Doc No. TMDA/DMC/MRE/G/016
Rev.#01

UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

GUIDELINES ON GOOD REVIEW PRACTICES

A Guide for Applicants and Assessors on Good Review Management Principles and Practices for Applications of Marketing Authorization of Medicinal Products

April, 2023

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TABLE OF CONTENTS

ABBREVIATIONS AND ACRONYMS

MAB	-	Ministerial Advisory Board
MAH	-	Marketing Authorization Holder
MoH	-	Ministry of Health
TMDA	-	Tanzania Medicines and Medical Devices Authority
WHO	-	World Health Organization
GRevP	-	Good Review Practices
GMP	-	Good Manufacturing Practices
TPD	-	Health Canada's Therapeutic Products Directorate
QM	-	Quality Management
QMS	-	Quality Management System
QRM	-	Quality Risk Management
NMRAs	-	National Medicines Regulatory Authorities
SOP	-	Standard Operating Procedure
MRE	-	Medicines Registration

ACKNOWLEDGEMENTS

I wish to take this opportunity to thank all who in one way or another assisted in the review of this guidance document.

I would like to sincerely thank the TMDA staff for their tireless efforts in reviewing the previous version of the Guidelines on Good Review Practices. Special thanks are extended to the following staff: -

- Mr. Felchism Apolnary
- Mr. Denis Mwangomo
- Dr. Athanas Mseki
- Ms. Diana Njiu
- Mr. Peter Hamisi
- Mr. Tryphone Gujema
- Mr. Begumisa Casmil

I would also like to extend my gratitude to the WHO GBT benchmarking assessors whose recommendations during auditing made valuable inputs in accomplishing the review of these guideline.

Lastly, the TMDA Management team is acknowledged for its constructive comments and endorsement of the first revision this document.

Dr. Yonah H. Mwalwisi
DIRECTOR OF HUMAN AND VETERINARY MEDICINES

GLOSSARY OF TERMS

The definitions given below apply to the terms used in this document. They may have different meanings in other contexts.

“Act” means the Tanzania Medicines and Medical Devices Act, Cap 219;

“Authority” means the Tanzania Medicines and Medical Devices, or the acronym “TMDA” established by Section 4 of the Act;

“Applicant” means a person or company who submits an application for marketing authorization of a new medical product, an update to an existing marketing authorization or a variation to an existing marketing authorization;

“Application” means the information provided by the applicant to the Authority for evidence-based evaluation and marketing authorization decision;

“Assessor or reviewer” means any qualified personnel who participate in the technical aspects of medicinal product evaluation and registration process;

“External assessor/reviewer” means assessor outsourced from outside TMDA;

“Evaluation” means highly complex, multidisciplinary assessment of medicinal products applications to determine whether they meet scientific and evidentiary standards for safety, efficacy and quality. It forms the scientific foundation for regulatory decisions;

“Evaluation procedure” means the approach or plan of action that an assessor uses to process and evaluate a medical product application;

“Good review practices (GRevP)” means documented best practices for any aspect related to the process, format, content and management of a medicinal product evaluation and registration process;

“Marketing authorization” means approval to market a medicinal product in Tanzania. It is a legal document issued by the Authority that permits the marketing or free distribution of a medicinal product in Tanzania after evaluation of safety, efficacy and quality. In terms of quality, itestablishes inter alia the detailed composition and formulation of the product and the quality requirements for the product and its ingredients. It also includes details of the packaging, labelling, storage conditions, shelf-life and approved conditions of use;

“Principles (of a good review)” means the important GRevP elements to implement in order to achieve successful evaluation and registration outcomes;

“Project management (for the evaluation and registration process)” means the planning,

organization and resources to achieve a complete and high-quality review of an application withina specified time frame;

“Quality management (QM)” means the coordinated activities that direct and control an organization with regard to quality;

“Quality management system (QMS)” means an appropriate infrastructure, encompassing the organizational structure, procedures, processes and resources and systematic actions necessaryto ensure adequate confidence that a product or service will satisfy given requirements for quality;

“Regulatory convergence” means the process whereby regulatory requirements, approaches and systems become more similar or aligned over time as a result of the adoption of internationally recognized technical guidance, standards and best practices;

“Standard operating procedure (SOP)” means an authorized written procedure giving instructionsfor performing operations (both general and specific); and

“Transparency” means defining policies and procedures in writing and publishing the written documentation, and giving reasons for decisions to the public.

FOREWORD

This is the first revision of the Guidelines on Good Review Practices published by TMDA. This review has been instituted as a result of the recommendations from the WHO-Global Re- benchmarking assessment. The document describes the internal processes conducted during the evaluation and registration of products and provides recommendations to stakeholders on good review management principles and practices for the review of medicinal product dossiers submitted in support of applications for registration.

The review incorporats the requirement for confirmation of GMP compliance of the finished product manufacturing facilities before granting Marketing Authorization. Moreover, technical editorial changes have been effected as a result of knowledge and experiences gained during the implementation of the first edition.

Good review practices ensure that the evaluation and registration process is managed in a consistent and efficient manner, thereby decreasing the number of evaluation cycles necessary for approval and enhancing patients' timely access to essential medicines and other therapeutic technologies.

In general, this guidance document does not establish legally enforceable responsibilities. Instead, the guidance prescribes the Authority's current thinking on the topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. Albeit, these guidelines do not legally bind TMDA, appropriate justification and supervisory concurrence are always placed before departure from the outlined procedures.

Good Review Practices form good regulatory practices in relation to the processes, format, content, and/or management of medicinal product evaluation and registration which have been developed based on the Authority's collective experience to provide consistency to the overall evaluation process.

TMDA continues to work to improve the management of applications for the registration of medicinal products to meet challenging registration targets while maintaining the highest standards of evaluation of product quality, safety, and efficacy.

This document is envisioned as one building block in a set of tools and is sufficiently expandable to accommodate additional annexes or ancillary documents in the future. GRevP guidelines will from time to time be updated as responses to changing regulatory environments, feedback from stakeholders accrue ongoing efforts will further be staged to improve and standardize internal processes across evaluation and registration processes, including quality systems implementation as well as innovations.

Adam M. Fimbo
DIRECTOR GENERAL

1. INTRODUCTION

Tanzania Medicines and Medical Devices Authority (TMDA) is an Executive Agency under the Ministry of Health (MoH) responsible for regulating the quality, safety and effectiveness of medicines, medical devices, diagnostics, biocidal and tobacco products. The functions of TMDAare provided for in the Tanzania Medicines and Medical Devices Act, Cap. 219.

TMDA has consistently documented GRevP through standard operating procedures, assessment templates and other guidance documents. However, developing and documenting GRevP as a single set of guidance may address problems with evaluation processes, enhance evaluation practices of medicinal products and provide clarity to applicants on our internal procedures.

The guidelines highlight the following areas: –

- Implementation of good review practices;
- The structural arrangement of medicines evaluation and registration;
- Management of the evaluation process;
- Critical thinking during dossier assessment; and
- Communications and managing domestically manufactured products.

A list of documents governing the medicines review process is provided in form number TMDA/DMC/MRE/F/036 which is available at www.tmda.go.tz

1.1 Objective of this document

The objective of this document is to provide high-level guidance on the principles and processes of good review practice (GRevP) for use in the process of submission of applications and evaluation of medicinal products within TMDA. It is not intended to provide detailed instructions on how to conduct a scientific review, hence this guideline should be read in conjunction with the existing documents related to the marketing authorization of medicines.

1.2 Scope

This document applies to the evaluation of quality, safety and efficacy data in medicinal product applications submitted to TMDA for marketing authorization. Although this document is developed to provide guidance on pharmaceutical and biological products used in humans, the principles may be applied to other categories of medicines including veterinary and herbal medicinal products. Similarly, the concepts will also be applied to the entire product life cycle from investigational testing to new product applications, variations to existing marketing authorizations and maintenance of registration of the product within the TMDA register.

2. IMPLEMENTATION OF GOOD REVIEW PRACTICES

The main objective of GRevP is to help achieve timeliness, predictability, consistency, transparency, clarity, efficiency and high quality in both the content and management of evaluation and registration processes. This is done through the development of assessment tools and learning activities.

The Authority has implemented various assessment tools including, marketing authorization guidelines, assessment guidance and templates, standard operating procedures, monitoring and evaluation systems. There are separate assessment procedures and templates for new applications, re-registration applications, query responses and variation applications.

Core Values

GRevP are developed based on the Authority's core values of Teamwork, Integrity, Customer focus, Transparency, Accountability and Quality. Therefore, the evaluation processes are all governed by these attributes. These core values and their applicability to medicines evaluation and registration are summarized the table below.

Core value	Implementation
Teamwork	Evaluation and registration of medicines is supported by various Sections including ICT, Inspectorate and Laboratory Services. This fosters a cooperative approach to ensuring that the public gets access to quality, safe and efficacious medicines.
Integrity	Personnel involved in medicines registration and evaluation are held to the highest standards of conduct and commitment while acting in the best interest of the country.
Customer focus	GRevP guides evaluators to ensure that the customers' needs and expectations are at the forefront of our work.
Transparency	Stakeholders have access to Authorities publications (Act, regulations, and guidelines) for technical assistance with regards to the evaluation and registration of medicines. Communications regarding the decisions and reasons are made timely to applicants governed by Client Service Charter.
Accountability	The Authority's roles, requirements and responsibilities for evaluation and registration of medicines are outlined in Regulations making the Authority accountable for timely accessibility of quality, safe and efficacious medicines.
Quality	Quality control procedures are implemented throughout the marketing authorization process. These procedures are governed by GRevP that enables consistency and efficiency hence ensuring the utmost quality of evaluation and the resultant regulatory action,

Principles of a good review

The principles of a good review describe the GRevP elements that are important to implement in order to achieve successful evaluation outcomes in line with the objectives of GRevP. The Authority has adopted 10 key principles of a good review to serve as a solid GRevP foundation upon which the Authority will continue to build. The principles are as follows:

1. Balanced
   A good review is objective and unbiased.

2. Considers context
   A good review considers the data and the conclusions of the applicant in the context of the proposed conditions of use and storage, and may include perspectives from patients, health-care professionals and other RAs' analyses and decisions.

3. Evidence-based
   A good review is evidence-based and reflects both the scientific and regulatory state of the art. It integrates legislative, regulatory and policy frameworks with emerging science.

4. Identifies signals
   A good review comprehensively highlights potential areas of concern identified by the applicant and the reviewers.

5. Investigates and solves problems
   A good review provides both the applicant's and the reviewers' in-depth analyses and findings of key scientific data and uses problem-solving, regulatory flexibility, risk-based analyses and synthesis skills to devise and recommend solutions and alternatives where needed.

6. Makes linkages
   A good review provides integrated analysis across all aspects of the application: preclinical; nonclinical; clinical; chemistry/biocompatibility; manufacturing; and risk management plan. It includes timely communication and consultation with applicants, internal stakeholders and, as needed, with external stakeholders who have expertise relevant to the various aspects of the application.

7. Thorough
   A good review reflects adequate follow-through of all the issues by the reviewers.

8. Utilizes critical analyses
   A good review assesses the scientific integrity, relevance and completeness of the data and proposed labelling, as well as the interpretation thereof, presented in the application.

9. Well-documented
   A good review provides a well-written and thorough report of the evidence-based findings and

conclusions provided by the applicant in the dossier, and the reviewers' assessment of the conclusions and rationale for reaching a decision. It contains clear, succinct recommendations that can stand up to scrutiny by all the parties involved and could be leveraged by others.

10. Well-managed
    A good review applies project and quality management processes, including clearly defined steps with specific activities and targets.

3. MEDICINES EVALUATION AND REGISTRATION

Within TMDA, the Directorate of Human and Veterinary Medicines through Medicines Registration Section (MRE) is responsible for actively managing the medicinal product evaluation and registration process. This is done to maximize both the potential for a positive public health impact and the effective and efficient use of resources. Effectiveness of the process is dependent on multiple factors, principles and systems as described below.

3.1 Monitoring and evaluation (Project Management)

Planning, monitoring and evaluation of registration activities are performed by all staff of the section led by the Manager, Medicines Registration (MRE). This, coupled with timely, informative communications and clearly defined work instructions ensures that registration timelines are met.

Principles of project management are implemented during dossier assessment for planning, organizing and resource allocation. This aids achievement of complete and high-quality assessment of applications within a specified time frame. All applications are made electronically through an online application portal which allows complete electronic management of each stage of evaluation.

Monitoring of applications is achieved using an electronic technique. This electronic system has evolved with changes in technologies, techniques, regulatory practices, TMDA resources and workload. It is expected that continuous use of the system will necessitate further advancements, however at all times the system shall enable:

a) Receiving, pre-checking and invoicing of applications;

b) Assigning and distribution of applications for evaluation;

c) Interpretation of the data to show the progress of one application as well as that of many applications under evaluation at any one time;

d) Interpretation of the data to help in decision-making with respect to balancing workload against resources; and

e) Monitoring that can be performed and/or interpreted by the Authority.

3.2 Quality Management

Quality Management System is an integral part of the MRE procedures. The QMS principles include standardized procedures to ensure that GRevP are in place, regularly monitored and subject to continuous improvement. In addition to standardizing processes and procedures to provide consistency and predictability, QM plays a significant role in robust regulatory decisions and actions.

Implementing QM is an interactive cyclic process that incorporates lessons learned with regard to improved processes and decision-making. All personnel involved in evaluation and registration processes are responsible for the continual implementation of quality management principles.

The quality cycle implemented by the Authority consists of four key components:-

a) say what we do
b) do what we say
c) prove it
d) improve it.

This cycle ensures that GRevPs are not just esoteric guidelines (say what we do) but become embedded in the daily practice of the Authority (do what we say). Quality management is also in place to review the Authority's practice (prove it) and evolve where necessary, either in response to evolving regulatory science or through the adoption of a new review process and procedures (improve it). A description of the key components of QMS is presented in table 1 below.

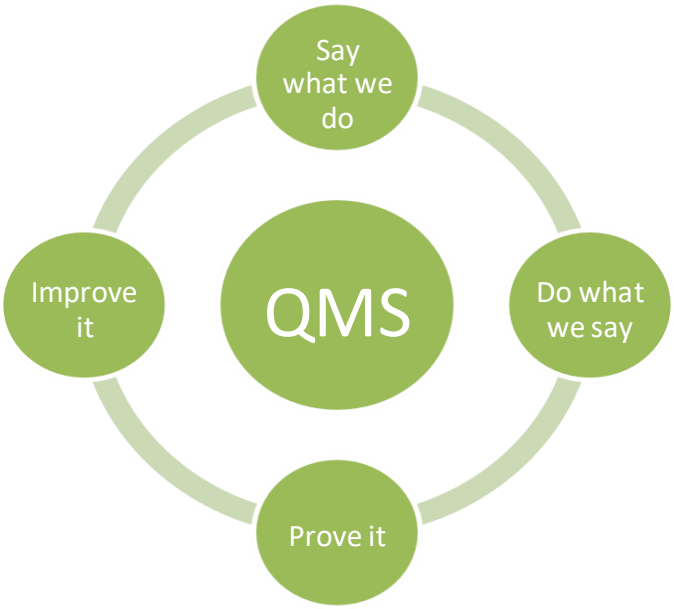

Figure 1: Cyclic representation of the key components of Quality Management Systems

Table 1: Key components of the Quality Management Cycle

QMS component	**Interpretation**
Say what we do	Availability key documents, such as SOPs assessment guidances and templates. Defined processes for decision-making, such as decision frameworks, time frames for completion and communication of reviews, use of external assessors, public meetings and peer-review.
Do what we say	Record and collect key documents, such as minutes of meetings and teleconferences, memoranda, letters and reports.
Prove it	Ensure that review procedures and templates are being consistently interpreted and applied through the assessment of various inputs, such as internal and external feedback and periodic evaluation of practices by internal and external assessors. Assess public health impacts of regulatory decisions, such as through a lessons-learned session that could include assessing the impact on disease, the health-care system and any unintended consequences.
Improve it	Review documentation and decision-making processes regularly. Introducing improvements to the review and decision-making process specifically in internal assessment of a review; peer review; internal quality audits; self-assessments; analyses of feedback from stakeholders; post-approval analysis of the decision in collaboration with other authorities; the public and applicants; and analysis of impact on public health. Implement new and improved work practices, the latest evaluation techniques, and scientific and technological advancements.

3.3 Standard Operating Procedures (SOPs)

Handling of each application is guided by specific SOPs which: -

a) Outline the workflow processes that facilitate project management when there are multiple applications to process;
b) Enables handling and evaluating applications in a consistent manner; and
c) Facilitate staff training.

MRE Section has developed SOPs for managing the marketing authorization process from receiving and handling applications and samples, distribution and assigning documents as well as for technical evaluation and communicating to applicants. The SOPs are used in conjuncture with additional tools and guidance to support effective implementation of the tasks. Such tools include assessment guidance tools, templates; forms, register and checklist to provide detailed instructions on conducting a particular procedure and give advice on handling different situations in the course of performing the procedures.

In addition, the Authority has developed training program and procedures to ensure consistent training of all assessors involved in medicinal dossier assessment. This is coupled with implementation of various guides including SOP for induction training, Competency requirements and Training structure for assessors. Furthermore, procedures for administratively handling applications after final recommendations are also implemented. These include the process of convening technical committees and publishing information on registered products and approval or rejection of medicinal products.

To promote continuous improvement, all SOPs and accompanying templates, registers, checklists and forms are reviewed every three (3) years and guidelines including guidance documents are reviewed every five (5) years. Nevertheless, all these documents may be reviewed any time technological advances occur or scientific and regulatory thinking evolves. This evolution could be related to influences including scientific progress, international harmonization of guidelines, changes in review strategy, available resources, and increased volume of applications, collaborative work-sharing and national laws and regulations, among others.

While these SOPs, assessment guidance, templates, registers and checklists are internal documents, the guidelines are made available to provide stepwise instructions to applicants on how to fulfil regulatory requirements. Guidelines and guidance documents for applicants use include guidelines on documentation for submission of new applications (pharmaceuticals, biotherapeutics including biosimilars and vaccines), re-registration and variations.

A list of documents governing the medicines review process is provided in form number TMDA/DMC/MRE/F/036 which is available at www.tmda.go.tz

4. MANAGING THE EVALUATION PROCESSES

4.1 Roles and responsibilities

4.1.1 Applicant

Applicants are expected to be conversant in international regulatory requirements as well as TMDA specific requirements. It is the responsibility of the applicant to:-

a) Provide authentic and complete scientific documents to support their applications;
b) Ensure that all submissions (of additional data) are submitted within the deadlines;
c) Ensure that their product meets all requirements to be retained in the register of registered medicines;
d) Updating, when necessary, a summary of product characteristics and package inserts for thepurpose of enabling a correct and safe use of the product;
e) Submit any variations to the Authority in line with the requirements stated in the variation guidelines;
f) Renew their registration every five (5) years; and
g) Conduct market surveillance activities once the product has been granted marketing authorization.

4.1.2 Authority

Ultimately, the responsibility of the Authority is to ensure the quality, safety and efficacy of medicinalproducts. To achieve this, assessors are expected to become thoroughly familiar with pertinent GRevP and to adhere to these GRevP during evaluation unless a particular part of a GRevP is not applicable to a particular review or the reviewers receive supervisory instruction to do so otherwise. Any deviation from the GRevP should be adequately documented and justified.

The Manager, MRE is responsible for: -

a) Ensuring that GRevP are developed, implemented, updated and followed by assessors;
b) Communicating specific instructions to deviate from the GRevP when appropriate;
c) Conducting training needs assessment and planning appropriate in-house training;
d) Overseeing the mentoring of assessors; and
e) Advising Management on content and policy within GRevP and appropriate training courses for assessors.

4.2 Evaluation procedures

Evaluation and registration of medicines is a collaborative process between the Authority and the applicant. The applicant initiates the first step by lodging an application online. Once the application is received, invoiced and paid for, it is scheduled for evaluation. The Authority has established different routes of applications and it lies with the applicants to choose their preferred route as follows: -

a) The national procedure: This is the normal procedure conducted by TMDA for all applications applied for registration. Essentially this is the default route and in absence of any declaration, it is assumed that the applicant intends to use this route. When following this route, the applicant may opt to apply for fast-track registration which entails a higher fee and reduction in registration timelines;
b) The EAC joint assessment procedure: This procedure is a collaborative process with all EAC NMRAs established as means of harmonizing regulatory requirements throughout the EAC. TMDA is the lead NMRA in medicines evaluation and registration under the EAC-MRH program hence works in close collaboration with the EAC Secretariat to coordinate this procedure;
c) The SADC joint assessment procedure: is a collaborative procedure for Southern African Development Community (SADC) countries commonly known as ZAZIBONA in which national regulatory authorities jointly assess medicines for registration purposes;
d) The WHO Collaborative Registration Procedure; is a voluntary procedure where by an applicant agrees to share with TMDA the assessment reports developed during WHO prequalification;
e) TMDA Emergence Use Authorization: This is an expedited review procedure prescribed in the Guidelines on Emergency Use authorization of medicinal products; and
f) Orphan medicine procedure: This is designed to facilitate registration of orphan medicines. It

is prescribed in the Tanzania Medicines and Medical Devices (Orphan Medicines) Regulations in force.

4.3 Stages of evaluation and registration

4.3.1 Pre-checking of applications

Evaluation and registration of medicines start with pre-checking of applications to confirm the completeness of the application in order to facilitate the subsequent scientific review. This comprises examining the application to ensure that it is well-organized and complete. Identifying missing documents in the application prior to scientific review enables the Authority to avoid spending time and review resources on an application that does not allow regulatory decision-making.

It is essential that applicants are aware of the Authority's expectations at both stages, including the target time frames, guidelines, requirements, templates and checklists. This results in a more predictable and clear process for applicants. In turn both parties' benefit when complete documents are submitted at the outset.

4.3.2 Dossier assessment

The second stage is dossier assessment where a scientific review is undertaken. This stage has three critical steps; first assessment, second assessment then quality assurance of the assessment report. This means that each application is assessed by two assessors assigned based on first-in first out concept while taking into consideration the competency, expertise and experience of the assessor. These stages are put in place as a safeguard to ensure that no critical issue is overlooked and that GRevP are followed.

Throughout the evaluation process, there is constant communication between MRE Section and Medicines Inspection and Enforcement Section regarding GMP status of the manufacturing sites. Additional communication with the laboratory is conducted when the need for sample analysis arises. Furthermore, during evaluation of re-registration applications (renewals), communication with the inspectorate regarding any quality or safety issues observed during routine inspections is undertaken.

This stage is complete once communications have been drafted and sent to applicants. The dossier assessment stage is usually the longest as it may require multiple rounds of communications to ensure that the data provided satisfies the regulatory requirements.

4.3.3 Legal and Administrative Procedures

Once the assessment has been completed and a final recommendation reached including compliance of the facility to GMP requirements, the legal and administrative procedures begin. At this stage, the Authority presents the outcome of the evaluation and recommendations before the technical committee for the registration of medicinal products for consideration.

MRE has two technical committees;

a) The Human Medicines Registration Technical Committee (HMRTC) is constituted by impartial external experts in the field of internal medicine, pharmaceutics, clinical pharmacology, biostatistics, microbiology/virology, toxicology, drug analysis and clinical pharmacy; and
b) The Veterinary Medicines Registration Technical Committee (VMRTC) is constituted of experts in the field of public health, clinical veterinary practices, microbiology/virology, pharmacology, toxicology and drug analysis.

Nevertheless, the Director General may co-opt additional members depending on the need and the matter to be discussed.

Both committees serve for three years and have similar functions of advising the Director General on matters related to:-

a) Quality, safety and efficacy of medicines and vaccines referred to the committee for technical guidance;
b) Registration of medicines and vaccines;
c) Medical and Scientific evaluation of applications for registration of medicines and vaccines (e.g., new chemical entities, fixed-dose combinations, biotechnological products etc);
d) Scheduling of medicines and vaccines into distribution categories;
e) Promotion and advertisement of medicines;
f) New developments in the field of medicines and vaccines including registration; and
g) Any matter related to the evaluation and registration of medicines and vaccines.

The recommendations of the technical committee are presented to the Director General for final approval and thereafter the decision is communicated to the applicant.

4.4 Medicinal dossier assessors

The quality, timeliness and success of medicinal product application processing are dependent on adequate human resources. The MRE Section contains assessors from different academic disciplines including Pharmacy, Human medicine, Veterinary medicine, Chemistry and Herbal medicine. In addition, multiple staff have been trained in different speciality areas such as assessment of biotherapeutics, vaccines, promotional materials and clinical safety and efficacy data. In order to ensure sufficient number of assessors to perform registration activities, the Authority uses experts from other Sections as well as external assessors from outside TMDA.

All assessors employed by the Authority are bound by the Code of Ethics and Conduct for Public Services and sign the declaration of conflicts of interest every calendar year as part of the requirements of the Public Service Regulations.

External Assessors

External assessors are selected following a rigorous screening of applications to ensure the integrity of product evaluations and recommendations. Only qualified personnel that are free of actual or perceived conflicts of interest are listed as external assessors. To be free of any conflictof interest means the evaluation decision or recommendation is not likely to be influenced by personal, family, financial or professional motives, including those of employers when an external assessor is also a consultant to the regulated applicants. All external assessors sign confidentiality agreements and declarations of conflict of interest at the beginning of their tenure. During the performance of any TMDA activity, the external assessors are mandated to adhere to TMDA's code of conduct for external assessors; failure to comply with the code of conduct may lead to the de-listing of the external assessors before the end of his/her tenure.

The tenure for all external assessors is one financial year which can be renewed indefinitely based on individual performance. The performance of external assessors is monitored annually through performance appraisal which is conducted at the end of each year to determine the overall quality of assessments done by the individual assessor. This process guarantees that each external assessor upholds our core values and consistently provides quality output. Following this appraisal, the list of external assessors is updated. If an assessor's appraisal deems that his/her work is unsatisfactory, he/she shall be delisted.

4.4.1 Assessor expertise, competencies and training

The professional qualifications of medicine assessors include holders of Bachelor Degrees in Pharmacy, Human Medicine, Pharmacology, Toxicology, Biotechnology, Microbiology and Immunology; Laboratory Technology, Bio-Medical Engineering, Veterinary Medicine, Chemistry, Herbal Medicine or equivalent qualifications from recognized institutions.

Assessors' capacity relates to many factors including scientific knowledge and skills, regulatory knowledge and experience as well as abilities and attitudes of the assessor including consistency in assessment, social skills and language fluency. These form the core competenciesfor personnel involved in the various aspects of managing and conducting dossier evaluation. TheAuthority has implemented guidance on Competency Requirements for Medicinal Dossier Assessors to aid in categorizing assessors based on their level of expertise.

Effective training is a requirement for maintaining core competencies thus, the Authority has developed training program and procedures in order to provide consistent quality of training for all assessors. Moreover, training needs assessment is done on an annual basis in order to determine knowledge gaps for individual assessors as well as knowledge gaps of the whole Section.

5. CRITICAL THINKING DURING DOSSIER ASSESSMENT

Critical thinking requires an objective and systematic approach to analyzing information and to problem-solving. It relies on the collection of data and evidence-based decision-making instead

of generalizing from one's own experience, intuition or trial and error. Decisions should be reproducible and clearly understood by others.

Nevertheless, every regulatory decision involves judgment. Therefore, core competence in public health and bioethics, and the ability to integrate up to-date scientific knowledge with an understanding of the evidentiary standards for regulatory action (including the flexibility inherent in those standards and regulations), also guide decisions.

Beyond their professional qualifications, assessors have the ability to critically appraise the information presented in an application and do not just accept it as presented. This skill is be developed and strengthened during the training process or routine quality assurance.

Discussion among assessors on application-specific issues is done regularly to ensure critical regulatory thinking and problem-solving.

Assessors focus on the important issues in the application, rather than on data that provide more information, but will not ultimately affect the outcome of an application i.e. need to know information versus good to know information. Nevertheless, good judgment is required to come to ensure a balanced decision. This includes, where applicable, using international harmonized regulatory requirements and adopting regulatory approaches that show flexibility to maximize public health benefits while minimizing adverse, unintended consequences.

Regulatory decision-making and recommendations from assessors are influenced by the following factors: -

a) The current science and state of knowledge;
b) The public health needs of the country; and
c) The health-care system.

Consideration of our health-care delivery system may necessitate changes in scheduling of a particular medicine or refusal of registration of a medicine that is known to meet quality, safety and efficacy standards because of the potential of misuse or abuse.

In decisions to grant marketing authorization the benefits must, on balance, outweigh the risks, based on sound scientific evidence. Within the assessment report, assessor provide the scientific rationale for decision making while taking into account the regulatory requirements. This provides a record to ensure integrity of the evaluation processes. The assessment report is the decision-to ensure integrity of the evaluation processes. The assessment report is the decision-making document used by the Authority to make a final recommendation. Therefore, it addresses dissenting, evidence-based views and clearly identifies the information that was considered.

6. COMMUNICATIONS

Good communication is critical and has many advantages for the Authority, applicants and the public. Clear and timely communication improves the efficiency of the marketing authorization process, allowing patients faster access to important medical products. It also contributes to

improvement in the quality of the evaluation and registration process by providing access to additional expertise.

The Authority actively communicates with its stakeholders through the official TMDA website. Specifically, any changes made or new requirements introduced are articulated to applicants via public announcements, updating on website or through emails. The aim of this communication is to provide insight into the Authority's current thinking and expectations hence, allowing applicants to provide better quality applications.

Moreover, new guidelines, regulations and regulatory requirements are shared with stakeholders for comments prior to implementation. This ensures that the requirements are mutually agreed upon and understood; thus, improving compliance. Open communication ultimately improves the efficacy of evaluation process allowing patients faster access to medicines.

6.1 Intra-agency

Evaluation is conducted in a collaborative environment requiring expertise from different Sections within the TMDA. This collaboration is fostered throughout the medicine's life-cycle. Pre-registration, during evaluation MRE communicates with the laboratory for sample analysis and the inspectorate for the GMP status of the manufacturing facilities. Post-registration, as the product enters the Tanzanian market, MRE interacts with Clinical Trial and Pharmacovigilance Section with regard to post marketing scientific disciplines and pharmacovigilance. Additionally, two-waycommunication with the Inspectorate and Zone Offices regarding the results of inspection or requeststo withdraw products from the market is done.

6.2 Inter-agency

Section 5 of the Act provides the main function upon which the Authority should execute. Among the functions is to collaborate and cooperate with other national and international organizations. That being the case, the Authority engages with other NMRAs on various regulatory-related issues to facilitate greater regulatory convergence. During the evaluation process, the Authority may access information from other NMRAs' public websites, such as guidelines, application decisions and product recalls. However, the decision to adopt and implement the information depends on the overall impact to the Tanzanian general public health. The Authority also engages in joint assessment procedures through the EAC-MRH Programme and the SADC-MRH Programme. These Regional Economic Communities driven initiatives are governed by information-sharing arrangements and procedures. Participation in EAC-MRHProgramme is mandated by the EAC treaty and Cooperation framework agreement of EAC partner states NMRAs while participation in SADC-MRH Programme activities is governed by a Memorandum of Understanding. Regardless of these arrangements, protection of confidentialityof commercial data, trade secrets and personal information is always considered. Therefore, priorconsent from applicants is always sought before divulging any confidential/proprietary information.

6.3 With applicants

Communication with individual applicant on specific applications throughout the assessment process can be done through official letters, online application portal notifications, telephones and electronic mails. The latter being used for minor clarifications and requests. These communications aim at: -

a) Fostering efficient medicinal product development through the provision of scientific advice;
b) Increasing applicants' understanding of evolving regulatory expectations in a changing medical and scientific environment;
c) Increasing the Authority's understanding of challenges and trade-offs with various requirements;
d) Fostering applicants' compliance with requirements; and
e) Informing applicants about the progress and status of the review of their applications.

The Authority strongly encourages input from applicants, particularly feedback on guidelines development and implementation as it creates dialogue regarding regulatory practices. The feedback enables the Authority to address any procedural or technical shortcoming and to improve services.

6.4 With external assessors

The Authority engages external assessors and technical committee members through telephone, electronic mail and official letters.

Expertise in the scientific assessment of the quality safety and efficacy of medicinal products is not limited to applicants and NMRAs. When needed, the Authority may identify and outsource experts from different institutions inter alia Academia consulting companies, health institutions, health programmes and, departments, pharmaceuticals, medical associations and individual experts.

6.5 With the general public

The Authority communicates with the general public about its mission and accomplishments in order to foster greater public awareness, understanding and confidence in the Authority. For the TMDA, transparency initiatives usually involve web-based information about how it is organized and operates, its decision-making processes and criteria, and its actions, such as application approvals and product recalls. Additionally, there are mechanisms in place whereby the public can provide input on medical needs, efficacy expectations and risk tolerances, such as through public meetings and advisory committee. Providing the public with the opportunity to comment will permit enhanced content and feasibility of proposed guidelines and regulations.

The general public may also be consulted on specific applications under evaluation by the Authority where public opinion is considered to be required. There are various mechanisms, by

which this can be achieved, such as surveys, focus groups, public meetings, workshops and appointments to advisory boards.

7. DOMESTICALLY MANUFACTURED PRODUCTS

Effective interaction between TMDA and applicants of domestically manufactured products during product development is critical to maximizing first-cycle marketing application review efficiency. Execution of a high-quality development program is the applicant's responsibility. However, there are important reasons for applicants to discuss development plans with TMDA and consider the review team's feedback. Assessors can provide valuable scientific and regulatory advice to the applicant, including technical assistance in complying with regulatory requirements in the form of pre-submission meetings and consultations before and during the assessment process.

8. LIST OF DOCUMENTS GOVERNING THE MEDICINES REVIEW PROCESS

A list of documents governing the medicines review process is provided in form number TMDA/DMC/MRE/F/036 which is available at www.tmda.go.tz

9. DOCUMENT REVISION HISTORY

Revision Number	Date	Author	Description of change	Section(s) Modified	Approvals
00	September, 2022	MMRE	First revision	N/A	DMC
01	April, 2023	MMRE	TMDA Head Office address from Dar es Salaam to Dodoma	Cover page	DMC
			Inclusion of requirement of GMP compliance of the facility for the products tabled for technical committee meeting	Section 4.3.3	DMC
			Replace table of documents governing medicines review process with a statement indicating the location of the respective documents in the TMDA website	Section 8	DMC
			Inclusion of table for document revision history	Section 9	DMC

10. BIBLIOGRAPHY

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