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MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

GOOD REGULATORY PRACTICES FOR MEDICAL PRODUCTS

A Guide for TMDA staff and stakeholders in maintaining a stable and well-functioning WHO maturity level (ML3) and in strengthening medical products Regulatory Systems

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ABBREVIATIONS AND ACRONYMS

CSC	-	Client Service Charter
GBT	-	WHO Global Benchmarking Tool
GRevP	-	Good Review Practices
GRP	-	Good Regulatory Practices
ICH	-	International Council for Harmonization
IDPs	-	Institutional Development Plans
MoH	-	Ministry of Health
NMRAs	-	National Medicines Regulatory Authorities
QMS	-	Quality Management System
RIMS	-	Regulatory Information Management System
SP	-	Strategic Plan
SOP	-	Standard Operating Procedure
TMDA	-	Tanzania Medicines and Medical Devices Authority
WHO	-	World Health Organization

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I am delighted to present the First edition of the Guidelines on Good Regulatory Practices, developed by TMDA in 2023. My appreciation goes out to the various stakeholders who provided valuable feedback and insights, which significantly shaped the final version of the guidance. Without their collaboration and input, this document would not have been possible. I extend special thanks to the following team of TMDA experts who prepared the guidance, whose dedication and hard work have contributed significantly to its quality and relevance:

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- Mr. Salum Mkata

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Director of Human and Veterinary Medicines

FOREWORD

This is the first edition of the guidance on implementing good regulatory practices published by TMDA. This guidance aims to guide TMDA staff and stakeholders in implementing recognized good regulatory practices to maintain a stable and well-functioning NRA, strengthen medical product regulatory systems, and overcome challenges such as globalization of markets, complex supply chains, and limited global resources. Additionally, the document guides prioritizing TMDA's regulatory activities based on available resources, national goals, public health policy, and medical product policy.

The regulation of medical products has become increasingly complex with the globalization of product development, production and supply and the rapid pace of technological and social change in the context of limited financial and human resources. The importance of robust regulatory systems was recognized by the Sixty-Seventh World Health Assembly when it endorsed resolution WHA 67.20,
Regulatory system strengthening for medical products. The resolution noted that "effective regulatory systems are an essential component of health system strengthening and contribute to better public health outcomes", that "regulators are an essential part of the health workforce" and that "inefficient regulatory systems themselves can be a barrier to access to safe, effective and quality medical products".

A sound system of oversight requires that regulatory authorities be supported by an effective framework of laws, regulations and guidelines and that they have the competence, capacity, resources and scientific knowledge to deliver their mandate efficiently and transparently. The extent to which a regulatory framework fulfils its policy objectives depends on the quality of its development and implementation. Thus, Good Regulatory Practices (GRP) are critical to the efficient performance of the TMDA regulatory system and, consequently, to the public's confidence in the system, while also setting clear requirements for regulated entities.

The implementation of GRP is essential for all key players, including those within and outside TMDA, to ensure appropriate requirements and decisions that are clear, transparent, consistent, impartial, proportionate, timely, and based on sound science. The guidance emphasizes the importance of regulated parties and other stakeholders in creating an efficient regulatory environment to ensure the availability of quality-assured medical products for patients. I expect that TMDA staff and stakeholders will find this guidance useful in maintaining a stable and well-functioning TMDA.

Adam M. Fimbo
DIRECTOR GENERAL

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;

“Global Benchmarking Tool (GBT)” means a globally standardized assessment tool developed by the WHO to serve as the primary means of objectively evaluating regulatory systems, as per provisions of the World Health Assembly Resolution 67.20 on Regulatory System Strengthening for medical products;

“Good Regulatory Practices (GRP)” means a set of principles and practices applied to the development, implementation and review of regulatory instruments – laws, regulations and guidelines – to achieve public health policy objectives most efficiently;

“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;

“Medical products” means medicines and vaccines;

Quality management (QM)” means the coordinated activities that direct and control an organization about quality;

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

“Stakeholders” means an individual, group or organization that has an interest in the organization and delivery of health care;

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

1. INTRODUCTION

The Tanzania Medicines and Medical Devices Authority (TMDA) is an Executive Agency under the Ministry of Health (MoH) that is tasked with regulating the quality, safety, and effectiveness of medicines, medical devices, and diagnostics. The authority's functions are outlined under section 5 of the Tanzania Medicines and Medical Devices Act, Cap. 219.

In November 2018, TMDA achieved WHO maturity level three (ML-3), becoming the first NRA in Africa to receive such recognition. This achievement was made possible by implementing Institutional Development Plans (IDPs) recommended by the WHO benchmarking team in May 2018. The maturity level applies to all regulatory functions related to medicines and vaccines, except for lot release as Tanzania is not a human vaccines producing country to date These regulatory functions include regulatory system strengthening, marketing authorization, licensing establishment, regulatory inspections, vigilance, clinical trial oversight, marketing control and surveillance and laboratory testing.

TMDA has a strong legal framework that is constantly updated to align with TMDA's good regulatory practices and those of other reputable organizations, such as the International Council on Harmonization (ICH), WHO, and other relied regulatory authorities. This has allowed TMDA to effectively regulate medical products while maintaining the quality, safety, and effectiveness of the products.

To maintain a stable and well-functioning WHO maturity level 3 (ML3), strengthen medical product regulatory systems, and address challenges such as globalization of markets, complex supply chains, limited global resources, and workload, TMDA has developed and implemented a guide on good regulatory practices (GRPs) for use by TMDA staff, regulated parties, and other stakeholders. All key players within and outside TMDA should be guided by GRPs in setting appropriate requirements and formulating decisions that are clear, transparent, consistent, impartial, proportionate, timely, and based on sound science. Regulated parties and other TMDA stakeholders also play important roles in ensuring a clear, efficient regulatory environment so that quality-assured medical products are accessed and available to the public.

1.1. Objective of the document

The objective of this document is to present high-level principles of GRP as a benchmark to guide TMDA staff and other stakeholders in the regulation of medical products. It also aims to help TMDA staff prioritize regulatory functions based on available resources, national goals, public health policy, and the medical product environment. This document is supplemented by related guidance on TMDA's best regulatory practices, including good reliance practices, good review practices, and quality management systems. Together,

these documents provide comprehensive guidance to help TMDA improve its performance.

1.2. Scope

The document presents principles and considerations for the development and use of regulatory instruments that support TMDA's regulatory systems for medical products. It also outlines broader practices and attributes that define well-performing regulatory systems. The principles and considerations presented in this document apply to all TMDA regulatory functions, regardless of available resources or geographical location. These high-level principles are equally relevant to regulatory systems and functions implemented in TMDA's head office and zone offices. The document is also intended to promote cooperation with other parties such as the Pharmacy Council of Tanzania, the National Institute for Medical Researches of Tanzania, and the Medical Stores Department of Tanzania.

2. KEY CONSIDERATIONS

The medical products sector is highly regulated due to the potential impact that its diverse range of products can have on health and society, as well as the difficulty in assessing their quality, efficacy, performance, and safety. Lessons learned from past public health crises have also emphasized the need for effective regulation. Additionally, the development, production, supply, and monitoring of medical products are complex processes that require careful oversight to ensure they consistently perform as intended. As a result, TMDA has developed increasingly sophisticated sets of laws, regulations, and guidelines to control all aspects of the medical product life cycle. TMDA has also adopted modern regulatory models that are responsive to resource constraints while meeting the challenges posed by scientific advancements, globalization, rising public expectations, and public health emergencies.

In fulfilling publicly entrusted mandates, TMDA has a duty to regulate in a manner that achieves public policy objectives. This requires establishing and implementing a coherent regulatory framework that provides the necessary level of oversight and control, while also facilitating innovation and access to safe, effective, and high-quality medical products. To ensure the regulatory framework is flexible and responsive, particularly in managing public health emergencies and addressing new technologies and best practices, TMDA promotes international regulatory cooperation and collaboration.

Consistent application of Good Regulatory Practices (GRP) in all aspects of oversight is essential to provide a foundation for a well-performing and respected regulatory system. GRP are principles and practices applied to the development, implementation, and review of regulatory instruments, such as laws, regulations, and guidelines, to achieve public health policy objectives most efficiently. Therefore, GRP promotes a culture of best

practices within TMDA and parties involved in regulatory oversight under TMDA's supervision to ensure that regulations are applied in a fair, consistent, and effective manner.

3. PRINCIPLES OF GOOD REGULATORY PRACTICES

TMDA has developed and implemented nine (9) principles of good regulatory practices. These principles were developed based on the experience gained during WHO benchmarking in May 2018, the WHO Global Benchmarking Tool (GBT), TMDA's core values (Teamwork, Integrity, Customer Focus, Transparency, Accountability, and Quality), and international best practices, including the published WHO Principles of Good Regulatory Practices (2021).

The nine (9) principles of good regulatory practices that have been developed and implemented by TMDA are summarized in the table below:

Principle	Implementation
Legality	All TMDA regulatory systems/functions and decisions are based on legal provisions provided in the Tanzania Medicines and Medical Devices Act, Cap. 219 and respective regulations.
Consistency	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. Its regulatory oversight of medical products is consistent with existing government policies and legislation. implementation and enforcement are applied consistently and predictably.
Independence	TMDA operates in an independent, authoritative manner and discharges its duties independently from politicians and regulated entities (researchers, manufacturers, distributors and wholesalers, as well as from the procurement system). TMDA raise funds through fees and charges for medical products applications and enforcement activities. TMDA has a well-structured mechanism for managing the funds allocated and/or generated internally and from outside.
Impartiality	All regulated parties are treated equitably, fairly and without bias. Its regulatory decision is always science and evidence-based and the same criteria are applied to all regulated parties regardless of the origin of or destination for the medical products.
Proportionality	Regulation and regulatory decisions are proportional to risk and to the TMDA’s capacity to implement and enforce them.

Flexibility	TMDA is not usually prescriptive but rather flexible in responding to a changing environment and unforeseen circumstances. It has a mechanism for responding timely to a specific need and in particular to public health emergencies. TMDA has non-routing procedures in implementing its function including during public health emergencies.
Clarity	TMDA regulatory requirements are accessible to the users. The documents developed provide clear and proper interpretations to the users. The language used as well as terminologies are consistent with international norms.
Efficiency	TMDA has developed CSC and SP to efficiently achieve its goals. Different mechanisms have been developed for the efficient use of available limited resources including the application of good reliance practices.
Transparency	TMDA operates transparently. Regulatory requirements and decisions are publicly accessible.

3.1 Legality

"Regulatory systems and the decisions that flow from them must have a sound legal basis".

TMDA is an Executive Agency under the Ministry of Health (MoH) that is responsible for regulating the quality, safety, and effectiveness of medicines, medical devices, diagnostics, biocides, and tobacco products. All of TMDA's regulatory systems, functions, and decisions are based on legal provisions provided in the Tanzania Medicines and Medical Devices Act, Cap. 219, and respective regulations. The Act clearly outlines TMDA's power in regulating medical products, as well as its functions and responsibilities.

As cross-jurisdictional issues become more complex, regulatory authorities must cooperate. Therefore, a modern legal framework for medical products should promote various forms of cooperation, such as convergence, harmonization, information sharing, work-sharing, reliance, and recognition. The Tanzania Medicines and Medical Devices Act includes legal provisions that support and encourage these forms of cooperation, particularly work-sharing, reliance, and recognition, for effective and efficient regulation.

TMDA is legally accountable to the public, regulated bodies, and the government for its actions and decisions, as part of good governance and accountability. Legal provisions exist to allow for the review of regulatory decisions, including internal and judicial appeals based on procedural fairness, due process, scientific, and administrative grounds. These provisions ensure that TMDA's decisions are transparent, consistent, and based on the

applicable laws and regulations and that any affected party has the right to seek redress through the established legal channels.

3.2. Consistency

"Regulation of medical products should be consistent with government policies and legislation and be applied consistently and predictably".

TMDA's regulation of medical products is aligned with the national legal framework, government policies, public health objectives, Regional Economic Communities (such as East Africa and Southern Africa Member States), and international agreements, including WHO Collaborative procedures.

Effective consultation, cooperation, and coordination systems among different levels of government are essential for promoting national uniformity of regulatory requirements while respecting local responsibilities.

All TMDA regulatory functions and activities are efficiently integrated to ensure the uniformity of the regulatory system. Similar considerations apply when more than one institution or department at the same level of government is responsible for different, or the same, regulatory functions and products – a situation that is not uncommon. Formal mechanisms for proper coordination have been established during the execution of regulatory instruments and the operations of bodies charged with the regulation of medical products.

TMDA strives for consistency in all regulatory actions and decisions to ensure similar outcomes. This is achieved by applying similar criteria in providing regulatory decisions and maintaining the Regulatory Information Management System (RIMS), which serves as an institutional database for recording all regulatory activities and decisions. Through RIMS, TMDA ensures that all parties receive fair and equal treatment in future situations. Moreover, TMDA provides clear regulatory guidance based on international guidelines whenever possible and conducts orientation and training programs for staff to ensure they have a solid understanding of regulatory practices. Lastly, TMDA fosters regular, transparent interactions with regulated parties and other stakeholders such as industry associations, patients, healthcare professional associations, and relevant government institutions to maintain consistency and promote collaboration.

The application of a well-functioning quality management system that covers all regulatory activities is critical for regulatory consistency. TMDA has a stable and well-functioning Quality Management System (QMS) that has been in place since 2008. This enables the

Authority to continually audit itself against evolving requirements of the ISO 9001 standard and statutory requirements, including TMDA's legal mandate, its regulations, and other relevant laws. Through the QMS, the Authority continually improves regulatory services and addresses customers' needs and expectations without compromising the quality, safety, and effectiveness of medical products. TMDA also uses performance-based indicators, internal reviews, and external audits to ensure consistency in the application of regulations and regulatory operations.

3.3. Independence

"Institutions responsible for the regulation of medical products should be independent".

To ensure that TMDA conducts its activities correctly and achieves the right policy outcomes, procedures and policies have been developed to protect regulatory decisions and activities from inappropriate or undue influence. Good governance and anti-corruption measures have been documented in TMDA's formal documents to prevent actual or perceived conflicts of interest, unfounded bias, or improper influence by stakeholders. To maintain public confidence, the Authority operates, and is seen to operate, independently, authoritatively, and impartially and discharges its duties independently of the regulated entities, such as researchers and industries.

TMDA has a legal mandate to collect and use the funds generated internally under the Fees and Charges Regulations (80% collections), government subvention (10%), and donor support (10%)}. Strong financial accountability measures are in place. The financial reports are audited by the Controller and Auditor General (CAG) annually. TMDA has been receiving clean audits from different auditors. In addition, the nomination and appointment of the regulator's leadership are based on transparent and accountable processes. Clear rules to avoid conflicts of interest are in place to ensure independent behavior during and after employment.

3.4. Impartiality

"All regulated parties should be treated equitably, fairly and without bias".

TMDA ensures competitive neutrality by treating all regulated parties equitably, fairly, and without bias. Regulatory decisions are always science- and evidence-based and aligned with regulatory requirements. The same criteria are applied to all regulated parties, regardless of the origin or destination of the medical products. The Authority operates impartially and discharges its duties independently of the regulated entities.

To ensure the impartiality and integrity of regulatory decision-making, TMDA applies this principle to researchers and other experts who sit on scientific and medical product registration technical committees. Declarations of interest and confidentiality forms are required to be filled and reviewed before any discussions to maintain the committee's

impartiality and integrity in making recommendations to the regulatory authority on regulatory policies or the authorization of medical products. The Authority also does not engage in the activities it regulates, nor is it hierarchically subordinate to institutions that perform regulated activities, such as the procurement of medical products by a ministry of health or other government institution.

3.5. Proportionality

"Regulatory oversight and regulatory decisions should be proportional to the risk and to the regulator's capacity to implement and enforce the decisions".

The principle of proportionality demands that any action taken should not exceed what is necessary to achieve the intended objective. TMDA applies this principle in all aspects of its regulatory system. Regulations, guidelines, and guidance are developed only when necessary and appropriate for the aim, and not excessive. Regulatory requirements are developed based on both the issue being addressed and the risk it poses. The enforcement and inspection regimes conducted by TMDA are also proportionate to the risk and severity of an infraction to mitigate health risks. A proportionate, risk-based approach allows TMDA to allocate resources where the need is greatest, while also ensuring that the cost of complying with regulations is proportional to the risk involved.

The assessment of medical products by TMDA is based on a thorough benefit-risk evaluation, which considers the evidence presented on the quality, safety, efficacy, or performance of the product. This evaluation weighs all demonstrated benefits against identified risks. TMDA has developed various procedures and guidance based on international best practices to guide assessors of medical products in applying the benefit-risk evaluation. To ensure that the authorized medical product continues to comply with established standards, appropriate surveillance and vigilance are implemented to continuously monitor the benefit-risk profile and take any necessary actions.

3.6. Flexibility

"Regulatory oversight should be flexible to respond to a changing environment and unforeseen circumstances".

Flexibility is essential to ensure that regulatory frameworks and regulatory systems remain "fit for purpose". The design and use of regulatory instruments must therefore be appropriate. A meaningful, understandable, enforceable regulatory framework should contain sufficient detail to ensure clarity. It should also allow flexibility to respond to new technologies and innovations and changes in the regulated environment and to ensure a timely response to unforeseen public health threats.

TMDA is not usually prescriptive but rather flexible in responding to a changing environment and unforeseen circumstances. It has a mechanism for responding timely to a specific need and in particular to public health emergencies. TMDA has non-routing procedures in implementing its function including during public health emergencies. There are legal provisions that allow TMDA to make decisions based on the best available science and benefit–risk considerations. There are also provisions relating to the reduction or exemption of dues, taxes, tariffs or fees in defined situations for public health interest.

3.7. Clarity

"*Regulatory requirements should be accessible to and understood by users".*

Compliance with and consistent application of regulatory requirements and processes require a clear understanding of what is expected. Both the regulator and the regulated party should understand the conduct that is expected and the consequences of non-compliance.

TMDA regulatory requirements are understandable and accessible to the users. The documents developed provide clear and proper interpretations to the users. The language used as well as terminologies are consistent with international norms. Development of TMDA regulatory requirements (Regulation, guidelines, procedures or guidance) is usually done in collaboration with legal personnel in considering the objectives of the legal instrument, the intended audience, other stakeholders who may be impacted and internal and external subject matter experts. Meetings between TMDA and regulated entities in clarifying the application of regulatory requirement(s) are usually conducted before approval and implementation of the new regulatory requirement(s).

Furthermore, Regulations and supporting guidelines are reviewed periodically and/or when the need arises to ensure that they reflect the authority's current practices and expectations, are adapted to scientific and technological developments as well as align with current international standards and guidelines, when applicable.

3.8. Efficiency

"Regulatory systems should achieve the intended results within the required time and at reasonable effort and cost".

An efficient regulatory system must be based on science and evidence and the principles of risk assessment and management and embed a strategy of international regulatory cooperation into daily business. A regulatory system in which sound decisions cannot be made in a timely, consistent fashion is not effective. Its efficiency depends not only on sufficient resources but also on the type of resources and their effective use, irrespective

of size. In this context, a lack of integrity in the overall regulatory system is a barrier to regulatory efficiency.

TMDA has developed Client's Service Charter and Strategic Plan (reviewed every 5 years) to efficiently achieve its goals. This strategic plan has clear strategic objectives, key performance indicators and targets. Periodic performance assessments are conducted to evaluate the actual efficiency of regulatory instruments to ensure that the foreseen benefits are realized and, if so, the direct and indirect costs.

Different mechanisms have been developed for the efficient use of available limited resources including the application of good review practices, good reliance practices and quality management systems.

3.9. Transparency

"*Transparency is the hallmark of a well-functioning regulatory system and is essential for building public trust and enabling international cooperation".*

Transparency is in the interests of patients, consumers, governments, healthcare workers and manufacturers, as it increases public trust and confidence in the regulation of medical products. Transparency in regulatory requirements and actions results in better-informed decisions about investment in the public and private sectors and discourages discriminatory, corrupt or abusive practices.

With transparency, all affected and potentially interested parties – domestic, foreign, public and private – have a meaningful opportunity to be informed of new or amended regulations and guidelines and to make their views known before they are enacted. With transparency, once medical product regulations and guidelines are adopted, they are readily available and accessible to stakeholders and the general public.

TMDA operates transparently. Regulatory requirements and decisions are publicly accessible. Relevant laws, regulations, guideline documents, public assessment reports, inspection reports, product information for health care professionals, performance targets & results, annual reports, substandard or falsified medical products, advisory notices, recalls and other time-sensitive information of public health interest. a searchable registry of approved, suspended and withdrawn products and licensing status of premises are posted on the authority's website (www.tmda.go.tz).

4. ENABLERS OF IMPLEMENTATION OF GOOD REGULATORY PRACTICES

An enabling environment facilitates the successful implementation of GRP. Below are some of the elements that enable TMDA to effectively implement principles of good regulatory practices: -

a) Political and government-wide support;
b) Effective organization and good governance supported by leadership;
c) Inter- and intra-organizational communication, collaboration and coordination;
d) A robust, well-functioning quality management system;
e) Sustainable financial resources;
f) Competent human resources;
g) Organizational ethics and values; and
h) Science- and data-driven decision-making process.

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