

**Ethiopian Food and Drug Authority**

**Medical Gas Manufacturing Establishments Control Directive No. XXXX/2024**

**Oct 2024**

**Addis Ababa, Ethiopia**

**PREAMBLE**

WHEREAS, it is necessary to protect patients by regulating medical gas manufacturers to ensure that the safety, quality and effectiveness of medical gasses are maintained;

WHEREAS, it is necessary to prevent the presence of contaminants in medical gases that lead to serious health risks and adverse outcomes to patients;

WHEREAS, it is necessary to implement appropriate requirements for production, quality control, storage and distribution of medical gases to guarantee that gases for medicinal use are of assured quality when they reach the patients;

WHEREAS, there is an urgent need to scale-up the production of quality assured medical gases, particularly oxygen, meeting the quality specifications;

WHEREAS, due to the nature of the product, manufacturing process and set-up, specialized equipment required; it necessary to establish uniform and consistent enforcement mechanisms that ensure the safety, quality, and effectiveness of medical gas in the country;

NOW, therefore, the Ethiopian Food and Drug Authority issue Medical Gas Manufacturing Establishment Control Directive in accordance with article 71(2) of the Food and Medicine Administration Proclamation No. 1112/2019

**PART ONE**

**GENERAL**

1. **Short Title**

This directive may be cited as “Medical Gas Manufacturing Establishment Control Directive Number xxx/2024”

1. **Definitions**
2. **Active substance gas means a**ny gas intended to be an active substance for a medical product or medicinal gas.
3. **Air separation means t**he separation of atmospheric air into its constituent gases.
4. **Compressed gas** means a gas that, when packaged under pressure for transport, is entirely gaseous at -50 °C; this category includes all gases with a critical temperature less than or equal to –50 °C.
5. **Container means a** cryogenic vessel (tank, tanker or other type of mobile cryogenic vessel), a cylinder, a cylinder bundle or any other package that is in direct contact with a gas.
6. **Cryogenic gas means a** gas that liquefies at 1.013 bar at temperatures below -150 °C.
7. **Cylinder means a** container, usually cylindrical, suited for compressed, liquefied or dissolved gas, fitted with a device to regulate the spontaneous outflow of gas at atmospheric pressure and room temperature.
8. **Cylinder bundle means a**n assembly of cylinders that are fastened together, interconnected by a manifold, transported and used as a unit.
9. **Evacuate means t**o remove residual gas from a container or system to a vacuum level of 0.84 bar absolute at sea level using a vacuum system.
10. **Gas** means any substance that is completely gaseous at 1.013 bar and +20 °C or has a vapour pressure exceeding 3 bar at +500 °C.
11. **Maximum theoretical residual impurity means a** gaseous impurity coming from a possible backflow that remains after a cylinder’s pretreatment before filling. The calculation of the maximum theoretical residual impurity is only relevant for compressed gases and supposes that these gases act as perfect gases.
12. **Medical gas** means any gas or mixture of gases classified as a medical product.
13. **Rejected material** means any medical gas either as bulk medical gas or filled into medical gas cylinders where either it has been found to be outside the specification limit by the quality control checks or qualified person or end user.
14. **“Authority”** means the Ethiopian Food and Drug Authority.
15. **“Proclamation”** means the Food and Medicine Administration Proclamation No.1112/2019.
16. **“Person”** means a natural or juridical person.
17. Other definitions provided under article 2 of the proclamation shall be applicable.
18. Any expression in the masculine gender shall also apply to the feminine gender
19. **Scope of Application**

This Directive shall be applicable to all medical gas manufacturers for human use. This Directive focuses on the production, control, storage and distribution of medical gases.

**PART TWO**

**CERTIFICATE OF COMPETENCE**

1. **Issuance of Certificate of Competence**
2. No person shall engage in manufacturing of medical gases on any premises unless the Authority issued a certificate of competence.
3. Any person who wants certificate of competence shall meet the following requirements:
	1. Pay the appropriate service fee.
	2. Complete an application and submit to the Authority as per the form prescribed by the Authority through the electronic regulatory information system
	3. The following original documents shall be accompanied with the application.
4. Educational evidence of the technical manager, quality control manager, production manager and quality assurance manager.
5. Employment agreement or contract of technical manager, quality control manager, production manager and quality assurance manager
6. Working experience letter of technical manager, quality control manager, production manager and quality assurance manager
7. Professional license of technical manager, quality control manager, production manager and quality assurance manager
8. Passport size photo of technical manager
9. House rent contract or carta or leasehold title certificate authenticated by government body.
10. If the applicant is a private limited company, establishment documents and administrative regulation attested by the government body.
11. If the application submitted via electronic regulatory information system does not fulfill the requirements and is returned to the applicant for correction, the applicant can re-apply after correction.
12. If the application submitted fulfills the requirements, the medical manufacturing site will be inspected on-site by a team of at least two inspectors.
13. The Authority will evaluate the duly filled inspection checklist by inspectors against the set requirements.
14. Where the requirements have not been met, the applicant shall be informed about the decision in writing by the Authority.
15. Applicants who do not fulfill the requirements shall be notified through electronic regulatory information system; two-round re-inspection shall be carried out after the appropriate service fee payment.
16. Notwithstanding sub-Article (7) of this Article, applicants who do not fulfill the requirements after the conduct of two round re-inspections for certificate of competence, the submitted application shall be rejected.
17. The inspection reports prepared by the inspectors shall be uploaded in the electronic regulatory information system.
18. **Content of the Certificate of Competence**

Any certificate of competence issued in accordance with this directive shall have the following information.

1. Name and address of the medical gas manufacturer
2. Owner name of the medical gas manufacturer
3. The technical manager’s name and professional license number
4. Type of service given by medical gas manufacturer
5. Date of issue and expiry date of the certificate of competence
6. Signature of authorized person who issued the certificate of competence and stamp of the Authority
7. Certificate of competence number
8. Taxpayer identification numbers
9. Detail conditions and notice on the license
10. **Renewal of Certificate of Competence**
11. Any medical gas manufacturer shall renew a certificate of competence every year.
12. Without prejudice to sub-article (1) of this article, if any force majours supported by objective evidence and confirmed by the authority, then the certificate of competence may be renewed upon providing an extension support letter.
13. To renew a certificate of competence, the medical gas manufacturer shall apply for renewal not earlier than three months before the certificate of competence expires, and not later than five working days before the date of validity.
14. A certificate of competence shall be renewed.
15. Upon confirmation of the medical gas manufacturing requirements set by the authority are met
16. If any, upon confirmation that decisions made by the Authority such as recall of products and disposal of products are done; and
17. Confirmation of payment of required service fee
18. If the medical gas manufacturer cannot renew the certificate of competence on the timelines stated in sub-article (1) of this article, the applicant may renew the certificate of competence upon paying the required penalty fee as per the service fee regulation.
19. If the certificate of competence is not renewed in accordance with sub-article (1) of this article, the certificate of competence shall be considered canceled.
20. Where the Authority does not accept renewal application requests, it shall notify the manufacturer by stating the reasons in writing.
21. **Change of address, ownership, technical personnel, product type/service type or other change**
22. No medical gas manufacturer shall change location, ownership, technical personnel, types of products/services, change of rooms, or modification without prior permission of the Authority.
23. Any medical gas manufacturer who wants to make a change shall apply using the electronic regulatory information system.
24. Notwithstanding sub-article (2) of this article to make changes stated in annex 1 of this directive, the applicant shall fulfill the requirements stipulated in annex 1.
25. **Replacement of Certificate of Competence**

Any medical gas manufacturer whose certificate of competence has wrong information made by the Authority or damaged or lost may request replacement by fulfilling the following conditions:

1. When the certificate of competence is damaged, the manufacturer shall return the damaged certificate of competence and pay the required service fee
2. When the certificate of competence is lost or burnt, the manufacturer shall provide proof of evidence from law enforcers and pay the required service fee.
3. For certificates containing wrong information, the manufacturer shall return the previous certificate of competence and pay the required service fee.
4. Without prejudice to this article sub article 3 for typographic error arising from the authority side the applicant is not required to pay service fee.
5. **Return of Certificate of Competence**
6. Where a medical gas manufacturer wants to return the certificate of competence granted by the Authority due to reasons, it shall submit a letter of declaration that describes status of the manufacturing facility with respect to products available such as materials, equipment, components and, previously issued certificate of competence and application letter.
7. Without prejudice to sub-article (1) of this article, any manufacturer shall return when:
	1. Confirmed that manufactured medical gases that are expired or contaminated are disposed
	2. Confirmed that medical gases that are decided to recall are recalled
	3. Confirmed that unsold or unused manufactured medical gases have been transferred to another equivalent institution in accordance with the law.
	4. Confirmed that equipment that is used for medical gas manufacturing transfer or managed properly.

**PART THREE**

**REQUIREMENTS FOR ESTABLISHMENTS OF MEDICAL GAS**

1. **Location, layout and design requirements**
2. The premises shall be located away from **sites or activities** where safety, quality and efficacy of the products can be compromised.
3. The premises where medicinal gases are manufactured shall be located,  designed, constructed and maintained to suit the operations to be carried out.
4. The premises shall have a physical address to include plot and house number, street, district and region where the business is to be carried out.
5. The facility layout and design shall ensure the integrity of the medicinal gases produced, stored, and distributed.
6. The layout and design of the premises shall be designed to minimize the risk of errors, mix ups, contamination and cross-contamination.
7. The layout and design shall allow effective cleaning and maintenance without any adverse effect on the quality of the medical gas.
8. All processes within the facility shall be organized to ensure unidirectional flow of materials, personnel, and products, and ensure safety and quality of the medicinal gas.
9. Raw material storage areas shall be separate from production areas and adequately equipped to handle gases in accordance with their specific chemical and physical properties and may include buffer zones for staging gases to prevent contamination during transport to the main production area.
10. Bulk storage areas shall be located at a safe distance from the production facility, in accordance with national fire safety codes, and should be fitted with fire suppression systems.
11. The premises shall provide sufficient space for manufacturing, quality control testing and storage operations.
12. Production areas shall be specifically designed for gas compression, blending, and filling, with clear separation from non-production areas.
13. There shall be separate zones for filling, purification, and compression of medical gas to ensure workflow efficiency and product safety.
14. The purification unit shall be designed and installed in compliance with internationally recognized standards for medical gas production
15. The purification unit shall be installed in a clean, dry, and well-ventilated area to avoid contamination and ensure proper function.
16. Compressors or generators for compressing gases into cylinders or liquid forms shall be vibration-isolated to prevent interference with other processes.
17. Cylinder filling areas shall have automated or semi-automated machines for filling cylinders.
18. For medical gases distributed directly to hospitals, the system may include a manifold and a piped distribution network.
19. There shall be a packaging and labeling area, which includes a dedicated space for fitting valves, sealing, and labeling cylinders that enables to ensure cylinders are correctly coded and prepared for distribution.
20. There shall be Maintenance and Utility Rooms, which are easily accessible spaces designed to house equipment such as air compressors, vacuum systems, and gas tanks to ensure smooth and efficient plant operations.
21. Finished product storage shall be isolated from raw material storage to prevent contamination and shall provide secure conditions for storing medical gases.
22. **Building Requirements**
23. Building shall be designed and constructed and located at an appropriate site recommended by the relevant body.
24. The walls**,** ceilings**,** andfloors shall be finished with materials that are non-combustible and designed to be easytoclean.
25. The materials used for finishing the walls, ceilings and floors shall be smooth, durable, non-combustible and chemical-resistant surfaces such as epoxy-coated finishes, bricks, stainless steel, or other fire-resistant materials.
26. The building shall be kept clean at all times and regularly maintained. safe and hygienic environment.
27. Sufficient lighting and ventilation shall be provided to enable all operations to be carried out.
28. Buildings shall protect products from mix-up, contamination and deterioration, including protection from excessive heat.
29. Entry to building and critical areas such as gas compression, filling, and quality control areas shall be restricted to authorized personnel only.
30. Appropriate control measures, including access logs or digital access systems, shall be implemented to ensure traceability and compliance.
31. Receiving and dispatch bays shall protect products from the extreme climate conditions and It shall be designed and equipped to allow containers of incoming products to be cleaned.
32. The building shall be equipped with emergency ventilation systems capable of evacuating harmful gas concentrations in the event of a leak or accidental release.
33. **Equipment, System and Utilities**
34. Equipment and utilities shall be selected, located, constructed and maintained to suit the operations to be carried out.
35. The numbers of equipment, systems, and utilities shall be adequate and be aligned with the size of the room and operation.
36. The layout, design, installation, and use of equipment and utilities shall minimize the risk of errors and permit effective cleaning and maintenance to avoid cross-contamination, buildup of dust or dirt, and adverse effects on the quality of products.
37. The manufacture of medicinal gases and the filling of medicinal gas cylinders shall be carried out in closed pipework, containers, and tanks.
38. The equipment and parts of equipment that directly contact the product shall not be reactive, additive, or absorptive. Risk assessment shall be carried out and cover the premises, equipment, processing, filling, storage, and distribution of medicinal gases.
39. All equipment for the manufacture, cylinder filling, and quality control of medicinal gases shall be qualified, calibrated, and maintained to suit its intended purpose.
40. Automatic, mechanical, and electronic equipment, or other types of equipment, including valves, shall be checked according to a written program designed to ensure proper performance.
41. Critical instruments used for measuring, weighing, recording, and controlling shall have specific calibration periods using appropriate validated methods.
42. Computerized systems, including hardware and software, used in the manufacturing, processing, and holding of medical gases shall be validated for their intended use.
43. Automated systems, if used, shall be qualified and validated and shall have backup systems in place to prevent critical failures.
44. Design Qualification, installation Qualification, operational qualification, and performance qualification shall be performed for medicinal gases Equipment and Utilities
45. Approved procedures, protocols, and reports and records should be maintained.
46. The manufacturer shall have standard operating procedures for repair and maintenance, including the measures to be taken after repair and maintenance operations.
47. Repair and maintenance operations (including cleaning and purging) of equipment shall not adversely affect the quality of medicinal gases. The design of manufacturing and cylinder filling equipment shall be designed to permit easy and effective cleaning and evacuation to remove any internal contamination.
48. The manufacturer shall have written standard operating procedures covering the appropriate methods of purging and cleaning of all equipment and putting the system back into operation.
49. The manufacturer shall have a documented preventative maintenance programme for major equipment.
50. Containers for medicinal gases shall conform to appropriate national or international technical specifications.
51. Cylinder valves shall undergo regular maintenance and periodic testing to prevent leaks and ensure compliance with regulatory durability standards.
52. The cleaning of internal surfaces of pipelines, tanks, and equipment using appropriate cleaning materials such as detergents, water, steam, and/or sanitizing agents shall be performed.
53. Cleaning using steam or chemical agents to sterilize the internal surfaces shall be performed.
54. Defective equipment shall be clearly labeled as defective and, if possible, be removed as soon as possible from the manufacturing, production or quality control areas.
55. The medical gas manufacturing facility shall at least have the following equipment and utilities
	* 1. Air compressor,
		2. gas concentrator,
		3. dryer, vacuum pumps,
		4. oxygen or other gases generator (as applicable),
		5. manifolds and piping,
		6. storage tank,
		7. vacuum insulated piping,
		8. high-pressure valves, filters, filing racks
		9. cylinders
		10. electrical power with backup generator,
		11. gas supply, compressed air, steam, water, vacuum system,
		12. ventilation system,
		13. alarm system,
		14. fire protection systems and drains
56. **Personnel Requirements**
57. The manufacturer shall ensure adequate staffing levels to maintain safe, consistent, and efficient production of medical gases
58. The qualifications of personnel involved in the manufacture, control, certification, or release of a batch, storage, and distribution of medicinal gases shall possess appropriate qualifications.
59. Personnel shall receive appropriate training in relevant laws and guidelines covering medical gas manufacturing, specific equipment operation, gas purity standards, safety protocols, good manufacturing practices (GMP), storage, distribution, and regulatory requirements.
60. All staff shall understand and follow GMP requirements, including hygiene, contamination control, potential hazards and risks to products and patients, Good documentation practice, and record-keeping.
61. Personnel shall be trained in handling high-pressure gasses, cylinder safety, equipment safety, emergency procedures, and personal protective equipment (PPE) usage.
62. Personnel of outsourced service providers shall be appropriately trained, especially where activities could influence the quality of medical gasses and containers, such as the maintenance and cleaning of cylinders or valves
63. The manufacturing facility shall have key personnel position for Technical manager, production, quality control, and quality assurance
64. Without prejudice to sub-article 7 of this article, the manufacturing facility shall have a maintenance manager as required.
65. The Production and quality control personnel shall be independent of each other
66. Key personnel shall have appropriate education and experience as indicated in table below.

|  |  |  |
| --- | --- | --- |
| **Key personnel** | **Minimum required qualification** | **Required experience** |
| Technical manager | Shall have bachelor degree in chemical engineering, biomedical engineering, mechanical engineering, electromechanical engineering, industrial engineering or pharmacy | A minimum of 3 years’ experience in manufacturing areas |
| Quality Assurance (QA) Manager | Shall have bachelor degree in Pharmacy or Chemistry | A minimum of 3 years’ experience in quality assurance  |
| Production Manager | Shall have bachelor degree in Pharmacy, chemistry, Chemical Engineering, Industrial Engineering, biomedical engineering, mechanical engineering, or electromechanical engineering  | Minimum 3 year experience in manufacturing areas |
| Quality Control (QC) Manager | Shall have bachelor degree Pharmacy or Chemistry | Minimum of 3 year experience in relevant quality control activities |

1. All personnel shall adhere to strict hygiene and health protocols to prevent contamination of medical gases.
2. Personnel shall undergo medical examinations prior to employment and at periodic intervals
3. Personnel shall wear appropriate personal protective equipment.
4. Personnel shall be restricted from direct contact with manufacturing processes if they have health problems, including lesion that may compromise product integrity
5. **Production**
6. Materialflow shall be designed to prevent contamination.
7. Incoming starting material shall be physically or administratively quarantined immediately on receipt or after processing, and held until they have been formally released for use.
8. Raw materials, intermediates, and final products shall not cross paths to avoid cross-contamination risks.
9. Personnel movement between clean and unclean areas shall be minimized, and staff shall adhere to hygiene protocols, including regular hand washing and wearing appropriate protective equipment.
10. Bulk gasses intended for medicinal use may be prepared by chemical synthesis or obtained from natural resources, followed by purification steps.
11. Bulk medicinal gasses classified as APIs should align with GMP requirements, and specific quality standards should be defined.
12. Materials can only be released once they meet predefined quality standards and have successfully passed all relevant quality control checks
13. All types of medical gas production, including the production of bulk medicinal gasses and the filling of medicinal gas cylinders, shall fully comply with Good Manufacturing Practice (GMP) standards.
14. Process flow charts for each process or part of the process shall be available to the operator for reference.
15. All process flow charts shall include identified critical control points (CCPs) and undergo regular updates to reflect any changes in the process.
16. Additional information shall also be available to the operator, specifying the purity of the gas and other components and the possible impurities that could be present in the source gas and at specified purification steps, as applicable.
17. All critical steps in bulk processing, cylinder filling process, and packaging of medical gases shall be validated in accordance with approved operating procedures.
18. Any in-process controls shall be recorded with the batch records and a control log to capture deviations and corrective actions during production, ensuring accountability and traceability for each stage of the process shall be implemented
19. The gas mixing method shall be validated to demonstrate effectiveness and should undergo periodic reviews to ensure uniformity and homogeneity of mixtures across each batch.
20. Re-validation schedule shall be implemented to ensure that these critical parameters remain effective over time.
21. Validation records for each stage, processing, packaging, and distribution, shall be maintained and made available for inspection when requested by the regulatory body.
22. New cylinders and cylinders that have undergone statutory testing shall be subject to an internal inspection to ensure they are dry and free from contamination before the cylinder valve being fitted
23. Returned cylinders for refilling shall be prepared in order to minimize the risk for contamination.
24. All minimum pressure retention valves shall be tested before refilling to verify their functionality and ensure effective contamination prevention.
25. A cylinder filled with more than one gas, the filling process shall ensure that the gases are correctly mixed in every cylinder and are fully homogeneous.
26. All medicinal gas cylinders in a filling batch shall be inspected prior to filling to ensure that they are in a suitable condition for filling.
27. Medicinal gas cylinder filling systems shall be organized so that each medical gas cylinder filling manifold dedicated to filling of a single medical gas or a specific mixture of gasses at set concentrations
28. All manifolds utilized for cylinder filling shall be meticulously cleaned and inspected between batches to prevent cross-contamination.
29. Each filling batch shall be clearly defined and documented ,and shall be related to the analysis of the gas sample from the batch. batch and any inspections conducted during the process
30. All filled cylinders shall be kept in quarantine until released by the Qualified Person for supply to the patient.
31. Released medicinal gas cylinders shall be stored in a designated storage area.
32. The manufacturer shall check post filling of medical gas for filling confirmation, lick testing, labeling and documentation of all containers in the batch.
33. Rejected filled cylinders shall be clearly marked or labeled and stored separately in a defined restricted area.
34. The manufacturer shall establish traceability system for medicinal gas cylinders, batch, and valves used for medical gas supply
35. Cylinders shall be cleaned, tested and maintained appropriately.
36. Cleaning and purging of filling equipment and pipelines shall be carried out in accordance with standard written procedures
37. Cleaning and maintenance records shall be documented for each cylinder, and any cylinders stored for extended periods shall be inspected
38. **Packaging**
	1. Cylinder labels and patient information leaflets shall be quarantined when they are received from an approved supplier
	2. Labels shall only be issued for use by an authorized person
	3. Labels and leaflets shall be stored under secure conditions to prevent unauthorized access and protect against damage.
	4. The printing on product labels shall be clear and resistant to fading when exposed to day light for a period appropriate to the product's shelf life
	5. The durability of the label material and print should be validated to ensure compatibility with the product's shelf life and quality standards
	6. All obsolete and outdated labels and leaflets shall be removed from the filling and / fitting areas.
	7. Each cylinder shall be correctly labeled and colour-coded in compliance with EFDA regulations and in accordance with the marketing authorization.
	8. Any unused batch labels shall be made unusable and the count of these labels number recorded on in the batch record.
	9. The manufacturer shall follow the requirements about labeling and leaflet information stated in the standards for medical gas
	10. The containers for medical gas and associated components shall be
39. A stainless steel cylinder of SS 304 grade or higher
40. Comply with ISO 5145 standards, and cylinder valve outlets for gases and gas mixtures meet ISO 5145:2020 specifications.
41. Valves or taps shall not be lubricated with oil or grease, to prevent contamination risks.
42. Cylinder color coding in accordance with ISO 32 standards or
43. **Labeling Requirements**
44. The medical gas cylinder has the following marking Requirements
45. Color coding of the cylinder as per the ES ISO 32:2016
46. specified materials of construction.
47. physical dimensions; and
48. design code, design pressure and the maximum working pressure of the storage tank;
49. The medical gas storage tanks containing refrigerated liquefied gases shall at least bear the following information:
50. The generic names of ‘’medical gas’’ along with its chemical formula written on the container body in white letters of the size not smaller than 1/8 of the cylinder diameter
51. Name and address of the manufacturer
52. Lot identification
53. Volume in liter at pressure 1Bar and filling pressure in Bar at the temperature of 27±2°C.
54. Water capacity of the tank appropriate for the medical gas.
55. Shelf life or Expiry date
56. Storage tanks periodic inspection status.
57. any internal cleanliness requirements, the acceptance limits for both new and re-tested tanks, and a warning statement or marking such as "No smoking", "No ignition" or "Stay away from flammable substance"
58. The numbers, letters or markings indicated in the medical gas storage tank shall be legibly, accurate and clear.
59. Labels that are obsolete or outdated shall be removed.
60. **Quality Control**
	1. The manufacturer shall establish, implement and maintain a quality assurance system appropriate for the production of medical gases.
	2. The established quality assurance system shall ensure that:
61. The equipment and procedures used for the production and quality control of medical gas are designed and developed in accordance with the requirements of Good Manufacturing Practices.
62. Managerial responsibilities are clearly specified
63. All necessary controls on starting and packaging materials, intermediate products, and any other in-process controls, validations, and quality checks are carried out and documented. The bulk medical gases and the filled medical gas cylinders are correctly processed and checked, according to the defined Standard Operating Procedures.
64. The medical gases are stored, distributed and handled in a manner that maintains medical gas quality and cylinder condition throughout their shelf life with documented procedures for monitoring these conditions
65. There is a procedure for self-inspection and quality audit which regularly appraises the effectiveness and applicability of the Quality Assurance systems.
66. The quality of production operations and materials monitored by the quality unit throughout the lifecycle of the product.
	1. The manufacturer shall:
67. establish an independent quality unit in charge of quality assurance and quality control activities.
68. allocate adequate resources for carrying out quality assurance and quality control activities effectively and consistently
69. ensure that the quality unit is independent of other departments and it is under the authority of a person with appropriate qualifications and experience
70. ensure availability of adequate facilities, trained personnel and approved procedures for sampling, inspecting, and testing starting materials, packaging materials, and intermediate, bulk, and finished products as well as product release
71. perform self-inspections and annual product quality review and conduct management reviews in a timely manner.
72. retain records of management review minutes, self-inspection reports and annual product quality review reports.
	1. There shall be authorized person for sampling of starting materials, packaging materials, intermediate products, bulk products and finished products
	2. The manufacturer shall ensure that all tests are performed before product release following accepted specifications and shall possess appropriate testing equipment to carry out these tests.
	3. The manufacturer shall retain:
73. Records demonstrating that all the required sampling, inspections and testing procedures have been completed according to quality documentationRecords of any deviations investigations and investigation results
74. Records of any deviations investigations and investigation results
75. Records that show the test results of inspecting and testing the raw materials, intermediate, bulk and finished medical gases against specifications
76. **Raw material and intermediate testing**
77. A medical gas manufacturer shall have written procedures prepared by qualified personnel to ensure that the medical gas meets the required specifications
78. Batches of gases used in manufacturing medical gas mixtures shall fulfill the following:
79. Each lot or batch of raw material shall be tested and meet specifications prior to its use in the production of a specific medical gas.
80. Each lot or batch of raw material must be tested and meet specifications prior to its use in the production of a specific medicinal gas
81. No lot or batch of raw material may be used in manufacturing unless that lot or batch of raw material complies with the specifications for that raw material.
82. Lots or batches of raw materials or packaging or labeling materials shall not be used in the manufacture or packaging or labeling of a medicinal gas prior to approval by the person in charge of the quality control.
83. without prejudice to sub-article 2 of this article, if any property of a raw material may change during storage, that material shall be retested after an appropriate interval to confirm compliance before use.
84. The manufacturer shall ensure that each lot or batch of the medical gas is manufactured, packaged, labeled and tested in compliance with approved written procedures.
85. A heat of compression checks on the exterior surface of each cylinder to demonstrate proper filling shall be performed during the manifold filling sequences of high pressure non-liquified compressed gases
86. Pressure leak test shall be performed on each container during filling and appropriate method, such as applying leak detection solution to the valve shall be applied to detect valve packing leaks, safety plug leaks and other valve leaks.
87. A second leak test shall be performed on each container after filling to detect valve outlet leaks
88. The manufacturer shall not use any leak test solutions that can cause corrosion or leave films.
89. **Finished Product Testing**
90. Each lot or batch of a medical gas shall be tested against the specifications before it is made available for further use in fabrication or for sale
91. Identity, purity or assay and impurity tests shall be carried out for each batch of medicinal gas to ensure that the finished medical gases contain ingredients complying with the qualitative and quantitative compositions.
92. Written specifications shall be approved by the person in charge of the quality unit. The approved specifications must include:
93. a description of the medical gas, including all properties and qualities (such as identity, purity and potency)
94. tolerances, and a description of all tests or analyses used to measure compliance with the established tolerances
95. the name or identification mark that will be used for each medical gas throughout the processing operation
96. Specifications shall be equal to or exceed a recognized standards
97. The test method shall be validated, and the validation results be documented
98. The manufacturer shall verify suitability of any transferred technology
99. All test results shall be documented properly, clearly and concisely
100. Sampling plans and the analysis to be performed on cylinders shall comply with the following requirements:
101. In the case of a single medicinal gas filled via a multi-cylinder manifold, the gas from at least one cylinder from each manifold filling cycle shall be tested for identity and assay each time the cylinders are changed on the manifold.
102. In the case of a single medicinal gas filled into cylinders one at a time, the gas from at least one cylinder of each uninterrupted filling cycle shall be tested for identity and assay. In this directive, *uninterrupted filling cycle means a one shift's production using the same personnel, equipment, and batch of gas to be filled.*
103. In the case of a medicinal gas produced by mixing two or more gases in a cylinder from the same manifold, the gas from every cylinder should be tested for assay and identity of each component gas.
104. Without prejudice to sub article (c) of this article, fewer cylinders may be tested in case of a validated automated filling system.
105. Without prejudice to sub article (c) of this article, premixed gases may follow the same principles as single gases when continuous in-line testing of the mixture to be filled is performed.
106. Without prejudice to sub article (e) of this article; premixed gases should follow the same principle as medicinal gases produced by mixing gases in the cylinders when there is no continuous in-line testing of the mixture to be filled.
107. Testing for water content shall be performed for all types of gases
108. The manufacturer is not required to retain reference and retention samples unless subscribed by the authority to do so for justifiable reason
109. The manufacturer shall not release medical gas for sale or supply prior to approval by the quality unit
110. The procedures for product release shall include review and evaluation of relevant production documentation and an assessment of deviations from specified procedures;
111. Deviations shall be investigated and reported by qualified person and the quality unit shall approve the reports and maintain records of such deviations
112. **Stability Testing**
113. The manufacturer shall conduct and document stability of the finished medicinal gas and propose specific shelf life and storage conditions based on properties of the constituent gas.
114. Without prejudice to sub article (1) of this article, the manufacturer may not be required to carry out stability study or to perform on-going stability studies for the finished medical gas that have been used for a long time and packaged in containers that have also been used for a long time, if bibliographic data is available.
115. **Specifications and Test parameters**
116. There shall be well established specifications for medical gas raw material, packaging and labeling materials in accordance with the requirements of the pharmacopeias recognized by the authority or Ethiopian national standard.
117. Without prejudice to article --- sub article .. of this directive, the manufacturer may use validated in-house methods if shown to be equivalent and accepted by the authority
118. The specification of the medicinal gas shall include the following test parameters:
119. Identification
120. Assay of the product
121. Maximum allowable impurity levels for those contaminants specified in the product specification and total impurities. The test for impurities; as appropriate, shall include test for:
122. Oxygen
123. N2, NO, NO2
124. Hydrogen
125. Carbon monoxide and Carbon dioxide
126. Methane
127. Hydrocarbons
128. Air
129. SO2
130. Oil
131. Acidity or Alkality
132. Chlorine
133. Odour
134. Reducing substances
135. Oxidizing substances
136. **Environmental and Safety requirements**
137. All medical gases shall be handled according to established safety protocols that minimize risk to personnel, facilities, and the environment.
138. All personnel shall use appropriate personal protective equipment (PPE) when handling gases.
139. All gas handling systems, including piping, valves, and storage containers, shall be constructed of materials compatible with the gases being handled, and shall be maintained in safe working condition at all times.
140. All gas storage and handling systems shall be equipped with leak detection sensors that trigger alarms in the event of leaks.
141. Facilities shall implement contamination control measures to prevent environmental contamination in the event of a gas release.
142. Spill kits, containment barriers, and emergency shutoff systems shall be installed and regularly maintained.
143. Expired, contaminated, or otherwise unfit for use medical gases shall be disposed of in compliance with local environmental protection regulations. Disposal shall be carried out by licensed hazardous waste disposal firms.
144. All medical gas facilities who dispose of medical gases shall maintain records of gas disposal activities, including the type and volume of gases disposed of, the method of disposal, and the name of the disposal company.
145. Every medical gas manufacturing facility shall have a written Emergency Response Plan in place including procedures for handling gas leaks, fires, explosions, and other accidents.
146. Emergency procedures for gas leaks shall include immediate evacuation, shutoff of gas supply, and activation of the emergency ventilation system. Emergency drills shall be conducted regularly to ensure employee preparedness.
147. Fire suppression systems designed for gas-related fires, such as gas-rated extinguishers and automatic sprinkler systems, shall be installed. Emergency exits shall be marked and unobstructed, and personnel shall be trained in fire response procedures.
148. Facilities shall have trained personnel or medical staff to administer first aid in the event of exposure to hazardous gases. The facility may have procedures in place for contacting emergency medical services.
149. **Storage**
150. There shall be sufficient capacity for orderly storage of cylinders and provide separate marked areas for different gases to avoid the risk of mix-up.
151. The method used to achieve the various levels of segregation may depend on the nature, extent and complexity of the overall operation. Marked-out floor areas, partitions, barriers, labels, signs or other appropriate means shall be used to identify storage areas.
152. Storage areas shall be appropriately located, designed, constructed, maintained, kept clean and dry, ventilated, and shall not be located in close to any installation that may have a fire risk or other hazard.
153. The Medical gases manufacturers shall establish and implement written procedures appropriate for the storage of medical gases.
154. The medical gas storage and shed shall be equipped with the proper emergency handling systems or kits, as well as safety equipment including hand gloves, gas masks, breathing apparatus, goggles, and gumboots.
155. Sorted empty cylinders and full cylinders shall be stored in nominated storage areas, preferably under cover and not subjected to extremes of weather conditions and ambient temperature.
156. All staff members who undertake domiciliary visits in the warehouse shall be trained in the use of portable medical gas cylinders and hazards associated with them.
157. The manufacturer shall specify any special storage conditions. Where special storage conditions are required, these shall be provided, controlled, monitored and recorded.
158. Periodic stock reconciliation shall be performed at defined intervals by comparing the actual and recorded stocks. Discrepancies shall be identified, investigated and appropriate corrective action shall be taken.
159. Precautions shall be taken to prevent unauthorized persons from entering storage areas.
160. A written cleaning program shall be available indicating the frequency of cleaning and methods to be used to clean the storage areas.
161. There shall be a written program for pest control.
162. The appropriate signs and warnings, where required, shall be visible on the warehouse.
163. The record of issue shall include name of gas, size of cylinder, date of issue and name of recipient.
164. Medical gases that have been improperly stored shall not be returned to usable stock.
165. Returned medical gases shall be stored in a controlled manner in a dedicated area, identified and kept until a decision is made.
166. Cylinders and their associated equipment shall be protected from contact with oil, grease, hand creams, bituminous products, acids and other corrosive substances.
167. During storage of medical gases;
168. Cylinders shall be stored in a cool, dry, and well-ventilated area, away from heat and potential ignition sources, such as open flames and electrical equipment.
169. Cylinders shall be stored in a secure and upright position, with the valve protection cap in place and tightened.
170. Cylinders shall be labeled with type of gas, name of manufacturer, and cylinder's test or inspection date.
171. Cylinders shall be regularly inspected and maintained to ensure that they are in good condition and safe to use.
172. Personnel involved in the storage, handling, conveyance and transport of medical gases shall be trained on the medical gas related issues, hazards and emergency procedures.
173. The facility shall implement an emergency evacuation plan and shutdown procedures in case of leakage.

**Part five**

**Pharmaceutical Quality System**

1. **Complaint requirements**
2. There shall be written procedure to handle complaints related to medical gas quality defects including identify the cause of complaint and actions to be taken in the event of receipt of complaint
3. All complaints concerning quality defects in cylinders and medical gas shall be carefully reviewed and recorded.
4. Each complaint shall be investigated by designated or authorized personnel of the company and maintain records of investigation and remedial action.
5. Complaints records shall be reviewed regularly, and document and retain records of complaint, subsequent investigations, and corrective actions taken.
6. Complaints may include faulty or damaged cylinders, expired cylinders, modification or tampering with medical gas, bad odour and other quality and safety related defects.
7. **Recall Requirements**
8. There shall be a written procedure for effective recall of products.
9. The manufacturers shall recall medical gases if there is evidence of impurity of gas, contamination, mislabelling issues, loss of more than 5% of its tare weight, gas cylinders used did not use standard colour or other products defects that causes temporary or medically reversible adverse health consequences.
10. Recalled medical gases shall be identified and stored separately in a secure area while awaiting a decision and records of recalled procedures shall be documented accordingly.
11. The Authority shall be immediately informed if a manufacturer is considering any recall action following the possible faulty manufacture, deterioration or any other quality problems.
12. Recall shall be initiated promptly and evaluated for recall effectiveness.
13. **Traceability**
14. There shall be records for the dispatch including relevant information to allow traceability.
15. During transportation, traceability shall be maintained to ensure that gases are handled properly and remain within the appropriate temperature and pressure ranges.
16. There shall be written procedures and records for each batch of medical gas cylinders distributed to ensure traceability of the products.
17. There shall be a system to ensure the traceability of cylinders, cryogenic vessels and valves stored in the manufacturing facilities.
18. There shall be labeling requirements for the filled medical gas cylinders for traceability of the product.
19. The manufacturer shall use barcodes on the cylinders for traceability, when required.
20. **Self-audit**
21. There shall be a procedure for self-inspection and quality audit that regularly appraises the effectiveness and applicability of the quality assurance systems.
22. The manufacturers shall perform self-inspections routinely and as well as on special occasions.
23. The facility shall maintain records of self-inspection.
24. The manufacturer shall conduct annual product quality reviews of all medical gases with the objective of verifying consistency of existing processes, and appropriateness of current specifications for both starting materials and medical gas and identify improvements on products and processes.
25. The manufacturer shall document annual product quality reviews
26. The manufacturers shall consider the following during conducting product quality reviews, taking into account previous reviews.
27. critical in-process controls, finished product testing results, and specifications
28. all batches that failed to meet established specification(s) and their investigation
29. all significant deviations or non-conformances, their related investigations, and the effectiveness of corrective and preventative actions taken
30. all changes carried out to processes, analytical methods, raw materials, packaging materials or critical suppliers
31. all product quality-related returns, complaints and recalls, and the investigations performed at the time
32. the qualification status of relevant equipment used for manufacturing and packaging of medical gases
33. **Waste Disposal and Management**
34. Medical gases and cylinders shall be identified and classified as either hazardous or non-hazardous waste in compliance with national and/or regional laws and guidelines
35. Unfit for use medical gases shall be segregated and stored separately, and appropriately disposed in the presence of authorized expert;
36. Unfit for use medical gasses, raw materials; packages, gas cylinders, and finished products shall be disposed of in compliance with the national or regional disposal laws and guidelines.
37. All medical gases and cylinders shall be disposed of using approved disposal methods, which include:
38. Returning cylinders to the manufacturer or supplier for proper disposal.
39. Participating in recycling programs for metal cylinders, ensuring that they are emptied and cleaned before recycling.
40. Conducting controlled release of non-hazardous gases into the atmosphere in compliance with regulatory limits.
41. Neutralizing hazardous gases as required before disposal.
42. **Documentation**
	* + 1. **General**
43. Good documentation is an essential part of any quality assurance system used for the production of bulk medicinal gases and the filling of medicinal gas cylinders. Written documentation prevents errors and permits the tracing of the batch history. Specifications, standard operating procedures, work instructions, and records shall be controlled and available to all of the relevant personnel either in written or electronic format.
44. A manufacturer shall be responsible for establishing a comprehensive documentation system to ensure compliance with regulatory standards and Good Manufacturing Practices (GMP) for medical gas. Documentation shall reflect the manufacturing process, quality control measures, and traceability of medical gases from production to delivery.
	* + 1. **Specific Requirements**
45. Specifications, SOPs, and all related documentation for the manufacturing, control, storage, and distribution of medical gases shall be established, implemented, and maintained according to the quality management system (QMS) in place.
46. Documents shall be carefully designed, prepared, reviewed, and distributed in line with the QMS.
47. All documents shall be approved, signed, and dated by appropriate and authorized persons before implementation. No changes shall be made to a document without prior authorization and approval.
48. Documents shall have unambiguous content; and identification number and they shall be laid out in an orderly fashion and be easy to check. The title, nature and purpose shall be clearly stated.
49. All documents shall be regularly reviewed and kept up-to-date.
50. Obsolete or superseded documents shall not be used under any circumstances. These documents shall be marked or removed from circulation to prevent unintentional use during production.
51. Documents shall not be hand-written; although, where documents contain data that require data entry, they shall follow the ALOCA+ principle to ensure compliance with good documentation practices and data integrity requirements. Sufficient space should be provided for such entries.
52. Any alteration made to the entry on a document shall be signed and dated; the alteration should permit the reading of the original information. Where appropriate, the reason for the alteration shall be recorded.
53. Labels shall be easily legible, clearly comprehensible and indelible and in full compliance with national legislation. The labeling shall be presented in English and/or Amharic. Appropriate placement of the label shall ensure access and visibility to all users.
54. Labels on the cylinders of medicinal gases shall contain at least the information as recommended in the pharmacopoeia, where applicable, as well as the following information:
55. The name of the medicinal gas
56. The batch number assigned by the manufacturer
57. The expiry or use-before date (if applicable)
58. Any special storage conditions or handling precautions that may be necessary directions for use
59. Warnings and precautions
60. The name and address of the manufacturer
61. Test date (month and year).
62. All authorized specifications and testing procedures shall be readily available.
	* + 1. **Standard operating procedures and records**
63. There shall be formally authorized production methods, SOPs, and work instructions for the production of each medicinal gas and the filling of each medicinal gas cylinder.
64. SOPs for production, quality control operation and storage of medical gases should be approved, signed and dated.
65. The manufacturer shall maintain documented information and the SOPs shall cover the following but not limited to:
66. Production of medical gases;
67. Purging of cylinders, pipelines, and storage tanks;
68. Filling of cylinders;
69. Pre-fill and Post fill inspection of cylinders;
70. Sampling and Testing of medical gases: Identity, purity or assay and impurity tests;
71. Calibration and maintenance of equipment;
72. Qualification and validation
73. Packaging and labeling;
74. Cleaning and sanitization of premises and equipment;
75. Training and personal hygiene;
76. Complaints, recalls, and returns;
77. Internal audit or self-inspection.
78. The batch numbering system shall be detailed in SOPs, ensuring that every batch of medicinal gas is given a unique batch number for traceability.
79. Any discrepancies or failures to meet specifications, including out-of-limit test results, shall be fully investigated, even if the batch is already distributed. Manufacturers shall keep records of these investigations, including conclusions and follow-up actions.
80. Written procedures for the release and rejection of products shall be in place, particularly for the release of finished products for sale.
	* + 1. **Specification**
81. There shall be appropriately authorized and dated specifications for all starting materials, bulk products, packaging materials, and finished medicinal gases.
82. Specifications for starting and packaging materials used for the production of medical gases or the filling of medical gas cylinders shall include, as appropriate:
83. The description of all of the starting and packaging materials
84. The chemical formula of the starting material
85. The designated name
86. Internal code reference for each component
87. The original producer and the approved suppliers of the materials
88. a specimen of the product label
89. The detailed methods for the sampling and testing of the starting materials, including any specified analytical procedures and equipment
90. The qualitative and quantitative testing requirements of the starting materials with the acceptance limits.
91. The storage conditions and precautions.
92. Where appropriate, specifications shall also be available for bulk medicinal gas and finished medical gas
93. There shall be detailed specifications for medical gas cylinders, including water capacity, design code, material of construction, colour coding, and internal cleanliness requirements.
94. Cylinder valves shall have detailed specifications, including materials of construction, design pressure, testing criteria, and maintenance requirements for approval.
95. Specifications shall cover printed cylinder labels and patient information leaflets, including label material, printed text details with version control, and approved suppliers.
	* + 1. **Records**
96. Batch records shall provide a comprehensive history of each batch of bulk medicinal gas produced or each batch of medicinal gas cylinders filled, including all details pertinent to the final product quality.
97. Batch records shall be designed to ensure traceability of each defined batch by documenting all significant activities involved in the manufacturing or filling processes. All records shall be dated and signed by the quality controller or their nominated deputy.
98. A batch of bulk medical gas shall be defined as a product produced in a bulk storage tank, a product transferred to a bulk gas tanker, or a continuous production within a defined period.
99. For continuous production processes, the batch records shall reference only the in-process quality control checks performed, while defined batches shall have separate batch records.
100. Batch records shall be based on the currently approved manufacturing procedures and processing instructions, designed to minimize transcription errors, and shall include the batch identity number.
101. Data included in the records for each batch of cylinders or mobile cryogenic vessels shall ensure that each filled cylinder is traceable to significant aspects of the relevant filling operations. The following shall be entered, as appropriate:
102. Master formula and batch size
103. the name of the product;
104. batch number;
105. the date and the time of the filling operations;
106. identification of the person(s) carrying out each significant step;
107. line clearance;
108. quantity of cylinders or mobile cryogenic vessels filled;
109. pre-filling operations performed;
110. In-process Quality Control;
111. results of appropriate checks to ensure the containers have been filled;
112. sample of the batch label;
113. specification of the finished product and results of quality control tests;
114. Quantity of rejected cylinders or mobile cryogenic vessels with reasons for rejections, if any;
115. details of any problems or unusual events, and signed authorization for any deviation from filling instructions;
116. Certification statement by the Authorized Person, date and signature;
117. Distribution record.
118. Records shall be maintained for all major and critical equipment. These records shall include information on any qualifications, calibrations, maintenance, cleaning, or repair operations, along with the dates and identities of personnel performing these tasks
119. Records of analysis for each batch shall be maintained, providing evidence of compliance with the required specifications.
120. Records shall be maintained for each batch of gas manufactured, including all relevant production and quality control information.
121. Records shall be completed immediately when any significant action is taken to maintain full traceability of all activities. These records shall be retained for a minimum period of until the expiration date of the batch. If a batch of medical gas is not labeled with an expiration date, the related records shall be retained for at least 3 years from the batch distribution date.
122. After completing the cylinder batch, the batch record shall be dated and signed by the person responsible for the filling operation, ensuring accountability and traceability of actions taken during the filling process.

**PART FOUR**

**ADMINISTRATIVE MEASURE**

1. **General**
2. A person who violates the requirements of this directive or other applicable laws may be subjected to appropriate administrative measures in accordance with the provisions of the Proclamation, the Directive on Administrative Measure Taking and Complaint Handling Procedure and other applicable laws.
3. Administrative measures shall be taken considering the severity of the offense, the circumstances of its execution, and the amount of damage it has caused or could have caused.
4. The person against whose product or whom an administrative measure is taken in accordance with sub-article (1) of this article may lodge complaint in accordance with the Directive on Administrative Measure Taking and Complaint Handling Procedure
5. When the certificate of competence is suspended or revoked, the Authority shall inform the relevant parties.
6. **Issuance of warning letter**

Without prejudice to grounds of warning provided under the proclamation and/or according to Directive on Administrative Measure Taking and Complaint Handling Procedure, the Authority may issue warning letter where the offense committed by the manufacturer is unintentional and doesn’t cause any harm to human health or body, and where it is not punishable with suspension or revocation.

1. **Suspension**
2. Without prejudice to grounds of suspension provided under the proclamation and the Administrative Measure Taking and Complaint Handling Procedure Directive, and based on the severity of the violation, the Authority shall suspend certificate of competence of the manufacturer of medical gas, if it:
3. Manufacturing medical gas without authorization by the authority
4. make changes on professionals, premises, services and products without notifying to the authority
5. impedes the work of inspectors during inspection; and
6. manufacture medical gases with the absence of authorized personnel;
7. suspended by other government organs (for the same duration of time), until reversal of such suspension is sought by the concerned government body.
8. issued warning letter three times or more in the validity period of the certificate competence and found to be failure to take corrective actions for the identified violations
9. The Authority shall notify the institution in written on action taken by the Authority and reasons thereof.
10. **Revocation of certificate of competence**
11. Without prejudice to grounds of revocation provided under proclamation, and based on the severity of the violation, and Administrative Measure Taking and Complaint Handling Procedure Directive, the Authority shall revoke certificate of competence, if it ;
12. obtained its certificate of competence through fraudulent acts or by submitting false information or documents
13. intentionally distribute and sale a medical gas to any health facility with no certificate of competence;
14. add or mix any substance to the medical gas so as to increase its bulk or weight, or for any other similar purpose;
15. possess or sale any unauthorized, adulterated, falsified; expired or unlabeled/mislabeled medical gas;
16. Fails to recall or discontinue supplying manufactured medical gas having safety or quality defects.
17. Resumption of suspended business in violation of the suspension imposed by the authority
18. Found to transfer the certificate of competency issued to another third party.
19. Commit violations indicated in article 27 twice and more
20. prohibited from doing its business by other appropriate government organs.
21. Once the certificate of competence is revoked as per sub-article one of this article, the manufacturer shall not participate in this business using certificate competence of other professionals and institutions.
22. The authority shall revoke the certificate of competence when the manufacturer stops to do business for its own reasons.
23. The Authority shall revoke the certificate of competence on the basis of cancellation of the business license of the manufacturer by another concerned government body, until reversal of such cancellation is sought by the concerned government body.
24. The Authority shall have an obligation to notify the manufacturer and other concerned bodies in writing on the above administrative measures taken.
25. **Reversing of Suspension and revocation**

The suspension and revocation of certificate of competence imposed on the manufacturer shall be reversed after review and accepting the complaint submitted as per Administrative Measure Taking and Complaint Handling Procedure Directive.

1. **Return of Certificate of competency certificate**
	1. The manufacturer may return its certificate of competence when
2. Change to manufacturing premises, location, technical person or other critical change is required to the existing certificate of competency issued.
3. The certificate of competency suspended, revoked or fails to renew.
4. The technical manager with whom the certificate of competency issued has been dead
5. The Authority believes that the service provided has imposed public health risk or may impose sudden public health problems
6. In such cases, the certificate of competency shall be returned to the Authority within two days.

**PART FOUR**

**MISCELLANEOUS**

1. **Complaints and appeal handling**
2. The manufacturer shall establish a system for addressing customer complaints regarding medical gases.
3. Each complaint received must be documented with necessary details.
4. The manufacturer shall have a dedicated person or unit responsible for handling process complaints.
5. Every complaint shall undergo a thorough investigation to determine the root causes of the complaint.
6. After thorough investigation, a resolution shall be provided within a reasonable timeframe.
7. If the customer is unsatisfied with the resolution, it shall be informed of the process for filing an appeal.
8. Appeals shall be managed by personnel who were not involved in the initial complaint resolution.
9. All decisions made during the appeal process shall be documented and promptly communicated to the customer.
10. If serious quality issues affecting patient safety are identified, the competent authorities shall be informed immediately.
11. **Duties to collaborate**
12. All relevant stakeholders involved in the manufacturing, handling, distribution, and regulation of medical gases must collaborate with each other.
13. Stakeholders shall share information and provide access to records when required to ensure compliance.
14. Manufacturers shall collaborate with regulatory bodies to ensure all processes comply with national and international standards.
15. In the event of health or safety concerns, manufacturers shall cooperate fully with the authority to address and mitigate risks.
16. The manufacturers are responsible for the maintenance and repair of cylinders, vessels, and valves. If subcontracted, only approved subcontractors with appropriated established contracts and technical agreements shall be involved in activities.
17. **Record keeping and reporting**
18. Manufacturers shall maintain detailed records for all manufacturing, quality control, distribution, recalls, and returns related to medical gases.
19. Records shall be kept for a minimum of five years or as per legal requirements, ensuring traceability for all production and distribution activities.
20. Any deviations or incidents shall be reported to the regulatory authority within a specified timeframe, with detailed documentation of the deviation and rationale for the deviation.
21. Regular reports should be submitted to authorities, including production volumes, quality control results, safety incidents, and batch-specific data.
22. Records for each batch shall include the product name, batch number, date/time of filling, personnel identification, equipment used, and any deviations or unusual events.
23. Standard Operating Procedures (SOPs) for processes such as raw material receiving, manufacturing, cleaning, and distribution shall be documented, authorized, and available during inspection.
24. **Service Fee**

Any person who seeks regulatory service under this directive may be required to pay applicable service fees in accordance with appropriate regulations.

1. **Inapplicable laws**

Any law which is inconsistent with this directive shall not be applicable with respect to those matters provided for in this directive.

1. **Effective date**

This directive shall be effective as of the date registered with in the Ministry of Justice and uploading on the EFDA website.

**Annexes**

**Table 1:** Type of changes and requirements for change

|  |  |  |  |
| --- | --- | --- | --- |
| **SN**  | **Type of change** | **Requirements for change** | **Remarks** |
| 1 | Change ofphysical location | * House rent contract or carta or leasehold title certificate authenticated by the appropriate government body.
* Payment of service fee
* Previous original certificate of competence
* Two passport size photos (not more than six months old) of the technical manager
* Description of the premises, including pictures or videos of both the interior and exterior, if required
* Self-inspection result
 | Inspection isrequired |
| 2 | Change ofKey personnel  | * Employment agreement of the new key personnel
* Educational credentials
* Current original release and experience letter
* Professional license
* Payment of service fee
* Previous original certificate of competence
* Two passport-size photos (not more than six months old) of the new key personel
 | Inspection is notrequired |
| 3 | Change of name of establishment | * Trade registration license
* Payment of service fee
* Previous original certificate of competence
 | Inspection is notrequired |
| 4 | Change of owner | * Memorandum of establishment
* Payment of service fee
* Previous original certificate of competence
 | Inspection is notrequired |
| 5 | Modification ofpremises | * Payment of service fee
* Previous original certificate of competence
* Proposed modification process management plan
 | Inspection isrequired |