GENERAL INFORMATION

This guideline is intended to provide recommendations to applicants wishing to submit applications for the registration of medicines. It represents the South African Health Products Regulatory Authority's (SAHPRA) current thinking on the safety, quality and efficacy of medicines. It is not intended as an exclusive approach. SAHPRA reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine in keeping with the knowledge current at the time of evaluation. Alternative approaches may be used but these should be scientifically and technically justified. SAHPRA is committed to ensure that all registered medicines will be of the required quality, safety and efficacy. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications. This guideline is relevant only to human medicines, including biological and complementary medicines. Separate guidelines apply to the registration of veterinary medicines, medical devices and other health products.

Guidelines and application forms are available from the office of the CEO and the website www.sahpra.org.za.

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GENERAL INFORMATION

NOTE: These guidelines outline the format and data requirements for preparation and submission of an application for registration of medicines, and should be read in conjunction with the Medicines and Related Substances Act, 1965 (Act 101 of 1965), and the Regulations to this Act.

1 INTRODUCTION

The registration of medicine in South Africa is governed by the provisions and requirements of the Medicines and Related Substances Act, 1965 (Act No. 101 of 1965), (hereafter 'the Act') and the regulations and guidelines published in terms thereof.

These guidelines describe the information required for the registration of "medicines" and for an application to amend a registered medicine. The information submitted will be evaluated in terms of the provisions of the Act.

The aim of this guideline is to assist applicants in the preparation of documentation for the registration of medicines for human use. The types of medicine include a new medicine for a new chemical entity (NCE), a multisource (generic) product, a product line extension, a biological medicine, and a complementary medicine.

Medical devices including *in vitro* diagnostics are addressed in separate guidelines.

It is a legal requirement that data submitted for evaluation should substantiate all claims and should meet technical requirements of **quality**, **safety** and **efficacy** of the product for the purposes for which it is intended. The guidelines are meant to guide the applicant in meeting the requirements of the Act. It is acknowledged, however, that in some instances scientific developments may dictate alternative approaches. When a deviation from a guideline is decided on, a detailed motivation giving the reason(s) for the deviation and justification for the alternative approach should be included in the expert report submitted with the application.

Whenever there is doubt, applicants are advised to consult SAHPRA for confirmation and / or clarification before completing and submitting the application form; refer to the website for contact details. Applicants should always refer to the **current** version of the relevant guidelines and the addenda thereto before completing the application form.

Guidelines are constantly evolving due to of scientific developments and harmonisation of the requirements of regional and international regulatory authorities. SAHPRA endeavours to regularly update the guidelines to reflect current thinking and keep its technical requirements and evaluation policies in line with "best international medicines regulatory practice".

2 GENERAL

2.1 Scope

Legislation requires that SAHPRA shall register every medicine before it may be sold / marketed. An application for the registration of a medicine should therefore be submitted for evaluation and approval.

These guidelines are relevant only to human medicines including biological and complementary medicines. Separate guidelines apply to the registration of veterinary medicines and medical devices.

2.2 Applicant / PHCR / HCR

The term 'applicant' can refer either to the proposed holder of the certificate of registration (PHCR), as in the case of a new registration, or to the holder of the certificate of registration (HCR), as in the case of a variation application. Throughout this document, the term 'applicant' is used to refer to either the PHCR or the HCR, based on whichever is applicable in the context.

Eligibility to apply for registration of a medicine is governed by Regulation 16 of the Act. An application may be made by any of the following:

a) a person, body corporate / juristic person, company, residing and doing business in South Africa;

b) a close corporation incorporated in South Africa; or

c) a company in South Africa with at least
   - a responsible delegated person residing in South Africa and
   - an authorised person residing in South Africa who must be a person with appropriate knowledge of all aspects of the medicine and who shall be responsible for communication with Council.

The application submitted should be signed by the pharmacist authorised to communicate with Council. This pharmacist should be in the full-time employ of the company and may be:

- the Responsible Pharmacist in terms of the Pharmacy Act, 1974 (Act 53 of 1974) as amended, or
- another registered pharmacist responsible for regulatory affairs and with appropriate knowledge of all aspects of the medicine.

This should be an original signature (scanned signature not acceptable).

The following should be included:

- proof of **current** registration (copy of certificate) of the pharmacist who signed the dossier, and
- proof of **current** registration of the Responsible Pharmacist in terms of Act 53;
- an individualised, person-specific letter of authorisation for the signatory, issued by the person responsible for the overall management and control of the business (CEO). *(Note that such a letter is not required for the Responsible Pharmacist if the Responsible Pharmacist signs the application.)*

An applicant should submit a Site Master File (SMF) in accordance with the Site Master File Guideline (document 4.08). For subsequent applications, reference to the allocated SMF number will suffice.

2.3 Confidentiality / Secrecy

The confidentiality of information submitted to SAHPRA is governed by Section 34 of the Act. The Authority, advisory committee members or staff of the Authority may NOT

- disclose to any person, any information acquired in the exercise of powers or performance of functions under the Act and relating to the business affairs of any person, except
  - for the purpose of exercising his / her powers, or for the performance of his/her functions under the Act, or
  - when required to do so by any competent court or under any law, or
  - with the written authority of the CEO, or
- use such information for self-gain or for the benefit of his employer.

SAHPRA may insist on written confirmation of the identity and affiliation of an individual inquiring telephonically, or in person, about a medicine. No information shall be disclosed telephonically unless the Authority staff member knows the enquirer is entitled to receive the information.

2.4 Language

In terms of Regulation 22(4) of the Act, all applications and supporting data submitted to SAHPRA should be presented in English (UK)). Original documents not in English should be accompanied by an English translation.

2.5 Where to submit applications

Applications should be delivered to the SAHPRA Document Reception, CSIR, Building 38a, Meiring Naudé Road, Brummeria, Pretoria, where they will be logged and acknowledged. All correspondence should be addressed to the Chief Executive Officer and should be clearly coded as indicated in section 8 of this guideline.

SAHPRA will not take responsibility for documents posted or delivered to any other place or in any other manner.

2.6 When a product should be registered

A product is liable for registration with SAHPRA if any of the following apply.

i) Any of the ingredients of a product is listed in one of the Schedules to the Act;

ii) The product is a medicine by virtue of the definition of a medicine in the Act.

The Act defines a medicine as:

> "any substance or mixture of substances used, or purported to be suitable for use, or manufactured or sold for use in;
>
> (a) the diagnosis, treatment, mitigation or prevention of disease, abnormal physical or mental state, or the symptoms thereof in man; or
>
> (b) restoring, correcting or modifying any somatic or psychic function in man;
>
> and includes any veterinary medicine."

iii) If the product falls under any of the pharmacological classifications as specified in Schedule 1 Annexure to the Regulations

iv) The intended use of a product and the text / words used in promoting the product, even if no claims are reflected on the label, render the product registerable. A substance not ordinarily eaten or drunk by man cannot be considered a foodstuff just because no apparent medicinal claims are made for it.

The relevant provisions and guidelines shall apply to a medicine called up as a complementary medicine.

2.7 Types of applications

Medicine applications for registration for humans are divided into the following types for the determination of fees and allocation to reviewers for evaluation:

New chemical entity applications that include **non-clinical** and **clinical** information in support of the efficacy and safety of the formulation / dosage form, indication(s) and dosage regimen.

Multisource / generic applications and innovator product line extension applications that include clinical information in support of efficacy and safety of the formulation / dosage form, or indication(s) or dosage regimen.

Multisource / generic applications and innovator line extension applications that include comparative bioavailability / bioequivalence studies as proof of efficacy.

Multisource / generic applications and innovator line extension applications

- that include comparative dissolution studies as proof of efficacy
- that include any other comparative studies as proof of efficacy

- others, not mentioned above e.g. liquids / solutions.

Complementary Medicines

Biological medicines: Biopharmaceuticals and Biosimilars

Biological medicine: A medicine where the active ingredient and / or key excipients have been derived from living organisms or tissues, or manufactured using a biological process. Biological medicines can be defined largely by reference to their method of manufacture (the biological process). These include *inter alia* medicines prepared from the following substrates:

(i) Microbial cultures (fermentation);

(ii) Plant or Animal Cell cultures (including those resulting from recombinant DNA or hybridoma techniques);

(iii) Extraction from biological tissues; and

(iv) Propagation of live agents in embryos or animals.

The living substrate may be genetically modified in a number of ways to provide the required active ingredient, including recombinant DNA technology or hybridoma techniques**.**

Biological Medicines include, but may not be limited to the following:

(i) Plasma-derived products, e.g. Clotting factors, Immunosera;

(ii) Vaccines;

(iii) Biotechnology-derived medicinal products (rDNA products) e.g. rHu-antihemophilic factors, Hormones, Cytokines, Enzymes, Monoclonal antibodies, erythropoietins;

(iv) Human Gene therapy.

It has been the practice, in South Africa, that SAHPRA will decide that certain well-characterised low-molecular weight medicinal biological compounds, such as antibiotics, insulin etc. be excluded from biological medicine status, and they are, therefore, not reviewed by the Biological Medicines Committee.

Biopharmaceutical: Patented biological medicine.

Biosimilar: A biological medicinal product referring to an existing biological medicinal product for which registration has been applied for.

2.8 Evaluation pathways

Medicines applications for new registrations and variations in South Africa will follow one of four evaluation / 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 (link here, page 15) as "[t]he 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." Wherever possible, SAHPRA will leverage these pathways, relying on the

evaluation efforts of Recognised Regulatory Authorities (RRAs) in order to reduce evaluation times. Note that pathways (b), (c) and (d) replace the prior Abbreviated Medicines Review Process (AMRP).

The application of and use-cases for reliance-based evaluation pathways differ between the Clinical and ME&R units (see Section 2.8.2 below). For further guidance, please refer to the Clinical Guideline (document 2.09) and Quality and Bioequivalence Guideline (document 2.02). General descriptions of the evaluation pathways are provided below:

a) Full review

A comprehensive / thorough review of all aspects of the dossier, based primarily on the evaluation of data (and summaries thereof) submitted by the applicant. This is the default evaluation pathway for new registrations and variations not previously approved by SAHPRA or a RRA, or where reliance documentation provided to SAHPRA is deemed to be insufficient.

b) Abridged review

A streamlined review based primarily on un-redacted assessment reports from RRAs, replacing the need to evaluate all of the data (and summaries thereof) submitted in support of an application.

c) Verified review

A streamlined review based primarily on verifying, instead of evaluating, information submitted in the application against information which has already been approved by SAHPRA or a RRA. Note that un-redacted reports are required for ME&R verified reviews as a fall-back option for evaluators.

d) Recognition

A streamlined registration / approval process based on directly recognising the outcome of a review from a RRA with which SAHPRA shares a recognition agreement.

Note: 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.

The abridged and verified review processes do 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 need to review data in the dossier as required (even when presented with un-redacted reports).

2.8.1 SAHPRA's Recognised Regulatory Authorities

To qualify for a reliance evaluation pathway, an application must have been approved by one or more of the RRAs with which SAHPRA aligns itself. SAHPRA's current RRAs include:

- European Medicines Agency Centralised Procedure (EMA CP)
- European Medicines Agency Decentralised Procedure (EMA DCP)
- Health Canada
- Medicines and Health Products Regulatory Agency (MHRA), UK
- Ministry of Health, Labour and Welfare (MHLW), Japan

- Swiss Agency for Therapeutic Products (Swissmedic)
- Therapeutic Goods Administration (TGA), Australia
- 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

2.8.2 Independent application of reliance for ME&R and Clinical

A given application often differs in complexity for Clinical versus ME&R evaluation. For example, a typical application for a generic / multisource medicine requires a relatively straightforward verification of PIs for Clinical, yet ME&R faces the added complexity of bioequivalence. As a result, SAHPRA's reliance pathways are applied *independently* for ME&R and Clinical. This has the following two key implications:

- Evaluation pathways may differ for ME&R and Clinical evaluation (e.g., Clinical may follow a verification procedure, while ME&R follows a full review based on the nature of the application and the quality of reliance documents submitted)

- The RRAs referenced in an application may differ for ME&R and Clinical evaluation (e.g., Clinical may refer to the SAHPRA-approved local innovator PI and latest EMA SmPC as part of a verified review, while the ME&R evaluation makes reference to information approved by the TGA)

This approach widens the use of reliance, by not limiting an application to the same pathway / reference RRA for ME&R and Clinical evaluation.

While this guideline is the central source of information regarding evaluation pathways, applicants must refer to the Clinical Guideline (document 2.09) and Quality and Bioequivalence Guideline (document 2.02) for guidance on their exact application (e.g., document requirements and the types of applications qualifying for reliance pathways for Clinical and ME&R).

2.8.3 Technical screening of applications

Applicants are to provide SAHPRA with the intended evaluation pathways for ME&R and Clinical evaluation, along with a brief motivation. The intended evaluation pathways should be indicated on the new registration / variation validation template in the relevant sections. Providing the intended pathways prevents unnecessary screening for reliance documentation in instances where a full review is intended by the applicant.

Decisions related to an application's final evaluation pathway and the extent of reliance on a RRA's evaluation are fully at SAHPRA's discretion and will depend on the availability and quality of reliance documentation submitted. SAHPRA will share screening queries with applicants regarding insufficient reliance documentation to ensure that as many applications as possible qualify for abridged and verified reviews. Where applicable, applications will default to a full review in the absence of a suitable reliance pathway.

2.8.4 Un-redacted assessment reports and the Letter of Access

Where indicated as a requirement for an abridged or verified review, applicants are to provide SAHPRA with full, un-redacted assessment reports from a RRA (submitted in Module 1.10). The following requirements apply:

- Un-redacted assessment / evaluation reports should at least include safety, efficacy and quality report(s) prepared by the RRA upon which the registration / approval decision was based

- Where un-redacted assessment / evaluation reports from the RRA are in a language which is not English, translated versions need to be provided

In instances where applicants do not have access to relevant un-redacted assessment reports, SAHPRA requires a signed Letter of Access appended to the letter of application in Module 1 (see appendix for a template) included in the application (appended to the letter of application). This allows SAHPRA to request un-redacted reports from the associated RRA(s). However, SAHPRA does not guarantee that these reports will be obtained. For a given RRA, only one letter should be signed covering both ME&R and Clinical access to the un-redacted reports. The Letter of Access must also be signed by the MAH in the associated RRA country or by the principal from whom the dossier is purchased.

Note that SAHPRA prefers receiving un-redacted reports directly from the applicant, and has introduced the Letter of Access only for instances where this is not possible.

2.9 Expedited review process

Refer to the latest version of SAHPRA's Expedited Review Guideline (document still in draft)

2.10 Fees

The fees payable are published in the Government Gazette and are also available on the website.

Methods of payment: Electronic payment / direct transfer. Cheques are no longer accepted as a method of payment.

Refer to the Bank Details for Direct Payment of Fees to SAHPRA Guideline (document 17.02) for electronic payment / direct transfer.

Proof of electronic payment / direct transfer must be submitted in a separate envelope attached to a **copy** of the letter of application of the relevant submission(s).

To ensure evaluation of the relevant submission(s) a copy of proof of payment must also be attached to the original letter of application of the relevant submission.

2.11 Same or separate applications

For the purpose of registration the following products will be regarded as either being the same product or separate product applications:

TYPE OF APPLICATIONS	Application	
	Same	**Separate**
2.11.1 Each individual dosage form of a particular medicine		X
2.11.2 Variations of the active pharmaceutical ingredient (API) of a product		X
2.11.3 Tablets / Capsules / Suppositories / Lozenges		
a) Different pack-sizes of exactly the same strength and formulation.	X	
b) Different strengths and formulations.		X
c) Uncoated and coated tablets of the same strength and formulation.		X
2.11.4 Syrups / Liquids / Solutions (excluding parenterals) / Creams / Ointments		
a) Different container sizes of the same strength and formulation.	X	
b) The same container size of different strengths and formulations.		X

TYPE OF APPLICATIONS	Application	
	Same	**Separate**
2.11.5 Ampoules and Vials and Large Volume Parenterals		
a) Ampoules or single dose vials containing identical solutions of the same strength but of different volumes (i.e. resulting in different total doses).		X
b) Ampoules containing solutions of different strengths.		X
c) Ampoules and single dose vials containing e.g. dry powder, crystals of different mass.		X
d) Ampoules and single dose vials containing the same respective masses of e.g. dry powder, crystals.	X	
e) Ampoules, single dose vials, as well as pre-filled disposable syringes and cartridges containing identical solutions of the same strength and same volume of liquid.	X	
f) Dental cartridges containing different volumes of fluids of the same strength (provided the dose remains constant).	X	
g) Ampoules containing “water for injection”, but of different volumes.	X	
h) Special ampoules of dry powder and “water for injections” contained in the same unit, but intended for mixing at the time of injection if water for injections is fully described in dossier.	X	
i) Ampoules containing identical solutions of different volumes used only as diluent in the reconstitution of a preparation for parenteral use.	X	
2.11.5 Ampoules and Vials and Large Volume Parenterals - continued	**Same**	**Separate**
j) Multidose vials containing different volumes of the same strength and formulation with the same dosage schedule.	X	
k) Multidose vials and a single dose ampoule or vial of the same formulation if the single-dose ampoule or vial corresponds to the dose indicated for the multidose vial.	X	
l) Multidose vials containing dry powder of different mass of the same formulation, and the same concentration when reconstituted.	X	
m) An ampoule of diluent packed together with any preparation including biological medicines if diluent is fully described in dossier.	X	
n) Infusion solutions of the different volumes and of the same formulation which are packed in containers of exactly the same type of material depending on the relevant information submitted.	X	
o) Infusion solutions of the same formulation and of the same or different volume which are packed in containers made of different types of materials.	X	
p) A preparation, packed in plastic containers, intended to be marketed in glass containers containing the same volume and the same formulation.	X	
q) Products with the same strength and formulation but with different colours and / or flavours.		X

TYPE OF APPLICATIONS	Application	
	Same	Separate
r) Applications containing the same API(s) applying for additional indications which render the product in a different scheduling status, or different pharmacological classification, or have any other restrictions imposed other than the original application.		X
s) Removal of antimicrobial preservative from single dose presentation of registered vaccine that included a preservative in the original approved formulation		X
2.11.6 Same formulation with different proprietary names whether of the same or different applicants		X

2.12 Cancellation or withdrawal of applications

HCRs of medicines and applicants should, before applying to the Authority, carefully consider any decision to cancel or withdraw, as the case may be, a registration or application for registration, as the Authority, after consideration of all issues involved, has resolved the following with immediate effect.

Any medicine

- of which the registration has been cancelled, or any "old medicine" of which the application for registration has been withdrawn by notice in the Government Gazette, and
- for which a written application or request to the CEO has been submitted by the holder of a certificate of registration or by the applicant,

will under no circumstances be re-instated.

Should the applicant desire to re-register such medicine, a new application for registration of a medicine must be submitted in accordance with the requirements of the Act and the relevant Regulations.

An application for registration of a medicine may at whatever stage of processing be withdrawn by written application to the CEO. The withdrawal shall under no circumstances be reversed once such an application is approved and the approval confirmed in writing. A new application for registration must be submitted should the applicant wish to proceed with registration thereafter.

3 REQUIREMENTS OF AN APPLICATION

From 1 June 2011 submissions in ZA CTD (Common Technical Document for South Africa) format is mandatory (excluding veterinary medicines). Please refer to the Guidance for the Submission of the South African CTD / eCTD General & Module 1.

For digital submission, the format should preferably be eCTD (electronic Common Technical Document), but eSubmissions will be accepted for a limited period. For further information on the accepted submission formats and timelines for implementation of digital requirements, refer to the following guidelines

- Guidance for submission of regulatory information in eCTD format (document 2.23)
- Guidance for submission of regulatory information in eSubmission format (document 2.58)
- ZA CTD and ZA eCTD Implementation Roadmap (document 2.26)

Specific guidelines also apply to the requirements of an application for complementary medicines.

4 PROPRIETARY NAME POLICY [Section 15 (3) of the Act]

Refer to the current version of the Guideline on Proprietary Names for Medicines (document 2.15)

5 MANUFACTURING REQUIREMENTS

Only medicines manufactured, packed and quality controlled at sites compliant with the current principles of Good Manufacturing Practice (GMP) as prescribed by SAHPRA will be considered for registration.

SAHPRA's general policy is that the standard to be used to assess compliance with current Good Manufacturing Practice (cGMP), is the South African Guide to Good Manufacturing Practice (SA guide to GMP) (latest edition)

Under Section 22C of the Act, all South African manufacturers should be licensed (effective 2 May 2004).

The aim of these licensing requirements and standards is to protect public health by ensuring that medicines meet defined standards of quality and are manufactured in conditions that are clean and free of contaminants.

The Act requires that overseas manufacturers of medicine supplied to South Africa should comply with the same or equivalent manufacturing standards as expected of South African manufacturers.

Evidence in relation to compliance with Good Manufacturing Practices of the overseas manufacturer is required for applications for registration of imported medicines. When acceptable evidence of GMP compliance is not available, overseas manufacturers are inspected by the GMP Inspectorate before registration of the medicine is approved.

6 SAMPLES

All medicine applications for registration must include a sample of a unit pack, Section 15(1) of the Act.

7 STANDARDISED PROFESSIONAL INFORMATION WARNINGS AND INFORMATION

Please refer to the current version of Professional Information for Human Medicines: Standardised Texts Guideline (document 2.20).

8 CODING OF SUBMISSIONS

Coding of applications / submissions / correspondence facilitates distribution, processing and tracking. The following codes, placed on the **first page of each letter of application in bold lettering,** should be used for submissions to SAHPRA to reduce the possibility of misdirection.

The code indicates the Unit to which the correspondence should be directed. The specific request should be stated in the letter of application. When more than one code is applicable, each should be indicated. For general correspondences, which do not have a letter of application, include a brief description in the subject line well as the code. All supporting documentation must be included with the letter of application.

8.1 Submission codes

CODE	SUBJECT
ANA	All new-registration applications (including extension applications)
AGC	General enquires and correspondence – Health Product Authorisation
BGC	General enquires and correspondence – Inspectorate and Law Enforcement
CGC	General enquires and correspondence – Clinical Evaluations
MGC	General enquires and correspondence – Complementary medicines
PGC	General enquires and correspondence – Medicines Evaluation and Research (ME&R) Directorate
QGC	General enquires and correspondence – Biological Medicines
SGC	General correspondence involving enquiries on policy issues and changes that are not product-specific
TGC	General enquires and correspondence – Clinical Trials
VPA	All variation applications

8.2 Responsibilities of each unit

In order to facilitate the correct coding of correspondences, examples of the responsibilities of each unit are outlined below

8.2.1 Medicines Evaluation and Research (ME&R)

The Medicines Evaluation and Research (ME&R) Directorate is responsible for the evaluation of

a) Quality of the drug substance (API) and drug product (finished pharmaceutical product);

b) Bioequivalence of generic medicines to their innovator counterparts.

8.2.2 Inspectorate and law enforcement

The Inspectorate and Law Enforcement Unit is responsible for

a) inspection and evaluation of sites for the manufacturing, packing, and testing of medicines nationally and internationally, as well as inspection and evaluation of all storage and distribution sites for medicines;

b) investigation of complaints regarding registered and unregistered medicines;

c) monitoring compliance to the Act and prosecution in case of non-compliance;

d) monitoring the importation and exportation of medicines in consultation with customs authorities;

e) evaluation of proprietary names and changes thereto.

8.2.3 Clinical evaluation

The Clinical Evaluation Unit is responsible for

a) evaluation of clinical and pre-clinical data;

b) evaluation of clinical aspects of the Professional Information and relevant changes to Professional Information.

8.2.4 Clinical trials

The Clinical Trials Unit is responsible for the evaluation of

a) clinical trial applications and clinical trial amendments;

b) reports of adverse events arising from a clinical trial;

c) applications for named patient use of unregistered medicines;

d) applications for the use of unregistered medicines for clinical trial purposes.

8.2.5 Complementary medicines

The Complementary Medicines Unit is responsible for

a) evaluation and review of applications for the registration of Complementary Medicines;
b) receiving and collating initial and subsequent responses to the call-up notice as published in Government Gazette Number 23128 (22 February 2002);
c) evaluation and review of applications for the amendment of the register for Complementary Medicines;
d) issue of temporary permits for the manufacture, distribution and dispensing of Complementary Medicines.

8.2.6 Biologicals

The Biologicals Sub-Unit is responsible for

a) biological new registration applications and responses to resolutions, and matters pertaining to biological medicines during review for registration;

b) evaluation of technical changes to registered biological medicines and "old" biological medicines;

c) evaluation of clinical aspects of the Professional Information and relevant changes to Professional Information for biological medicines;

d) technical support to other units with respect to biological matters.

Note: For biologicals:

- For any other activities not described above, the applications and / or queries should be directed to (and properly coded for) the relevant Units.
- Relevant supportive documentation should be attached as per the Annexures described in the relevant CTD format.
- Applicants are to submit electronic application, bookmarked, cross-referenced and virus free in CD and USB respectively.

8.2.7 Health Product Authorisation

The Health Products Authorisation Directorate is responsible for the following:

a) receiving and acknowledging applications for registration of medicines and for amendment of registration dossiers;
b) receiving correspondence dealing with administrative processes, registration and other application forms, and registration policy information documents and guidelines;
c) applicant transfers and applicant name and address changes ;
d) cancellations of registered medicines and withdrawal of applications for the registration of medicines
e) co-ordination of reports on the evaluation of medicines

9 APPENDIX – LETTER OF ACCESS FOR RELIANCE DOCUMENTATION

To be completed by the applicant / holder of certificate of registration[1] / principal from whom the document was purchased for submission in South Africa, based on which party submitted the dossier to the RRA:

Details of foreign registration	
Recognised Regulatory Authority(ies) (RRAs)	{Insert name of recognised regulatory authority(ies) here}
Proprietary name(s) of reference product(s) registered with RRA(s)	{Insert the proprietary name(s) of the associated product(s) which has been registered with the RRA(s) listed above}
Active Pharmaceutical Ingredient(s) (APIs)	
Registration date	
Date(s) of approval of post-registration variation(s) if applicable	
Details of SAHPRA application	
SAHPRA application number	
Product / proprietary name proposed to SAHPRA	

I hereby authorise SAHPRA to contact the above-specified regulatory authority or authorities to obtain reliance documentation for registered products. Reliance documentation includes, but is not limited to:

- The full, unredacted assessment / evaluation reports and inspection outcomes / reports
- Results of laboratory testing
- Assessment and inspection reports of other regulatory authorities, provided that these authorities gave their written consent to the use of such reports

Full name of Responsible pharmacist / Person authorised to communicate with the authority:
Job title, company:
Email address:
Telephone number:

Signature:

Date: Place:

[1] Also referred to as marketing authorisation holder

10. UPDATE HISTORY

Date	Reason for update	Version & publication
May 2003	First publication released for implementation and comment	Version 1 May 2003
November 2003	Release for additional comment	Version 1, Nov 2003
November 2003	Deadline for comment	
December 2003	Date for finalisation / implementation	Version 1, Dec 2003
May 2006	General editing – page numbers in index, 2.5, 3.1.2, 3.1.3 a) b), 4.1, 4.4, 4.17, 8, 10, and amendment of sections 2.2.2, 2.9, 3.1.4, 4.2, 4.5, 4.6, 4.7, 4.14, 5, 5.2, 13.1, 13.2, 13,3, 13.4, 13.5, 13.6, 13.7, Attachment A	May06 v2, June 2006
12 July 2006	Date for implementation	
May 2007	Additions to 2.7.5, 2.10.5, 13.4; amendments to 4, 5.2, Attachment A	Version 3, May 2007
25 June 2007	Date for implementation	
March 2008	Amendment of sections 2.9, 2.10.5, 3.1.3 a), 4, 4.7, 4.10, 5.1, 5.2, 13.3, 13.4, Attachment A	Version 4 March 2008
1 May 2008	Date for implementation – except 3.1.3 a), b)	Version 4 April 2008
1 August 2008	Date for implementation of 3.1.3 a), b)	
August 2009, January 2010	1 Removal of section 12 “Standardised package insert warnings” and inclusion in new “Package Insert Standardised Texts” guideline 2 Removal of Attachment B re package insert information 3 Amendment to section 4.9	Version 5 January 2010
March 2010	Date for implementation	
June 2010	Inclusion of references to the ZA CTD – sections 2.11, 3, 4, 4.14, 5, 13.1	Version 6 June 2010
1 July 2010	Date for implementation	
	Amendment of section 2.5	
21 June 2010	Date for implementation	
	Amendment, for clarity, of sections 2.10.5 k), 3.1.2, 3.1.3 c), 3.1.4, 3.4, 3.5, 4.3, 4.5, new 4.6, 4.9 (original 4.8), 4.10 (original 4.9), 4.17, 5.2, 5.4, 13.3, 13.9 & new section 3.1.1 p)	
With immediate effect	Date for implementation	
March 2011	Amendment of name of “Post-registration Amendments”, “Guidance for submission of SA CTD / eCTD Module 1" guidelines, and administrative amendments: Sections 2.5, 3, 3.1.1o), 4, 4.5, 5, 5.2.6, 5.2.8, 5.4, 13, 13.1, 13.2, Attachment A; new 4.11 and renumbered. Amendment of 2.2.2 for clarification & in line with CTD guideline. Clarification of 4.3 & 4.4 in accordance with Biostudies guideline 3.9 & 4.4 and insertion of 4.11 in accordance with Quality and Bioequivalence Guideline 2.1.2.11. Deletion of “independent” in 6.2 & 8.1.	Version 7 March 2011

Date	Reason for update	Version & publication
	Insertion of "(including batch specific)" for shelf-life extension under working code VSE in accordance with Amendments guideline Type C Inspectorate category 19.	Version 7 March 2011
With immediate effect	Date for implementation	
June 2011	13.1 Correction	Version 7_1, June 2011
July 2012	Deletion of section 9 on Proprietary Names, Attachment A (pre-screening check-list) Amendment of 2.11, 3.1.4, 4, 4.2, 5.2.8, 6, 13.2, 13.9	Version 8, August 2012
With immediate effect	Date for implementation	
With immediate effect	Transition from MCC to SAHPRA *To include sections changed or deleted*	Version 9, May 2019
With immediate effect	Updated to align with new processes and guidelines	Version 10, July 2019