MINISTRY OF HEALTH

PHARMACY AND POISONS

ROADMAP FOR THE IMPLEMENTATION OF BIOEQUIVALENCE REQUIREMENTS FOR MULTISOURCE DRUG PRODUCTS IN KENYA

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For clarifications, comments, or suggestions, please contact:

The Chief Executive Officer

Pharmacy and Poisons Board

P.O. Box 27663 – 00506, Nairobi

Telephone: 0709770100

Email: info@pharmacyboardkenya.org

Website: www.pharmacyboardkenya.org

HPT/PER/POL/018	**ROADMAP FOR THE IMPLEMENTATION OF BIOEQUIVALENCE REQUIREMENTS FOR MULTISOURCE DRUG PRODUCTS IN KENYA**	**Revision No. 0**	**Effective Date:** 30/09/2023 **Review Date:** 31/08/2028

Prepared by Deputy Director, Product Evaluation and Registration

Sign.....

Date.....19/09/2023.....

Reviewed by Director, Health Products and Technologies

Sign.....

Date.....21/09/2023.....

Checked by Head, Quality Management

Sign.....

Date.....22/09/2023.....

Authorized by CEO

Sign.....

Date.....26/09/2023.....

ABBREVIATIONS, ACRONYMS AND DEFINITIONS

BCS	Biopharmaceutical Classification System
BE	Bioequivalence
EAC-MRH	East African Community-Medicines Regulation Harmonization
GCP	Good Clinical Practices
MAH	Market Authorization Holder
MSDPs	Multisource Drug Products
OOS	Out of Specifications
PPB	Pharmacy & Poisons Board
RLD	Reference Listed Drug
WHO	World Health Organization

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LIST OF AUTHORS/CONTRIBUTORS

1. Dr. Fred M. Siyoi, Chief Executive Officer, Pharmacy and Poisons Board
2. Dr. Ahmed Mohammed – Director, Health Products & Technologies (DHPT)
3. Dr. Kariuki Gachoki, Deputy Director, Product Evaluation and Registration (DPER) Department, Directorate of Health Products and Technologies
4. Dr. Ali Arale, Principal Regulatory Officer, Drug Product Evaluation and Registration (DPER) Department, Directorate of Health Products and Technologies.
5. Dr. Felistas Chepwogen, Head, Bio-equivalence Division, Product Evaluation and Registration (DPER) Department, Directorate of Health Products and Technologies & Focal Person EAC-MRH Programme, Pharmacy and Poisons Board, Kenya
6. Dr. Sarah Chesaro, Principal Regulatory Officer, Directorate of Health Products and Technologies.

REVIEWERS

1. Dr. Anthony Toroitich, Deputy Director, Product Safety Department, Directorate of Health Products and Technologies
2. Dr. Sichei Cheworei, Deputy Director, Quality Control Laboratory.
3. Dr. Brayhan Kariuki, Regulatory Officer, Drug Product Evaluation and Registration (DPER) Department, Directorate of Health Products and Technologies.

Table of Contents

1. Introduction

The Pharmacy and Poisons Board (PPB), Kenya's national regulatory authority, has the crucial mandate to regulate clinical trials and issue marketing authorization based on assessment of quality, safety, and efficacy documentation submitted by the Market Authorization Holder/applicant. Part of the essential requirements for acquiring market authorization in Kenya is the submission of Bioequivalence (BE) data, crucial to proving the interchangeability of multisource products.

This comprehensive roadmap delineates the specific timelines within which Market Authorization Holders (MAHs) must submit Bioequivalence study data. The primary objective is to prove that multisource (generic) pharmaceutical drug products are therapeutically equivalent and interchangeable with their corresponding innovator's products. The roadmap not only outlines the criteria for scheduling of mandatory bioequivalence for both new applications and already marketed products but also incorporates a phased approach to ensure the compliance of all marketed products that require bioequivalence are compliant with the standards of quality, efficacy, and safety.

1.1 Purpose of the Roadmap

The roadmap is meant to ensure the same criteria are applied for assessing applications regardless of the origin or destination of the medical products. It ensures the demonstration of bioequivalence of multisource local and foreign products marketed in Kenya conform to prescribed standards of quality, safety, and efficacy. This roadmap is in compliance with WHO requirements following a formal benchmarking assessment on the status of the Kenyan regulatory system against the WHO's Global Benchmarking Tool (GBT).

1.2 Scope

The scope of this road map will cover all eligible multisource products both locally manufactured and imported products marketed in Kenya. The roadmap will cover all new applications and marketed products spanning from the year 1982 and all future market authorizations applications.

1.3 Legal framework

The regulation for the conduct of clinical trials is governed under the provisions of the Pharmacy and Poisons Act, Cap 244[1] Laws of Kenya

[1] Laws of Kenya (1989). The Pharmacy and Poisons Act, Chapter 244. Nairobi:

(hereinafter referred to as the "Act") and the Subsidiary Legislation thereunder. Since the submission of Bioequivalence data is also part of the requirements for issuance of market authorization in Kenya to prove the interchangeability of multisource products, the Board is mandated under provisions of CAP 244 Act, of 2019, section 3B(2)(p) ensure that all medicinal products manufactured in, imported into or exported from the country conform to prescribed standards of quality, safety, and efficacy; and 3B(2)(o) approve the use of any unregistered medicinal substance for purposes of clinical trials and compassionate use, and (p) approve and regulate clinical trials on medicinal substances.

1.4 Eligibility Criteria

All multisource (generic) products that require demonstration of therapeutic equivalence already marketed or intended to be marketed in Kenya are eligible for mandatory Bioequivalence studies.

This mandatory requirement for demonstrating therapeutic equivalence for all new applications and marketed products shall be implemented over an 11-year period beginning from January 2024 and progressing through phases as discussed under the section outlining the **criteria for scheduling of mandatory bioequivalence study requirements in Kenya** below.

2. Guidelines for Submission of Bioequivalence Studies

This roadmap will be implemented in line with the Guidelines on Bioequivalence Requirements in Kenya and the Framework for Implementation of Bioequivalence in Kenya, Pharmacy and Poisons Board, 2023.

3. Criteria for scheduling of mandatory bioequivalence study requirements in Kenya

This roadmap encompasses three processes; implementation plan for new applications, applications pending review and products issued with marketing authorization.

To enable a gradual and structured implementation of the mandatory Bioequivalence as per the Guidelines on Bioequivalence Requirements in the Compendium of Guidelines of Medicines Evaluation and Registration (HPT/PER/GUD/016), the Board has adopted a phased-out approach;

3.1.1 Criterion 1: All new Applications submitted after implementation of this roadmap

Effective 1st January 2024, all new applications for eligible generic products manufactured locally and imported products requiring marketing authorization shall submit bioequivalence studies under the Clinical Study Reports within Module 5 of the Common Technical Document (CTD).

3.1.2 Criterion 2: All applications pending review prior to implementation of this roadmap

All applications for eligible generic products that will not have been registered by 31st December 2023 will be subject to rescreening to ensure compliance with mandatory bioequivalence requirements under the Clinical Study Reports within Module 5 of the CTD.

3.1.3 Criterion 3: All eligible generic medicines with Marketing Authorization prior to implementation of this roadmap

The PPB shall apply BE requirements to all marketed medicines products on a phased-out approach based on the Biopharmaceutics Classification System (BCS) as follows;

a) All eligible marketed products registered before 2010 (local and foreign manufactured) when the BE requirement was made mandatory will be required to demonstrate Bio-equivalence.
b) Bioequivalence studies data of all eligible marketed products registered after 2010 shall be verified.
c) All locally manufactured products registered after 2010, when BE studies were waived, will be required to demonstrate Bio-equivalence.

4. Implementation roadmap

Already marketed products that meet the criteria 2 and 3 will be required to provide BE studies data in accordance to the time buckets specified in this roadmap effective from January 2025. The time buckets will be implemented for 10 years. The review of BE data will be aligned to the renewal cycle of 5 years. The Board will undertake the following strategies to ensure compliance of all marketed products to the BE Requirements as follows;

a) Mapping out all BCS class 2 and 4 products issued with marketing authorization in Kenya since 1982 (see table 1 below).
b) Re-registering all mapped BCS class 2 and 4 products according to the time buckets implemented over a period of 10 years effective 2025 (see table 1 below)

c) BCS class 2 and 4 products contained in the priority list developed under the following criteria, shall be required to demonstrate bioequivalence irrespective of the time buckets stated in (b) above;
    1. BCS class 2 and 4 products with market complaints for the past two years following post-market surveillance that fail comparative dissolution studies effective 2024.
    2. BCS class 2 and 4 products with Out of Specifications (OOS) for the past two years, effective 2024.
    3. BCS class 2 and 4 products have proven to have been registered without BE data.

4.1 Time Buckets of implementation of mandatory bioequivalence studies in Kenya.

The time buckets are designed to cluster the products according to the years when marketing authorization was issued. For the purposes of this roadmap, the mandatory BE requirements will apply to all eligible marketed products from 1982 to 2023.

Note the first-time market authorization in Kenya for products under BCS class 2 and 4 was issued in 1982.

Time Buckets

The following are the time buckets that will be implemented in this roadmap for eligible BCS class 2/4 registered products as follows:

Year 1: 2024 - the effective date for new applications and priority-listed products

Year 2 (2025): BCS 2/4 and priority listed products.

Year 3 (2026): BCS 2/4 and priority listed products.

Year 4 (2027): BCS 2/4 and priority listed products.

Year 5 (2028): BCS 2/4 and priority listed products.

Year 6 (2029): BCS 2/4 and priority listed products.

Year 7(2030): BCS 2/4 and priority listed products.

Year 8: (2031): BCS 2/4 and priority listed products.

Year 9: (2032): BCS 2/4 and priority listed products.

Year 10(2033): BCS 2/4 and priority listed products.

Year 11(2034): BCS 2/4 and priority listed products.

Years of implementation	2024 **(Year 1)**	2025 **(Year 2)**	2026 **(Year 3)**	2027 **(Year 4)**	2028 **(Year 5)**	2029 **(Year 6)**	2030 **(Year 7)**	2031 **(Year 8)**	2032 **(Year 9)**	2033 **(Year 10)**	2034 **(Year 11)**
	All new products	All new products	All new products	All new products	All new products	All new products	All new products	All new products	All new products	All new products	All new products
Time Bucket	N/A	As per Renewal Cycle	As per Renewal Cycle	As per Renewal Cycle	As per Renewal Cycle	As per Renewal Cycle	As per Renewal Cycle	As per Renewal Cycle	As per Renewal Cycle	As per Renewal Cycle	As per Renewal Cycle
	As per priority list	As per priority list	As per priority list	As per priority list	As per priority list	As per priority list	As per priority list	As per priority list	As per priority list	As per priority list	As per priority list

Note: This is a live document and thus remains dynamic based on performance of every year

5. Stakeholder management and sensitization

The PPB has established systems for public participation and shall undertake periodic stakeholder sensitization of pharmaceutical industry, and all relevant government institutions.

The PPB shall foster collaborations with national, regional, continental and international agencies/institutions to harmonize bioequivalence standards and facilitate information sharing.

As part of collaboration, the PPB will participate in national, regional and international forums to share knowledge, expertise, and best practices for bioequivalence implementations.

6. Bioequivalence regulatory process

The PPB will issue a circular on mandatory BE to applicants/MAH, review the Priority list in the Bioequivalence Roadmap from time to time, and take necessary regulatory actions.

7. Post-Market Surveillance

The Board will continuously monitor the safety and efficacy of approved and marketed products through pharmacovigilance and post-marketing surveillance programs including active market surveillance, investigations of market complaints, out of specifications, and conducting comparative dissolution studies of both BCS Class 2 and 4 pharmaceutical drug products.

8. Periodic Review and updates of the roadmap

A proactive approach to continuous improvement and review will be adopted in the implementation of this roadmap. The Board shall therefore review and update this roadmap to reflect advances in scientific knowledge and technology. In addition, the Board shall continuously evaluate and improve the effectiveness of bioequivalence requirements and regulatory actions.

9. Reference

1. South African Health Products Regulatory Authority (2022). Medicines Registration Renewals Implementation Framework. (Issue No.: HPA 01-2022/23)
2. World Health Organization (2021). WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory Systems of Medical Products, Revision VI. Geneva. License: CC BY-NC-SA 3.0 IGO.
3. Laws of Kenya (1989). The Pharmacy and Poisons Act, Chapter 244. Nairobi:

P. O. Box 27663 00506 Lenana Road Opposite Russian Embassy Nairobi,
Tel:+2540212345/6789, Fax: +2540212345,

Website: www.Pharmacyboardkenya.org.ke,

Email: info@pharmacyboardkenya.org.ke