SAHPRA
South African
Health Products
Regulatory Authority

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

COMMUNICATION TO STAKEHOLDERS

Issue No.: HPA01-2022/23

7 November 2022

Medicines Registration Renewals Implementation Framework

Document History

First publication – Version 1	22 June 2022
Update – Version 2	07 November 2022

This document sets out the proposed approach that SAHPRA undertakes to implement the process of health product registration renewals ensuring a consistent approach to benefit all stakeholders to ensure quality, efficacious and safe products are available to the public. This will be a "living document" and will be updated as required. This communication is an interim document.

INTRODUCTION

To comply with the legal provisions as set out in by the Medicines and Related Substances Act (Act 101 of 1965), as amended – SAHPRA will be implementing a process to renew the validity of Health Products registrations.

Implementing this process will ensure that SAHPRA complies with the legal provisions but also it will enable the regulator to comply with the requirements as set out by the WHO in the Global Benchmarking Tool. It is SAHPRA's intention to attain Maturity Level 3 status and then to progress to Maturity Level 4 and be listed as a WHO Listed Authority. This step is of particular importance to the regulator and industry alike, as it may allow for Regulators from other regions to rely on SAHPRA's

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

regulatory decision for products registered, to facilitate shorter timelines for registrations in other markets.

The framework will cover the health product registration renewals for all medicines as governed by the Medicines and Related Substances Act (Act 101 of 1965), as amended.
The process that has been proposed in the guideline, is the product of research and consultations with the WHO, other regulatory authorities in the SADC Region, other WHO Maturity Level 3 African Regulators, and considering as well best practice from regulators in the Middle East & North Africa MENA region.

The relevant legal provisions that may be referenced can be found in the Medicines and Related Substance Act No. 101 of 1965, as amended.

- Section 2B (1) (c) provides for the periodic re-evaluation or re-assessment and monitoring of medicines, medical devices and IVDs.
- Section 15(6)(a)(b) provides for the Registration of medicines, medical devices or IVDs. It further states that any registration under this section may be made subject to such conditions as may be determined by the Authority; and shall in the case of medicines, be valid for a period of five years.
- Section 2B (1) (c) provides for the periodic re-evaluation or re-assessment and monitoring of medicines, medical devices and IVDs. There are benefit risk assessments performed throughout product life cycle, reviews of annual reports of registered medicines.

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

2. RENEWALS PROCESS IMPLEMENTATION

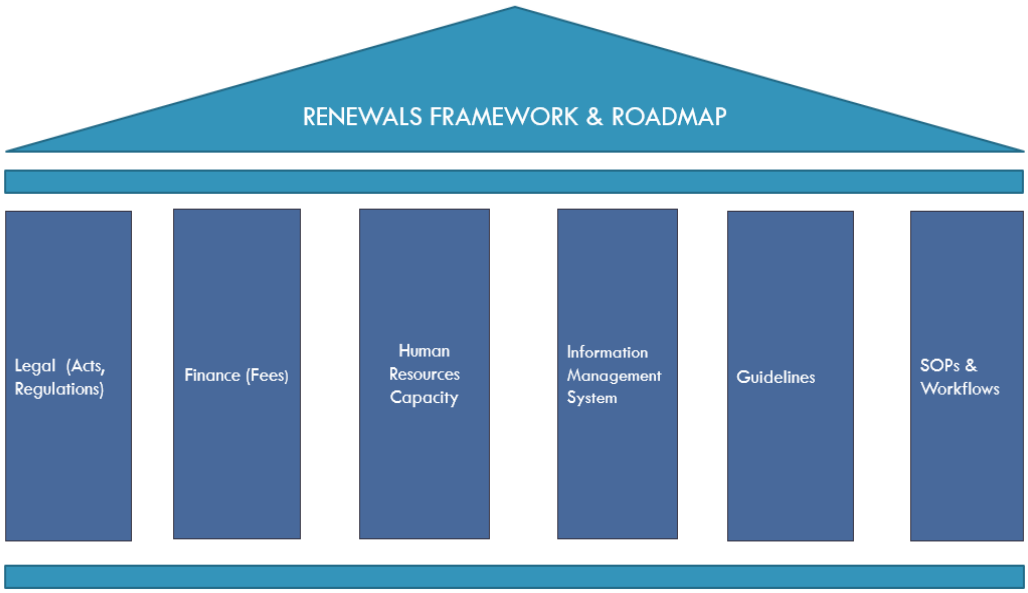
The renewal application must be submitted to SAHPRA six (6) months prior to the expiry of the health product registration and the required fees paid. The fees, as per the standard practice will be published in the government gazette, along with the other SAHPRA fees.

Failure to submit a complete and compliant renewal application may result in the registration then expiring and the product registration no longer being valid -- *If the product registration has expired the applicant must submit a new product registration application all together in line with the General Guideline for new health product registrations.*

Once a complete and compliant renewal application has been received, the product status will be updated to reflect "renewal in progress".

The guideline sets out the details of what information should be submitted for the products that will be due for renewal – including specific requirements for the older products (2017 and older).

Product submission roadmaps by applicant will be shared with applicants by the 14th of July 2022 – listing then the detail for which products are to be submitted for renewal in a specific quarter for the



specified year. To Note: in Year one of renewals there are only 46 applicants with 185 product lines

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

requiring renewal from registration year 2018. The first submissions are expected on or before the 15th of March 2023. Thereafter applicants will be required to complete submissions monthly as detailed on their schedule. Applicants can already now assess their own lists of registered products and identify the 2018 registration year items if they wish to start planning, but the formal roadmap schedules will then be shared as indicated, in July 2022

To note: each applicant's roadmap is customized – and has considered the number of product lines for which they have to do submissions for, to allow reasonable notice based on the time it takes to compile an eCTD submission – as confirmed by various industry colleagues, and due consideration has been given to this and has been incorporated in the timeline schedules.

SAHPRA will also be introducing a change to the current registration certificate – to allow for an expiry date to be added. This change will take effect in Q3 2022.

The renewals process will be implemented in line with the high-level roadmap as per Annexure B, in January 2023 – with applications for the Quarter expected on or before 20 March 2023, to allow adequate time for preparation of the information and seeking guidance from the regulator where it is required, as we embark on the new process.

3. GUIDELINES

A guideline for the submission of documentation for Renewal of Registration of Human & Veterinary Medicinal Products is attached for review and comments. The Guidelines comments form should be used.

4. ASSESSMENT PROCESS

The process **will primarily consist of a benefit/risk balance re-evaluation**, based on a consolidated version of the file and any relevant new information affecting the benefit/ risk for the product. Serious public health concerns should be addressed as part of the renewal process and the product will not be renewed if serious public health issues remain at the end of the

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

procedure or if an existing suspension on the product registration or marketing authorisation cannot be lifted. The process will also be varied with more comprehensive reviews for higher risk products. For products not previously registered, these will - in line with the joint approach between SAHPRA and BOMRA be considered for a full review and registration during this process. It is for this reason that these products are also included towards the very latter part of the schedule, as this will allow at least 8 years of planning and compiling the required information before these items are due for full eCTD submissions

A **separate** workstream will be put in place to process the renewal applications. An adequate number of resources will be put in place, based on the predictable volumes as set out in the schedule, to process the reviews according to the approved standard operating procedure, and the number of resources will be aligned over the course of the next few years as we scale up the volume of renewal applications to match the workload demands accordingly.

5. FEES FOR RENEWALS PROCESS

SAHPRA will charging a fee for applications to be renewed. The fees will be derived from a cost to serve analysis. The new fee structure will be shared with ITG for comments in August 2022. In October 2022 it will be published for public comment and then duly be published in the Government Gazette.

6. PILOT PHASE

A workshop will be arranged with industry to take them through the detail of the guideline on 14 July 2022. A Pilot Phase will be conducted in September through to October 2022. Specific products have already been identified – and they include a spread of products from a variety of registration years. These products and applicants have been selected in a joint exercise with the Registration team from BOMRA. SAHPRA and BOMRA have specifically looked at applications which then have been submitted to BOMRA for renewal – to ensure that it is possible for applicants to do a similar submission then to SAHPRA in mid-September 2022.

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

We will be conducting this renewals review as well as a joint exercise in September-October 2022 so both regulators can take learnings from this process and refine the approaches to align our standardised renewal practice principles.

During this Pilot process, we will identify any process improvements or further guidance notes that we can provide to industry to make the process robust and clarify criteria so it is easy to submit compliant applications.

7. RESPONSES TO SCHEDULES

Thank you very much for the responses to the schedules that we have been sending out. We appreciate the ongoing engagement and the questions we have received so far. By means of providing further clarity and also guidance we would like to confirm the following with regards to the communicated schedules:

1. For our current list of active products – we have taken all products and have plotted them over a 13 year period to try and spread the planning period and administrative burden across a reasonable time frame.
2. For the submissions of products then currently registered – and on this schedule – we have divided them into different years and quarters per year so we can receive the renewal submission for the relevant products in the **first month** of each of those identified quarters i.e if a product appears in PHASE 2 Q3 – we would want to receive the submission(s) in July 2024, if it was PHASE 1 Q2 – it would be April 2023.
3. Once the new registration certificate comes into effect at the end of October 2022 – there will be an expiry date on the new certificates – and for these products then registered with the new certificates from November 2022 – the expiry date minus 6 months – will be the your submission window in 5 years' time.
4. The SIAMED column is an internal vlookup reference marker – this data field that has bearing on industry's renewals and can be ignored by industry colleagues.
5. Regarding the fees for the renewals process , our Finance colleagues will engage with industry on the proposed renewal fee during October 2022.

SAHPRA
South African
Health Products
Regulatory Authority

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

6. Old Medcines not registered do not form part of the renewals process

7. No variations will be allowed during a renewals review, variations must please follow their normal submission processes.

8. The renewals process requirement is for a QIS and QOS – the SCoRE will not be required.

9. Renewals for Vetenary products can be submited as per the current CTD format

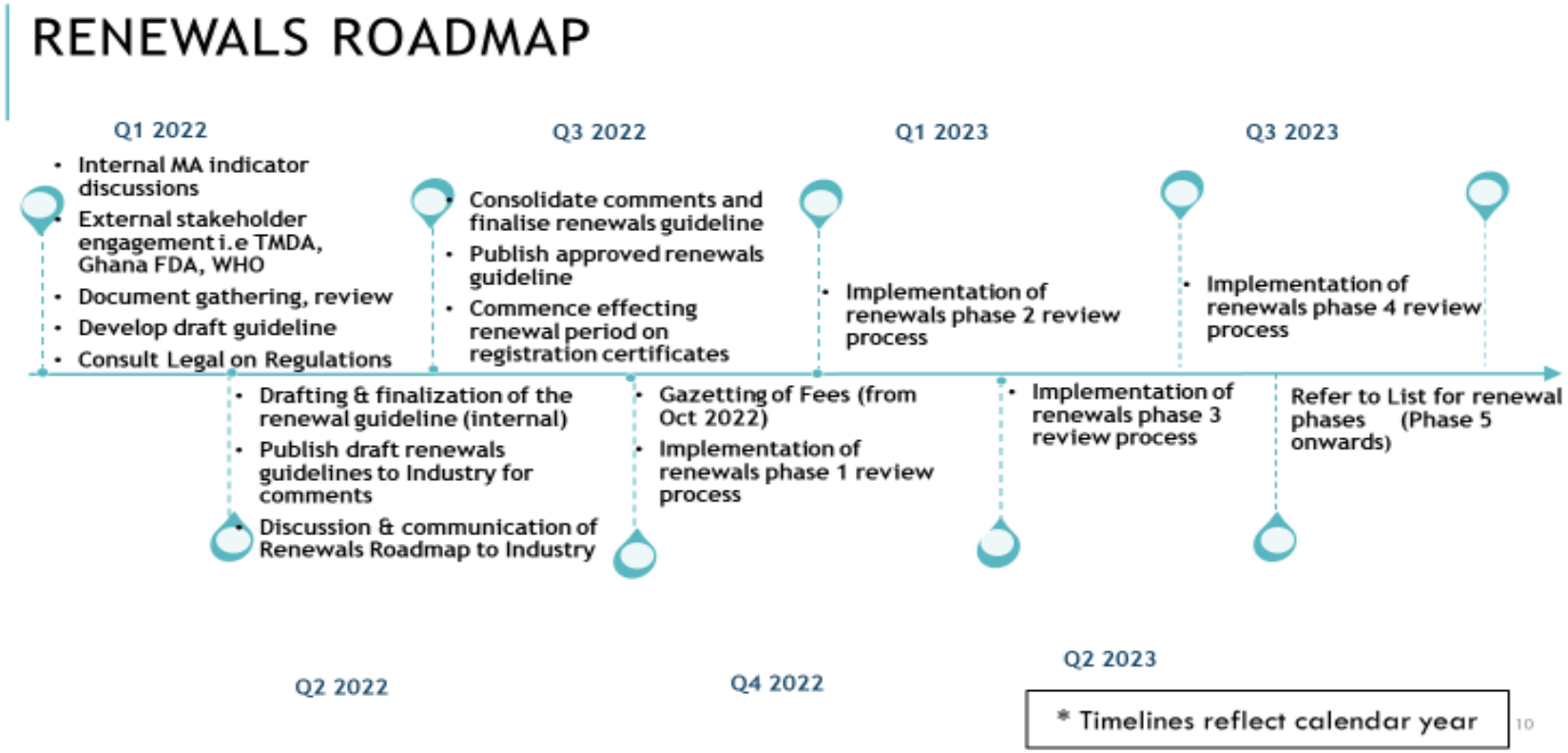
10. For Old registered Medicines and Products registered in the year 2017 and dating further back – a full eCTD baseline (0000) submission in line with the General Guidelines for registration will be required, which should be accompanied with sequence 0001 which contains the documents for the renewals process.

11. The practicality of the requirement to reflect all amendments made in the preceding 5 years by means of underlining on the Professional Information (PI)/Patient Information Leaflet (PIL), will be tested in the Renewals pilot. Depending on the outcome of the review process in the pilot this will allow us to look at the proposal of rather submitting a tabular summary instead.

SAHPRA
South African
Health Products
Regulatory Authority

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

ANNEXURE A



SAHPRA
South African Health Products Regulatory Authority

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

ANNEXURE B

	Time buckets									
	1969 to 1979	**1980 to 1989**	**1990 to 1999**	**2000 to 2009**	**2010 to 2017**	**2018**	**2019**	**2020**	**2021**	**2022**
No of Lines	744	1008	2317	3544	3282	185	205	867	1626	TBC

		Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10	Y11	Y12
	Renewal year due	***2023***	***2024***	***2025***	***2026***	***2027***	***2028***	***2029***	***2030***	***2031***	***2032***	***2033***	***2034***
1	*Registration years due for renewal*	2018	2019	2020	2021 & 2010-2017	2022 & 2010-2017	2023 renewals and new registrations(2023) & 2010-2017	2024 renewals and new registrations(2024) & 2000-2009	2025 renewals and new registrations(2025) & 2000-2009	2026 renewals and new registrations(2026) & 1980-1989	2027 renewals and new registrations(2027) & 1980-1989	2028 renewals and new registrations(2028) & 1990-1999	2029 renewals and new registrations(2029) & 1969-1979
2	No. of new registrations	new regs23	new regs24	new regs25	new regs26	new regs27	new regs28	new regs29	new regs30	new regs31	new regs32	new regs33	new regs34
3	*Older applications to be reviewed*				Initiate 1/3rd of 2010-2017 bucket	Initiate 1/3rd of 2010-2017 bucket	Initiate 1/3rd of 2010-2017 bucket	Initiate 1st half of 2000-2009 bucket	Initiate 2nd half of 2000 to 2009 bucket	Initiate first half 1980 to 1989	Initiate 2nd half 1980 to 1989	Initiate 1990 to 1999	Initiate 1969 to 1979
TOTAL	*No of Lines*	185	205	867	= 1626 + 1094	= new reg22 + 1094	=185 +new reg23 + 1094	= 205 + new reg24 + 1772	= 867 + new reg25 + 1772	=1626 + 1094 + new reg26 + 504	= new reg22 + 1094 + 504 + new reg27	=185+new reg23+1094+new reg28 + 2317	=205+ new reg24 +1181 +new reg29 + 744
		PHASE 1	PHASE 2	PHASE 3	PHASE 4	**PHASE 5**	**PHASE 6**	**PHASE 7**	**PHASE 8**	**PHASE 9**	**PHASE 10**	**PHASE 11**	**PHASE 12**
REFER TO INDIVIDUAL APPLICANT LIST FOR PRODUCTS RENEWALS TO BE SUBMITTED		*PHASE 1 Q1*	*PHASE 2 Q1*	*PHASE 3 Q1*	*PHASE 4 Q1*	*PHASE 5 Q1*	*PHASE 6 Q1*	*PHASE 7 Q1*	*PHASE 8 Q1*	*PHASE 9 Q1*	*PHASE 10 Q1*	*PHASE 11 Q1*	PHASE 12 Q1
		PHASE 1 Q2	*PHASE 2 Q2*	*PHASE 3 Q2*	*PHASE 4 Q2*	*PHASE 5 Q2*	*PHASE 6 Q2*	*PHASE 7 Q2*	*PHASE 8 Q2*	*PHASE 9 Q2*	*PHASE 10 Q2*	*PHASE 11 Q2*	PHASE 12 Q2
		PHASE 1 Q3	*PHASE 2 Q3*	*PHASE 3 Q3*	*PHASE 4 Q3*	*PHASE 5 Q3*	*PHASE 6 Q3*	*PHASE 7 Q3*	*PHASE 8 Q3*	*PHASE 9 Q3*	*PHASE 10 Q3*	*PHASE 11 Q3*	PHASE 12 Q3
		PHASE 1 Q4	*PHASE 2 Q4*	*PHASE 3 Q4*	*PHASE 4 Q4*	*PHASE 5 Q4*	*PHASE 6 Q4*	*PHASE 7 Q4*	*PHASE 8 Q4*	*PHASE 9 Q4*	*PHASE 10 Q4*	*PHASE 11 Q4*	PHASE 12 Q4

SAHPRA
South African
Health Products
Regulatory Authority

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

Dr Boitumelo Semete-Makokotlela
SAHPRA Chief Executive Officer (CEO)