RWANDA FDA
Rwanda Food and Drugs Authority

GUIDELINES ON RELIANCE FOR REGULATORY DECISION-MAKING

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GUIDELINES DEVELOPMENT HISTORY

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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 Nº CBD/TRG/010 governing the registration of human medicinal products, regulations Nº CBD/TRG/011 governing control of medicated cosmetics; Regulations Nº CBD/TRG/012, governing registration of medical devices, Regulations Nº CBD/TRG/013, governing the registration of pesticides, laboratory and cleaning chemicals; regulations Nº CBD/TRG/015 governing the conduct of Clinical Trial, regulations Nº 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 on reliance for regulatory decision 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 well-resourced 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 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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ACCRONYMES 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 Harmonisation 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

1.0. 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 widely 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 on the capacities of these reference authorities.

Consistency:

Reliance on a specific process/evaluation/ decision should be established for 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 in order 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 the 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 routine acceptance of the regulatory decision of another regulator or other trusted institution. Recognition indicates that evidence of conformity with the regulatory requirements of country A is sufficient to meet the regulatory requirements of country B.
Recognition should be based on evidence of conformity that the regulatory requirements of the reference regulatory authority is sufficient to meet the regulatory requirements of the relying authority. 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 drugs, 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.).

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.

Well-resourced or reference Regulatory Authority

In this guideline a well-resourced or reference regulatory authority refers to:

a) a member of ICH prior to 23 October 2015, namely: the US Food and Drug Administration, the European Commission and the Ministry of Health, Labour and Welfare of Japan also represented by the Pharmaceuticals and Medical Devices Agency of Japan
b) an ICH observer prior to 23 October 2015, namely: the European Free Trade Association, as represented by Swissmedic and Health Canada; or
c) a regulatory authority associated with an ICH member through a legally binding, mutual recognition agreement prior to 23 October 2015

Work-sharing

The work sharing is a process by which the regulatory Authority of two or more jurisdictions share 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 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

2.0. **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. The aim of these guidelines is to speed up the submission and/or evaluation of authorization applications towards the timely approval of 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 well-resourced regulatory authorities that operates within the ICH region and other reference countries (FDA Ghana, 2019).

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

3.0. SCOPE

These Guidelines covers 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 laboratory testing (QC).

4.0. 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.

4.1 Sovereignty:

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

4.2 Legal basis:

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

4.3 Transparency:

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.

4.4 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 on the capacities of well-resourced regulatory authorities

4.5 Consistency:

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

5.0. **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 well-resourced 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 of products, public health needs and priorities, level of resources and expertise available in a well-resourced regulatory authority, and opportunities for reliance in Rwanda (WHO, 2020).

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

1. **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.

2. **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 a medicine as well as quality parameters, especially in relation to the stability under different climatic conditions, appropriate justification should be provided by the Applicant.

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

4. **Joint assessment or work-sharing** between two or more regulatory authorities where a primary review by one authority, second review by another authority followed by a joint assessment session to finalize the assessment report and comments.

6.0. AREAS OF RELIANCE FOR REGULATORY DECESION

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:

6.1 Marketing Authorization of medical products;

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

1) Product should have been evaluated and listed as a WHO Prequalified Product through the WHO PQ collaborative registration procedure between WHO and the Authority.
2) Product should have been evaluated and listed as a product of either the WHO collaborative registration pilot for stringently authorized products, including through the European Union (EU) Article 58 Procedure or the Swissmedic Marketing Authorization for Global Health Products or the International Generic Drug Regulatory Programme (launched July, 2014).
3) The product should have been registered and/or granted marketing authorization in either an ICH founding regulatory member state or region [such as EMA, United States Food and Drug Administration, Japan (MHLW/PMDA) or an ICH standing regulatory member state or region (such as Health Canada, Swissmedic).
4) The product should have been jointly evaluated and listed as an output of the East African Community (EAC).
5) Further, products registered by WHO listed agencies may be considered through the reliance pathways on a case-by-case basis.

6.2 GMP/GCP Inspections

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

1. Product should have been evaluated and listed as a WHO Prequalified Product through the WHO PQ collaborative registration procedure between WHO and the authority and the manufacturing facility should have been inspected by the Regulatory authority (ies) in the country of origin and the WHO pre-qualification team.

2. The product should have been evaluated and listed as a product of either the WHO collaborative registration pilot for stringently authorized products, including through the European Union (EU) Article 58 Procedure or the Swissmedic Marketing Authorization for Global Health products or the International Generic Drug Regulatory Programme (launched July, 2014), and the manufacturing facility should have been inspected by the Regulatory Authority in the country of origin and/or the WHO pre-qualification team.

3. The product should have been registered and/or granted marketing authorization in either an ICH founding regulatory member state or region such as EMA, United States Food and Drug Administration, Japan (MHLW/PMDA) or an ICH standing regulatory member state or region (such as Health Canada, Swissmedic). The manufacturing facility should have been inspected by the Regulatory Authority in the country of origin and/or EMA, United States Food and Drug Administration, Japan (MHLW/PMDA) or an ICH standing regulatory member state or region (such as Health Canada, Swissmedic).
4. The product should have been jointly evaluated and listed as an output of the East African Community (EAC). The manufacturing facility should have been inspected by the Regulatory Authority in the country of origin and/or EAC joint GMP inspection has been conducted.
5. Further, products registered by WHO listed agencies may be considered through the reliance pathways on a case-by-case basis. The manufacturing facilities within which the products are manufactured should have been inspected by the regulatory authority (ies) in the country of origin.

6.3 Reliance in Vigilance related 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 well-resourced regulatory authority (ies) on the safety of medical products that impact negatively on the health of patients.

The regulatory decisions of the Authority leveraging safety decision from well-resourced or reference regulatory authority (ies) are geared towards ensuring appropriate and safe use of registered medical products.

The medical product of concern should have been registered and/or granted marketing authorization in either an ICH founding regulatory member state or region such as European Commission (EMA), United States (United States Food and Drug Administration), Japan (MHLW/PMDA) or an ICH standing regulatory member state or region such as Canada (Health Canada), Switzerland (Swissmedic). Further, Vigilance decisions on products registered by WHO listed agencies may be considered through the reliance pathways on a case-by-case basis.

6.4 Clinical Trials Authorization

The Authority may apply reliance procedures for Clinical Trial Authorization if:

1. The product under investigation has already been evaluated and listed as a WHO Prequalified Product through the WHO PQ collaborative registration procedure between WHO and the Authority.

2. The product under investigation has already been evaluated and listed as a product of either the WHO collaborative registration pilot for stringently authorized products, including through the European Union Article 58 Procedure or the Swissmedic Marketing Authorization for Global Health products or the International Generic Drug Regulatory Programme (launched July, 2014)
3. Either trial or the investigational product has been authorized or granted marketing authorization in either an ICH founding regulatory member state or region such as European Commission (EMA), United States (United States Food and Drug Administration), Japan (MHLW/PMDA) or an ICH standing regulatory member state or region such as Canada (Health Canada), Switzerland (Swissmedic).
4. Further, products registered by WHO listed National Regulatory Authorities (NRA) under investigation may be considered through the reliance pathways on a case-by-case basis.
5. Either the trial or the investigational product has been evaluated and judged satisfactory at a joint review meeting facilitated by the World Health Organization under the African Vaccine Regulatory Forum (AVAREF).
6. Clinical trial authorized or the investigational product has been evaluated and judged satisfactory in the National Regulatory Authority that has signed memorandum of understanding/Agreement with Rwanda FDA.

6.5 Quality Control (QC) Testing related decisions

Quality Control Laboratory (QCL) of the Authority leverages a provision that allows the Authority to rely or recognize analytical reports from 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,

7.0. RELIANCE PROCEDURES

7.1 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 a well-resourced 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 well-resourced or the reference regulatory authority. In addition, there should be an assurance that the product is either identical or similar to that approved by the well-resourced 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 well-resourced or reference regulatory authority.

The authority reserves the right to subject all submissions for approval to an 'abridged' evaluation of a certain part of the application (e.g., relevant to use under local condition) such as product quality data in relation to climatic conditions and distribution infrastructure and a benefit-risk assessment in relation to use in the local ethnic population, medical practice/culture and patterns of disease and nutrition. **Depending on the type of the verification pathway, the regulatory decision will be approved within (30) working days.**

7.2 Reliance Documentations

In addition to the full assessment report from the well-resourced or the reference regulatory authority, the applicant shall be required to submit a full Clinical Trial Application, full Application for Marketing Authorization, Full application for GMP inspection as required by the Authority guidelines towards authorization of the application through the reliance pathway.

7.3 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

8.0. REFERENCES

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

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