South African Health Products
Regulatory Authority
Building A
Loftus Park
Arcadia
Pretoria

GUIDELINE ON HOW TO APPLY FOR AN AMENDMENT TO A LICENCE GRANTED BY SAHPRA FOR MANUFACTURING, IMPORTING OR EXPORTING, AND WHOLESALING MEDICINES AND SCHEDULED SUBSTANCES.

June 2022

This guideline is intended to provide recommendations to applicants wishing to submit an application for an amendment to their current licence to manufacture, import or export, and wholesale medicines or scheduled substances. It is not intended as an exclusive approach and should not be taken as a complete or authoritative statement of the law. SAHPRA reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine or scheduled substance in keeping with the knowledge current at the time of evaluation. SAHPRA is committed to ensure that all registered medicines or scheduled substances will be of the required quality, safety, and efficacy and that the manufacturer, importer or exporter, wholesaler and/or distributor complies with acceptable quality assurance principles, good manufacturing, good wholesaling, and good distributing practices as determined by SAHPRA. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.

The guidance in this Guidelines and the applicable application forms are available from the Office of the Chief Executive Officer of SAHPRA and the SAHPRA website www.sahpra.org.za.

Document History

Version	Implementation Date	Reason for amendment
Version 1	June 2022	First Publication released for implementation

BOITUMELO SEMETE-MAKOKOTLELA

CHIEF EXECUTIVE OFFICER

Contents

Table list

List of abbreviations and definitions

Table 1: List of Abbreviations

Act 53 of 1974	The Pharmacy Act 53 of 1974 as amended
Act 101 of 1965/Medicine Act	The Medicines and Related Substances Act, 1965(Act 101 of 1965) as amended
CEO	Chief Executive Officer
GDP	Good Distribution Practices
GMP	Good Manufacturing Practices
GWP	Good Wholesaling Practices
HCR	Holder of the Certificate of Registration
MD	Managing Director
SAHPRA	South African Health Products Regulatory Authority (also known as The Authority)
SMF	Site Master File
POP	Proof of Payment
SAPC	South African Pharmacy Council

Table 2: List of Definitions

Holder of a certificate of registration	means a person in whose name a registration certificate has been granted and who is responsible for all aspects of the medicine, including quality and safety and compliance with conditions of registration;
Importer and/or Exporter	(i) A manufacturer wherein the manufacturing is contracted out to a third-party manufacturer. The third-

	party manufacturer could be located within or beyond the borders of South Africa. (ii) Wherein the product is registered by SAHPRA. (iii) Wherein the scheduled substance is to be used in the manufacture of a SAHPRA registered product.
Manufacture	means all operations including purchasing of material, processing, production, packaging, releasing, storage and shipment of medicines and related substances in accordance with quality assurance and related controls.
Manufacturer	means a person manufacturing a medicine and includes a manufacturing pharmacy
Wholesaler	including a wholesale pharmacy means a person who holds, stores, delivers or purchases medicines or Scheduled substances from a manufacturer and sells them in terms of section 22H of the Act

1. Introduction

The South African Health Products Regulatory Authority (SAHPRA) regulates medicines and scheduled substances for human and animal use, in accordance with the provisions of the Medicines and Related Substances Act, 1965 (Act 101 of 1965) and the relevant Regulations made there under. (Hereafter referred to as the Medicines Act.)

Amongst other things, the Medicines Act provides for a system of licences, certificates and exemptions from the regulation and control of the manufacture, import, export, and wholesale of medicines and scheduled substances in South Africa. Legislation in respect of medicines and scheduled substances is in accordance with the provisions of the Medicines and Related Substances Act, 1965 (Act 101 of 1965). These medicines and scheduled substances must, unless exempt, be registered by SAHPRA, or must have an application number (regarded as “old Medicines”) and their manufacturer, importer, exporter, wholesaler and/or distributor must hold an appropriate licence. The manufacturer, importer, exporter,

wholesaler and/or distributor licence is required by Section 22C of the Medicines and Related Substances Act 101 of 1965 read together with Regulation 23 of the same Act 101 of 1965.

The manufacture, import and /or export, wholesale and/or distribute of veterinary medicines or scheduled substances for animal use, registered with the South African Health Products Regulatory Authority in terms of the provisions of the Medicines and Related Substances Act 101 of 1965 (Act 101 of 1965), is subject to the same legislation and the requirements are similar.

Any changes (amendments) to the Licence granted as per Section 22C (1) (b) of the Medicine Act to a manufacturer, importer, exporter, wholesaler and/or distributor of medicines and scheduled substances must be reported to the CEO of SAHPRA in writing within 30 days of such a change as per Regulation 23(9) of the Medicine Act. These amendments can only be implemented after the Licence Holder receives an approval from SAHPRA through the office of the CEO of SAHPRA.

2. Purpose

This guideline is intended to provide recommendations to applicants wishing to submit an application for an amendment to their current licence to manufacture, import or export, and wholesale medicines or scheduled substances.

3. Background

On 01 June 2017, the President of the Republic of South Africa signed into effect Amendment Act 72 of 2008 (and effectively therefore also Amendment Act 14 of 2015), which broadened the regulatory scope of the Medicines and Related Substances Act, 1965 (Act 101 of 1965; the "Act")

4. Scope

This document lays down guidelines for how to apply for an amendment to a licence granted by SAHPRA, for the Manufacturing, Importing, Exporting, Wholesaling and Distributing Medicines and Scheduled Substances. It applies equally to medicines and scheduled substances for human and for veterinary use as per Act 101 of 1965. and exclude applications for Complementary Medicines licenses (Category D medicines). Information relevant to the Complementary Medicines licensing can be accessed on the website: www.sahpra.org.za/e-services/complementary medicines licensing/

In this Guideline, the word "should" indicates requirements that are expected to apply unless shown to be inapplicable or replaced by an alternative demonstrated to provide at least an equivalent level of quality assurance, so that the safety, efficacy and quality of the medicine and scheduled substance is maintained at the same standard as per the requirements of its registration.

This guideline applies to all changes made to the Manufacturing, Importing, Exporting, and Wholesaling licences as granted by SAHPRA also known as the Authority.

5. Guiding Principles

5.1. Any facility involved with the manufacturing, importing, exporting, wholesaling, and distribution of medicines and/or scheduled substances is responsible for the effective, efficient, and safe handling of all the materials (both raw and packing materials), manufacturing processes, and storage and distribution conditions of such medicines and/or scheduled substances. The facility must ensure that the quality, safety, and efficacy of the medicine and/or scheduled substance is maintained at the same standard as per their registration requirements throughout the supply chain, and any changes to these requirements must be reported to SAHPRA.

5.2. Any amendments (changes) to the facility such as: address change, key personnel(as outlined in existing licence),manufacturing and wholesaling activities and conditions(general and site specific)provided for by the licence and the inspection resolution letter, name of the licence holder, medicines or scheduled substances manufactured, imported, exported, and wholesaled, must as per Regulation 23(7) of Act 101 of 1965 be reported to the CEO of SAHPRA through the submission of an application to the SAHPRA Licencing Unit. The application to include proof of payment of the current prescribed amended fee found on the SAHPRA website www.sahpra.org.za

5.3. As per the Regulation 23(8) of Act 101 of 1965, the Authority (SAHPRA) may following the evaluation of the application form and its supporting documents submitted by the Licence Holder requesting the amendment of their current licence, issue a new licence provided that:

a) The Authority is satisfied that the application complies with all the provisions of Act 101 of 1965 or any condition as determined by the Authority

b) Either-

i. the original licence is returned to the Authority; or

ii. an affidavit is submitted to the Authority stating that the original licence has been lost

c) All the applicable licence fees have been paid in full.

6. Who must apply for the amendment of their Licence granted by SAHPRA.

6.1. Any facility/company/individual who are holders of the following licences, which are current and issued by SAHPRA:

i. Licence to manufacture, import or export a medicine or scheduled substance

ii. Licence to import a medicine or scheduled substance

iii. Licence to export a medicine or scheduled substance

iv. Licence to act as a wholesaler of or distribute a medicine or scheduled substance.

7. Why should a Holder of a Licence granted by SAHPRA apply for an amendment of their license.

The Authority (SAHPRA) grants a licence to a facility, company, or an individual with conditions (which are general and/or site specific) based on Section 22C (1)(b) of Act 101 of 1965 read together with Regulation 23 of the same Act 101 of 1965.

Any changes (amendments) to these conditions of the Licence issued by SAHPRA must be reported to SAHPRA, by submitting to the Chief Executive Officer of SAHPRA an application, on a form obtainable from the Authority, accompanied by the prescribed fee, requesting the amendment of their current licence.

These amendments are classified as either Administrative or Technical.

A. Administrative details:

7.1 Administrative Amendments include but are not limited to the following;

- Change in the Responsible Pharmacist, Quality Assurance Head and/or Production Head.
- Change in the Natural Person who is responsible to SAHPRA as per Act 101 of 1965, e.g., the CEO/MD of the company.
- Faulty Licence, e.g., incorrect postal code or street number.
- Change in the Licence activity (Deletion only)

B. Technical details:

7.2 Technical Amendments include but are not limited to the following;

- Change of company name, i.e.: Importer and/ or Exporter (Holder of Certificate of Registration (HRC)); Manufacturer; Packer; Laboratory; Wholesaler
- Change of address of a Manufacturer, HCR (Importer/Exporter-who stores Medicines and /or Scheduled substances on site/facility), Testing Laboratory, Packer, and a Wholesaler.
- Change of Applicant (Importer and/or Exporter) HCR address, where no medicines and/or scheduled substances are stored at the site/facility.
- Addition of Activity by Manufacturer, Packaging (primary and secondary), Testing Laboratory, Materials handled or stored at the site.
- Addition of an Import and/or Export activity.
- Addition of manufacturing activity.
- Addition of a distributor activity.
- Addition of material to be handled as finished packed product (MANUFACTURER only).
- Addition of major equipment, technology and/or lines to the facility.
- Structural changes to the facility which directly affect product.

8. How to apply for an amendment of a Licence granted by SAHPRA.

8.1. The site(facility), company and/or individual holding a licence issued by SAHPRA, wishing to be applying to SAHPRA for the amendment of their current licence must submit the following documents;

8.1.1. A cover letter stating the reason(s) for the amendment application (or reasons for requesting an amendment to the current licence)

8.1.2. A completely filled licence application form with the declaration signed.

8.1.3. Proof of payment with the correct reference as per Annexure A - SAHPRA Fee Categorisation Guideline (see the SAHPRA website www.sahpra.org.za)

8.1.4. Latest Inspection resolution letter

8.1.5. A copy of the existing Licence being amended

8.1.6. CIPC/CIPRO/DTI CERTIFICATES OR DOCUMENTS proving ownership of the

business

8.1.7. NDOH PREMISES LICENCE

8.1.8. REGISTRATION AS RESPONSIBLE PHARMACIST

8.1.9. SAPC CERTIFICATE OF RECORDING OF A PHARMACY

8.1.10. SAPC CERTIFICATE OF RECORDING OF A PHARMACY OWNER

8.1.11. Copy of POP of the licence annual retention fee for all preceding years if licence is older than a year.

8.1.12. Product List with POP of annual retention fee.

8.2. A signed copy of the proposed SMF with a comprehensive history of changes (see the SAHPRA website www.sahpra.org.za for the guideline)

The applicant must submit all these documents as per the instruction from the website www.sahpra.org.za

or

https://www.sahpra.org.za/inspectorate-and-regulatory-compliance/

9. Inspections

9.1. The Program 3: Inspectorate and Regulatory Compliance carry out regular and repeated inspection of manufacturing, importing, exporting, and wholesaling sites in the Republic of South Africa. The Inspections enables the Inspectorate and the Regulatory Compliance Units to confirm that licence holders are complying with the conditions of their current licence, with the provisions of the Medicines Act, with Good Manufacturing Practice (GMP), with Good Wholesaling Practice (GWP) and Good Distribution Practice (GDP).

9.2. It is therefore the responsibility of the current licence holder to report to SAHPRA any changes (whether planned or not planned) to their licence conditions, for SAHPRA to evaluate these changes and their impact on quality, safety and efficacy of the medicine and/or schedule substance.

9.3. Amongst other things, Inspectors are empowered Section 28 of the Medicine Act to:

a) Enter any place or premises from which

- The holder of a licence to manufacture, import, export, and wholesale medicines and scheduled substances conducts business

- The holder of a certificate of registration of a medicine conducts business

b) Inspect the premises used in the manufacture, packing, testing, storage, and distribution of medicines and scheduled substances and inspect any documentation or records relating to the manufacture, packing, storage and distribution of these medicines and scheduled substances

c) Take samples of any medicine or schedule substance for the purpose of testing or analysis

d) Seize any book, record, documentation or medicine or scheduled substances.

It is required by legislation that licence holders shall make their premises available for inspection by the Inspectorate at any reasonable time.

9.4 Following an inspection, the Inspector prepares a report of his/her findings. A report is sent to the licence applicant or holder noting any deficiencies found and asking for proposals to remedy them. In the event of serious non-compliance with GMP, GWP or GDP, the report is referred to SAHPRA for formal action, which can include the refusal to amend the licence, suspension or revoking of a licence, or part of a licence as per Section 22E of the Medicine Act/Act 101 of 1965.

9.5 Where quality control testing is contracted to a third party, the testing site should also be made available for inspection and should also obtain a licence authorizing it to test medicines and/or scheduled substances.

9.6 Any amendments to the current licence conditions must firstly be authorized by SAHPRA before they can be implemented.

10. Fees Payable

10.1. The Medicines and Related Substances Act 101 of 1965 introduced provisions in terms of Section 35 (1) (xxxi) and (xxxii) read together with Section 35 (4) for the payment of fees for licences, certificates, and inspections. The current fees legislation for medicines and scheduled substances is contained in the Medicines Regulations as amended.

10.2. A schedule of the current fees is available from the Office of the Chief Executive Officer of SAHPRA or on the SAHPRA website at www.sahpra.org.za

10.3. When SAHPRA plans to make changes to the amount or frequency of fees, licence holders are consulted and given the opportunity to comment on the new fee proposals. Details of the new fees are published in the government gazette and on the South African Health Products Regulatory Authority's website at www.sahpra.org.za

10.4. The fees currently payable for the amendment of a licence are the following:

a) Licence amendment application

b) Licence issue

c) Performance of an inspection

d) Annual fees applicable for the retention of the licence as per regulation 24 of the Regulations to the Medicines Act.

11. Contacts

Refer to SAHPRA website: https://www.sahpra.org.za/key-contacts/ and

https://www.sahpra.org.za/inspectorate-and-regulatory-compliance/

12. Summary of Licence Amendment Requirements:

Table 3: Amending a License for Administrative Details

AMENDING A LICENCE FOR ADMINISTRATIVE DETAILS ONLY:		
CHANGE REQUIRED	**REQUIREMENTS**	**FEES**
CHANGE of the Responsible Pharmacist; Quality Assurance and / or Production Person	• New Application (with all the supporting documents included). • Copy of the Current Licence • Cover Letter-stating the reason(s) for the requested change.	See current SAHPRA gazetted fees
CHANGE in natural person responsible for compliance with Act 101 of 1965, e.g., CEO, Managing director	• New Application (with all the supporting documents included). • Copy of the Current Licence • Cover Letter from the Company-stating the reason(s) for the requested change.	See current SAHPRA gazetted fees
LICENCE CONTENT ERROR DUE TO THE APPLICANT, e.g., incorrect street address, postal code, name and/or surname of one of the key personnel, etc.	• New Application (with all the supporting documents) • Copy of the Current Licence • Cover Letter from the Company-highlighting the faulty part of the licence.	See current SAHPRA gazetted fees
CHANGE IN ACTIVITIES: **Deletion** of any Activity **Only**	• Cover Letter from the Company stating reason(s) for the requested deletion. • New Application (with all the supporting documents included). • Copy of the Current Licence	See current SAHPRA gazetted fees

Table 4: Amending the License for Technical Details

AMENDING THE LICENCE FOR TECHNICAL DETAILS ONLY:		
CHANGE REQUIRED	**REQUIREMENTS**	**FEES**
NAME change of the company i.e.: Importer, Exporter (Holder of Certificate of Registration (HRC)); Manufacturer; Packer; Laboratory; Wholesaler of the licence holder	• New Application (with all the supporting documents included). • Cover Letter from the company stating the reason(s) why the name is being changed. • Copy of the current Licence. • An Inspectorate approval is required prior to the approval of the name change.	See current SAHPRA gazetted fees.
Addition of a Distributor activity	• New Application (with all the supporting documents included). • Cover Letter from the Company stating the reason(s) why they request the addition of this activity onto their licence. • Copy of the Current Licence. • An Inspectorate approval is required prior to the granting/re-granting of the licence with the additional distributor activity included.	See current SAHPRA gazetted fees
CHANGE OF ADDRESS: • Manufacturer • Laboratory • Packer • Wholesaler • Importer/Exporter (HCR)Applicant	• New Application (with all the supporting documents included). • Cover Letter from the Company stating the reason(s) why the licence address is being changed. • Copy of the Current Licence. • An Inspectorate approval is required prior to the granting/re-granting of the licence with the new address.	See current SAHPRA gazetted fees.
CHANGE OF ADDRESS by HCR (Importer, Exporter) /(Applicant) **only who does not store or handle any medicines/scheduled substances at the site/facility.**	• New Application (with all the supporting documents included). • Copy of the Current Licence • Cover Letter-stating the reason(s) for the requested change	See current SAHPRA gazetted fees

	• An Inspectorate Approval is required prior to re-granting of the licence with the new address.	
ADDITION IN ACTIVITY: • Manufacturer • Packaging (Primary and Secondary) • Testing • Materials to be handled as: open product by manufacturer. **Packaging:** Addition of material to be handled as finished packed product **(MANUFACTURER only)**	• New Application (with all the supporting documents included). • Cover Letter from the Company stating the reason(s) why they request the addition of these activities to their licence. • Copy of the Current Licence. • An Inspectorate approval is required prior to the granting/re-granting of the licence with the additional activities included.	See current SAHPRA gazetted fees.
Addition of an Export & Import activity	• New Application (with all the supporting documents included). • Cover Letter from the Company stating the reason(s) why they request the addition of this activity onto their licence. • Copy of the Current Licence. • An Inspectorate approval is required prior to the granting/re-granting of the licence with the additional Import and/or Export activities included.	See current SAHPRA gazetted fees.
Addition of manufacturing activity	• New Application (with all the supporting documents included). • Cover Letter from the Company stating the reason(s) why they request the addition of this activity onto their licence. • Copy of the Current Licence. • An Inspectorate approval is required prior to the granting/re-granting of the licence with the additional manufacturing activity	See current SAHPRA gazetted fees

	included.	
Addition of major equipment, technology and/or lines to the facility.	• New Application (with all the supporting documents included). • Cover Letter from the Company stating the reason(s) why they request the addition of the major equipment, technology and/or lines into their facility. • All the validation protocols should be made available for evaluation by the Inspectorate. • Copy of the Current Licence. • An Inspectorate approval is required prior to the additional major equipment, technology and/or lines being used for production in the licensed facility.	See current SAHPRA gazetted fees.
Structural changes to the facility which directly affect the product.	• New application (with all the supporting documents included). • Cover Letter from the Company stating the reason(s) why they request the approval of structural changes to their facility. • All the new facility's floor plans, validation protocols and any other document related to these changes, should be made available for evaluation by the Inspectorate. • Copy of the Current Licence. • An Inspectorate approval is required prior to the use of these new changed structure for production in the licensed facility.	See current SAHPRA gazetted fees.

13. References

Related Legislation

- The Pharmacy Act 53 of 1974 as amended
- Medicines and Related Substances Act 101 of 1965 as amended