بسم الله الرحمن الرحيم

Maldives Food and Drug Authority

Ministry of Health

Male', Maldives

Guideline for Good Regulatory Practice

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Guideline for Good Regulatory Practice

1 INTRODUCTION

Management of regulatory processes is vital for ensuring the quality, efficacy and safety of medicine and therapeutic goods and keeping such items in compliance with legal, scientific, ethical and administrative requirements. It is important that the processes used to implement regulations and verify compliance serve their intended purpose effectively.

Regulations have the following features:

- **Accountable:** Mandated to a specific institution for implementation and responsibilities of the stakeholders and public.
- **Clear:** Accessible and understandable
- **Effective:** Produce good effects on the society and economy with feasible enforcement.
- **Proportional:** Should outweigh economic and social impacts and adverse effects.
- **Transparent:** Objectives understood and compiled with public consultation and evidence based.
- **Impartial:** Free of conflicts of interest and equal to all.
- **Legal basis:** with existing legislations both local and international
- **Efficient:** achieve intended results within the required effort, time and expenditure
- **Consistency:** regulations should be clear and predictable such that both regulators and stakeholders understand the expected behavior and consequences of any noncompliance.
- **Flexibility:** should accommodate for unforeseen circumstances and changing environment.

Implementation and enforcement of regulations shall be carried out in a way that achieves the purpose and does not hinder features of regulations.

Outcomes from the regulation can be achieved by assuring effective implementation and enforcement of the regulations. Incorporating Good Regulatory Practices (GRP) in the quality management system of MTG/MFDA is vital to the effective implementation of its mandate with regard to pharmaceuticals. This guide ensures that regulations;

- Serve clearly identified policy goals.
- Are effective in achieving those goals.
- Produce benefits that justify costs.
- Promote innovation, are fair and equitable.
- Are clear, simple, and practical for users.
- Are consistent with other regulations and policies.

This guide is divided into two main parts, which are management requirements and implementation and enforcement requirements for assuring effective execution of regulations.

2 PURPOSE OF THE GUIDE

This guide is developed to define the role and responsibilities of MTG division within MFDA, mandated to it in the implementation and enforcement of the regulations established by the government of the Maldives. It effectively describes the practices applied by MTG in the protecting the rights of the people of the Maldives to good quality, safe and efficacious medicines.

3 SCOPE

This guide is applicable to all the processes and activities used in the implementation and enforcement of all the regulations mandated to Maldives Food and Drug Authority (MFDA) in regulation of medicines and therapeutic products. This guideline is intended to assist the Medicines and Therapeutic Division within MFDA to implement GRP in enforcing the current regulatory system in the Maldives for medicines and therapeutic products.

4 MANAGEMENT REQUIREMENTS

4.1.1 Organization

4.1.1.1 The management system shall cover all work and activities that need to be carried out for the implementation and enforcement of regulations mandated to the organization.

4.1.1.2 The management system shall cover work carried outside the site of the main office of the organization and away from its permanent facilities, or in associated temporary or mobile facilities.

4.1.1.3 If the organization is part of an organization performing activities other than enforcement and implementation of the regulations, the responsibilities of key personnel in the organization that have an involvement or influence on enforcement and implementation activities shall be defined in order to identify potential conflicts of interest.

4.1.1.4 The organization shall;

a) Have managerial and technical personnel who, irrespective of other responsibilities, have authority and adequate resources needed for the enforcement and implementation of the regulations;

b) Have arrangements to ensure that its management and personnel are free from any undue internal and external commercial, financial and other pressures and influences that may adversely affect the quality of their work;

c) Have policies and procedures in place for the collection and management of data to ensure data integrity;

d) Have policies and procedures in place to ensure the protection of its clients' confidential information and proprietary rights, including procedures for protecting the electronic storage and communications;

e) Have policies and procedures to avoid involvement in any activities that would diminish confidence in its competence, impartiality, judgement or operational integrity;

f) Define the organization and management structure of the organization, its place in any parent organization, and the relationships between quality management, technical operations and support services;

g) Define other institutions or agencies or personnel who are assigned work in **other agencies**, for the enforcement and implementation of regulations, and their responsibilities and services (for the purpose of decentralization of work);

h) Specify the responsibility and accountability, authority and interrelationships of all personnel who manage, perform or verify work related to enforcement and implementation;

i) Provide adequate supervision of enforcement and implementation works, including trainees, by persons' familiar with methods and procedures, purpose of each activity, and with the assessment of the activity;

j) Have technical management which has overall responsibility for the activities and the provision of the resources needed to ensure the required quality;

k) Ensure key technical personnel are replaced timeously whenever they leave the organization

l) Appoint a member of staff as quality manager (however named) who, irrespective of other duties and responsibilities, shall have defined responsibility and authority for ensuring that the management system related to quality is implemented and followed at all times; the quality manager shall have direct access to the highest level of management at which decisions are made on enforcement and implementation processes or resources;

m) Appoint deputies for key managerial personnel

n) Ensure that its personnel are aware of the relevance and importance of their activities and how they contribute to the achievement of the objectives of the management system, and receive awareness training at least once annually.

o) Have in place a system that promotes and allows management to communicate the QMS to all personnel through various forums.

4.1.2 Premises

4.1.2.1 Premises should be designed and maintained in good order to provide sufficient space to suit the activities being carried out and should allow efficient work flow and should permit effective communication and supervision.

4.1.2.2 Premises must be structurally sturdy and safe for all personnel working within the premise. All movements and activities should take into account the health and safety of personnel working in the premises.

4.1.2.3 Premises must be equipped with adequate and appropriate facilities to control/handle any predictable hazards such as fire, chemical spills or other injuries to staff.

4.1.2.4 Premises design shall ensure controlled and where required, limited access, to authorized personnel only.

4.1.2.5 Physical and non-physical working conditions e.g. environmental factors, area of work , etc., should be such that the quality of the activities carried out is influenced in a positive manner.

4.1.2.6 All necessary equipment for the activities to be performed efficiently should be provided, e.g. computer hard and software, printers, copiers, archives and means of communication.

4.1.2.7 Personnel should be instructed in the proper use of equipment and the risk of errors occurring should be minimized by effective systems.

4.1.3 Quality Management System

4.1.3.1 An effective and a practical quality management system shall be set up by the organization for all the activities under its obligation. The system shall have, but not limited to, the following attributes:

a) The organization shall establish, implement and maintain a quality management system appropriate to the scope of its activities.

b) The management system's documentation shall be communicated to, understood by, available to, and implemented by the appropriate personnel.

c) The management system shall be designed and implemented to ensure that statutory, regulatory and the customer requirements fulfilled.

d) Commitment from top management system towards development and continual improvement of the system must be evident.

e) Top management shall ensure that the integrity of the management system is maintained at all times with any changes.

4.1.4 Documentation

4.1.4.1 Documents that form part of its management system shall be established and maintained inclusive of internally prepared and those of external sources (such as regulations, standards, normative documents, methods, software, specifications, instructions, manuals etc.).

4.1.4.2 All documentation must be approved and controlled; and reviewed regularly and kept up to date. Amendments should be dated, authorized and signed by the appropriate personnel.

4.1.4.3 An appropriate system should be in place to ensure traceability of documents and their different versions. This may best be achieved by help of a commercially available electronic document management system.

4.1.4.4 Duplication of documents must be controlled. Photocopying of controlled documents must be authorized.

4.1.4.5 All documentation should be securely stored.

4.1.4.6 Data should be protected against loss or damage, e.g. use of backup procedures. Only authorized personnel should be allowed to enter or edit data. Such edits should be recorded.

4.1.4.7 Documentation should be readily accessible to regulatory authority personnel in so far as it is required for them to perform their duties.

5 Procedures

5.1.1 SOPs shall be developed for all activities required for the implementation of regulations and compliance verification activities.

5.1.2 SOPs shall be established on how to implement relevant legislation and codes and the consequences for the organization's policy.

5.1.3 They shall be readily available and be checked and updated regularly in accordance with the SOP for amending and reviewing SOPs.

5.1.4 The organization shall develop policies for situations in which changing legislation and codes make it necessary or desirable to adapt to it.

5.1.5 Adopted (approved) SOPs shall be adapted and /or renewed whenever new or amended standards become available.

5.1.6 Procedures shall cover the different areas within the regulatory authority to specify responsibilities and organization

5.2 Maintenance of records

5.2.1 The organization shall have policies and procedures to store records related to the regulations, implementation and compliance verification processes.

5.2.2 Policies and procedures to control access to records shall be established and implemented.

5.2.3 A good archiving system is mandatory. It shall be described in a procedure which will describe, both for the documentation and the electronic documents, the archiving plan, the management of the different versions, frequently asked questions and answers, the traceability and the measures taken to ensure regular backup.

5.3 Availability / accessibility of regulations

5.3.1 In order to ensure availability of regulations, Master copies (printed versions) of the regulations shall be maintained and made available to staff.

5.3.2 A Master list of the regulations relevant to the organization detailing the name, date published, version number of the regulation and publisher must be maintained. Other details such as URL links, websites of published issue may also be recorded in the list.

5.3.3 Controlled copies of the most recent versions (printed or electronic versions) of the regulations must be made available to all staff. Locations of the controlled copies must be communicated to the staffs responsible for the implementation and enforcement of regulations and the communication recorded.

5.3.4 Electronic Versions of the regulations (if available) may be saved and a register of the regulations maintained.

5.4 Updating

5.4.1 Periodic checks of websites and documentation shall be done to see if newer versions have been published. The date, person carrying out the check and the sites and documentation checked should be recorded.

5.4.2 Whenever an update or an amendment to a regulation is issued and published, the regulation shall be updated and the most recent versions of the regulations shall be incorporated into the documentation system.

5.4.3 A period to maintain older versions of the regulations shall be decided and followed and documented.

5.4.4 It is important that parallel and necessary amendments are brought to the SOPs when regulations are amended by assigning individual staff to evaluate amendments and review SOPs under supervision of Division Head.

5.4.5 Amendments brought to the regulations and to the SOPs, shall be informed / communicated in writing to the respective staffs.

5.4.6 Changes brought to the SOPs and other documentation shall be approved by the Technical Committee to check its feasibility for implementation and enforcement.

5.5 PERSONNEL

5.5.1 Availability of staff

5.5.1.1 The Authority shall

a) Ensure that sufficient number of staffs shall be available who have the ability, education, training, experience and appropriate professional skills to perform the tasks assigned to them.

b) Provide adequate supervision of enforcement and implementation works, including trainees, by persons' familiar with methods and procedures, purpose of each activity, and with the assessment of the activity; (Also in organization)

c) Have technical management which has overall responsibility for the activities and the provision of the resources needed to ensure the required quality; (Also in organization)

d) Appoint a member of staff as quality manager (however named) who, irrespective of other duties and responsibilities, shall have defined responsibility and authority for ensuring that the management system related to quality is implemented and followed at all times; the quality manager shall have direct access to the highest level of management at which decisions are made on enforcement and implementation processes or resources; (Also in organization)

e) The management may authorize specific personnel to perform particular activities and to give opinions and interpretations.

f) Persons shall be designated to deputize for them in their absence and should be clearly defined in their job descriptions.

5.5.2 Responsibilities of staff

5.5.2.1 Staff shall be made aware of their responsibilities and importance of their contribution.

5.5.2.2 Current Job descriptions of all staff (managerial, technical and support staff) within the organization shall be maintained.

5.5.2.3 Key personnel in responsible positions and supervisory positions should be identified and shall be accountable for authorizing procedures and tasks and have adequate supporting staff.

5.5.2.4 The laboratory shall maintain records of the relevant authorization(s), competence, educational and professional qualifications, training, skills and experience of all technical personnel, including contracted personnel. This information shall be readily available and shall include the date on which authorization and/or competence is confirmed.

5.5.2.5 Where contracted and additional technical and key support personnel are used, the organization shall ensure that such personnel are supervised and competent and that they work in accordance with the organization's management system.

5.5.2.6 The organization shall have a policy requiring that all personnel concerned within the organization familiarize themselves with the quality documentation and implement the procedures in their work.

5.5.2.7 The organization shall have a policy requiring that all personnel concerned within the organization familiarize themselves with the codes of practices laid down and follow those.

5.5.3 Competency of staff

5.5.3.1 Records of qualification and competency must be maintained for all personnel, and used in the assignment and allocation of work.

5.5.3.2 Personnel performing specific tasks shall be qualified on the basis of appropriate education, training, experience and/or demonstrated skills, as required.

5.5.3.3 The laboratory management shall ensure the competence of all who perform analytical work;

5.5.3.4 Special skills such as inspection of sites, premises, goods and services shall be available and at the disposal of the Authority.

5.5.3.5 Authorized personnel shall evaluate results, and sign reports and certificates.

5.5.3.6 When using staffs that are undergoing training, appropriate supervision shall be provided.

5.5.3.7 All personnel shall be trained regularly in the tasks assigned to them.

5.5.3.8 Ideally, all graduate personnel should have a multidisciplinary background, scientific expertise, communication and negotiation skills, regulatory knowledge, planning capacity and be able to work in teams, to organize multidimensional projects and to work in a multidimensional manner.

5.5.4 New staff

5.5.4.1 Newly recruited staff shall be familiarized with the regulations via an orientation program based on his/her job description within 30 days of recruitment and records maintained.

5.5.4.2 An orientation package for new recruits may be prepared and used for the above purpose. This package shall be verified and authorized for its contents before usage by a named designation.

5.5.4.3 The organization shall have procedures to conduct assessment of new staff and assigning work to new staff.

5.5.4.4 Works assigned to new staff must be closely monitored and supervised.

5.5.5 Training and Familiarization On Regulations

5.5.5.1 In order to achieve the objectives of the regulations, ensure consistency in the implementation and enforcement of regulations and improve efficiency of the organization, staff responsible for the implementation and enforcement shall be familiarized with the regulations and trained on the procedures in place.

5.5.6 Planning Annual Training Program and Requirement

5.5.6.1 Trainings required must be identified individually for each staff member and recorded in the appraisal forms by respective immediate supervisors. A list of trainings required must be prepared every year by incorporating all these.

5.5.6.2 If an area or skill is found to be weak and observed to require improvements among majority of staffs, a training program may be conducted for all.

5.5.6.3 Refresher trainings shall also be periodically held and their frequencies decided and recorded as decided by the Technical Committee.

5.5.6.4 External trainings (within country and abroad) can also be sought as much as possible to address the gaps in the implementation and enforcement process.

5.5.7 Assessing and performance check

5.5.7.1 Any training held must be accompanied by an assessment. The effectiveness of the training actions taken shall be evaluated

5.5.7.2 Periodic performance checks for skills required by staff for the implementation and enforcement activities shall be checked to see if consistency is maintained in the implementation and enforcement process.

5.5.8 Training for new regulations

5.5.8.1 When a new regulation is in place, familiarization program for the staff concerned shall be drawn up and followed. If the implementation and enforcement of the regulation requires new skills, plans to train staff shall be formulated and conducted.

5.5.8.2 For skills, in which trainers are not available within the organization, training programs should be sought outside the organization or abroad if budget is available.

5.5.8.3 These trainings should be refreshed in the coming years by including those in the annual training requirement and plan.

5.5.9 Resources and technical tools

5.5.9.1 Tools and equipment, such as thermometers, required for activities shall be made available to the implementation staff.

5.5.9.2 Accuracy of measurement tools (e.g. thermometer) shall be calibrated and their calibration records maintained.

5.5.9.3 Resources shall be made available to develop and implement tools

a) to manage documents and information submitted

b) to maintain accurate records with a numbering system applications, amendments and notifications

c) to manage other information such as general inquiries

d) to ensure security and maintain confidentiality of records

5.5.9.4 Checklists shall be developed with regard to implementation of regulations and these shall be checked by managerial staff and authorized in accordance to the SOP for approving documents.

5.5.9.5 Codes of practice in relation to the regulations shall be formulated, communicated and familiarized to all staff involved. All staff shall abide by these codes. The communication and familiarization and declaration to abide by the codes of practice shall be recorded.

5.5.9.6 Documents pertaining to resources and technical tools used for the purpose of the implementation of regulations shall be incorporated in to the documentation system of the organization.

5.6 Requirements for implementation and enforcement

5.6.1 Planning and Coordination

5.6.1.1 **Strategic Action Plan:** A strategic action plan defining the objectives, strategies and the activities that the regulations oblige the organization to fulfill shall be prepared. The action plan shall consist of the objectives, strategies and action steps or activities.

5.6.1.2 **Develop objectives:** Regulations shall be researched and reviewed to determine the objectives of the regulation. The objectives that shall be developed must be;

a) **Specific:** That is, they tell how much (e.g., 40%) of what is to be achieved (e.g., what behavior of whom or what outcome) by when (e.g., by 2020)?

b) **Measurable**: Information concerning the objective can be collected, detected, or obtained from records (at least potentially).

c) **Achievable:** They must be feasible and possible for the organization to carry pull them off.

d) **Relevant**: The organization shall ensure that these objectives fit in with the overall vision and mission of the organization or the regulation.

e) **Timed:** A timeline (a portion of which is made clear in the objectives) by which they will be achieved shall be developed.

f) **Challenging**: They stretch the group to set its aims on significant improvements that are important to members of the community.

5.6.1.3 Develop an action plan composed of action steps or activities and strategies that address the objectives. The plan should be complete, clear, and current. The following questions can be used as guidelines to follow to write action steps:

a) What action or change will occur?

b) Who will carry it out, supervise and evaluate the activity

c) When it will take place, and for how long and the frequency of the activity

d) Determine resources needed to implement tasks (i.e., money, staff) – currently available resources and additional requirements

e) Determine the data that needs to be collected from each activity and incorporate the documents, forms, lists and records into the document management system and records of the organization

f) Consolidate functions which can be combined with other activities of the organization so as to avoid duplication and overlaps of activities within the organization and make the best use of the available resources.

g) Share the plan with relevant staffs to obtain their remarks.

h) Finalize plan and communicate the plan to related personnel and record the communication.

5.6.1.4 Create a schedule of the action steps and activities;

a) For daily activities and activities that are frequent (more than once a month), new tasks, duties and responsibilities should be incorporated into the job description of staffs that will carry out the actions.

b) For activities with low frequency (less than once a month), it is recommended to draw up a schedule for activities in consideration with the frequency of the activity, staff availability and resources.

c) The schedule should be communicated to the relevant staff and the communication recorded.

d) It is recommended to have substitute staffs in the schedule.

e) Periods/ dates for assessment and evaluation of the activities are to be included in the schedule.

f) For recurring activities schedules shall be made on a regular basis and prior to the end of the current schedule.

g) It is recommended to allocate an overall staff, irrespective of other duties, to monitor/supervise the progress of the activities in the schedule.

h) Activities requiring heavy finance shall be budgeted and included in the coming year's financial plan of the organization.

5.6.2 Compliance Verification

5.6.2.1 Regular and periodic inspection and audits shall be carried out to check the practices applied by practitioners and if the sites of practice are in accordance with regulations or standards set by a regulation.

5.6.2.2 Regulations that require registrations of products, places, processes, persons etc., shall be registered. A register of such categories shall be maintained (preferably via a database or electronic means) and shall be readily available.

5.6.2.3 Regulations requiring certification shall be awarded certificates to compliant clients/customers. Copies of these certificates shall be maintained.

5.6.2.4 Sanctions for non-compliant products, parties, places, people etc. shall be laid down clearly and penalties implemented accordingly.

5.6.2.5 SOPs for compliance verification activities above shall be prepared, authorized and maintained.

5.6.2.6 Compliance verification activities shall be incorporated into the action plan of the organization.

5.6.2.7 Records of the compliance verification activities shall be maintained.

5.6.2.8 Qualified staff shall be appointed to supervise and authorize the documents and records of the compliance verification activities and procedures to verify the staff involved in the activities shall be in place.

5.6.2.9 Criteria for compliance shall be laid down (if not available in the regulation or standards) and incorporated in to the documentation system of the organization.

5.6.2.10 Laid down criteria shall be applied in the decision making process during verifying compliance. The organization shall have procedures to follow for cases where contradictions occur in decision making.

5.6.2.11 For regulations requiring inputs from other governmental agencies and other non-governmental institutions a committee shall be formed constituting members from related institutions. Meetings of the committee shall be held periodically and whenever need arise and records maintained.

5.6.2.12 A Technical Committee comprising of members within the organization and or experts from outside shall be formed and meetings regularly held and records maintained.

5.6.2.13 Consultation with experts on complex scientific, medical, or regulatory issues shall be facilitated and the Authority shall make use of advisory committees.

5.6.3 Monitoring and Evaluation

5.6.3.1 Consequences of all activities shall be evaluated and reviewed by the managerial staff at the end of a periodic cycle (quarterly and then annually) to conclude the necessary changes to plans, activities, policies, strategies and when required ammendements to regulations.

5.6.3.2 Periodic self-inspections and audits of activities shall be carried out in order to evaluate the processes in accordance with the approved schedule.

5.6.3.3 Surveys to get feedback from stakeholders may be conducted on a regular basis and the results evaluated for continual improvement.

5.6.3.4 Procedures shall be in place to establish a mechanism to get comments and suggestions from public and analyze those.

5.6.3.5 A system to record complaints from clients and public shall be established. Complaints thus received shall be reviewed and a response given to the client

5.6.3.6 Data and evidence collected from activities shall be used to analyze the risks to manage risks involved and improve the costs involved both to the organization and the public and stakeholders.

5.6.3.7 A system to record deviations from procedures shall be established and implemented.

5.6.3.8 Where deviations from procedures occur, corrective actions shall be duly taken and recorded.

5.6.3.9 Programs to raise public and stakeholder awareness on the regulations shall be conducted periodically and following amendments to regulations.

5.6.3.10 Additionally, meetings with stakeholders and target groups may be conducted, irrespective of their requests for such a program.

5.6.3.11 Procedures to disseminate information (to the public) shall be established and implemented. Information disseminated during awareness programs shall undergo careful scrutiny and research for its content for clarity, accuracy, consistency and alignment against regulations and preferably a trial round shall be conducted to check its effectiveness, understandings and impacts.

6 REFERENCES

1. ISO/IEC 17025:2005(E), General requirements for the competence of testing and calibration laboratories
2. Guide to Good Regulatory Practice, EUROPEAN INDUSTRIAL PHARMACISTS GROUP
3. Draft 2016, Good regulatory practices: guidelines for national regulatory authorities for medical products, WHO