anesthesia, therapy, or diagnosis."
As a therapeutics gas are prescribed as an anesthetic, drug delivery agent, or remedy for an occurring illness, pneumatic power source for surgical and dental tools.
Medical gases are provided by licensed manufacturers who meet the quality controls which have been established by a jurisdiction's prescription drug regulating agency.
Medical gases must be extremely pure, with at least 99.995% of the gas congruent to how it is identified.
With the exception of medical-grade oxygen, all medical gases are delivered in compressed gas cylinders constructed of aluminum, stainless steel, or some other non-corrosive and non-reactive metal.
Since medical gases are used in healthcare facilities, pipelines are routed from a cylinder storage location, through a gas manifold, and to the rest of the facility wherever access to medical gases is critical to patient care. Pipelines are devoted to a particular type of gas, and these systems will also include a medical vacuum and waste anesthesia exhaust system. Lines are accessible by outlets located around the facility.
The proper installation and maintenance of these gas lines is critical to patient care. Many professionals contribute to this system, including anesthesiologists, pharmacists, nurses, engineers, maintenance personnel, and gas suppliers. Accompanying these pipeline systems are various alarms, gauges, and testing instruments to ensure that the pipeline maintains pressure and flow. Occasionally, pipelines may need to be serviced to maintain service.

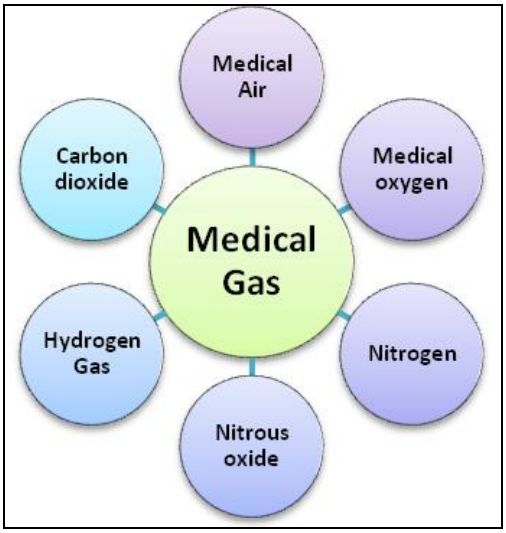

Fig 1: various medical gases

Pharmaceutical Gases [4, 5]

Pharmaceutical gases are defined as gaseous materials that are manufactured for the use in pharmaceutical industries and laboratories in the production of pharmaceutical merchandise and medicines. They may be used in the synthesis of these items, to sterilize such items, to test the item's packaging, or to insulate them from undesirable environmental effects such as oxidation.

As an analytical agent, to calibrate medical devices or to diagnose a patient by exposing cultures or a biopsy to the gas and examining the reaction.

As an atmosphere in environments in which air composition must be regulated.

Production and Atmosphere: Medical gases are occasionally valued for their ability to expel other gaseous fluids from a container or environment. Most often, nitrogen or carbon dioxide is introduced to a pharmaceutical product to reduce oxygen and humidity within the packaging environment, both of which greatly contribute to the decay and ineffectiveness of the drug. Furthermore, gases may be used to suspend cells and tissues in a cryogenic state after freezing, as is the case with nitrogen.

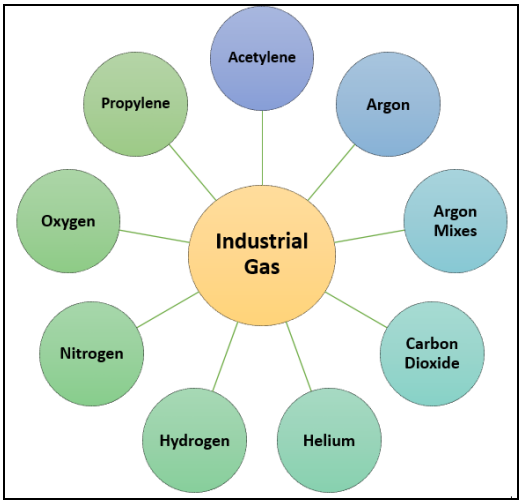

Fig 2: various pharmacetical gases

Overview on regulation of medical as well as pharmaceutical gases [7]

The physical and chemical composition of a medical gas, the maximum levels of its contaminants and the way in which it is administered and packaged are governed by the regulatory authority.

"Gases used for human healthcare are strictly controlled by both legislation and industrial standards so as to not impair human physiology. "

Gases of this nature may be manufactured as pure gases or as compounds, but are always filtered to the highest quality possible. The application of each individual gas determines its production and distribution.

The equipment with which medical gases are applied to a patient, production process, or other task is strictly controlled. More than 225 standards relating to pharmaceutical and medical gases are available through the IHS (Information Handling Service) Global Standards Store.

All individuals who install or maintain medical gas systems must receive appropriate training and complete the Medical Gas Installer Exam. Those who administer or prescribe pharmaceutical-grade gases undergo extensive medical training and licensing programs.

Until a certification has been granted, anyone marketing a medical gas for human or animal drug use without an approved application under section 505 or 512 of the FD&C Act is marketing an unapproved new drug.

There are two main standards in use internationally that provide best practice guidance for medical gas systems and products:-NFPA 99(US) and HTM 02 01 (UK) (Health Technical Memorandum 02 Medical gases)

Regulations in USA [9]

Medical gases are considered prescription drugs because their use as drugs is unsafe without the supervision of a licensed practitioner or by properly instructed emergency personnel. Regulations regarding the purity of these substances are established by the United States Pharmacopeia/National Formulary (USP/NF).

Specifically, medical gases are under the scrutiny of the United States Pharmacopeia and National Formulary, whose recommendations are legally enforced by the Food and Drug Administration.

Medical gases are the most frequently administered drugs in the United States, the FDA is attempting to heighten both consumer and industry awareness about this specialized category of regulated products. Such related delivery hardware as regulators and tubing is also regulated as medical devices.

Medical gases (*e.g.*, oxygen, carbon dioxide, helium, nitrogen, nitrous oxide, medical air, and combinations of these) are drugs regulated by section 201(g) of the Federal Food, Drug, and Cosmetic Act. The United States Pharmacopeia (USP) sets standards for all medical gases, including those that address quality, strength, purity, packaging, labeling, and identification. The proper handling of medical gases has been called into question during the past several years because of incidents resulting in patient harm and even death that have been documented by the US Food and Drug Administration, by the Joint Commission on Accreditation of Healthcare

Organizations (JCAHO), and by USP through its Medication Errors Reporting Program. In most cases, the deaths and injuries occurred to patients who were thought to be receiving medical-grade oxygen but instead were receiving a different gas (*e.g.*, nitrogen or argon) that had been mistakenly connected to the oxygen supply system.

The FDA's Compressed Medical Gas Guidelines and Manufacturing Guidelines for Medical Gases serve as the foremost instruments of patient safety. Due to the fact that medical gases can be combustible or act as oxidants, medical gas systems must adhere to NFPA 99.

Title 21 of the Code of Federal Regulations (CFR) designates medical gases as drugs, and mandates the Secretary of the Treasury and the Secretary of Health and Human Services to promulgate regulations for the efficient enforcement of the Federal Food, Drug, and Cosmetic Act (FDA) (drug portion of 21 CFR).

Regulations in Europe [10]

A medical gas pipeline system (MGPS) is installed to provide a safe, convenient and cost-effective system for the provision of medical gases to the clinical and nursing staff at the point of use. It reduces the problems associated with the use of gas cylinders such as safety, porter age, storage and noise. The manufacturing of gases should be according to the cGMP.

British compressed GAS Association

Many BCGA member companies are licensed by the Regulatory Authorities to manufacture and distribute the medical gases used within the UK and provide a range of associated equipment and services. Within BCGA, all aspects of medical gases are managed by Technical Sub-Committee (TSC)

BCGA CP 44

The storage of gas cylinders.

BCGA GN 26

Medical gas cylinders. Selection and maintenance of seals used on high pressure cylinders.

BCGA GN31

Medical Gases: The use of valves incorporating residual pressure devices.

BCGA GN 32

Medical gases. Good distribution practice.

BCGA L 7

The dangers of industrial gas abuse.

BCGA L 13

Medical oxygen in a vehicle.

BCGA L 16

The safe use of electronic cigarettes and other electronic devices used near medical oxygen.

BCGA TIS 6

Cylinder identification. Colour coding and labeling requirements.

BCGA TIS 20

Medical gas cylinders. BCGA policy statement on colour coding.

BCGA TIS 21

Medical gas cylinders. BCGA policy statement on valve outlets.

BCGA TIS 36

Medical gases. The safe handling and use of gas cylinders fitted with valves with integrated pressure regulators.

BCGA TIS 37

Medical Gases. Gas Cylinder cleanliness standards.

BCGA TIS 39

Medical Gases. Quality control and QP batch certification of bulk medical liquid oxygen.

Regulations in India [7, 10]

Healthcare sector in India offers a huge potential to grow in terms of service facilities as well as healthcare infrastructure. This is one of the major reasons expected to drive the future demand for medical gases in India over the next five years. The country is receiving substantial support from the government for the improvement of healthcare.

Standards for Cylinders in India

GAS cylinders rules

1. **General Provisions**
   - Filling, possession, import and transport of cylinders
   - Valves
   - Safety relief devices
   - Marking on cylinders
   - Markings on valve
   - Identification colors
   - Labeling of cylinders:
   - Restriction on delivery or dispatch of cylinders
   - Repairing of seamless gas cylinders during use
   - Repairing of welded or brazed cylinders
   - Prohibition of employment of children and intoxicated persons.
   - Prohibition of smoking, fires, lights and dangerous substances
   - General & Special precautions against accidents
   - Competent person to be in charge of operations
   - Handling and use
   - Restrictions on filling
   - Loading, unloading and transport of cylinders
   - Storage of cylinders
   - Purity of gas
2. Importation of cylinders
3. Examination and testing of Cylinders
4. Dissolved acetylene gas cylinders
5. Filling and possession
6. Accidents and inquiries
7. Powers

Static and Mobile pressure vessels (unfired) rules (1981)
Bureau of Indian Standards Act (1986)
Bureau of Indian Standards is of particular interest to the public, particularly disadvantaged communities and those engaged in the pursuit of education and knowledge, the attached public safety standard is made available to promote the timely dissemination of this information in an accurate manner to the public.
Such other regulatory bodies as the Department of Transportation (DOT) and national organizations [e.g., the Compressed Gas Association (CGA) and the National Fire Protection Association (NFPA)] write regulations and standards for compressed Gases.

Conclusion
In this study United states and European countries have very stringent regulations for the medical and pharmaceutical gases while in India very few acts and regulations available. So to reduce the rate of morbidity and mortality the strict regulations over the medical and pharmaceutical gases are important and need the improvement in the future.

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