FOOD AND DRUGS AUTHORITY

PROGRESSIVE LICENSING SCHEME

GUIDELINE FOR LICENSING OF PREMISES FOR MANUFACTURING MEDICAL DEVICES

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It is acknowledged that, in the development of this Guideline, reference was made to the following sources:

- ISO 13485: 2016 (Medical Devices – Quality Management Systems – Requirements for regulatory purposes)
- Global Harmonization Task Force (GHTF) Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Manufacturers (GHTF/SG4/N30:2010)
- Health Products Regulatory Authority (HPRA) Guide to Distribution of Medical Devices, including in vitro diagnostic Medical Devices
- Health Sciences Authority's Medical Device Technical Specification on Good Distribution Practice for Medical Devices Requirements (TS-01)
- Public Health Act, 2012 (Act 851)
- The EU New Medical Devices Regulation (MDR) (2017/745/EU) and the In-vitro Diagnostic Medical Devices Regulation (IVDR) (2017/746/EU)
- US FDA Center for Devices and Radiological Health (CDRH) web page for multimedia industry education – CDRH Learn.
- US Food and Drug Administration (USFDA), Guide to Inspections of Quality Systems, Quality System Inspections Technique (QSIT)
- US Food and Drug Administration (US FDA) Quality System Regulation – 21 CFR 820

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1.0 INTRODUCTION

In pursuance of sections 115, 130, 131 and 148 of the Public Health Act, 2012 (Act 851), this Guideline is hereby made to provide information on the requirements for the registration and licensing of premises or facilities for the manufacture of medical device in Ghana and also for the upkeep of already licensed manufacturing facilities. This includes information on Quality Management Systems/Good Manufacturing Practice (QMS/GMP) requirements for medical device manufacturing companies.

This Guideline applies to all persons manufacturing medical devices in Ghana. In accordance with Section 130(1) of the Public Health Act, 2012 (Act 851), these persons shall not manufacture medical devices except in premises registered and licensed by the Food and Drugs Authority (FDA) for that purpose. In addition, pursuant to Section 118(1), medical devices manufactured by these persons are required to be registered with the Authority.

Premises for the manufacture of medical devices shall be subjected to pre-licensing and post-licensing QMS audit/GMP inspection in accordance with the requirements of the current ISO 13485 (medical devices-quality management systems-requirements for regulatory purposes). The audit/inspection will be risk-based, and will be informed by factors such as product and process risk, the manufacturer's compliance history, risk associated with the use of the device, and relevant recalls carried out.

The purpose of this audit/inspection is to verify that medical devices designed, developed, produced, stored and distributed by the manufacturer consistently meet applicable regulatory requirements and ensure customer satisfaction in the interest of public health and safety. The QMS audit/GMP inspection observations, if found to be satisfactory, will guide the Authority in its decision to issue a new manufacturing licence or renew an existing manufacturing licence in accordance with Section 131 of the Act. With micro, small and medium scale enterprises manufacturing low risk medical devices, a progressive licensing scheme will apply.

Applicants are therefore advised to observe the provisions of this Guideline before submitting an application for registration and subsequent licensing or renewal of licence of their premise(s) for the manufacture of medical devices.

Progressive Licensing Scheme

Given the springing up of homemade face mask and other low risk medical devices manufacturing by micro, small and medium scale enterprises (with few being large scale), this guideline is also aimed at facilitating progressive licensing of these enterprises. Manufacturing Licences to be issued to these enterprises has therefore been stratified or categorized into three based on the QMS/GMP compliance level and risk associated with the product being produced. With respect to this, one of the three licence categories as listed below would be issued to medical device manufacturing facilities based on total scores obtained following inspection of the facility by Officers of the Authority using the current ISO 13585:

(1) **Green:** A green licence shall be issued to a medical manufacturing facility that is 75-100% compliant to QMS/GMP. Such a facility is expected to maintain or make better it's QMS/GMP compliance status.

(2) **Yellow:** A yellow licence shall be issued to a medical device manufacturing facility that is 45-74% compliant to QMS/GMP. Such facilities shall be given a year to be fully QMS/GMP compliant and the medical device being produced should be a low risk device

(3) **Pink:** A pink licence shall be issued to a medical device manufacturing facility that is 30-44% compliant to QMS/GMP. Such facilities shall be given two years to be fully QMS/GMP compliant and the medical device being produced should be a low risk device.

This Guideline is hereby promulgated for information, guidance and strict adherence by all concerned.

2.0 GLOSSARY

In this Guideline, unless the context otherwise requires, the following terms have the assigned meanings:

2.1 **Accessory:** An article which, whilst not being itself a medical device, is intended by its manufacturer to be used together with one or several particular medical device(s) to specifically enable the medical device(s) to be used in accordance with its/their intended purpose(s) or to specifically and directly assist the medical functionality of the medical device(s) in terms of its/their intended purpose(s). Accessories shall be classified in their own right separately from the device with which they are used.

2.2 **Applicant:** Product owner or licence holder. May either be the trademark owner or person authorized by him, who has rights to sell a product and is responsible for placing the product on the Ghanaian market. Representatives of licence holders may not hold themselves as applicants unless they own the product.

2.3 **Authority:** Food and Drugs Authority

2.4 **Authorized Representative (or Local Agent):** Legal person established within the jurisdiction who has received a written mandate from the manufacturer to act on his behalf for specified tasks with regard to the latter's obligations under the jurisdiction's legislation.

2.5 **Complaint:** Written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, usability, safety or performance of a medical device that has been released from the manufacturer's control or related to a service that affects the performance of such medical devices.

2.6 **Component:** Any raw material, Substance, piece, part, software, firmware, labelling, or assembly which is intended to be included as part of the finished, packaged, and labelled device.

2.7 **Correction:** Action to eliminate a detected nonconformity. A correction can be made in conjunction with a corrective action. A correction can be, for example, rework or regrade.

2.8 **Corrective Action:** Action to eliminate the cause of a detected non-conformity or other undesirable situation. Corrective action is taken to prevent recurrence.

2.9 **Design and development file/ design history file:** Is a compilation of records which describes all the design and development activities. It may also be referred to as design history file (DHF) in which case it is defined as compilation of records which describes the design history of a finished device.

2.10 **Design Input (Design and development inputs):** The physical and performance requirements of a device that are used as a basis for device design.

2.11 **Design Output (Design and development outputs):** The result of a design effort at each design phase and at the end of the total design effort. The finished design output is the basis for the device master record. The total finished design output consists of the device, its packaging and labelling, and the device master record.

2.12 **Device History Record (DHR):** A compilation of records containing the production history of a finished device.

2.13 **Device Master Record (DMR):** A compilation of records containing the procedures and specifications for a finished device. It may also be referred to as medical device file.

2.14 **Design review (Design and development review):** A documented, comprehensive, systematic examination of a design to evaluate the adequacy of the design requirements, to evaluate the capability of the design to meet these requirements, and to identify problems.

2.15 **Design Validation** (**Design and development validation):** Establishing by objective evidence that device specifications conform to user needs and intended use(s).

2.16 **Entity:** Any legal person, engaging in the manufacture, importation, exportation, storage, transportation and wholesale distribution of medical devices.

2.17 **Labelling:** Label, instructions for use, and any other information that is related to identification, technical description, intended purpose and proper use of the medical device, but excluding shipping documents.

2.18 **Management with Executive Responsibility**: Senior employees of a manufacturer who have the authority to establish or make changes to the manufacturer's quality policy and quality system.

2.19 **Manufacture:** Manufacture may include specification development, production, fabrication, assembly, processing, packaging, repackaging, labelling, relabelling, sterilization, installation, or refurbishing of a medical device; or putting a collection of devices, and possibly other products, together for a medical purpose.

2.20 **Manufacturer:** Any entity that manufactures.

2.21 **Medical device:** An instrument, apparatus, implement, a medical equipment, machine, contrivance, implant, in vitro reagent or any other similar or related article, including a component, part or an accessory which is:

(a) Recognized in the official natural formulary or pharmacopoeia or a supplement to them, or
(b) Intended for use in the diagnosis of a disease or any other condition, or in the cure, mitigation, treatment or prevention of disease in humans and animals, or
(c) Intended to affect the structure or a function of the body of the human being or other animal and which does not achieve any of its principal intended purposes through chemical action within the body of the human being or any other animal and which is not dependent on being metabolized for the achievement of any of its principal intended purposes.

2.22 **Medical Device Family:** Group of medical devices manufactured by or for the same manufacturer and having the same basic design and performance characteristics related to safety, intended use and function.

2.23 **Product:** result of a process.

2.24 **Preventive Action:** Action to eliminate the cause of a potential non-conformity or other undesirable situation.

2.25 **Process validation:** Establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications.

2.26 **Purchased product:** Product provided by a party outside the manufacturer's quality management system.

2.27 **Packaging/ Packaging material:** The container and other materials including printed material in which medical devices are supplied. Primary packaging materials are those that are in direct contact with the product.

2.28 **Packaging process/Operations:** All operations, including filling and labelling, that a bulk product has to undergo in order to become a finished packaged product.

2.29 **Quality policy:** The overall intentions and direction of a manufacturer with respect to quality, as established by management with executive responsibility (or top management).

2.30 **Quality management system (QMS):** A formal system that documents the structure, processes, roles, responsibilities and procedures required to achieve effective quality management. For the purpose of this document "quality management system" means requirements for manufacturing of medical devices as specified in the current ISO 13485.

2.31 **Rework:** Action taken on a nonconforming product so that it will fulfil the specified DMR requirements before it is released for distribution.

2.32 **Risk:** A combination of the probability of occurrence of harm and the severity of that harm.

2.33 **Specification:** Any requirement with which a product, process, service, or other activity must conform.

2.34 **Top management:** The people who direct and control an organization at the highest level.

2.35 **Verification:** Confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.

3.0 REQUIREMENTS

3.1 APPLICATION REQUIREMENTS

3.1.1 New Applications

3.1.1.1 An application to register and license a new facility for the manufacture of medical devices shall be made in writing by submitting a completed application form with a cover letter addressed to:
The Chief Executive Officer
Food and Drugs Authority
GA-237-7316
Accra

3.1.1.2 The completed application form (FDA/MCH/MID/APM-LMD/2019/02) shall be dated, signed and stamped by the applicant and shall provide the following minimum information as part of the licence acquisition:

(a) The name, full business address, location/site address and telephone numbers (including mobile numbers) of the applicant.
(b) Addresses, telephone numbers, and the names of contact persons for all facilities used by the applicant for the manufacture of medical devices

3.1.1.3 The completed application form shall be accompanied by:

(a) Non-refundable application fee as specified in the FDA's Fee Schedule
(b) Certified true copies of Certificate of Incorporation and Certificate to Commence Business from Registrar General's Department.
(c) Quality Manual which shall also outline the structure of the documentation used in the quality management system where applicable (Refer to Appendix 1).
(d) Permit from the Environmental Protection Agency (EPA), where applicable.
(e) Basic floor plan showing plant installation, where applicable
(f) Architectural engineering permit issued by the local authority, where applicable
(g) Technical Management Agreement with any entity, where applicable

3.1.1.4 In situations where the manufacturing site is more than one, a separate application is required in respect of each premise, except where a group of buildings on one or more sites are engaged in making the same kind of product under the same direct production and quality control management.

3.1.1.5 The Authority shall consider, as a minimum, the following factors in reviewing the qualifications of applicants:

(a) Any convictions of the applicant relating to FDA-regulated products;
(b) The applicant's history of regulatory compliance in the manufacture, importation, exportation or distribution of FDA-regulated products, where applicable;
(c) The applicant's information provided to the Authority which is found to be misleading, false or fraudulent in respect of its application for FDA-regulated products;

(d) The applicant's licence has been suspended or revoked by the Authority for violation of any FDA law; and
(e) Any other requirements the FDA may from time to time prescribe.

3.1.1.6 The Authority may approve, defer or refuse an application following assessment including QMS/GMP audit findings which shall be duly communicated to the applicant.

3.1.1.7 A manufacturing licence shall be valid for one year and shall be renewable.

3.1.1.8 The Authority shall exercise the right to cancel or suspend a licence in accordance with the law.

3.1.1.9 An applicant shall submit any and all changes in their application information to the Authority prior to amending or changing its existing records and information.

3.1.2 Renewal Applications

3.1.2.1 The registration and licensing of the premises shall be renewed annually.

3.1.2.2 An application for renewal of registration and licensing of premises shall be made at least 3 months before the expiry of the existing licence by submitting with a cover letter the following:
(a) Duly completed application form (FDA/MCH/MID/APM-LCH/2019/02).
(b) Non-refundable application fee in accordance with the FDA fee schedule

3.1.2.3 The applicant's compliance with QMS/GMP shall be a key determinant to the renewal of the registration and licensing of the premises.

3.1.3 Foreign Manufacturing Facilities / Premises

3.1.3.1 Where applicable, foreign manufacturing facilities or companies may be required to pay the facility inspection fee for the conduct of QMS /GMP audit/inspection in addition to other documentation required.

3.1.3.2 The manufacturing facility would be issued a GMP certificate following a satisfactory audit or inspection.

3.1.3.3 Based on the level of risk, foreign manufacturing facilities shall be inspected at least every 5 years provided there are no safety and quality issues related to the facility's products during this period.

3.1.3.4 In the event that an applicant for the registration of medical device(s) to be marketed in Ghana is not a registered entity in Ghana, the applicant is required to appoint a local agent (authorised representative) and duly notify the Authority.

3.1.4 Contract Manufacturing

3.1.4.1 Where the applicant for the registration of medical device(s) to be marketed in Ghana is not the manufacturer, a contract agreement between the applicant and the manufacturer will be required.

3.2 QMS/GMP REQUIREMENTS

As a general principle, manufacturers and potential manufacturers of medical devices intended to be marketed in Ghana are required to document a quality management system and maintain its effectiveness in accordance with the current ISO 13485 (medical devices-quality management systems-requirements for regulatory purposes). This should be appropriate for the specific medical device(s) designed, or manufactured, and should demonstrate their ability to provide medical devices and related services that consistently meet applicable regulatory requirements and ensure customer satisfaction in the interest of public health and safety.

Premises for the manufacture of medical devices shall therefore be audited/ or inspected using the requirements outlined in the current ISO 13485. The primary purpose of the audit or inspection is as follows:

(a) To determine if the procedures, equipment and processes used by the manufacturer can be expected to consistently produce medical devices that meet the specification/standard of the medical device being produced.
(b) To verify that the production procedures and processes are carried out as described in the product dossier and quality manual summaries submitted to the FDA as part of the registration process.
(c) To do an in-depth assessment of the medical device manufacturing operation and not just a general assessment of the ISO 13485 documentation.

Manufacturers are to note that the ISO 13485 is not prescriptive; it should therefore be used together with the applicable technical regulation.

Where a manufacturer outsources any process likely to affect the quality and safety of the medical device(s), the manufacturer shall ensure control over such process to ensure that the outsourced process conforms to specified requirements. Technical agreements should be in place for all outsourced processes and should at least describe the roles and responsibilities of both parties including details on production, quality control and release.

For the purpose of auditing, the ISO 13485 QMS/GMP requirements for medical devices have been divided into subsystems (as per the Global Harmonization Task Force (GHTF) guidelines for regulatory auditing of quality management systems of medical device manufacturers). These are:

(1) Management subsystem (Clause 4,5,6,8)
(2) Design and development subsystem (clause 7)
(3) Product documentation subsystem (clause 4,7)
(4) Production and process controls subsystem (clause 4,6,7,8)
(5) Corrective and preventive actions (CAPA) subsystem (4,5,6,7,8)
(6) Purchasing controls subsystem (clause 7)
(7) Documentation and records subsystem (clause 4)
(8) Customer related processes subsystem (clause 7)

The highlights of these subsystems are described below:

3.2.1 Management subsystem (Clause 4,5,6,7,8)

There should be top management's active participation in the QMS. Top management is therefore required to provide adequate resources for operations within the manufacturer's quality management system, establish adequate effective quality system and effective monitoring of the quality system, making any necessary adjustments where required. The following specifics are required with respect to management subsystem:

3.2.1.1 *Management Commitment:* Top management is required to provide evidence of their commitment to the development and maintenance of the established quality management system and maintenance of its effectiveness by carrying out at least the following:

(i) Establish a *quality policy* and a *quality objective* and ensure that this is understood and implemented by all employees
(ii) Establish a *quality plan* which defines the quality practices, resources and activities relevant to the devices that are designed and manufactured
(iii) Establish an *organizational structure* that defines clear responsibilities and authorities within the organization. These responsibilities shall be independent of every function affecting quality
(iv) Provide *adequate resources* to assure quality objectives can be achieved
(v) Appoint a *management representative* to ensure that the quality system is maintained and monitored making any necessary adjustments based on information obtained from periodic monitoring
(vi) Conduct *management reviews* to measure the firm's quality system

3.2.1.2 *Personnel Training:* Management shall ensure adequate personnel with the necessary educational background, training and experience.

3.2.1.3 *Internal Audit:* The manufacturer shall conduct internal audits at planned intervals in accordance with its SOP to determine whether the quality system complies and is effective.

3.2.2 Design and Development subsystem (Clause 7)

Properly established design and development control systems must be in place, and must include the following:

(a) Design and development planning
(b) Design and development inputs
(c) Design and development outputs
(d) Design and development review
(e) Design and development verification
(f) Design and development validation
(g) Design and development transfer
(h) Control of design and development changes
(i) Design and development files (design history file).

3.2.3 Product Documentation subsystem (Clause 4,7)

The applicable manufacturer's documentation on the manufacturer's products should provide credible evidence to show that the products meet customer and regulatory requirements. Thus, for any typical product of the manufacturer selected based on product risk, complaints or known problems, age of design, the underlisted documentation should be available and should be found to be credible and satisfactory:

(a) Evidence of conformity to requirements, including standards used
(b) Medical device description including instruction for use, materials and specification
(c) Summary of design verification and validation documents including clinical evidence
(d) Labelling
(e) Risk management documents
(f) Manufacturing information including major suppliers
(g) Any other relevant additional documentation.

3.2.4 Production & Process Controls subsystem (clause 4,6,7,8)

The production processes and the infrastructure within which it operates including personnel, materials, and documents shall be sufficiently controlled to consistently produce devices that meet established specifications. The ISO 13485 describes infrastructure to include as appropriate, buildings, workspace and associated utilities, process equipment (both hardware and software) and supporting services (such as transport, communication, or information systems). The following are to be considered with respect to the Production and Process Controls subsystem:

3.2.4.1 *Production process:* Manufacturers are required to develop, conduct, control and monitor production processes to ensure that a device conforms to its specification. The production processes shall be validated (process validation) where the resulting output cannot be or is not verified by subsequent monitoring or measurement. Similarly, when computers or automated data processing systems are used as part of the production process or the quality system, such software applications shall be validated prior to initial use and as appropriate after changes to such software or its application. In situations where there are production and process changes, these shall be controlled and

evaluated for their impact on the quality management system and on the medical devices produced.

3.2.4.2 *Buildings:* The building infrastructure is required to be suitably designed with sufficient work space to achieve conformity to product requirements, to prevent mix-ups and to assure orderly handling of product. It is also required that the building infrastructure is appropriately qualified and maintained.

3.2.4.3 *Equipment:* Process equipment (both hardware and software) are required to be suitable and appropriately designed, constructed, placed and installed to facilitate maintenance, adjustment, cleaning and use.

3.2.4.4 *Personnel:* Personnel of the entity are fundamentally required to be appropriately qualified and/or trained to implement /maintain the process. Additionally, the manufacturer is required to document requirements for health, cleanliness and clothing of personnel if contact between such personnel and the product or work environment could affect medical device safety or performance. The manufacturer must ensure that all personnel who are required to work temporarily under special environmental conditions within the work environment are competent or supervised by a competent person.

3.2.4.5 *Work environment and contamination control:* If the conditions for the work environment can have an adverse effect on product quality, the manufacturer shall document the requirements for the work environment and the procedures to monitor and control the work environment. In addition, and as appropriate, the manufacturer shall plan and document arrangements for the control of contaminated or potentially contaminated product in order to prevent contamination of the work environment, personnel, or product. Also, as appropriate, the manufacturer shall document requirements for control of contamination during assembly or packaging of sterile products. Thus, for sterile products, clean room requirements shall apply.

3.2.4.6 *Storage and Control of work in progress*: The manufacturer shall document procedures for preserving the conformity of product to requirements during processing and storage including work-in-progress. Thus, steps shall be taken by the manufacturer to ensure appropriate segregation, labelling, status identification, environment control and security of work-in-progress.

3.2.4.7 *Packaging Operations:* As appropriate, production controls shall include but not be limited to implementation of defined operations for labelling and packaging. Consequently, materials used for labelling and packaging, the packaging process, packaging equipment adequacy, product testing and controls, documentation and labelling, lot coding as well as the packaging environment shall be controlled.

3.2.4.8 *Monitoring, Testing and Controls (Quality Control):* The manufacturer shall determine the monitoring and measurement activities to be undertaken and the monitoring and measuring equipment needed to provide evidence of conformity of product to determined requirements. Monitoring and measurement of the characteristics of the product to verify that product requirements have been met shall be carried out at applicable stages of the product realization process in accordance with the planned and documented arrangements and procedures. The monitoring and measuring equipment shall be duly calibrated. An effective quality assurance system is therefore required for product release, delivery and post-delivery activities.

3.2.4.9 *Documentation:* Documented procedures, specifications, work instructions, and reference materials as necessary, are required to be available. Additionally, the manufacturer shall establish and maintain a record (device history records) for each medical device or batch of medical devices that provides traceability and identifies the amount manufactured and amount approved for distribution (device history records). The record shall be verified and approved.

3.2.4.10 *Handling, Storage and Distribution of finished products:* The manufacturer shall protect product from alteration, contamination or damage when exposed to expected conditions and hazards during processing, storage, handling, and distribution. It shall therefore document procedures for preserving the conformity of product to requirements during processing, storage, handling, and distribution. The preservation requirement shall as well apply to the constituent parts of a medical device.

3.2.4.11 *Installation and Servicing activities:* The manufacturer shall document requirements for medical device installation and acceptance criteria for verification of installation, as appropriate, and corresponding records kept. Similarly, if servicing of the medical device is a specified requirement, the manufacturer shall document servicing procedures, reference materials, and reference measurements, as necessary, for performing servicing activities and verifying that product requirements are met.

3.2.5 Corrective and Preventive Actions (CAPA) subsystem.

The manufacturer shall put systems in place to take appropriate and effective corrective action to correct existing quality problems and also preventive action to prevent reoccurrence of potential quality problems. The CAPA provisions of the QMS therefore require manufacturers to establish and maintain procedures for implementing corrective and preventative action, including analysing all sources of quality data to identify existing and potential causes of nonconforming product or other quality problems. The following amongst others are sources of quality data from where manufacturers are to collect data to analyse and trend to identify actual and potential product quality problems, investigate them and take appropriate and effective corrective and preventive actions:

(a) Customer feedback

(b) Complaints, returned products (as well as lawsuits)

(c) Medical device reporting and recall
(d) Internal audit and management reviews
(e) Monitoring and measurement of processes and products
(f) Non-conforming products including concessions
(g) Reworked products
(h) Work operations, Quality records and Service records
(i) Market surveillance

3.2.6 Purchasing Controls subsystem (Clause 7)

Device manufacturers shall select only those suppliers, contractors, and consultants who have the capability to provide quality product and services and that purchased or otherwise received products, components, materials and services provided by suppliers (including contractors and consultants) conform to specifications. This is particularly important when the finished product or service cannot be verified via inspection (e.g. sterilisation services). The purchasing control subsystem requires the following:

3.2.6.1 *Evaluation and selection of suppliers:* The manufacturer is required to establish criteria for the evaluation, selection, monitoring and re-evaluation of supplier capability or performance in meeting requirements for the purchased product and any necessary actions arising from these activities.

3.2.6.2 *Conformance to specified purchasing information:* The manufacturer is required to document procedure to ensure that purchased product conforms to specified purchasing information which shall include product specifications, requirements for product acceptance, procedures, processes and equipment, requirements for qualification of supplier personnel and quality management system requirements.

3.2.6.3 *Verification of purchased product:* The manufacturer shall establish and implement inspection or other activities necessary for ensuring that purchased product meets specified purchasing requirements.

3.2.7 Documentation and Records subsystem (Clause 4)

The manufacturer's documentation processes shall ensure that relevant documents and records are available and adequately controlled to provide evidence of compliance to the QMS. Documents required by the quality management system shall include:

(a) Documented statements of a quality policy and quality objectives
(b) A Quality Manual (Refer to Appendix 1)
(c) Documented Procedures and Records
(d) Documents, including records, determined by the manufacturer to be necessary to ensure the effective planning, operation, and control of its processes
(e) Other documentation specified by applicable regulatory requirements

In addition, for each medical device type or medical device family, the manufacturer shall establish and maintain a medical device file to demonstrate conformity to the

requirement of the quality management system and compliance with applicable regulatory requirements.

Control of the manufacturer's documents will require that:

(a) Documents are reviewed and approved for adequacy prior to issue;
(b) Documents are reviewed, updated as necessary and re-approved;
(c) Current revision status of and changes to documents are identified;
(d) Relevant versions of applicable documents are available at points of use;
(e) Documents remain legible and readily identifiable;
(f) Documents of external origin, determined by the organization to be necessary for the planning and operation of the quality management system, are identified and their distribution controlled;
(g) Prevention of document deterioration or document loss

Prevention of unintended use of obsolete documents and apply suitable identification to them.

3.2.8 Customer Related Processes Subsystem (Clause 7)

Manufacturers shall keep to high standards when dealing with products and services they offer to customers. The manufacturer's top management are therefore required to ensure that customer requirements (for example, requirements specified by the customer for delivery and post-delivery) and applicable regulatory requirements related to the product are determined, reviewed and met in the interest of the customer. Any user training needed to ensure specified performance and safe use of the medical device shall also be determined.

3.3 CLASSIFICATION OF INSPECTION FINDINGS / NON-CONFORMITIES

3.3.1 Non-conformities

Nonconformities identified following an inspection/audit may be classified as major or minor and they have to be corrected. These shall be communicated to the company and a corrective and preventive action to address them would be required of the company inspected.

3.3.1.1 *Major non-conformity:* A major non-conformity is a serious deficiency that could adversely affect product/service quality (i.e. performance requirement or specification). It could also be a single infraction that by itself constitutes evidence of persistent failure. Furthermore, a number of observations that individually are of small importance whose frequency indicates a serious deficiency can also be classified as major non-conformity.

3.3.1.2 *Minor non-conformity*: A minor non-conformity is an isolated instance of failure to conform with a specified requirement that does not have an effect on product/ service quality.

3.3.2 Other Observations

Inspection observations that are not non-conformities per se but worth noting may be expressed as opportunity for improvement or concern.

3.3.2.1 *Opportunity for Improvement:* Inspection findings that appear to be undesirable but cannot be cited as a non-conformity are described as "Opportunity for Improvement". Corrective action is not required.

3.3.2.2 *Concern:* An inspection or audit finding is said to be of "Concern" in situations in which there is no information at the time of the inspection/audit to determine if a non-conformity exists. The concern shall be noted in the inspection report for further regulatory action.

3.3.3 Stakeholder Training

The Authority will periodically conduct appropriate stakeholder training for manufacturers to enhance their level of compliance.

4.0 TIMELINES

4.1 Conducting the inspection

Barring unforeseen circumstances, inspection of the manufacturing facility will be carried out within 90 days upon receipt of application for local manufacturing companies and 180 days for foreign manufacturing companies.

4.2 Unannounced Inspections

Despite existing protocol with respect to planned inspections, the Authority shall, when it deems it necessary, conduct unannounced inspections for the purposes of ensuring that the manufacturer's operation conforms to applicable law.

4.3 Communication of Inspection findings

The inspection findings shall initially be communicated to the manufacturer during the closing meeting of the audit and an observation form shall be issued to enable the manufacturer to commence the necessary corrective and preventive action. This will be followed by a formal inspection observation letter within 21 days after the inspection for local manufacturing companies and 42 days for foreign manufacturing companies.

4.4 Response to nonconformities

The manufacturer is required to formally respond to the deficiencies/nonconformities identified in the inspection report as officially communicated within a specified timeframe (usually 15 working days on receipt of the formal inspection findings letter).

4.5 Issuing of manufacturing licenses/GMP certificates

4.5.1 After all corrections and corrective actions (action plans) have been submitted to the Authority, evaluated and found to be satisfactory, a manufacturing licence/GMP certificate would be issued to the inspected company to close out the inspection.

4.5.2 The licence will only be valid for the period stated on the license or certificate, provided there are no quality and safety issues on the product manufactured at the site inspected.

4.5.3 For a previously inspected manufacturer applying a licence, the licence will be issued within 30 days upon payment of the required application fee and satisfactory evaluation of the manufacturer's previous inspection Corrective and Preventive Action (CAPA).

4.5.4 The concept of progressive licensing will apply.

APPENDIX 1
CONTENTS OF A QUALITY MANUAL FOR A MEDICAL DEVICE MANUFACTURING FACILITY

An ISO quality manual is an official document created by a manufacturer that lays out how its quality management structure works. It should include the manufacturer's quality policy and objectives and a highly detailed explanation of the quality control system being used. According to the ISO 13485, a quality manual includes the following:

(a) The scope of the quality management system, including details of and justification for any exclusion or non-application;
(b) The documented procedures for the quality management system, or reference to them;
(c) A description of the interaction between the processes of the quality management system.

The quality manual shall also outline the structure of the documentation used in the quality management system.