Guidelines for Good Reliance Practices
MPD-G-LI-

Medical Product Division
Bhutan Food and Drug Authority

Medical Product Division
Bhutan Food and Drug Authority
Ministry of Health
Royal Government of Bhutan
Post Box 1556
Thimphu, Bhutan

List of Contributors

We would like to acknowledge following officials for their contributions in developing this guideline:

1. Jigme Tenzin, Chief Regulatory Officer, Medical Product Division, Bhutan Food and Drug Authority.
2. Jigme Dorji, Sr. Regulatory Officer, Medical Product Division, Bhutan Food and Drug Authority.
3. Kinley Penjor Tshomo, Sr. Regulatory Officer, Medical Product Division, Bhutan Food and Drug Authority.
4. Sonam Chophel, Sr. Regulatory Officer, Medical Product Division, Bhutan Food and Drug Authority.
5. Sangay Choden, Regulatory Officer, Medical Product Division, Bhutan Food and Drug Authority.
6. Sonam Jamtsho, Asst. Regulatory Officer, Medical Product Division, Bhutan Food and Drug Authority.
7. Gyelwa Kuenzom, Sr. Regulatory Officer, Medical Product Division, Bhutan Food and Drug Authority.

Compilation and Editing

1. Gyelwa Kuenzom, Sr. Regulatory Officer, Medical Product Division, Bhutan Food and Drug Authority.

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1. Introduction

The Medical Product Division (MPD) under the Bhutan Food and Drug Authority (BFDA) employs a comprehensive range of pre and post marketing risk assessment procedures to ensure the continued safe use of medicinal products. These procedures include evaluating the safety, quality and effectiveness of medicinal products before and after they are authorized. This involves clinical trials assessment, market authorization, compliance checks with regulatory standards, adverse event reporting, periodic safety updates and market surveillance and control to identify and mitigate potential risks to public health.

The increasing complexity of modern medicinal products and the emergence of new medicinal technologies that improve survival and quality of life have led regulators to recognize the importance of international cooperation through recognition and reliance. This approach is essential for ensuring the safety, quality and effectiveness of products used in the country. Adhering to Good Reliance Practices (GRP) involves leveraging existing regulatory work from trusted sources, thereby enhancing the efficiency and reliability of these processes.

By adopting reliance, regulators can access up-to-date scientific knowledge, share critical safety and efficacy data and harmonize standards, reducing duplication of efforts and resource constraints. This collaborative approach not only speeds up the approval and availability of safe and effective medicinal products but also ensures that regulatory decisions are informed by a broader global perspective, ultimately benefiting public health by providing timely access to quality medicinal products.

This guideline is developed to assist officials of the MPD at the BFDA in facilitating and accelerating access to quality-assured, safe and effective medicinal products through a streamlined reliance pathway for regulatory services. It is also intended to guide stakeholders in understanding the reliance procedures adopted by the Authority, thereby enhancing clarity and transparency across various regulatory service processes.

2. Scope

2.1. This guideline applies to the following regulatory activities for medicinal products:

- 2.1.1. Emergency Use Authorization
- 2.1.2. Market Authorization
- 2.1.3. Clinical Trials Approval
- 2.1.4. Regulatory Inspections
- 2.1.5. Vigilance Activities
- 2.1.6. Laboratory Testing
- 2.1.7. Lot Release
- 2.1.8. Market Control and Surveillance

3. Objective

3.1. To expedite and streamline the regulatory process by adopting reliance practices without compromising safety, quality or effectiveness of medicinal products.

3.2. To promote efficiency of regulatory operations and optimize resource allocation through reliance practices.

3.3. To promote transparency of the Authority's regulatory processes in reliance practices.

4. Normative Reference

4.1. The Medicines Act of the Kingdom of Bhutan 2003
4.2. Bhutan Medicines Rules And Regulation, 2025
4.3. Blood and Blood Product Regulation of Bhutan, 2016
4.4. Annex 10 Good reliance practices in the regulation of medical products: high level principles and considerations.

5. Definition

5.1. **Abridged Registration route** refers to the route of evaluation of medicinal product which is either prequalified by WHO, OIE, UN recognized international organizations or approved by at least one of the Medicine Regulatory Authority of PIC/s member country at the time of submission of application for registration
5.2. **Act:** It refers to the Medicines Act of the kingdom of Bhutan, 2003.
5.3. **Authority:** It refers to the Bhutan Food and Drug Authority.
5.4. **Collaborative Registration Procedure:** It refers to an accelerated registration procedure whereby information between WHO prequalification team, WLAs and NRAs are shared and registration is accelerated by leveraging assessment and inspection outputs produced by WHO-PQ and WLAs.
5.5. **Good Manufacturing Practice:** Good Manufacturing Practices (GMP, also referred to as 'cGMP' or 'current Good Manufacturing Practice') is the aspect of quality assurance that ensures that medicinal products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the product specification.
5.6. **IMDRF:** It refers to a voluntary group of medical device regulators who have come together to build on the strong foundational work of the Global Harmonization Task Force on Medical Devices (GHTF) and aims to accelerate international medical device regulatory harmonization and convergence.
5.7. **Medical Device:** It refers to all devices including an instrument, apparatus, appliance, implant, material or other article, whether used alone or in combination, including a software or an accessory, intended by its manufacturer to be used specially for human beings or animals which does not achieve the primary intended action in or on human body or animals by any pharmacological or immunological or metabolic means, but which may assist in its intended function by such means for one or more of the specific purposes of:
    5.7.1. diagnosis, prevention, monitoring, treatment or alleviation of disease;
    5.7.2. diagnosis, monitoring, treatment, alleviation of or compensation for an injury;
    5.7.3. investigation, replacement, modification, or support of the anatomy or of a physiological process;
    5.7.4. supporting or sustaining life;
    5.7.5. control of conception;
    5.7.6. disinfection of medical devices; or
    5.7.7. providing information by means of in-vitro examination of specimens

derived from the human or animal body.

5.8. **Medical Device Single Audit Program**: It refers to a program that allows an MDSAP recognized Auditing Organization to conduct a single regulatory audit of a medical device manufacturer that satisfies the relevant requirements of the regulatory authorities participating in the program.

5.9. **Medicinal products:** It refers refers to:

5.9.1. All substances intended for internal or external use of human or animals and intended to be used in the diagnosis, treatment, mitigation or prevention of any disease or disorder in human or animal;

5.9.2. Such substances intended to affect the functioning of any structure found in the human and animal body; and

5.9.3. Any other substance or device declared by the Board to be a medicinal product, and this may belong either to modern (allopathic) or traditional medicine.

5.10. **Mutual Reliance or Recognition:** It refers to a process which allows conformity assessments (of qualifications, product) carried out in one country to be recognized in another country. may be based on binding mutual agreements or treaties negotiated at the level of governments. Mutual recognition may be based on binding mutual agreements or treaties negotiated at the level of governments. A demonstration of the equivalence of regulatory systems is usually a prerequisite for mutual reliance or recognition. Work-sharing and joint activities are examples of mutual reliance.

5.11. **PQ-CRP:** It refers to collaborative registration procedure applied for WHO prequalified medicinal products.

5.12. **PSUR:** It refers to the documents intended to provide an evaluation of the risk-benefit balance of a medicinal product at defined time points after its authorisation.

5.13. **Recognition:** It refers to acceptance of the regulatory decision of another regulator or trusted institution. Recognition should be based on evidence that the regulatory requirements of the reference regulatory authority are 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.

5.14. **Reference Regulatory Authority:** It refers to a national or regional authority or a trusted institution whose regulatory decisions and/or regulatory work products are relied upon by another regulatory authority to inform its own regulatory decisions.

5.15. **Reliance:** It refers to 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.

5.16. **Sameness of Product:** It refers to two products having identical essential characteristics, i.e., the product being submitted to the relying authority and the product approved by the RRA should be essentially the same. (e.g., same qualitative and quantitative composition, same strength, same pharmaceutical form, same intended use, same manufacturing process, same suppliers of active pharmaceutical

ingredients, same quality of all excipients).

5.17. **SmPC:** It refers to a detailed document that provides information about a medicinal product. It is a crucial document for healthcare professionals to understand how to safely and effectively use a drug. The SmPC is a key part of the marketing authorization process for medicines and is updated throughout the product's lifecycle as new data emerge.

5.18. **Unilateral Reliance or Recognition:** It refers to a process when a country chooses to rely on or formally recognize an assessment from another country unilaterally and without reciprocity.

5.19. **Vigilance:** It refers to the collection, assessment, reporting and identification of trends in incidents resulting from the use of medicinal products.

5.20. **WHO-listed Authority (WLA):** A WHO Listed Authority (WLA) is a regulatory authority (RA) or a regional regulatory system (RRS) that complies with all the relevant indicators and requirements specified by WHO for regulatory capability as defined by an established benchmarking and performance evaluation process.

5.21. **WHO Prequalification:** WHO prequalification is a service provided by WHO to assess the quality, safety, and efficacy of medicinal products for priority diseases.

5.22. **WLA-CRP:** It refers to collaborative registration procedure applied for medicines and vaccines registered by WLAs.

6. Acronyms

6.1. BFDA: Bhutan Food and Drug Authority
6.2. CRP: Collaborative Registration Procedure
6.3. GHTF: Global Harmonization Task Force
6.4. GMP: Good Manufacturing Practices
6.5. GRP: Good Reliance Practice
6.6. IMDRF: International Medical Device Regulators Forum
6.7. MDSAP: Medical Device Single Audit Program
6.8. MPD: Medical Product Division
6.9. NRA: National Regulatory Authority
6.10. PIC/s: Pharmaceutical Inspection Co-operation Scheme (PIC/S)
6.11. PSUR: Periodic Safety Update Reports
6.12. PQ: Prequalification
6.13. RRA: Reference Regulatory Authority
6.14. SEARN: South East Asia Regulatory Network
6.15. SmPC: Summary of Product Characteristics
6.16. UMC: It refers to Uppsala Monitory Center
6.17. WHO: World Health Organization
6.18. WHO-PQ: World Health Organization Prequalification
6.19. WLA: WHO-listed Authorities

7. General Principles of Good Reliance Practice (GRP)

7.1. As per the provision under the Bhutan Medicines Rules and Regulation, the Authority may recognize relevant information on quality, safety and efficacy from other competent national regulatory authorities and international organizations.

7.2. The Authority may utilize prior decisions or assessments reports from Reference Regulatory Authority (RRA) and incorporate into the local regulatory decision-making process.

7.3. In adopting the reliance practices, the Authority should consider its needs and capacity, leveraging external authorities to enhance regulatory oversight for better-quality decisions and optimize resources.

7.4. The Authority should ensure the sameness of medicinal products with RRA where applicable.

7.5. The reliance approach may be prioritized for medicinal products intended for public health emergencies, priority/orphan diseases and pediatric formulations.

7.6. A risk-based approach to reliance should be adopted, considering factors like product type, available resources and public health needs to determine the level of reliance on external assessments.

7.7. The following principles are meant to complement and extend the basic principles of GRP:

7.7.1. **Universality:** Reliance applies to all National Regulatory Authorities (NRAs), regardless of their maturity level or resources, as a means to enhance regulatory capacity and efficiency.

7.7.2. **Sovereignty of Decision-Making:** The Authority should retain its independence and decision-making authority when practicing reliance, ensuring that it is a complementary strategy rather than outsourcing responsibility.

7.7.3. **Transparency:** The Authority should be transparent about the reliance processes, including the standards and rationale for using specific external information to foster trust and cooperation.

7.7.4. **Respect of National and Regional Legal Bases:** The Authority should align its reliance practices with national and regional legal framework ensuring clear mandates for implementation.

7.7.5. **Consistency:** The Authority should consistently apply reliance practices across well-defined categories of products and processes, ensuring predictable and transparent regulatory activities.

7.7.6. **Competence:** The Authority should have the necessary competency for critical decision-making and the authorities being relied upon should possess necessary competencies with robust and transparent regulatory systems.

7.8. The Authority will aim to promote reliance on its regulatory decisions by other

NRAs through measures including, but not limited to:

7.8.1. Publishing regulatory decisions and/or reports in a publicly accessible domains;
7.8.2. Participating actively in regional and international regulatory networks;
7.8.3. Executing Memoranda of Understanding (MoUs) or Confidential Disclosure Agreements with interested NRAs;
7.8.4. Enhancing its regulatory maturity via WHO benchmarking and accreditation; and
7.8.5. Offering capacity-building and technical exchange programs for peer regulators

8. Reference Regulatory Authority for reliance

8.1. For the purpose of regulatory reliance, RRA should meet any of the following criteria:

8.1.1. Be a WLA or Transitional WLA for the concerned product category and regulatory function;
8.1.2. Be a NRA operating at Maturity Levels 3 or 4 for the concerned product category;
8.1.3. Be a Member of IMDRF, particularly the founding members of the Global Harmonization Task Force (GHTF);
8.1.4. Be a Member of PIC/S;
8.1.5. Be a participating NRA for MDSAP;
8.1.6. Be member state of SEARN whose regulatory decision are considered highly relevant in national context as determined by the Authority; and
8.1.7. Any other NRAs whose regulatory decisions are highly relevant in the national context as determined by the Authority.

8.2. In addition, the following institutions will be recognised as RRA by the Authority for the purpose of reliance:

8.2.1. Uppsala Monitoring Center and
8.2.2. WHO Prequalification (WHO PQ) program

8.3. The Authority must ensure that any RRA considered for reliance meets the following additional criteria:

8.3.1. Strength of the RRA's regulatory system: There must be robust evidence of the RRA's capacity and credibility.
8.3.2. Availability of essential information: The RRA should provide the minimum required information (e.g., website access, Memorandum of Understanding, Confidential Disclosure Agreement) in a language accepted by the Authority.
8.3.3. Communication and responsiveness: The RRA should be responsive and easily reachable for any necessary clarification.

8.4. The scope and extent of reliance and recognition will vary based on the specific regulatory functions and categories of medicinal products involved.

8.5. The Authority may revise the criteria for RRAs in response to evolving regulatory needs based on recommendations from relevant technical committees or through stakeholder consultations.

9. Domains for reliance

9.1. Emergency Use Authorization

9.1.1. For medicinal products used during public health emergencies, the products must be listed for emergency use by the WHO or should have Emergency Authorization or special access for use of such products granted by RRA.

9.1.2. The applicants must adhere to the relevant guidelines for oversight of emergency use authorization.

9.2. Market Authorization

9.2.1. For the purpose of grant of marketing authorization (registration) of the medicinal product, following RRA will be relied on:

9.2.1.1. **Allopathic medicines:** The product must be registered with WLA for the concerned product category, NRAs operating at Maturity Levels 3 or 4 for the concerned product category, Transitional WLA for the concerned product category, PIC/s member country or WHO prequalified.

9.2.1.2. **Vaccines and biologics**: The vaccines must be registered with WLA or Transitional WLA or NRAs operating at Maturity Levels 3 or 4 for vaccines; and WHO prequalified.

9.2.1.3. **Medical Devices:** The medical devices must be registered or listed with WLA, IMDRF member countries (founding members of GHTF in particular), participating NRAs for MDSAP or prequalified by the WHO.

9.2.2. Product sameness verification is an important parameter for reliance where the product applied for marketing authorization should be essentially the same as the product registered by RRA.

9.2.3. The Authority may grant marketing authorization for medicinal product through the following reliance pathways:

9.2.3.1. **Abridged registration:** This is applicable for products that have been approved by at least one of RRAs. This is a unilateral reliance approach and the requirements for abridged registration are provided in the relevant guidelines.

9.2.3.2. **Collaborative Registration Process:** On expression of interest from the manufacturer, the Authority will apply the CRP procedure for the grant of marketing authorization through a reliance procedure. Both applications for PQ-CRP and WLA-CRP will be accepted. This process is based on a mutual reliance approach, promoting

collaboration and trust between different National Regulatory Authorities.

9.3. **Clinical Trial Oversight**

9.3.1. The Authority will rely on relevant clinical trial decisions, reports and information available or received from the following RRA with regards to clinical trial oversight in the interest of public health:

9.3.1.1. WLAs for the concerned product category;

9.3.1.2. Transitional WLAs for the concerned product category;

9.3.1.3. NRA operating at Maturity Levels 3 or 4for the concerned product category; and

9.3.1.4. IMDRF member countries (founding members of GHTF in particular)

9.4. **GMP Inspection**

9.4.1. Compliance to GMP is a mandatory consideration for market authorization of medicinal products.

9.4.2. The Authority may adopt the reliance approach to verify the GMP status of both domestic and foreign manufacturers by applying a risk-based inspection exemption when:

9.4.2.1. the same medicinal products is registered or granted marketing authorization in any of RRA;

9.4.2.2. the manufacturer GMP certificate (for applied dosage form facility) is available on EudraGMP website or USFDA website;

9.4.2.3. the manufacturing firm holds a valid WHO Pre-qualified status for the specific product;

9.4.2.4. the manufacturing firm of that medicinal product is approved by any PIC/s participating authority;

9.4.2.5. The manufacturer firm holds a valid GMP certificate issued by PIC/S member country; and

9.4.2.6. the manufacturing firm for medical devices is audited by MDSAP-recognized auditing organizations.

9.4.3. The reliance of the inspection for all the above criteria will be taken into account if the inspection is conducted within two years and/or the manufacturer holds a valid GMP certificate with a remaining validity of at least three months from the date of the receipt of the application of market authorization.

9.5. **Vigilance**

9.5.1. To ensure that safety issues are promptly identified and the necessary interventions implemented, reliance mechanisms should be implemented in the vigilance processes.

9.5.2. The Authority may adopt reliance approaches for the following vigilance/safety information issued by any RRA:

9.5.2.1. Safety signal detection and assessment report;
9.5.2.2. Safety variations, including changes in the SmPC and patient information leaflet
9.5.2.3. PSUR assessment
9.5.2.4. Risk communication (e.g. Dear doctors letters, Direct Healthcare professional communications)
9.5.2.5. Risk management plans
9.5.2.6. Benefit-Risk reviews

9.6. **Laboratory Testing**

9.6.1. The Authority may rely on or recognize analytical reports from laboratories that are WHO Pre-qualified or ISO/IEC 17025 accredited for recognition by an International Laboratory Accreditation Cooperation (ILAC) member on a case-by-case basis.

9.7. **Lot release**

9.7.1. The Authority may recognize the lot release certificate of vaccines from the NRA of the exporting country.

9.8. **Market surveillance and control**

9.8.1. The authority may rely on market surveillance and control decisions from RRA or WHO/Global surveillance and monitoring system (WHO/GSMS) or from the SEARN network on a case-by-case basis which are highly relevant in the national context

10. Links to Reference Regulatory Authorities

10.1. WLA: WHO List of World Listed Authorities
10.2. National Regulatory Authorities (NRAs) operating at Maturity Levels 3 or 4: WHO List of NRAs at ML3 and ML4
10.3. Transitional WHO Listed Authorities: WHO List of Transitional WLAs
10.4. PIC/S member countries: PIC/S Members
10.5. IMDRF member countries: IMDRF Members

Note: *The latest available version of each list must always be used to ensure up to date information.*

11. Reference

11.1. Reliance mechanism in regulatory processes “DRAP APPROACH ON GOOD RELIANCE PRACTICE” (2023) - Drug Regulatory Authority of Pakistan.

11.2. SEARN Strategy to facilitate reliance: https://searn-network.org/action-point-5-strategy-to-facilitate-reliance

11.3. Guideline on Reliance Practices in Marketing Authorization of Medicine (August 26, 2024) - National Medicine Regulatory Authority - Sri Lanka

11.4. Good Reliance Practices (March 2023) - Tanzania Medicines and Medical Devices Authority.

11.5. Guidelines on Reliance Practices During Registration of Medicinal Products (2024) - Egyptian Drug Authority

11.6. Guidelines on reliance for regulatory decision- making (2024) - Rwanda Food and Drugs Authority

11.7. Guideline on Good Reliance Practice for Regulation of Medicines - Maldives Food and Drug Authority

Quality Policy of Medical Product Division

"We commit to provide consistent regulatory operations with risk based planning and continual improvement in compliance with the recognized standards to meet our consumers' satisfaction and confidence"

Bhutan Food and Drug Authority
Royal Government of Bhutan
P.O 1556
Phone: 337074.337075, Fax: 33580
Email: bfda@gov.bt Website: www.bfda.gov.bt