MINISTRY OF HEALTH

Pharmacy and Poisons Board

RENEWALS FRAMEWORK FOR MEDICINES AND VACCINES IN KENYA

May 2023

Citation

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Recommended citation: *Republic of Kenya, Ministry of Health, Pharmacy and Poisons Board, Renewals Framework for Medicines and Vaccines in Kenya, Revision 0, 2023.*

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HPT/PER/POL/017	Renewals Framework for Medicines and Vaccines in Kenya	Revision No. 0	Effective Date: 31/05/2023 Review Date: 30/04/2026

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Glossary of Terms

Renewal:	Marketing Authorization renewal every five years.
Retention:	Maintenance of a Marketing Authorization upon payment of the prescribed annual fee.
Product Quality Review (PQR):	A mechanism (regular periodic or rolling quality reviews of all licensed medicinal products) to ensure that data captured by the Pharmaceutical Quality System (PQS) is reviewed for trends in order to verify the consistency of the existing process, the appropriateness of current specifications for both starting materials and finished products, highlight any adverse quality trends and to identify product and process improvements. The Product Quality review (PQR) is an effective quality improvement tool to enhance the consistency of the process and the overall quality of the product.
Pharmacovigilance:	the practice of monitoring the effects of medical drugs after they have been licensed for use, especially in order to identify and evaluate previously unreported adverse reactions.
Product complaints:	A complaint is a statement from a customer expressing dissatisfaction with the manufactured product, whether with the manufacturer's service, the product's packaging, the product's usability, or damage to the product.
Market Surveillance:	Activities carried out and measures taken by public authorities to ensure that products comply with the applicable legislations and do not endanger health, safety or any other aspect of public interest protection. It may include product traceability activities.
Risk management plan:	A risk management plan (RMP) provides information on a medicine's safety profile, describes the activities of the marketing authorisation holder to further characterise the safety profile during post-marketing (pharmacovigilance activities), and explains

	the measures that are taken in order to prevent or minimise the risks.
Product retention:	Means maintenance of a product in the register of licensed products.

Marketing Authorization (MA): Also means product registration

MA withdrawal:	Means voluntary withdrawal of a marketing authorization by the marketing authorization holder.
PRIMS:	Pharmaceutical Regulatory Information Management System

1.0 INTRODUCTION

1.1 Background

Pharmacy and Poisons Board, hereafter referred to as "The Board" is mandated under the Pharmacy and Poisons Act to regulate Health products and Health Technologies. Renewals of medicines and vaccines has become a crucial requirement, driven by assessments carried out by the World Health Organization's Global Benchmarking Tool (WHO-GBT). In response, the Board has developed comprehensive Guidelines and Standard Operating Procedures (SOPs) within a renewal framework. This framework encompasses all medicines and vaccines registered in Kenya since 1981. The framework provides guidance for both the regulator (PPB) and applicant in the preparation of a policy on Market Authorization renewal applications to The Board, while ensuring access of medicines and vaccines is not disrupted and that quality, safe and efficacious medicines and vaccines are available during their entire lifecycle. PPB has established and implemented documented procedures and tools for the renewal of medicine and vaccine registrations. Each stage of the renewal process, including application receipt, screening, review, and decision-making, must be thoroughly documented and rigorously implemented. These guidelines explicitly define the appropriate validity periods for initial registrations while outlining the requirements for renewing registrations, which are limited to a five-year cap as mandated by law.

1.2 Legal and Regulatory Framework:

Relevant Kenyan Legislation

The Board is empowered under Section 3A(c) of the Pharmacy and Poisons Act, Chapter 244 Laws of Kenya ("the Act") to grant or withdraw marketing authorization for medicines and vaccines

subject to appropriate conditions and revise such conditions for marketing authorization as necessary. These conditions include the validity period of the marketing authorization as specified in the Pharmacy and Poisons (Registration of Health Products and Technologies) Rules, 2022.

The Pharmacy and Poisons (Registration of Health Products and Technologies) Rules, 2022, under Rule 10 provide that an issued Certificate of Registration of Health Products shall be valid for a period of five (5) years from the date of issue.

Additionally, Rule 9 of the Pharmacy and Poisons (Registration of Health Products and Technologies) Rules, 2022, provides for the requirements for renewing the registration, which is required to be in compliance with the prescribed guideline for Renewal of medicines and vaccines.

1.3 **Scope**

The renewal initiative will begin with currently registered medicines and vaccines from the year 2018 and progressively extend backward in time to include medicines and vaccines registered as early as 1980. This phased approach considers the growth in the number of medicines and vaccines registered over the years, reflecting both the increasing number of applications received and those evaluated and granted market authorization.

1.4 **Historical Background**

The journey of market authorization for medicines and vaccines in Kenya has evolved significantly over the years:

1981 – 2015: The inception of market authorization for medicines and vaccines in Kenya dates back to the 1980s. During this period, the process was predominantly manual, lacking a structured

evaluation of data. Although manual dossier submissions were made, the capacity of PPB to thoroughly review the data was limited.

2016 – 2017: A pivotal transformation occurred in 2016 with the introduction of an online system. This system adopted a standardized electronic submission of applications in the Common Technical Document format, revolutionizing the evaluation of dossiers. This digital shift marked a significant step towards harmonization and structured assessment processes.

2018 – 2020: Post-market authorization, in 2018, a pivotal annual retention system was established. Initially, this system was founded on the principle of listing retained medicines and vaccines based on their potential market presence. This policy aimed to ensure the continued availability of medicines and vaccines in the market.

2021 – to date: Building on the progress made, 2021 witnessed a substantial upgrade in the retention system. The introduction of the "wallet system" represented a significant enhancement. This modernized approach further streamlined the retention process, contributing to a more efficient and responsive regulatory framework.

1.5 Purpose of the Framework

The purpose of this framework is to ensure that PPB complies with The Pharmacy and Poisons (Registration of Health Products and Technologies) Rules, 2022, under Rule 9 and 10 and the Global Benchmarking Tool (GBT), in ensuring that medicines and vaccines are consistently of Quality, Safe and efficacious.

The Requirement of Subsection MA04.02: of the GBT tool requires that “Documented procedures have been implemented to renew and/or to periodically review the MAs granted have been established and implemented. Similar to the initial registration and MA, the benefit-risk balance of the medical product is the core consideration

for marketing re-authorization by regulatory authorities. The procedures should be supported with guidance on the requirements to be reviewed, and on the SOPs to be implemented at the various stages of the renewal or periodic review process. Guidance should be available for each stage of the renewal process, including, for example, receipt of application, screening, reviewing, and decision making. The process flow should be documented and implemented."

It is the Pharmacy and Poisons Board's intention to attain Maturity Level 3 status then to progress to Maturity Level 4 and be listed as a WHO Listed Authority.

The framework will cover the health product registration renewals for all medicines as governed by the CAP 244 Laws of Kenya.

2.0 INTERNATIONAL GUIDELINES AND STANDARDS

International guidelines and standards play a crucial role in shaping the renewal process. The following key considerations are derived from the WHO Technical Report Series, No. 1019, 2019:

2.1 **Guidelines for Renewal:**

The validity of registration and renewal of registration will be based on the existing guidelines and regulations for renewal of registration of medicines and vaccines as applicable in PPB. These guidelines serve as the foundation for assessing the continued compliance and efficacy of registered medicines and vaccines.

2.2 **Compliance Verification:**

The renewal process presents a valuable opportunity to verify whether all commitments made by applicants during the initial registration phase have been satisfactorily fulfilled. This includes the assessment of approved variations, requalification for registered medicines and vaccines, and any updates or changes to the conditions of registration in the reference NRA.

2.3 **Consistency and Alignment:**

Ensuring consistency is essential. This involves verifying that the conditions of registration remain up to date and aligned with the nationally registered product. Collaboration with Product Quality Teams (PQT), reference SRAs (Stringent Regulatory Authorities), and national registration conditions is vital to maintain alignment and regulatory harmony.

Overview of the Medicines Renewal Process

In accordance with the Cap 244 laws of Kenya, the renewal of medicines and vaccines is a vital regulatory process that ensures the ongoing quality, safety, and efficacy of medicines and vaccines in the market. The process can be summarized as follows:

3.0 RENEWAL FREQUENCY:

Renewal is mandated to occur every five years. This regularity ensures that medicines and vaccines are continually evaluated and maintained to meet evolving standards.

3.1 **Renewal Fee:**

This fee is payable by applicants to support the regulatory process. The fee for both local and foreign applications will be as gazzetted in accordance with the gazette notice under Rule 9.

3.2 **Annual Product Retention:**

Following the issuance of market authorization, applicants are required to retain their medicines and vaccines annually. This retention is facilitated through the submission of product information and updates.

3.3 **Retention Fee:**

An annual fee of $300 USD per product is applicable for product retention. This fee contributes to the ongoing oversight and maintenance of registered medicines and vaccines.

3.4 **Variations and Changes:**

If any variations or changes to a product are necessary, applicants must submit these changes to the regulatory authority.

3.5 **Variation Fee:**

A fee of $200 USD per change is applicable for variations or modifications to a product. It ensures that the regulatory authority is informed and can assess the impact of changes effectively.

3.6 **Exemptions for Safety-Related Changes:**

Changes related to safety, such as Periodic Safety Update Reports (PSUR), are exempt from fees and are processed free of charge. This exemption encourages prompt reporting and ensures the safety of medicines and vaccines.

3.7 **Strategy Matrix**

To efficiently manage the renewal process, a strategy matrix has been established. It categorizes medicines and vaccines based on the number of registered products during specific time periods. This approach ensures a systematic and organized renewal process, addressing medicines and vaccines in a structured manner.

3.8 **Expected Time for Completion:**

The renewal process will start with medicines and vaccines due for renewal within the five-year renewal period.

The process will extend over a span of 10 years to accommodate all eligible medicines and vaccines.

This structured approach ensures that the renewal effort aligns with evolving regulatory standards and contributes to maintaining the quality, safety, and efficacy of medicines and vaccines in Kenya's market.

The stratification is as follows:

Time Buckets:

The purpose of using time buckets in data analysis can be summarized as follows:

i. Increase operational efficiency: Time bucketing can help process and report data more efficiently, as it simplifies the calculation process by grouping data into intervals of time
ii. Aggregate data: Time bucketing enables the aggregation of data by time interval, allowing for summary calculations such as average, maximum, minimum, or sum of values within a bucket.
iii. Group data: Time bucketing helps group data into intervals of time, making it easier to analyze trends and patterns over time
iv. Simplify calculations: Time bucketing can simplify calculations for time-series data, as it allows for rollups and down sampling of data
v. Improve performance: Pre-calculating time buckets can improve performance by reducing the amount of data that needs to be processed
vi. Provide flexibility: Time bucketing provides flexibility in bucket size and start time, allowing for customization of time intervals

Overall, time buckets are a valuable tool in data analysis, providing a way to group data into intervals of time for efficient processing, aggregation, and analysis.

a) 1980 to 1989
b) 1990-1999
c) 2000-2011
d) 2012-2014
e) 2015-2017
f) 2018 (Yearly)
g) 2019 (Yearly)
h) 2020 (Yearly)
i) 2021 (Yearly)
j) 2022 (Yearly)
k) 2023 (Yearly)

Time buckets											
Registration year	**1980-1989**	**1990-1999**	**2000-2011**	**2012-2014**	**2015-2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**
No. of applications	1785	4316	5874	1512	2021	559	337	318	471	798	403 (TBC)
Year of Implementation	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 6**	**Year 7**	**Year 8**	**Year 9**	**Year 10**	**Year 11**
	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034
Products under Renewal	2019 + fraction of 2018	2020 + fraction of 2018	2021 + fraction of 2015 to 2017	2022 + fraction of 2015 to 2017	2023 + fraction of 2015 to 2017	2024 + fraction of 2015 to 2017	2025 + 2012 to 2014	2026 + 2000 to 2011	2027 + 1990 to 1999	2028 + 1980 to 1980	2029

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

4.0 IMPORTANCE OF RENEWAL

1. Ensuring Safety and Efficacy through periodically reviewing and assessing the safety and efficacy of medicines and vaccines. This helps in identifying any new safety concerns or emerging risks associated with a particular medication.
2. Quality Control by providing an opportunity to re-evaluate the quality of medicines and vaccines in the market thus help identify issues with manufacturing or quality control processes that may have arisen since initial approval.
3. Continuous monitoring of adverse events and side effects associated with medicines and vaccines. This ongoing assessment ensures that any potential safety issues are addressed promptly.
4. Alignment with Current Standards by the fact that medicines and vaccines regulations and standards may evolve over time thus allow for alignment with the latest regulatory standards, pharmacopoeias, and guidelines.
5. Labeling and Packaging updates through Changes in labeling and packaging requirements to be addressed during renewal, ensuring that information provided to healthcare professionals and patients is up-to-date and accurate.
6. Continual Assessment of Benefit-Risk Profile following a benefit-risk profiles changes as new data become available thus providing an opportunity to reassess the balance between a medicine's benefits and risks.
7. Encouraging Innovation by maintaining a robust regulatory system that includes renewal, and encouraging pharmaceutical companies to continually invest in research and development to improve existing medicines and vaccines or develop new ones.
8. Streamlining the Market by removing outdated or unsafe medicines and vaccines from the market, streamlining the availability of medicines and vaccines, and reducing the risk of patients receiving ineffective or harmful treatments.

9. Global Harmonization through promotion and alignment with international standards and practices, making it easier for pharmaceutical companies to operate in multiple markets and reducing duplication of efforts in the review process.
10. Build Public Trust through regular renewal and ongoing oversight by PPB to enhance public trust in the safety and efficacy of medicines, which is crucial for healthcare systems.
11. Supporting Pharmacovigilance: Renewal can enhance pharmacovigilance efforts by requiring companies to submit updated safety data and ensuring that surveillance systems remain effective.
12. Compliance Monitoring: It allows PPB to monitor compliance with regulatory requirements over time, reducing the likelihood of non-compliance and ensuring that manufacturers adhere to quality standards.

5.0 PREPARING FOR RENEWAL AND STAKEHOLDER SENSITIZATION

As part of the comprehensive renewal process, effective stakeholder sensitization is paramount to ensure a smooth transition and cooperation from all parties involved. The Pharmacy and Poisons Board (PPB) has developed a structured approach to achieve this goal:

5.1 **Stakeholder Sensitization Workshop:**

To facilitate a clear understanding of the renewal process and guidelines, a workshop will be organized for industry stakeholders. This workshop will provide detailed insights into the regulatory requirements and expectations.

a) **Pilot Phase Implementation**

The sensitization process will be initiated through a pilot phase. In the first phase, which aligns with the 2018-time bucket, medicines and vaccines due for renewal in that year will be the primary focus.

This phased approach ensures that the stakeholders are well-prepared for the renewal process, starting with a manageable subset of medicines and vaccines.

b) **Sensitization Timeline:**

The stakeholder sensitization workshop for the pilot phase is scheduled to take place before end of December 2023.

During this workshop, industry representatives will receive comprehensive information about the renewal guidelines, procedures, and expectations.

c) **Application Process:**

To implement the process of health product registration renewals ensuring a consistent approach to benefit all stakeholders and to ensure quality, efficacious and safe medicines and vaccines are available to the public, the following approaches shall be taken:

i. Submitting the application: The completed renewal application form shall be submitted to the Pharmacy and Poisons Board online application process, along with any required supporting documentation. This will make the process more efficient and convenient for all stakeholders.

ii. Completing the renewal application form: The marketing authorization holder (MAH) shall complete and sign the renewal application form, appending a list of all authorized strengths, pharmaceutical forms, and presentations of the product concerned for which renewal is sought. This will help to ensure that the renewal process is completed accurately and efficiently.

iii. Clear instructions and user assistance: Clear instructions and user assistance shall be provided to guide applicants through the registration and renewal process. This will help to avoid errors and ensure that the process is completed correctly.

iv. Paying fees: Application fees are required to be paid for the renewal of health product registration

v. Timely renewal reminders: Timely renewal reminders should be sent to Market Authorization Holders (MAH) to ensure that they do not miss the renewal deadline. This will help to ensure that medicines and vaccines remain available to the public without any interruptions.

vi. Contact persons: Details of contact persons should be provided. This will help to ensure that any questions or issues that arise during the renewal process can be addressed quickly and efficiently.

vii. Review and approval: The regulatory authority will review the renewal application and supporting documentation to ensure that the product continues to meet the required standards for safety, efficacy, and quality

viii. Abbreviated renewal process: An abbreviated renewal process may be used for facilities that have not had any changes to their registration information since the last renewal. This will make the process more efficient for these facilities.

ix. Turnaround time: The turnaround time for health product registration renewal shall be within 120 Working days.

6.0 DATA COLLECTION AND REVIEW

6.1 **Documenting Existing Registrations:**

To effectively manage the renewal process, it is imperative to maintain a comprehensive database of all registered medicines and vaccines. This database will include the following categories of medicines and vaccines:

a. **All Manual Registered Medicines and vaccines:**

This category encompasses medicines and vaccines that were registered through manual submission processes. Their inclusion in the database ensures that all medicines and vaccines, regardless of the registration method, are accounted for.

b. **All CTD Registered Medicines and vaccines:**

Medicines and vaccines registered using the electronic submission of Common Technical Document (CTD) format are essential components of the database. This modern submission method is critical for efficient data management.

c. **List of All Retained Medicines and vaccines:**

An inventory of retained medicines and vaccines will be maintained. Retained medicines and vaccines are those for which annual retention is required. This list ensures ongoing compliance with regulatory requirements.

d. **List of All Withdrawn Medicines and vaccines** that have been withdrawn or removed from the market will also be documented. Tracking withdrawn medicines and vaccines is essential for regulatory oversight and market safety.

7.0 TIMELINES AND DEADLINES:

To ensure a systematic and efficient renewal process, specific timelines and deadlines have been established:

7.1 Application Timeline:

All applicants must submit their renewal applications at least 3 months before the expiry of their Market Authorization. This lead time ensures that the regulatory authority has sufficient time for evaluation and processing.

7.2 Phased Approach for Backlog:

To effectively manage the renewal backlog, a phased approach will be implemented. This approach spans a period of 10 years.

7.3 Initial Focus on Five-Year Period:

The renewal process will commence with medicines and vaccines that are due for renewal within the first five-year period.

7.4 **Five-Year Renewal Cycle:**

Subsequently, the process will continue to address medicines and vaccines according to their renewal due dates, aligning with the standard five-year renewal cycle.

8.0 APPLICATION FORMS AND REQUIREMENTS:

For the renewal process, applicants are required to adhere to specific guidelines and formats to ensure consistency and efficiency:

a) **Application Format:** All renewal applications must strictly adhere to the format outlined in the renewal guidelines.

b) **Submission**: The renewal process will be facilitated through the Pharmacy and Poisons Board's (PPB) online system known as the Pharmaceutical Regulatory Information Management System (PRIMs). Applicants are required to submit their applications through this dedicated platform.

9.0 RENEWAL FEES AND PENALTIES

The fee structure for renewal is as follows:

a) **Renewal Fee:** In accordance with the gazette notice under Rule 9, the renewal fee is set at USD 1,000 for foreign applicants and USD 500 for local applicants. This fee is essential to support the regulatory process and ensure ongoing compliance with renewal requirements.

b) **Good Manufacturing Practice (GMP) Fee:** The GMP fee is applicable across all medicines and vaccines, with the fee amount determined by the validity of the GMP certificate. For foreign applicants, the GMP fee as per the gazette fee. This fee contributes to the assessment of manufacturing practices and quality control standards.

c) **Penalty Fee:** To encourage timely compliance with renewal timelines, a penalty fee will be introduced for those who fail to renew their medicines and vaccines within the prescribed period. The penalty fee will apply accordingly for overdue renewals.

9.1 **Penalty Provisions for Non-Compliance:**

Past the sixth month of no renewal, it is presumed that market withdrawal will be instituted against such medicines and vaccines.

10.0 RECORD KEEPING AND DOCUMENTATION:

To maintain transparency, accountability, and regulatory oversight, a robust record-keeping system will be established:

a) **Online Application System:** All renewal applications will be submitted and processed through the Pharmacy and Poisons Board's online system known as PRIMS. This digital platform ensures the secure and organized handling of renewal applications.

b) **Record Maintenance:** Comprehensive records of all renewal applications, evaluations, and decisions will be meticulously maintained within the PRIMS system. This includes detailed information about each product's renewal process.

c) **Meeting Minutes:** During the renewal process, minutes of meetings and discussions will be documented. These minutes serve as a valuable resource for tracking decisions, actions, and discussions related to the renewal of medicines and vaccines.

10.1 **Documentation Requirements:**

All documentation requirements for the renewal process will be in strict accordance with the guidelines outlined in the Renewal Guideline. These guidelines provide comprehensive instructions and standards for the documentation necessary to support the renewal applications.

11.0 CONTINUOUS IMPROVEMENT AND REVIEW:

A proactive approach to continuous improvement and review will be implemented, these will be as done as follows:

a) **Quarterly Review Meetings:** Regular quarterly review meetings will be conducted to assess the status of the renewal framework. These

meetings serve as opportunities to identify areas that require improvement and to address any emerging challenges promptly.

b) **Renewal Committee:** A dedicated Renewal Committee will be established to oversee and coordinate the renewal process. This committee will play a pivotal role in ensuring the process runs smoothly and aligns with regulatory objectives.

c) **Periodic Process Review:** There will be periodic reviews of the entire renewal process to evaluate its effectiveness and relevance. This review process allows for adjustments and enhancements as needed to maintain the highest standards of regulatory oversight.

d) **Market Withdrawal for Non-Renewals:** Beyond the sixth month of non-renewal, it will be assumed that market withdrawal procedures will be initiated for medicines and vaccines that have not undergone renewal. This proactive measure helps maintain the integrity and safety of the market.

12.0 REFERENCING:

1. South Africa Re-registration Framework
2. WHO GBT Tool
3. Cap 244 Law of Kenya

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