24 December 2021
MCA-GL-109, version 1 2021
MCA Technical Working Group

Guideline for Reliance on decisions, reports, or information from other national medicines regulatory authorities (NMRAs) or regional and international bodies

Release for consultation by MCA The Gambia	07 December 2021
Start of public consultation	10 December 2021
End of consultation (deadline for comments)	21 December 2021
Agreed by MCA Technical Working Group	23 December 2021
Approved by MCA Executive Director	24 December 2021
Date of coming into effect	24 January 2022

Keywords	Reliance; Recognition; national medicines regulatory authority (NMRA); Reference institution (RI)

54 Kairaba Avenue, P.O. Box 3162, The Gambia
Telephone +220 4380632
Send a question via our website www.mca.gm or info@mca.gm

An agency of The Gambia

Guideline for Reliance on decisions, reports, or information from other national medicines regulatory authorities (NMRAs) or regional and international bodies

Table of contents

Executive summary

This document has been prepared for the purpose of inviting comments/suggestions and amendments on this draft, which will be considered in a subsequent exchange between the national medicines regulatory authorities (NMRA) of Ghana (FDA, Ghana Food and Drugs Authority), Liberia (LMHRA, Liberia Medicines and Health

Products Regulatory Authority), Sierra Leone (PBSL, Pharmacy Board of Sierra Leone), The Gambia (MCA, Medicines Control Agency) and the GHPP PharmTrain-Project Team of the Federal Institute for Drugs and Medical Devices (BfArM, Germany).

This guideline development process was initiated in March 2021 based on the outcomes and consensus of the meetings convened in January 2020 and February 2020 with participants from the national medicines regulatory authorities (NMRA) of Liberia (LMHRA), Sierra Leone (PBSL), The Gambia (MCA) and from the GHPP PharmTrain-Project Team. Version 1 of the draft Guideline on Reliance was finalised in November 2021.

The draft guidelines was adopted by the MCA Technical Working Group on 07 December 2021 for release for public consultation. After consultation the suggested changes were implemented and the MCA Technical Working Group agreed on the document for finalisation. The final guideline was approved by the MCA Executive Director for coming into effect.

1. Introduction (background)

The legal provision Medicines and Related Products Act 2014 mandates the MCA to regulate the importation, distribution, and manufacture of all medicines and related products in The Gambia.

NMRAs face an increasingly complex regulatory environment, with limited resources and a need to avoid duplication by communicating, collaborating, cooperating and forming coalitions to ensure product quality, safety and efficacy, as well as supply-chain security.

To this end, MCA is permitted to take into account and give significant weight to assessments performed and decisions made by another regulatory authority or trusted institution, or to any other authoritative information in reaching its own decision. Using reliance on the expertise and regulatory outcomes of recognised reference institutions (RI) facilitates and accelerates national registration processes.

Available assessment and inspection reports of reference institutions in addition to the registration dossiers, assure NMRAs of the positive benefit-risk of a product and its identical quality with the product already approved elsewhere, while allowing them to reflect their own judgement on the benefit-risk balance as it relates to their

specific country situation and the legislation in place. This contributes substantially to savings in regulatory resources, improvements in the quality of regulatory decisions and faster availability of needed therapies for patients.

Of note, MCA remains independent, responsible and accountable regarding the decisions taken, even when it relies on the decisions, assessments and information of other reference institutions.

1.1. Objectives

This guideline describes the prerequisites and information requirements of an application (for marketing authorisation or variation) for a medicine that has previously been approved by reference institutions.

The objectives of this guideline are to provide guidance and clarification to applicants, including sponsors and industry, on how MCA relies on foreign decisions, reports and information, in the assessment of medicines. It describes the practical steps for MCA regulators and applicants to effectively and efficiently implement and conduct the assessment activities using reliance on decisions, reports, or information from other NMRAs or regional and international bodies.

The MCA reserves the right to request information or material, or define conditions not specifically described in this guidance, in order to adequately assess the safety, efficacy or quality of a medicine. MCA is committed to ensure that such requests are justifiable and that decisions are clearly documented.

All final decisions on the approval of marketing authorisation or variation of medicines will be made by MCA.

2. Scope

This guideline provides guidance to applicants and MCA regulators on the requirements and process for the registration/approval of medicines, (both innovator and multisource (generic) finished pharmaceutical products (FPPs) and biologicals), in The Gambia that have been approved by a recognised reference institution. For details on the reference institutions see section 5 and **Annex I**.

By using the approach of reliance, MCA maximises the efficiency in using their own resources. Moreover, MCA is able to focus on value-adding activities. In addition, the burden of duplication of work done by reference institutions and duplication of work for applicants/manufacturers is reduced.

This guideline covers initial registrations/approvals and variations/post approval changes.

3. Legal basis

This guideline is coherent with national/regional frameworks and policies. The usage of reliance by MCA is supported/embedded in the Part XIII, section 82 (2) of the Medicines and Related Products Regulations, 2020.

4. Assessment activities

NMRAs have several options for organising their assessment activities.

In addition to a **full review**, there exist two reliance-based approaches to organise the assessment activities; verification or abridged/abbreviated review/regulatory pathway.

Verification is an administrative process to reach a regulatory decision, based on registration or authorisation by a reference institution. The NMRA formalises its decision by approving the product or submission and ensures the product for local registration and marketing. The NMRA does not undertake any further assessment activity on its own. This may apply to full submissions or parts thereof (see 'Definitions' for details on full and partial reliance). Verification is applied where conformity with requirements of the reference institution is sufficient to meet the requirements of MCA.

Abridged/abbreviated review is the assessment of suitability of use under local conditions and regulatory requirements, while relying partly or fully on prior assessment and inspection outcomes as well as Quality Control (QC) laboratory reports from the reference institution to inform the local decision (see 'Definitions' for details on abridged/abbreviated procedure).

5. Reference institutions

Regulatory authorities and regional and international bodies that are considered reference institutions by MCA for the purpose of reliance/use of relevant decisions, reports or information are stated in **Annex I** (see also "Definitions" for clarification).

6. Dossier requirements

MCA has published guidance documents and policies to assist applicants in the preparation and filing of medicine dossiers, for example, the common technical document CTD guideline (see reference list). Applicants should refer to the MCA website for applicable guidance documents.

This section provides guidance on the documentation specifically required for applying partial or full reliance mechanisms, as detailed in section 4.

6.1. Documentation Requirements

The format of the documentation should correspond to the CTD in accordance with MCA or International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) format/content.

Currency of the documentation, i.e. the sameness of the contents of the application with the documentation available and underlying any regulatory decision of the reference institution is mandatory (see section 6.2).

6.1.1. For marketing authorisation applications

A full dossier (CTD format) should be submitted including:

a. Module 1, regional administrative information, adapted, following the contents/format/structure laid out in **Annex II** ("Proposed documentation for the abridged procedure for reference institution-approved medicine").

b. Module 2, summaries, complete as submitted to the reference institution.

   Note: In the case of generic medicines for which a Clinical summary is not available, the Clinical overview (Module 2.5) should be included.

c. Module 3, quality documentation, as submitted to the reference institution, unless indicated otherwise according to the requirements of MCA. If climatic zone III–IV stability data are not available, the commitment and protocol should be provided for stability studies under the appropriate climatic conditions for The Gambia. Any preliminary data under the required climatic conditions for MCA should be provided. The stability data will be assessed by the reference institution, where applicable or possible.

d. Module 4, non-clinical documentation, to be provided except for generic/multisource medicines in addition to summary in module 2.

e. Module 5, clinical documentation, (in addition to summary in module 2).

   For innovative medicines to be provided.

   For generic/multisource products, complete documentation on bioequivalence studies should be provided in the submission in line with WHO guidelines (see reference list (WHO. Annex 6 Multisource (generic)….) on registration requirements to establish interchangeability and applicable national regulatory requirements for MCA.

6.1.2. For applications for variations

a. Module 1, adapted, following the contents/format/structure laid out in **Annex II** ("Proposed documentation for the abridged procedure for reference institution-approved medical products").

b. Module 2, complete as submitted to the reference institution.

   Note: In the case of generic medicines for which a Clinical summary is not available, the Clinical overview (Module 2.5) should be included.

c. Modules 3, 4 and/or 5 as submitted to the reference institution for the substantiation of the applied variation.

6.1.3. Additional information for marketing authorisation applications as well as for applications for variations

a. All review(s), assessment reports as well as inspection reports by the reference institution, substantiating the current authorisation status of the medicine, should be provided by the applicant when the submission is filed with MCA.

b. Written confirmation of permission for sharing reference institution-owned non-public information with MCA (see **Annex III**).

   Note for variation applications: If the confirmation has been obtained for the initial marketing authorisation application with unlimited validity, the confirmation does not have to be renewed with the reference institution. Nonetheless, the written confirmation should be part of each submission.

The legal information accompanying the dossier should be duly certified and authenticated under the procedure, in effect, in the country of origin, and issued by the appropriate entity.

c. Samples of the medicine from commercial batches, submitted to support the application as per sample schedule.

6.2. Requirements for Verification

The applicant should verify the “sameness” of the reference institution-approved medicine with the one applied for the purpose of reliance.

For this,

a. the “Quality information summary” (QIS) has to be provided (in CTD-module 1.2). Details on the information requested for finished pharmaceutical products (FPP) and for biologicals/biotherapeutic products (BTP) are provided in **Annex IVa** (QIS-RI-FPP) and **Annex IVb** (QIS-RI-BTP), respectively.

b. the applicant should confirm in writing that the review(s) provided is/are complete and unaltered. The applicant should confirm that the documentation filed in the submission is identical to that, on which the review(s) and authorisation decision was based. If it is not identical, all differences should be clearly indicated.

c. The product should have been registered, prequalified and/or granted marketing authorisation and is, in the latter case, actually on the market of the reference authority.

6.3. Requirements for abridged/abbreviated review

The abridged/abbreviated review may pertain to the full submission or parts thereof, depending on the suitability of use under local conditions and regulatory requirements.

An abridged/abbreviated review for **parts of the submission** may be applied for the active pharmaceutical ingredients (API). MCA recognises the Certificates of Suitability to the monographs of the European Pharmacopoeia (CEP) for API as well as the Confirmation of API Prequalification (CPQ) issued by the WHO Prequalification Team Medicines Programme (WHO-PQ) for APIs as a validation of the quality of a certain API.

For an abridged/abbreviated review of the **full submission**, in addition to the documentation/information requirements laid out in sections 6.1 and 6.2 of this guideline a so-called bridging report should be submitted by the applicant.

The bridging report:

The reference institution's assessments may not always account for specific circumstances that can significantly affect the benefit-risk of a medicine in other countries/regions. Hence, the reference institution's assessment reports may have to be considered incomplete, when a reference institution-approved product is submitted for the regulatory approval in The Gambia and the conditions of use or the benefit–risk profile of the medicine may differ. In these cases, the applicant should support the application by providing evidence of a positive benefit–risk profile for the proposed conditions of use in The Gambia.

Differences in target population, epidemiology and other features of the disease, concomitantly used medicines and hence the interaction potential, local treatment and diagnostic modalities, and other factors can substantially affect the benefit-risk profile of a medicine. There can also be issues related to certain quality parameters, especially in relation to the stability under different climatic conditions.

A bridging report should, in particular, justify the:

- comparability of the studied population to the target population (e.g. ethnicity, gender representation, age groups) as regards demonstration of efficacy and safety;
- relevance of reference institution-approved conditions of use as regards epidemiology and disease pattern in The Gambia as well as other implications for efficacy and safety, e.g. feasibility of monitoring and precautionary measures (e.g. resistance testing or therapeutic drug monitoring);
- interactions with food and with other medications relevant in The Gambia that are not discussed in the reference institution's assessment report;
- therapeutic role of a product and its recommended use according to relevant national and international treatment guidelines;
- quality issues, including but not limited to, storage conditions and conditions of administration and use;
- risk management plan for a new medicine (see 'Definitions' for details)

Provision of a bridging report is not mandatory, but may substantially facilitate conduct of the regulatory assessment, reduce the number of potential regulatory

questions and shorten the duration of the regulatory approval process. This report has to be dated and signed by the author and the author's CV be attached.

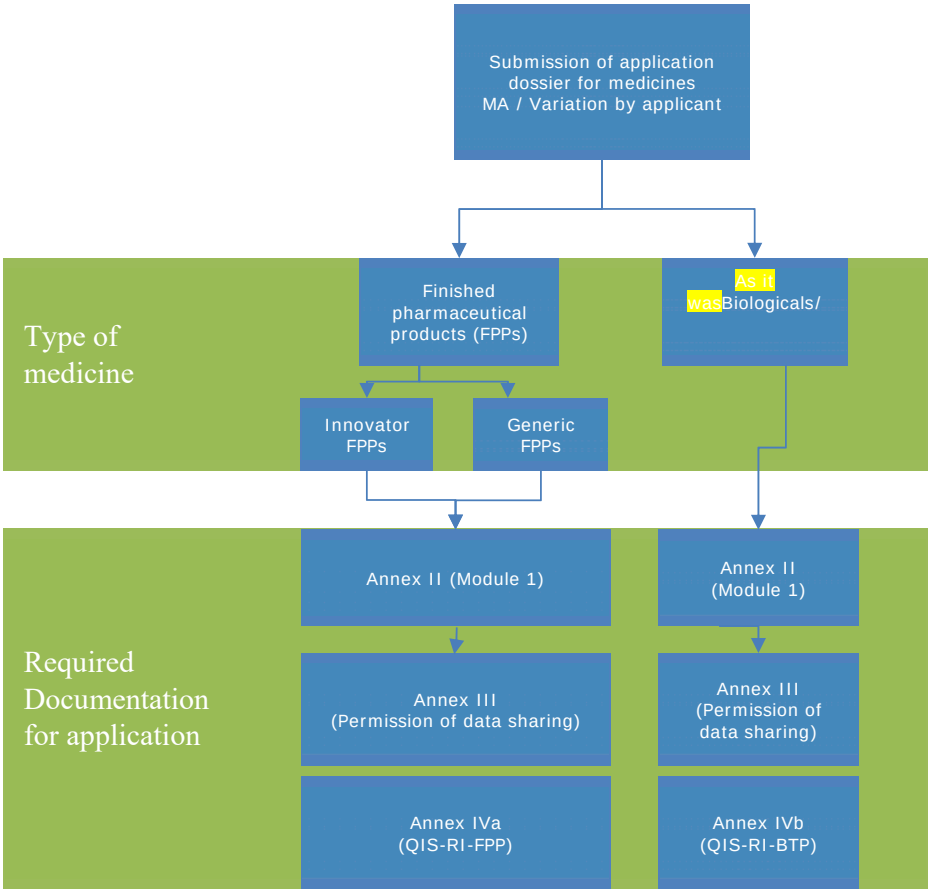

Figure 1: Documentation requirements in reliance-based approach for the application of marketing authorisation/registration or variations of medicines provided by the applicant

7. Guidance for Implementation

7.1. Guiding Principles

The MCA uses, where appropriate, reference institutions' reviews to perform ~~part of~~ the evaluation or to inform MCA's decision-making. MCA adheres to the following guiding principles when using reference institutions' reviews:

a. MCA may grant (or refuse to grant) a marketing authorisation or approve a variation based solely on the existence of a reference institution's review and its corresponding regulatory decision.

b. The use of reference institutions' reviews may be applicable, to variable degrees, to the regulatory review of medicines covered under the scope of this guideline and when available, are considered when determining the review strategy. However, an applicant will not be required to file a submission at a reference institution, nor will MCA unilaterally decide to delay the Gambian's review until a reference institution's review is available.

c. The extent to which a reference institution's review may be used to inform MCA's regulatory decision on a medicine will be guided by MCA's estimation of the benefits and risks/limitations of using that review (or components thereof) to inform the Gambian regulatory decision-making process.

d. The MCA 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.

e. While the use of reference institutions' reviews may enhance timely access to high quality medicines, it is essential that benefit-risk assessments of health products be made within the context of the Gambia's health care system. Final regulatory decisions on the granting or refusal or approval of a marketing authorisation or variation of medicines for the citizens are made by MCA.

f. In all cases, the Gambian's product labelling (e.g. summary of product characteristics or professional product information, package insert or patient information leaflet) will be reviewed by MCA to ensure it meets Gambia's requirements, in accordance with the Medicines and Related Products Regulations, applying MCA standard operating procedures and current practices.

g. Confidentiality of submitted data and non-disclosure to a third party is assured by the organisational policies applied by MCA.

7.2. Timelines

Formal deficiencies in the submitted application and the dossier will be communicated to the applicant, in line with the MCA procedures. Timelines for decisions from MCA as well as applicant response timelines are detailed in the respective registration guidelines.

7.3. Reliance Principles for variations

NMRAs are encouraged to establish alternative accelerated timelines for variations on medicines that have previously been approved by the other NMRAs. Accordingly, those NMRAs should create a list of the NMRA approvals they will recognise. As an expedite regulatory pathway the following approaches of accelerated timelines could be established:

- The MCA recognises the decision of other regulatory authorities and does not perform a review of supporting data but is informed of the change. Using this approach, MCA could allow changes to be implemented immediately after receipt of the change notification.
- The MCA performs an assessment of the decision of the NMRA of the licensing country to determine if recognition of the NMRA's decision is appropriate. Using this reliance-based approach, MCA established abbreviated review timelines detailed in the respective registration guidelines.
- The MCA performs a partial review and evaluation of a complete supporting data package, as originally submitted to the licensing country. Using this approach, timelines would be expected to be shorter than the timelines of a common approval of variation.

If a variation application is rejected by MCA, this will be communicated to the applicant with an explanation for the rejection. As appropriate, there should be an opportunity for dialogue between the MCA and the applicant, as necessary, with the aim of resolving the NMRA's concerns with the application.

Withhold/Suspension/Withdrawal of the product as authorised by the reference authority (or from the list of prequalified products) must be reported by the Marketing Authorisation Holder (MAH) to the MCA within 30 days including official

document stating the reason for this action. When applicable, this should be a letter/document issued by the reference authority.

Definitions

Abridged/abbreviated regulatory pathway/review

Regulatory procedures facilitated by reliance, whereby a regulatory decision is solely or partially based on application of reliance. This usually involves some work by the national medicines regulatory authority (NMRA) that is practising reliance. It is expected that use of reliance in these pathways will save resources and time as compared with standard pathways, while ensuring that the standards of regulatory oversight are maintained.

Applicant

The applicant means the product owner or licence holder in the reference institution, called supplier for WHO-prequalified products. Representatives of licence holders/suppliers may not hold themselves as applicants, unless they own the product.

Finished Pharmaceutical Product (FPP)

A finished dosage form of a pharmaceutical product that has undergone all stages of manufacture, including packaging in its final container and labelling.

Innovator finished pharmaceutical product

Generally, the innovator pharmaceutical product is that which was first authorised for marketing, on the basis of documentation of quality, safety and efficacy

Medicines

Innovator and multisource (generic) finished pharmaceutical products (FPPs) and biologicals/biotherapeutic products (BTPs).

Multisource (generic) finished pharmaceutical products

Pharmaceutically equivalent or pharmaceutically alternative products that may or may not be therapeutically equivalent. Multisource pharmaceutical products that are therapeutically equivalent are interchangeable.

Marketing Authorisation Holder (MAH)

A Marketing Authorisation Holder is an individual or a corporate entity possessing a marketing authorisation for a pharmaceutical product.

National medicines regulatory authority (NMRA)

A National medicines regulatory authority is a country's entity responsible for the registration, marketing authorisation, and other regulatory functions concerning medicines.

New Medicine

A generic copy of an innovator product, that has not been previously registered as a pharmaceutical or biological product in The Gambia or which has been marketed in The Gambia for a period of not more than ten (10) years or any other period to be determined by the Authority from time to time, for public health reasons.

Reliance (full and partial)

Reliance is the act whereby the regulatory authority in one jurisdiction takes into account and gives significant weight to assessments performed by another regulatory authority or trusted institution, or to any other authoritative information, in reaching its own decision. The relying authority remains independent, responsible and accountable for the decisions taken, even when it relies on the decisions, assessments and information of others. Full reliance means that the authority relies on the entire assessments/inspection and quality control reports performed by another NMRA. Partial reliance means that the authority relies on certain documents/parts of the assessments performed by another NMRA, while for the other part(s) an independent, full assessment of the documentation submitted by the Applicant is conducted.

Reference institution

A reference institution is an authority or organisation that agrees to provide outcomes of its regulatory expertise (especially assessment and inspection reports) to applicants/marketing authorisation holders or inspected manufacturers; agrees to sharing of these documents with other NMRAs. See also **Annex I** for clarification.

Variation

A variation is a change to the terms of a marketing authorisation. There are different types of variations with different regulatory requirements and procedures. For more detail for regulatory and procedural guidance proceed to MCA Guideline for Registration of Medicines.

References

WHO. Good Reliance Practices (GReP), Annex 11, 55th report of the World Health Organization Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP), WHO Technical Report Series No. 1033, 2021.

WHO. Guidelines on submission of documentation for prequalification of finished pharmaceutical products approved by stringent regulatory authorities, Annex5. World Health Organization, WHO Technical Report Series No. 986, 2014.

WHO. Good practices of national regulatory authorities in implementing the collaborative registration procedures for medical products, Annex 6. World Health Organization, WHO Technical Report Series No. 1019, 2019.

WHO. Collaborative procedure in the assessment and accelerated national registration of pharmaceutical products and vaccines approved by stringent regulatory authorities, Annex 11 (Appendix 3B, 4, 5). World Health Organization, WHO Technical Report Series, No. 1010, 2018.

WHO. Template: Quality Information Summary (QIS) of the Biotherapeutic Product Approved by Stringent Regulatory Authority (SRA) (QIS-SRA). June 2018 https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwjcr5OGoqT0AhWiQvEDHaBLCSoQFnoECA4QAQ&url=https%3A%2F%2Fextranet.who.int%2Fpqweb%2Fkey-resources%2Fdocuments%2Fwho-trs-1010-annex-11-appendix-4&usg=AOvVaw0Qd4TjGX1ERAsiU7OBV6oN (Access of website: November 2021)
Reference is made to the WHO "Guidelines on submission of documentation for the pilot procedure for prequalification of rituximab or trastuzumab approved by stringent regulatory authorities" (Access of website: November 2021)

WHO. Annex 6 Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability Republication of Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, WHO Technical Report Series, No. 992, Annex 7 with a new Appendix 2, 2017.

FDA Ghana. Guidelines for Registration of World Health Organization (WHO) Pre-Qualified Biological Products. FDA/SMC/BPU/GL-WPP/2013/03. Published by the Food and Drugs Authority of Ghana. Date of Issue: 2013/04/01.

FDA Ghana. Reliance Policy. FDA/GEN/POL-02. Published by the Food and Drugs Authority of Ghana. Date of Issue: 2ND January, 2019.

Health Canada. The Use of Foreign Reviews by Health Canada. Draft guidance document. Published by authority of the Minister of Health. Draft Date: 2012/09/11.

Collaboration, Not Competition: Developing New Reliance Models - Regulatory Collaboration. Exchange of Assessment Reports (ARs) with Regulators Outside the European Union (EU). World Health Organization, WHO Drug Information Vol. 30, No. 4, 2016.

MCA Reliance Policy, version 2, December 2021

MCA Guideline for Registration of Medicines, version 3, 15 April 2020

MCA Guideline for Registration of Herbal Medicinal Products, version 3, 15 April 2020

MCA Guidance for the Application in the Common Technical Document (CTD) Format, version 2, 15 April 2020

Annex

Annex I _List of reference institutions

Annex II_Documentation abridged procedure

Annex III_Confirmation of data sharing

Annex IVa_QIS-RI-FPP

Annex IVb_QIS-RI-BTP