IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
July 2020 Vol.:18, Issue:4

Regulatory Harmonisation in South Africa: A Critical Overview

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An official Publication of Human Journals
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Submission: 20 June 2020
Accepted: 27 June 2020
Published: 30 July 2020

Keywords: SAHPRA, EMA, SCORE, BTIF and RRA

ABSTRACT

The purpose of this article is to present a concise overview of changes in the variation of South African Health Products Regulatory Authority (SAHPRA) and its adoption of variation policies from the European Medicines Agency (EMA). Along with which we have also discussed the exclusions, additions of variation guidelines in different aspects. In this article, along with variation changes by SAHPRA, it also includes different reliance pathways adopted and also about the difference in document and data requirements by the authority for reliance based evaluations and principles involved in it. Latest documents to be involved as per Reliance Models have also been discussed e.g. Summary of Critical Regulatory Elements (Score) Document along with Bioequivalence Trial Information Form, Biowaiver and Bio study forms which are also mandatory for New Drug Submissions and Resubmissions along the details of data to be submitted to the agency and the pathways of registration an applicant can avail, categories a drug can be registered by SAHPRA. These forms include details about the drug summary and different studies carried out on the drug. It also includes a list of SAHPRA's recognized regulatory authorities (RRA). Finally, the article includes harmonization by SAHPRA in its variations guidelines and the adoption of different policies wherever required.

INTRODUCTION

Regulatory guidelines are regularly updating as a result of scientific developments and harmonization of their requirements of regional and international regulatory authorities. This article deals with the process of medicine registration in South Africa and its transformation in regulations involved in medicine registration. This article usually deals with the respect to South African regulations, which is mandated by the provisions of Medicines and Related Substances Control Act 101 of 1965 and guidelines published thereafter.

South African Health Products Regulatory Authority (SAHPRA) is a section 3A public entity that was formed by the South African government to oversee the regulation of health products which includes medicines, medical devices, in-vitro diagnostics devices and also radiation-emitting products. SAHPRA replaces the Medicines Control Council (MCC) as well as the Directorate of Radiation Control (DRC). It is usually responsible for monitoring, evaluating, regulating, investigation, inspection, registration, and review the matter to the usage of all health products in South Africa. They are also responsible for the control of human and veterinary medicines, scheduled substances, clinical trials and related matters.[1]

SAHPRA is a statutory body appointed by the Ministry of Health and it contains 11 active expert committees which comprise of Biological medicines, Clinical Trials, Complementary Medicines, GxP, Legal, Medical Devices, Names & Scheduling, Pharmaceutical & Analytical, Pharmacovigilance and Veterinary Clinical Committees.

South African Health Products Regulatory Authority (SAHPRA) has decided to harmonize certain SAHPRA medicine policies and procedures with those of the European Medicines Agency (EMA)[2]. These in turn are aligned to the framework of the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) as well as the International Co-operation on Harmonisation of Technical Requirements for Registration of Veterinary Medicines (VICH). By doing so, SAHPRA will reflect global best practices in terms of the safety, quality, and efficacy of health product regulation.

The different adaptations and adoptions involved in SAHPRA's regulatory system are enlisted below as follows:-

Amendments/Variations

Amendments to the registration dossier are necessary to maintain the safety, quality, and efficacy of a medicine and to ensure compliance with current technical requirements, to adhere to administrative aspects, to keep abreast of scientific progress, or to reflect new therapeutic indications/warnings or other safety matters.

It is, therefore, the objective of the SAHPRA to process, as quickly as possible, amendment applications made by the:

- Holder of the certificate of registration (HCR) to registered medicines
- Applicant of old medicines
- Proposed holder of the registration certificate (PHCR) / Applicant in response to committee recommendations

Amendments were classified during the earlier regime were classified as:

- **Type A** - Amendments that may be implemented without the intervention of or prior notification to Council.
- **Type B** - Amendments that require prior notification.
- **Type C** - Amendments that require prior approval.
- **Type D** - Amendments that should be considered new applications.

In the recent past from July 2019, SAHPRA has adopted the EU variation classification guidelines for orthodox human and veterinary medicines in full. With the full details (including the associated exceptions) published in the Variations Addendum for Human and Veterinary Medicines [2.08]. This includes information on the treatment of former Type C applications that have been re-classified as Type IA, Type IAIN and Type IB applications, submitted before the implementation date of the addendum. The fundamental principle for retrospective implementation of this guideline is that the evaluation period (e.g., 30 calendar days for Type IB) commenced on the date the application was initially submitted to SAHPRA. The implication is that many re-classified Type I applications will thus be deemed

immediately implementable and require only a notification to be provided to SAHPRA through the Digital Variations Portal for our records.

Variations as per EMA

A variation is a change to the terms of a marketing authorization. This section guides marketing authorization holders on the regulatory requirements and procedures for the different types of variations**.**

Variations are also any changes done to the product & hence to a product dossier in terms of P&A, labeling, clinical or pharmacovigilance system amounts for a variation.

The variations classified in EMA are as follows

- Minor Variations – Type IA, Type IA $_{IN,}$ Type IB
- Major Variations – Type II
- Extensions - New application

Type IA

- These changes have only a minimal or no impact on quality, safety and efficacy of the product and are also known as IA_{AN} = Notify change(s) within 12 months (‘Annual Report’).
- Type IA variations are generally expressed as “do and tell” i.e. in this case the applicant implements the change and then notifies the authority annually.
- If the implementation duration passes around 12 months or more without a variation being filed, a default Type IB should be submitted. This makes the application to get processed within 30 days.

Type IA $_{IN}$

- It is defined as a subtype of Type IA and comes under the category of “do and tell”.
- But the difference here is it obliges for “Immediate notification” i.e. notify the change before implementation to the authority within 15 days of the change being implemented.

Type IB

➢ This type of variation has minimal to moderate impact on the product's quality and comes under the category of "Tell, Wait and Do "procedure.

➢ The applicant submits, including all required supporting data, and wait for agency approval before implementing the changes. The process follows a defined assessment period of 30 days, but with agency questions, it can often take up to 90 days.

Type II

➢ These variations are termed as major and have a major, significant impact on the quality, safety, and efficacy of the product.

➢ It requires considerable supporting documentation and must be assessed and signed off by a qualified expert in the respective field.

➢ The process follows a defined assessment period of 60 days default timetable;

30 days for urgent variations and 90 days for changes / new indication. Implement the changes after 30 days of decision from authority.

Table No. 1: Comparison of amendments/variations of RSA and the European Union

South Africa	European Union
1. **Type A**: Amendments that do not require prior approval and that may be implemented without prior notification ▪ At any point when an amendment application is submitted for a product, all Type A amendments about the product should also be included.	1. **Type IA / IAIN: Type IA** procedures are classed 'do-and-tell' & or 'tell & do' i.e. implement the change before notification. ▪ Submit the application within 12 months of the non-immediate notification change being implemented ▪ Submit the application within 2 weeks of the immediate notification change being implemented.
2. Type B – Amendments that do require notification before implementation and shall be forwarded within 30 days to the office	2. **Type IB**: Submit the application and wait for a period of 30 days to ensure that the notification is deemed acceptable by the relevant authorities before implementing the change ("Tell, Wait and Do" procedure).
3. Type C –These require prior approval before implementation and Variations having a major impact on the product comes under this category. No conditions are required to be met for this type. **Inspectorate;** Amendments related to changes with respect to Manufacturer/Packer/FPRC/FPRR	**3. Type II –**These variations are more complex and have a significant impact on product quality. As a general rule, for major variations, there is a 60day evaluation period and 30,60 or 120 days to assess the application depending on the urgency or complexity
4. **Type D** -Amendments that are considered new applications ▪ Change in the API to a different API ▪ Inclusion or removal of an API(s) from a multi-component product unless specifically required by Council ▪ A change in the route of administration ▪ Change in the dosage form including, change from an immediate release product to modified-release dosage form or vice versa and change form liquid to powder for reconstitution or vice versa	4. Extensions -Although extensions are still considered a type of variation, their impact on a product is so significant that you will need to follow the application process to apply for a new MA. • changes to the active substance(s), including the salt/ester, isomer or biological active substance. • changes to strength, pharmaceutical form or route of administration

Variation Transformations in the newly adopted EU guidelines

SAHPRA will adopt the EU variation classification guidelines for human and veterinary medicines in full. This yields ongoing benefits as any updates to the EU guidelines will simultaneously be updates for SAHPRA. However, there will be specific exceptions for SAHPRA including:

- **Alterations**: EU codes/procedures adopted by SAHPRA with an adjustment for implementation in South Africa

- **Exclusions**: EU codes/procedures that will not be adopted by SAHPRA

- **Additions**: Additional codes created by SAHPRA

Examples for Alterations, Exclusions and Additions are given below:

Table No. 2: Examples for Alterations, Exclusions, and Additions

4.3.1	**Clarification**		
EMA/SAHPRA code	B.I.b.1a – B.I.b.1i	**EMA/SAHPRA classification**	Type IAIN (a); Type IA (b, c, d); Type IB (h, i); Type II (e, f, g)
Code description	Change in the specification parameters and/or limits of an active substance, starting material/intermediate/reagent used in the manufacturing process of the active substance		
Details	When changes to specifications parameters and/or limits result from adoption of a new monograph or a monograph from a different pharmacopeia, the variations codes in B.I.b.1 would also apply.		

4.3.2	**Exception Type**	**Alteration**	**EMA Code**	B.I.b.1i
EMA/SAHPRA classification	Type IB			
Code description	Change in the specification parameters and/or limits of an active substance, starting material/intermediate/reagent used in the manufacturing process of the active substance			
Details	Newly adopted monographs do not need to be from the European Pharmacopoeia or the national pharmacopeia of a European Union member state. SAHPRA will be accepting monographs from all Recognised Regulatory Authorities as stipulated in the General Information and Quality and Bioequivalence guidelines			

4.3.3	Exception Type	Alteration	EMA Code	B.II.b.1a, b, e, f
EMA/SAHPRA classification	Type IAIN (a, b); Type IB (e, f)			
Code description	Replacement or addition of a FPP manufacturing site for part or all of the manufacturing process of the finished product			
Details	For a site to be deemed GMP compliant: • SAHPRA requires that conditions 2, 4, 5 and the revised condition 1 (revision found below) be fulfilled in order for sites indicated in B.II.b.1 a, b, e and f to be deemed to be GMP compliant • Applicants are to provide the revised version of document 1 (revision found below) Please note the revision to condition 1: Satisfactory inspection in the last 3 years must have been conducted by a member of PIC/S or a country with a GMP MRA between said country's regulatory authority and SAHPRA Please note the revision to document 1: Proof that the proposed site is appropriately authorized for the pharmaceutical form of the product concerned. Applicants are to submit a certificate of GMP compliance or a manufacturing license issued within the last 3 years by SAHPRA or an authority in which a GMP MRA with SAHPRA exists (i.e., a PIC/S member state, Zazibona work-sharing agreement or WHO PQ).			

4.3.4	Exception Type	Alteration	EMA Code	B.I.b.1i
EMA/SAHPRA classification	Type IA			
Code description	Change in test procedure for the finished product			
Details	The monograph should be compliant with a monograph from one of SAHPRA's Recognised Regulatory Authorities as stipulated in the General Information and Quality and Bioequivalence guidelines.			

4.3.4	Exception Type	Alteration	EMA Code	A.2.b
EMA classification	Type IB		SAHPRA classification	Type II
Code description	Change in the proprietary name of the authorized medicine			
Details	Elevating a change in the product name of an authorized product to a high-risk variation to ensure that any changes are in line with current naming and scheduling policies			

4.3.4	Exception Type	Alteration	EMA Code	A.2.b
EMA classification	Type IB		SAHPRA classification	Type II
Code description	Change in the proprietary name of the authorized medicine			
Details	Elevating a change in the product name of an authorized product to a high-risk variation to ensure that any changes are in line with current naming and scheduling policies			

4.3.4	Exception Type	Addition	EMA Code	A.0.1
EMA classification	NA		SAHPRA classification	Type II
Code description	Application for a Transfer of Holder of Certificate of Registration (ToHCR) for a registered medicine			
Details	New code introduced allowing applicants to effect changes in the Holder of Certificate of Registration (i.e. change in product ownership). Note that ToHCRs do not apply for medicines that have yet to be registered. SAHPRA will issue separate guidance for a Transfer of Applicancy (ToA) of an unregistered medicine.			

Names and scheduling

To facilitate a smooth transition to the EU variation classification guidelines, SAHPRA has clarified the interpretation of selected EU codes. These are termed ‘clarifications.’ Note that clarified codes are still adopted by SAHPRA in full.

This guideline details the *exceptions* to the adoption and must be read in conjunction with the EU variation classification guidelines. Any guidance in the EU variation classification guidelines which is neither altered nor excluded in this guideline is implicitly adopted in full by SAHPRA.

But there is no need to submit additional data based on newer EU requirements and for its outstanding variations that were already submitted to the authority. Applicants will just have to reclassify and notify SAHPRA of the nature of implemented Type IA and IB variations through an online portal.

Any recently adopted data requirements will come to effect only after 6 months after the implementation date of this addendum. But the applicant can choose to comply with newer data requirements before the 6 month transition period has lapsed.

SAHPRA will adopt/follow the same timelines as the EU for the implementation of any future changes to the EU variation classification guidelines (e.g., if the EU implements a 3-month transition period associated with a new requirement, the same timelines will apply in South Africa).

To facilitate a smooth transition to the EU variation classification guidelines, SAHPRA has clarified the interpretation of selected EU codes. These are termed 'clarifications.' Note that clarified codes are still adopted by SAHPRA in full.

Documentation and Data Requirements

In this first step towards harmonization, not all of SAHPRA's directorates will fully adopt the documentation/data submission requirements provided in the EMA variation classification guidelines. This section outlines the associated exceptions and clarifications for selected directorates. SAHPRA implicitly adopts the document requirements stipulated in the EU variations classification guideline in full where no mention is made of any exceptions in this addendum/guideline.

General

Any reference to the "variation application form" in the EU guidelines should be read as the SAHPRA application form (available on SAHPRA's website) and amendments schedule (see appendix).

Introduction to reliance-based evaluation

A ME&R evaluation will follow one of the following review pathways:

a) Full review

b) Abridged review

c) Verified review

d) Recognition

Review pathways (b), (c), and (d) represent reliance-based evaluations. The World Health Organisation defines reliance as "the act whereby the regulatory authority in one jurisdiction may take into account and give significant weight to – i.e. totally or partially rely upon – evaluations performed by another regulatory authority or trusted institution in reaching its own decision. The relying authority remains responsible and accountable for decisions taken, even when it relies on the decisions and information of others."

Definitions of review pathways

5.4.1 Full review

A full review involves a thorough review of all aspects of the dossier, including:

- Module 1: Regional administrative data (as required)
- Module 2: Relevant summaries
- Module 3: Quality data
- Module 5: Efficacy data (for generic medicines)

All applications for products/variations that have not been registered/approved by an RRA, or that lack sufficient reliance documentation, will be considered for a full review. To reiterate, both new registrations and Type IB and Type II variations, for NCEs and generics, which meet these criteria will be considered for a full review.

5.4.2 Abridged review[3]

An abridged review is a reliance-based review comprising:

- Validation by SAHPRA to ensure that the product application submitted for registration by SAHPRA is the same as the product registered by the specified RRA.

- Evaluation of Module 1: Regional administrative information (as required)

- Evaluation of specific aspects of the dossier, depending on the type of application submitted.

The abridged review process does not involve an abbreviated application – all data and information required for a full review should be submitted, i.e. the full CTD module structure, as well as the SCoRE document. Evaluators may still wish to review data in the dossier as required.

An abridged review applies to the following types of applications:

i. For a new registration application for a generic medicine already registered by an RRA.

ii. For a new registration for a WHO PQ product:

- Applicants are required to follow SAHPRA's process for the WHO Collaborative Registration Procedure.

iii. Backlog-specific: For a new registration application for a generic or NCE medicine that has received prior P&A Committee approval, where any information relevant to P&A Committee approval has been updated since approval.

iv. For a Type II variation where the variation applied for has already been approved by an RRA.

5.4.3 Verified review[4]

A verified review is a reliance-based review comprising:

- Validation by SAHPRA to ensure that the product application submitted for registration by SAHPRA is the same as the product registered by the specified RRA.

- Evaluation of Module 1: Regional administrative information (as required)

The verified review process does not involve an abbreviated application – all data and information required for a full review should be submitted, i.e. the full CTD module structure, as well as the SCoRE document. Evaluators may still wish to review data in the dossier as required.

A verified review applies to the following types of applications:

i. For a new registration application for an NCE medicine already registered by an RRA.

ii. Backlog-specific: For a new registration application for a generic or NCE medicine that has received prior P&A Committee approval, where Module 1, 2 or 3 has not been updated since approval (i.e. the information relevant to the prior P&A Committee approval has not changed).

iii. For a Type IB variation where the variation applied for has already been approved by an RRA.

5.4.4 Recognition

SAHPRA is currently in the process of negotiating recognition agreements with RRAs. Once such an agreement is in place, SAHPRA will publish a framework for the practical implementation thereof. The guiding principle is that applications approved by RRAs with which SAHPRA shares a recognition agreement may not need to be evaluated separately by SAHPRA. Please note that this is not to be confused with collaborative / work-sharing procedures, e.g. Zazibona.

Documentation required for reliance-based evaluation

To qualify for a reliance-based review, an applicant needs to submit additional documentation to the documentation required for a full review.

Table No. 3: Documentation required for reliance-based evaluation

Document required	**Applicable types of applications**
• Completed abridged review template	5.4.2 i, ii
• Completed verified review template	5.4.3 i
• Full, unredacted assessment/evaluation reports from the RRA where the product is registered, **or** • If the applicant cannot obtain full, unredacted assessment/evaluation reports from the RRA where the product is registered, the Letter of access (Appendix in the General Information Guideline – 2.01) must be completed, and • Details of the outcomes of the application in all jurisdictions where it has been submitted, and • Foreign registration certificate(s), and • SmPC, a copy of the patient information leaflet (PIL) and label of the product that has been registered by the RRA, and • If available: initial scientific assessments, regulatory correspondence with the sponsor/applicant, follow-up assessments, and any other documentation from the RRA related to the final registration decision, and • If available and where applicable: risk management plans and on-site inspection reports (or equivalent), for example, GCP / GRP. Does not include the data package filed with the RRA	5.4.2 i, iv 5.4.3 i, iii
• Letter of approval from the RRA	5.4.2 iv 5.4.3 iii
• Declaration: Sameness (Appendix 2)	5.4.2 i, ii 5.4.3 i
• Declaration: Previous P&A Committee approval (Appendix 3)	5.4.2 iii 5.4.3 ii

Additional documentation requirements for the various types of applications may be stipulated in other sections of this guideline or other guidelines.

Additional documentation requirements for WHO PQ products are detailed in SAHPRA's process for the WHO Collaborative Registration Procedure.

Full, unredacted assessment/evaluation reports

- Please note that if the full, unredacted assessment/evaluation reports from the RRA where the product is registered are in a language that is not English, certified translated versions need to be provided as per SAHPRA guidelines.

- Please note that full, unredacted assessment/evaluation reports from the RRA where the product is registered should at least include safety, efficacy, and quality report(s) prepared by the RRA upon which the registration decision for the health product was based.

- If full, unredacted assessment/evaluation reports from the RRA are not provided by the applicant, SAHPRA may contact the RRA to obtain them, provided the Letter of access (Appendix in the General Information Guideline) has been provided. However, SAHPRA does not take responsibility for guaranteeing the obtainment of these reports. If the reports are not obtained, the application in question will most likely default to a full review, extending evaluation time.

SAHPRA's recognized regulatory authorities

To qualify for a reliance evaluation pathway, a product being applied for must be registered by one or more of the recognized regulatory authorities (RRAs) with which SAHPRA aligns itself. SAHPRA will leverage evaluation efforts done by RRAs to make its evaluation process more efficient and enhance market access. SAHPRA's current RRAs include:

- European Medicines Agency Centralised Procedure (EMA CP)

- European Medicines Agency Decentralised Procedure (EMA DCP) (no restrictions on which member state acts as the reference member state)

- Health Canada

- Medicines and Health Products Regulatory Agency, UK (MHRA)

- Ministry of Health, Labour and Welfare (MHLW), Japan

- Swiss Agency for Therapeutic Products (Swiss medic)

- Therapeutic Goods Administration, Australia (TGA)

- US Food and Drug Administration (US FDA)

Two additional procedures can be used for reliance / collaborative review, which are not strictly regulatory authorities:

- World Health Organisation Prequalification (WHO PQ)

- Zazibona collaborative procedure

Principles of reliance-based evaluation

The reliance-based evaluation will be based on the following principles:

- Reliance applies to both new registration and variation applications (Type IB and Type II).

- Reliance for Clinical and ME&R is applied independently, i.e. the review types selected by the units could differ based on unit-specific document requirements and the availability thereof.

- The application submitted for registration by SAHPRA should be the same as the most updated product on record at the RRA, i.e. all approved variations for the RRA's registered product should be incorporated in the application submitted for registration by SAHPRA. Pending variations with the RRA should not be included in the application submitted to SAHPRA for the application to qualify for reliance.

- All decisions regarding final evaluation pathway (i.e. full review or reliance-based review), as well as the extent of reliance on the RRA's evaluation of the product being applied for, are at the discretion of SAHPRA, based on the documents (and quality thereof) available for reliance-based evaluation.

- Any decisions regarding approval and final registration will be made by SAHPRA, in consideration of multiple factors including an RRA registration.

Full, unredacted assessment/evaluation reports

- Please note that if the full, unredacted assessment/evaluation reports from the RRA where the product is registered are in a language that is not English, certified translated versions need to be provided as per SAHPRA guidelines.

- Please note that full, unredacted assessment/evaluation reports from the RRA where the product is registered should at least include safety, efficacy, and quality report(s) prepared by the RRA upon which the registration decision for the health product was based.

- If full, unredacted assessment/evaluation reports from the RRA are not provided by the applicant, SAHPRA may contact the RRA to obtain them, provided the Letter of access (Appendix in the General Information Guideline) has been provided. However, SAHPRA does not take responsibility for guaranteeing the obtainment of these reports. If the reports are not obtained, the application in question will most likely default to a full review, extending evaluation time.

SUMMARY OF CRITICAL REGULATORY ELEMENTS (SCoRE) DOCUMENT[5]

- The Summary of Critical Regulatory Elements (SCoRE) document is required for all new registration applications, to facilitate more rapid evaluation by SAHPRA, and should be submitted with new registration application at the time of filing.

- For new registrations with a SCoRE document, a revised SCoRE will be required for each approved variation, to track the product lifecycle. For registered products where no SCoRE was submitted with the initial new registration application, a SCoRE will not be required for subsequent variation applications.

- When updating a SCoRE for a variation, the SCoRE document should be completed in its entirety (regardless of the proposed change), it should include information on all strengths, with any changes highlighted in yellow and it should be provided at the time of filing.

- It is to be noted that the SCoRE does not replace the Quality Overall Summary (QOS), nor does it replace the requirements outlined in the relevant guideline documents.

- The font used in the main text must be Arial, size 11.

- Hyperlinking or referencing sections in the QOS or other sections of the dossier is not acceptable; information needs to be summarised in the SCoRE.

- For dossiers in old formats (MBR, MRF) the applicant can request an exemption for sections not evaluated previously by stating “exemption” in the relevant section(s).

Bio study and Biowaiver review forms

If a Bio study has been included in the application, please review and complete the Bioequivalence Trial Information Form (BTIF) template [6.32].

For circumstances where a biowaiver is submitted (no bio study or bio study was done on a different product strength), please review and complete the following:

- IPRP template (for a BCS-based biowaiver)
- WHO template (for an additional strength biowaiver)

For the biowaiver templates, as well as additional information, please refer to the Quality and Bioequivalence Guideline [2.02].The location of where these documents should be placed in the dossier is indicated in the validation templates [6.16] and [6.30].

Extension applications

SAHPRA will adopt the EU classification of extension applications[6] for human and veterinary medicines, outlined in Annex I of the EU variations regulation (EC Regulation No. 1234/2008). These applications fundamentally alter the terms of the initial registration, and thus cannot be evaluated according to a variations procedure. Extension applications will typically be accompanied by a new registration certificate.

In terms of procedure, extension applications will be treated as new registrations by SAHPRA. Note the following exceptions in terms of documentation requirements:

- Data submitted in support of such applications should be limited to the extension (i.e. there is no need to submit data/references in support of the initial registration).
- Applicants should include the latest approved PI and PIL of the initial registered product.

Fees

The fees applicable to variations are published in the Government Gazette.[7] SAHPRA wishes to clarify the interpretation of "evaluation of the request for major technical amendments in respect of which data relating to quality must be evaluated (post-registration)", which refers to:

- The submission of one or more Type II quality ("B" code) variations which require the evaluation of data by SAHPRA's Medicines Evaluation and Research (ME&R) directorate.

Note that multiple Type II variations may be grouped in one submission, requiring a single payment of the fee stipulated in the Government Gazette.

CONCLUSION

The South African Health Products Regulatory Authority (SAHPRA) has the mandate to ensure the safety, quality, and efficacy of medicines available in South Africa. Part of this responsibility is revising its guidelines to reflect global regulatory best practices and to appropriately manage the regulatory burden on our industry partners to ensure access to quality, affordable medicines for all South Africans.

After consultation with our industry partners, the SAHPRA management team has decided to begin harmonizing certain SAHPRA human medicine policies and procedures with those of the European Medicines Agency (EMA). Harmonization will align South Africa with global best practices while decreasing barriers to trade and improving investor confidence.

The first step in harmonization will be the adoption of the EMA variation classification guidelines for human medicines. SAHPRA will fully adopt the EMA variation guidelines for P&A and GMP and are issuing harmonized guidelines for Clinical (attached herein). The core EMA variation guidelines can be found via a hypertext link or on the EMA website.1 When the new SAHPRA clinical guidelines and the EMA guidelines conflict, the SAHPRA guideline takes precedence.

Please note that the adoption only applies to the EMA variation classification guidelines. Data submission guidelines will stay the same. A mapping of EMA variation classifications to SAHPRA data submission guidelines will be provided and the data submission guidelines will be updated at a later point to further harmonize with the EMA variation guidelines.

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