RWANDA FDA
Rwanda Food and Drugs Authority

GUIDELINES ON RELIANCE FOR REGULATORY DECISION-MAKING

FEBRUARY, 2024

FOREWORD

Rwanda Food and Drugs Authority (Rwanda FDA) is a regulatory body established by the Law N° 003/2018 of 09/02/2018. One of the missions of the Authority is to build cooperation and partnership for harmonization of practices with regional and international bodies with similar missions as stipulated in article 8, paragraph 15 of the above stated law.

Considering the provisions of the technical regulations N° DFAR/HMDAR/TRG/001 governing the registration of medicinal products, regulations N° CBD/TRG/011 governing control of medicated cosmetics; Regulations N° DFAR/HMDAR/TRG/002, governing Registration of Medical Devices including In Vitro Diagnostics, Regulations N° CBD/TRG/013, governing the registration of pesticides, laboratory and cleaning chemicals; regulations N° FDISM/PVSM/TRG/001 governing the conduct and Inspection of Clinical Trials in Rwanda, regulations N° CBD/TRG/016, governing pharmacovigilance of pharmaceutical products and medical devices, and other relevant regulations, the Authority may rely on regulatory decisions from other regional and international regulatory authorities when deemed necessary.

The Authority has developed guidelines N° ODG/RAHC/GDL/001 on reliance for regulatory decision-making to promote a more efficient approach for regulatory oversight, access to quality-assured, effective and safe medical products. The reliance is an alternative /non-routine authorization pathway to the standard approval pathways - especially for applications where the safety and efficacy of the product have already been confirmed or when the Clinical Trial has been approved and/or initiated in a well–resourced regulatory authority (ies).

The reliance implies that the work done through Clinical Trial Assessment reports, Marketing Authorization (MA) assessment reports, GMP inspection reports, and Quality Control (QC) related decisions is shared by the regulatory authority while the Authority uses this work according to its own scientific knowledge and regulatory procedures and retains its own regulatory responsibilities.

The reliance can be unilateral, bilateral (mutual) or multilateral for the regulatory decision but the authority maintains its own regulatory responsibilities for decision-making

The Authority acknowledges all the efforts of key stakeholders who participated in the development and validation of these guidelines.

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DOCUMENT DEVELOPMENT HISTORY

First issue date	14/06/2021
Effective date of this revision	23/02/2024

DOCUMENT REVISION HISTORY

Revision number	Changes made and/or reasons for revision
Rev_0	First issued
Rev_1	Revision of section 6.1. Marketing Authorization of medical products by including a statement that capture all ICH members
Rev_2	1. ICH founding regulatory member state or region such as European Commission (EMA), United States (United States Food and Drugs Administration), Japan (MHLW/PMDA) or an ICH standing regulatory member state or region such as Canada (Health Canada), Switzerland (Swissmedic) countries were replaced by **WHO Transitional listed authorities** which includes also all countries which have attained ML3 or 4. 2. New Reference number assigned according to the new requirements of Document Control Revision 3. General rewarding of the whole document was effected
Rev_3	Revision of section 5.1 and 5.2, Marketing Authorization of medical products and GMP inspection respectively, by including the list of agencies recognized by the Authority for Reliance

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ACCRONYMS AND ABBREVIATIONS

AVAREF:	African Vaccine Regulatory Forum
CRO:	Contract Research Organizations
EAC:	East African Community
EC:	European Commission
EMA:	European Medicines Authority
EU:	European Union
GMP/GCP:	Good Manufacturing Practices/ Good Clinical Practices
ICH:	International Council on Harmonization of Technical Requirements for
ILAC:	International Laboratory Accreditation Cooperation.
ISO/IEC:	International Organization for Standardization and the International Electrotechnical Commission
MA:	Marketing Authorization**,**
MAGHP:	Marketing Authorization for Global Health Products Medical Devices Agency of Japan
MHLW/PMDA:	Ministry of Health, Labour and Welfare/ Pharmaceuticals and Medical Devices Agency.
QC:	Quality Control
USFDA:	United States Food and Drug Administration
WHO PQ:	World Health Organization Prequalification

GLOSSARY

In these guidelines, unless the context states otherwise:

Abridged regulatory pathways:
Abridged regulatory pathways are regulatory procedures facilitated by the use of reliance, whereby the regulatory decision is solely or partially based on the application of reliance. The expectation is that the use of reliance would save resources and shorten the timelines compared to the standard pathways while ensuring that the standards for regulatory oversight are maintained.

Authority refers to Rwanda Food and Drugs Authority or Rwanda FDA

Competency:
Reliance requires that national authorities build the necessary competencies for critical decision making for proper implementation. In most cases, they need to have a number of critical tools for implementation, whether information sharing arrangements or information platforms among others. Conversely, authorities being relied on should have and maintain competencies and performance in the given area and prove the use of internationally accepted standards. The competencies should be bench-marked by transparent processes that develop trust in the capacities of these reference authorities.

Consistency:
Reliance on a specific process/evaluation/ decision should be established for the specific and well-defined category of products/ practices and should as well be predictable. Thus, it is expected that reliance shall be applied consistently for all products/practices in the same predetermined category.

Joint activity is a form of work-sharing whereby a regulatory task is conducted by two or more regulatory Authorities in collaboration in order to share their assessments, benefit from each other's expertise and discuss any shortcomings of the data being evaluated. For example, a joint assessment is a procedure in which the same application is simultaneously submitted to two or more regulatory Authorities for the (assigned) regulatory Authority is to conduct their evaluations in parallel and share their respective scientific assessments with each other (e.g., the different modules for quality, nonclinical and clinical data can be assigned to different regulatory Authorities for review). The regulatory Authorities participating in the joint assessment can combine their list of questions or deficiencies to send to the manufacturer and base their respective independent regulatory decision on the outcome of these assessments. Similarly, a joint inspection is an inspection involving two or more regulatory Authorities sharing the activities and assessment performed during an inspection.

Legal basis:
Reliance should be coherent with national legal frameworks and supported by clear mandates/regulations that aim at efficient implementation.

Regulatory reliance:
Regulatory reliance is the act whereby the regulatory Authority in one jurisdiction may take into account and give significant weight to regulatory work performed by another regulatory or trusted institution for purposes of reaching its own regulatory decisions.

Recognition:
The recognition is a routine acceptance of the regulatory decision of another regulator or other trusted institution. Recognition indicates that evidence of conformity with the regulatory requirements of a recognized Authority is sufficient to meet the regulatory requirements of Rwanda FDA.
Recognition may be unilateral or mutual and may, in the latter case, be the subject of a mutual recognition agreement.

Sameness of product:
For the purpose of this document, the sameness of product means that two products have identical essential characteristics (i.e., the product being submitted to the relying authority and the product approved by the reference regulatory authority). All relevant aspects applicable to medicinal products, medical devices and in vitro diagnostics have to be considered in order to confirm that the product is the same or sufficiently similar (e.g., same qualitative and quantitative composition, same strength, same pharmaceutical form, same intended use, same manufacturing process, same active pharmaceutical ingredient suppliers, etc.). Additionally, the results of supporting studies of safety, efficacy and quality, indications and conditions of use should be the same.

Sovereignty:
Reliance should be a sovereign decision. National authorities should decide if they want to use reliance, on which they are going to rely and how.

Transparency:
Reliance processes should be transparent regarding standards and processes. In addition, the basis/rationale for relying on a specific entity should be disclosed and understood by all parties.

Reference Regulatory Authority:
In these guidelines, a Reference Regulatory Authority refers to a national, regional or international authority or a trusted institution such as WHO prequalification (WHO
PQ) and WHO transitional Listed Authorities (WLA) whose regulatory decisions and/or regulatory work products are relied upon by another regulatory authority to inform its own regulatory decisions.

Work-sharing:

Work sharing is a process by which the regulatory Authority of two or more jurisdictions shares activities to accomplish a specific regulatory task. The opportunities for work-sharing include, but are not limited to, jointly assessing applications for authorization of clinical trials, marketing authorizations or good practices in inspections, joint work in the post-marketing surveillance of medical product quality and safety, joint development of technical guidelines or regulatory standards, and collaboration on information platforms and technology.

1. INTRODUCTION

Reliance is seen by a growing number of regulatory authorities as an important means of improving the efficiency of regulatory operations in the oversight of medical products. It allows the Authority to make the best use of resources, build expertise and capacity, increase the quality of regulatory decisions, reduce duplication of effort and, ultimately, promote timely access to safe, efficacious and quality-assured medical products. By adopting reliance measures whenever possible within a well-structured framework, underpinned by national or regional policies and strategies, regulators may focus their resources on key activities that cannot be undertaken by others and that contribute to public health.

The principles and considerations presented in these guidelines should be taken into account when implementing regulatory reliance frameworks or strategies. Effective implementation of reliance will benefit not only the Authority but also patients/clients, healthcare providers, Marketing Authorization holders and Contract Research Organizations (CROs).

The Authority accepts that reliance can be unilateral, bilateral (mutual) or multilateral, and it will leverage the information in the shared reports and/or decisions to arrive at a regulatory decision but will maintain its own regulatory responsibilities for decision-making. These guidelines aim to speed up the submission and/or evaluation of authorization applications towards the timely approval of the application. Further, it focuses on risk-based evaluations, concentrating on what is locally critical (i.e., value-added in terms of resource/time investment) versus what can be leveraged/relied upon from decisions made by WHO transitional listed authorities.

The reliance is achieved in a variety of ways, including information and reports or work-sharing in Clinical Trial Assessment, dossier assessment, GMP/GCP inspection, Vigilance related decisions and QC Testing related decisions

2. SCOPE

These Guidelines cover reliance activities regarding all types of medical products and regulatory activities using reliance approaches. The reliance procedures shall apply to the registration and marketing authorization, GMP/GCP Inspections, Clinical Trial, Vigilance and Post Marketing Surveillance activities and laboratory testing (QC).

3. PRINCIPLES OF RELIANCE

The adopted principles of the Reliance are in line with the WHO recommendations to optimize innovative and more effective forms of collaboration in order to make the best use of available resources and expertise, avoid duplication in order to ensure the safety, quality and efficacy of locally used products.

Sovereignty:
Reliance is a sovereign decision. The Authority decides when and how to use reliance and in which circumstances.

Legal basis:
Reliance procedures are coherent with the Authority's legal frameworks and supported by clear mandates/regulations that aim at efficient implementation.

Transparency:
The reliance approach remains transparent regarding standards and processes. In addition, the rationale for relying on a specific entity should be disclosed and understood by all parties.

Competency:
The authority has the necessary competencies for critical decision making for proper implementation of the reliance guidelines. The competencies are bench-marked by transparent processes that develop trust in the capacities of reference regulatory authorities.

Consistency:
The Authority reliance decision shall be established for the specific and well-defined category of products and practices.

4. RELIANCE PATHWAYS TO FACILITATE REGULATORY DECISIONS

Reliance pathways are alternative /non-routine application approval pathways used by the authority in its regulatory decisions. The approval of any type of clinical trial, GMP/GCP compliance, quality control procedures, medical product marketing authorization, and vigilance decision, can be accelerated by reliance on prior regulatory decisions from a reference regulatory authority(ies). The reliance aims at reducing timelines compared to standard timelines applied when using normal regulatory practices. However, the authority shall remain responsible and accountable for decisions taken.

This is a risk-based approach and its implementation procedures shall consider factors, such as the type and source of products assessed, public health needs and priorities, level of resources and expertise available in the authority, and opportunities for reliance.

Reliance may take many forms and be applied to varying degrees in recognizing or taking account of the assessments, decisions or other authoritative information of other authorities and institutions. Recognition may be seen as a special and more formalized approach to reliance, whereby one regulatory authority recognizes the decisions of another regulatory authority, system or institution, obviating additional regulatory assessment to reach its own decision. Recognition usually requires formal and binding legal provisions.

Considering marketing authorization as an example, the following **four (4) reliance pathways** may involve additional tasks in the assessment process:

a) **Verification of sameness** of the product to ensure that the medical product is the same as the one that has been assessed by the reference regulatory authority. A critical aspect of the application of reliance is verification of the "sameness" of a medical product. Reliance can be practised only if the Authority has the assurance that the medical product being assessed is essentially the same as the one submitted to the reference regulatory Authority. The role of the manufacturer is essential to confirm the sameness of a product and to provide the same

documentation as submitted to the reference regulatory Authority, except for additional country-specific information submitted for review, such as product stability data according to the stability zone and the local product label. The manufacturer should confirm in the application that the product is the same and that the application contains essentially the same information, taking into consideration any potential national requirements. If the application is not submitted simultaneously to the agencies, the manufacturer should highlight any new information about the product acquired since the application was submitted to the reference regulatory Authority, with the corresponding assessment.

b) **Confirmation of applicability of the assessment outcomes** of another authority for regulatory decision-making in the national context, for example, in terms of legal and regulatory settings, benefit-risk assessment, co-morbidities, unmet medical needs, risk management plans and any quality-related specificities such as climatic zones for product stability. In case of differences, such as in target population, epidemiology and other features of the disease, concomitantly used medicines and other factors that can substantially affect the benefit-risk profile of medicine as well as quality parameters, especially in relation to the stability under different climatic conditions, appropriate justification should be provided by the Applicant.

c) **Abridged assessment** of the quality, safety and efficacy/performance data taking into account information in the assessment reports of the reference regulatory authority.

d) **Joint assessment or work-sharing** between two or more regulatory authorities where a primary review by one authority, a second review by another authority followed by a joint assessment session to finalize the assessment report and comments or distribution of the modules (quality, non-clinical and safety or efficacy) between the authorities.

Similar reliance-based regulatory pathways can be used for other regulatory functions, such as inspection, lot release or import testing.

5. AREAS OF RELIANCE FOR REGULATORY DECISION

The areas of reliance include registration and marketing authorization, GMP/GCP Inspections, Clinical Trial, Vigilance and Quality Control (QC) testing related decisions to ensure full implementation and compliance to the reliance route:

5.1. Marketing Authorization of medical products

The Authority may apply reliance procedures for granting Marketing Authorization in the following situations:

a) The product should have been evaluated and listed as a WHO Prequalified Product including the WHO PQ collaborative registration procedure between WHO and the Authority.
b) The product should have been approved by Stringent regulatory authorities.

c) The product should have been registered by a WHO listed Authorities (WLAs) and WHO transitional Listed Authorities (B category).

d) The product should have been recommended by Continental and Regional regulatory harmonization initiatives and networks such as EMA and EAC, through the Joint Dossier Assessments

e) The product should have been registered by ML3 functioning regulatory Authorities having Memorandum of Understanding (MoU) with Rwanda FDA.

5.2. GMP Inspections

The authority may apply reliance for GMP Inspections in the following situations:

a) Facilities located in countries and hold a valid GMP certificate from WHO listed Authorities (WLAs) and WHO transitional listed authorities (category B);

b) Facilities located in countries which are standing PIC/s members and hold a valid GMP certificate from relevant Authority;

c) Facilities inspected and approved under the framework of World Health Organization (WHO) prequalification program;

d) Facilities inspected and approved through EAC joint GMP Procedures.

e) Facilities that hold a valid GMP certificate issued by ML3 functioning regulatory Authorities having Memorandum of Understanding (MoU) with Rwanda FDA.

5.3. Vigilance

The Authority may recognize and/or rely on vigilance-related decisions, reports or information from other countries or regional or international organization and harmonization initiative when making national vigilance decisions.

The Authority shall continue to ensure the safety of marketed products through its established vigilance system. In order to ensure that safety issues are promptly identified and the necessary interventions implemented, the Authority considers decisions from WHO transitional listed Authorities on the safety of medical products that impact negatively on the health of patients.

Furthermore, the Authority can rely on Vigilance decisions taken by WHO Uppsala Monitoring Centre (WHO-UMC), joint vigilance decisions in EAC region and this may be considered through the reliance pathways on a case-by-case basis.

The Authority may, upon receiving proof of scientific information related to safety of medical products, recognise and take any corrective action to protect the public from any eminent safety concerns that may likely arise.

5.4. Clinical Trials

The Authority may rely and/or recognize relevant clinical trial decisions, reports and information from transitional WHO listed authorities and/or other regional or international harmonization initiatives such as EMA, AVAREF, African Medicines Agency (AMA), EAC Medicines Regulatory Harmonization (EAC HRH including those have MoUs with Rwanda FDA to take appropriate regulatory decisions in clinical trial oversight for public health protection.

In order to facilitate product development, regulatory decision-making, and access to promising new medical products, the Authority may consider the regulatory decisions taken by other regulatory authorities for the multi-country trials that are being implemented in Rwanda because of post-approval monitoring activities.

In case of emergency, the Authority applies reliance pathways as non-routine procedure for Clinical Trial Authorization.

5.5. Quality Control (QC) Testing

Rwanda FDA may rely on analytical reports/Certificate of analysis from National Regulatory Authority laboratories which are on WHO transitional listed Authorities. Detailed procedure will be developed

During the decision making, Rwanda FDA may rely on analytical reports from NRA laboratories which are WHO Pre-qualified or ISO/IEC 17025:2017 accredited and awarded by an International Laboratory Accreditation Cooperation (ILAC) member on a case-by-case basis.

5.6. Market surveillance and control

The authority may rely on market surveillance and control decisions from WHO transitional listed Authorities.

Furthermore, the Authority can rely on market surveillance and control decisions taken by WHO/Global surveillance and monitoring system (WHO/GSMS).

The Authority may rely on the market surveillance and control decision taken by regulatory authorities in East African Community and regulatory authorities that signed MoU with the Authority

6. RELIANCE PROCEDURES

6.1. Verification of Documentations

The Authority shall ‘verify’ that the product intended to be imported and distributed in Rwanda or the Clinical trial to be conducted in Rwanda has been duly registered or authorized respectively by the reference regulatory authority (ies).

In the case of marketing authorization, the product characteristics (use, dosage, precautions) for local registration should conform to that agreed in the authorization by the reference regulatory authority.

In addition, there should be an assurance that the product is either identical or similar to that approved by the reference regulatory Authority in terms of quality, safety and efficacy.

In case the reliance is for Clinical trial submissions, the application (protocol, Investigational brochure, nonclinical reports, previous study reports and other relevant documents) should be identical to that submitted, evaluated and approved by the reference regulatory authority.

Typically, the reliance pathway in case of marketing authorisation shall take ninety (90) working days (excluding clock stops) and sixty (60) working days in the case of Clinical Trial Authorization.

6.2. Reliance Documentations

In addition to the full assessment report from the reference regulatory authority (where possible), the applicant shall be required to submit the following;

In the case of marketing authorization, a full application for Marketing Authorization should be submitted as required by the Authority's relevant guidelines.

In the case of clinical trial, a full Clinical Trial Application should be submitted as required by the Authority's relevant guidelines.

In the case of GMP inspection, a full application for GMP inspection should be submitted as required by the Authority's relevant guidelines.

6.3. Assessment based on reliance procedures

The assessment or evaluation of the imported assessment report(s) shall be executed in accordance with laid down procedures to ensure appropriateness and completeness of the assessment findings and conclusions.

REFERENCES

FDA. (2019). FDA GHANA RELIANCE POLICY. January, 1–13.
WHO. (2020). Good reliance practices in regulatory decision-making: High-level principles and recommendations. WHO Drug Information, 34(2), 201–230.

ENDORSEMENT OF THE GUIDELINES

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