MINISTRY OF HEALTH

Pharmacy and Poisons Board

RENEWALS FRAMEWORK FOR MEDICNES AND VACCINES IN KENYA

December, 2023

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Table of Contents

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 authorization holder to further characterize the safety profile during post-marketing (pharmacovigilance activities), and explains the measures that are taken in order to prevent or minimize 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

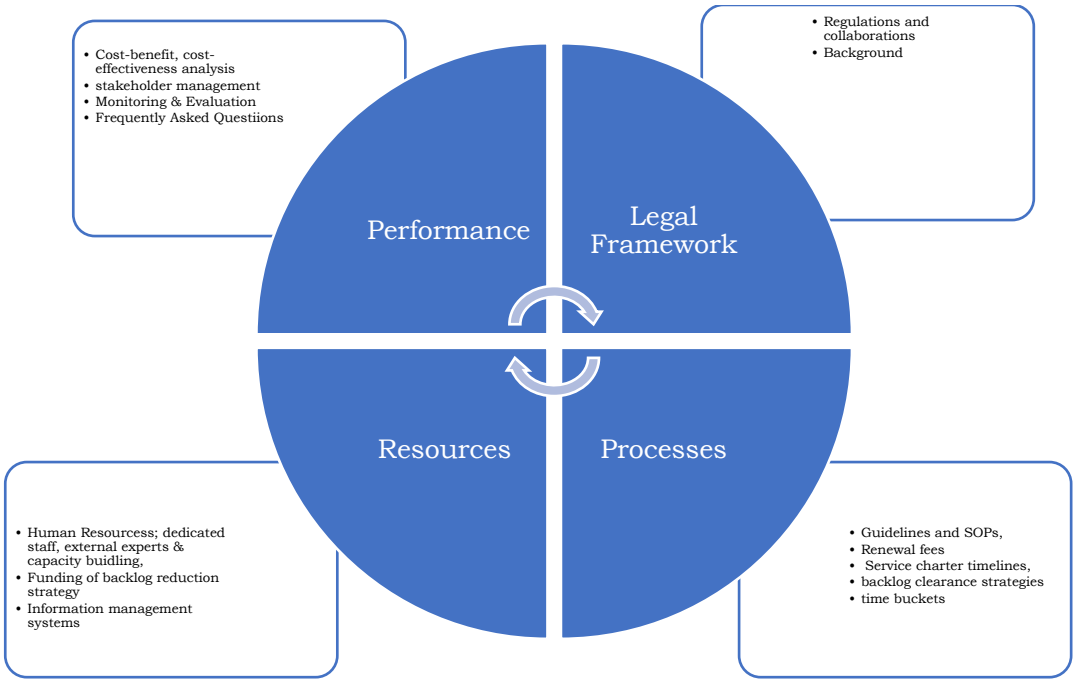
1.0 INTRODUCTION

1.1 Background

The 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 serves to provide the regulatory authority with cumulative changes/updates that may significantly impact on the quality, safety and efficacy of the product and ensuring that registered products continue to be safe, effective and of good quality for public use. It is the Board’s requirement that all registered medicines are retained annually and renewed after every five (5) years following issuance of marketing authorization.

In addition, renewals of medicines and vaccines has become a crucial requirement, driven by regulatory systems strengthening assessment initiative by the World Health Organization's Global Benchmarking Tool (WHO-GBT) of the Board in June 2022 in response, the Board 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 Renewals Framework



1.3 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 guidelines for Renewal of Medicines and Vaccines.

1.4 Scope

The five-year renewal cycle will begin with medicines and vaccines registered in 2019. The requirements will be applied both prospectively following a 5-year cycle and retrogressively to include products registered as early as from 1980 handled through the time buckets described herein. 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.

1.5 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.

1.6 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 in ensuring that medicines and vaccines are consistently of quality, safe and efficacious.

As part of regulatory systems strengthening, the Board is conforming to the WHO requirement of Subsection MA04.02: of the GBT tool "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 shall 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.

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 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.

2.2 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.

3.0 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:

3.1 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.

3.2 Renewal Fee:

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

3.3 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.

3.4 Retention Fee:

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

3.5 Variations and Changes:

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

3.6 Variation Fee:

A variation fee 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.

3.7 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.

3.8 Time buckets

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. In 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.

3.9 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 5 (five) 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.

Time Buckets:

Time Buckets	
Renewal Timeline	**Products Under Renewal (By Year of Registration)**
2024	2019 (Due)
2025	2020; 2013-2018
2026	2021; 2007 to 2012
2027	2022; 2000 to 2006
2028	2023; 1993 to 1999
2029	2024 1980 to 1992

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

4.0 PREPARING FOR RENEWAL

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:

4.1 Staffing and capacity building

It is envisaged that both the PPB and the MAH will assign responsibility of handling renewals applications and review to dedicated staff. For elimination

of backlog the PPB will adopt two strategies; building internal capacity and use of external experts.

4.2 Information management system

The online portal for renewal of registration of medicines and vaccines is part of the PRIMS. Applicants are required to commence the process for renewal by preparing the required documentation for submission as and when requested in line with the guidelines outlined in the Renewals Framework for Medicines and Vaccines in Kenya, 2023.

4.3 Stakeholder Sensitization Workshop:

To facilitate a clear understanding of the renewal process and guidelines, a periodic stakeholder consultative meeting will be conducted. This workshop will provide detailed insights into the regulatory requirements and managing stakeholder expectations.

4.4 Pilot Phase Implementation

The sensitization process will be initiated through a pilot phase in 2024. In the first phase, which aligns with the 2019-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.

4.5 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.

4.6 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:

a) Submitting the application: The completed renewal application form shall be submitted via the Pharmacy and Poisons Board online application portal, along with any required supporting documentation.
b) Clear instructions and user assistance in the form of a screening form shall be provided to guide applicants through the registration and renewal process to assist in avoidance of errors and ensure that the renewal process is completed correctly.
c) An application fees will be required to be made based on the prescribed gazette fee.
d) Timely renewal reminders will be sent to Market Authorization Holders (MAH) based on programmed time stamps to ensure that they do not miss the renewal deadline.
e) Details of contact persons will be provided and filled in into the application form to ensure that any questions or issues that arise during the renewal process can be addressed quickly and efficiently.
f) 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.
g) 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.
h) Turnaround time: The turnaround time for health product registration renewal shall be within 120 Working days.

4.7 Frequently Asked Questions (FAQ):

The Board shall supplement the stakeholder sensitization with periodic issues of FAQs and guidance documents to the industry to facilitate the process of renewals.

5.0 RENEWAL BACKLOG CLEARANCE STRATEGIES

PPB will employ several strategies to clear the backlog of marketing authorization applications:

5.1 Streamlined Data Management

a. Data Auditing: Conduct a comprehensive audit and data cleaning of the existing database to identify duplicate assessments (Manual vs electronic) and blank dossiers.
b. Data Validation: Improve on screening process during the dossier submission process to prevent the inclusion of blank or duplicate dossiers.

5.2 Streamlining and Eliminating Applications

Eliminating Old Applications: PPB will encourage industry stakeholders to 'opt-in' for applications submitted in 2018 or earlier, considering that these older applications may be out-of-date, duplicated, or of less commercial interest. Failure to 'opt-in' will result in the elimination of these older applications from the backlog.

5.2.1 Adoption of New Evaluation Models

PPB will explore new models of evaluation, such as focusing on specific sections of applications, especially for products with common API manufacturers and sources.

5.2.2 Segmenting and Prioritizing Applications

Applications will be segmented and prioritized based on public health need, locally manufactured, WHO listed Authorities & Stringent regulatory authorities.

5.2.3 Leveraging Reliance Pathways

PPB will establish reliance pathways to facilitate regulatory decisions, including recognition procedures, verification review procedures, and abridged review procedures. These pathways will optimize the use of assessments from stringent regulatory authorities.

5.2.4 Fast-Track submission and review of applications.

PPB will consider fast-track submissions and review.

5.2.5 Integration of New recruited Staff

a) Staff Roles and Responsibilities: Clearly define roles and responsibilities for new staff members within the assessment process.
b) Training and Orientation: Provide comprehensive training and orientation to new staff members, ensuring they are well-equipped to contribute effectively.
c) Collaborative Assessment: Encourage collaboration between experienced assessors and new staff to facilitate knowledge transfer and skill development.
d) Measuring and monitoring review timelines.

5.3 Funding for backlog reduction strategies;

The Backlog Reduction Strategy is expected to be a capital-intensive initiative and will require financial, human and time resources. To effectively manage the backlog and conform with service charter timelines, the Board will allocate specific budget to the process and in addition mobilize resources from development partners to supplement the Board's limited resources.

6.0 DOCUMENTATION REQUIREMENS 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 now integrated into an online submission model to ensure that their information is easily retrievable and accessible.

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

Medicines and vaccines registered using the electronic/online submission of Common Technical Document (CTD) format will be updated with the current information and changed will be trackable and updated information regarding the product made available over the product life cycle.

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 will be undertaking during the renewal period to help know what products still exist in the database and ensure 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.

7.2 Phased Approach for Backlog:

To effectively manage the renewal backlog, a phased approach will be implemented. This approach spans a period of five (5) 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 RENEWAL FEES AND PENALTIES

The fee structure for renewal is as follows:

a) **Renewal Fee:** The fee for both local and foreign applications will be as gazette in accordance with the gazette notice under Rule 9.

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.

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.

8.1 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.

9.0 RECORD KEEPING AND DOCUMENTATION:

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

a) **Online Application System and Record Maintenance:** All renewal applications will be submitted and processed through the Pharmacy

and Poisons Board's online PRIMS system. A Comprehensive record of all renewal applications, evaluations, and decisions will be meticulously maintained within the system.

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

9.1 Documentation Requirements:

All documentation requirements for the renewal process will be in strict accordance with the guidelines outlined in the Renewal Guideline.

10.0 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.

11.0 IMPORTANCE OF RENEWAL

a) 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.

b) 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.

c) 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.

d) 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.

e) 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.

f) 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.

g) 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.

h) 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.

i) 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.

j) 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.

k) Supporting Pharmacovigilance: Renewal can enhance pharmacovigilance efforts by requiring companies to submit updated safety data and ensuring that surveillance systems remain effective.

l) 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.

12.0 REVISION HISTORY

Revision No.	**Date**	**Author/Reviewer**	**Section(s) revised**	**Description of change**
Rev.1.	15/12/2023	Pharmacy and Poisons Board	1.2	Addition of Renewal Framework Section
	15/12/2023	Pharmacy and Poisons Board	3.9	Revision of Time Buckets
	15/12/2023	Pharmacy and Poisons Board	5	Addition of Renewal Backlog Clearance Strategies

13.0 REFERENCING:

1. Registration Renewals Implementation Framework South African Health Products Regulatory Authority Medicines, July 2023
2. World Health Organization Global Benchmarking Tool, 2018
3. The Pharmacy and Poisons Board Act, Cap 244 Laws of Kenya, amended 2019.

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