South African Health Products
Regulatory Authority
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Loftus Park
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Pretoria

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GENERAL INFORMATION GUIDELINE FOR REGISTRATION OF VETERINARY MEDICINES

This guideline is intended to provide recommendations to applicants wishing to submit applications for the registration of veterinary medicines. It represents the South African Health Products Regulatory Authority's (SAHPRA) current thinking on the quality, safety, and efficacy of medicines. SAHPRA reserves the right to request any additional information to establish the quality, safety, and efficacy of a medicine in keeping with the knowledge current at the time of evaluation. It is not intended as an exclusive approach. Alternative approaches may be used but these should be scientifically and technically justified. SAHPRA is committed to ensure that all registered veterinary medicines will be of the required quality, safety, and efficacy. Human medicines and medical devices including *in vitro* diagnostics are addressed in separate guidelines. Guidelines and application forms are available from the SAHPRA website

Document History

Final Version	Reason for Amendment	Effective Date
1	First issue and published for implementation	January 2004
2	Second issue and published for implementation	September 2019
3	Administrative changes to accommodate new registration process	July 2021
4	- Content structured on the new SAHPRA Guideline Template - Old document number 3.01 changed to SAHPGL-PEM-VET-04 - Administrative changes to accommodate new processes	June 2023

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Contents

Glossary

Abbreviation/ Term	Meaning
API	Active Pharmaceutical Ingredient
BCS	Biopharmaceuticals Classification System
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CoA	Certificate of Analysis
CTD	Common Technical Document
FPP	Finished Pharmaceutical Product
GCP	Good Clinical Practice
GRP	Good Regulatory Practice
LOD	Limit of Detection
MRLs	Maximum Residue Limits
NCE	New Chemical Entity
PI	Professional Information
Ph.Eur	European Pharmacopoeia
ROS	Residue Overall Summary

1. INTRODUCTION

This guideline describes the format, data requirements and information required for the preparation and submission of an application for registration of veterinary medicines and for an application to amend a registered veterinary medicine. The new medicines include new chemical entities (NCE), generics, clones and replicas and line extensions. 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 reasons for the deviation and scientific justification for the alternative approach should be included in the expert report.

Whenever there is doubt, applicants are advised to consult SAHPRA for clarification before completing and submitting the application forms. The contact details for queries are VETqueries@sahpra.org.za

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

1.1 Legislation

The registration of veterinary medicines in South Africa is governed by the provisions of the Medicines and Related Substances Act, 1965 (Act No. 101 of 1965) and the relevant regulations and guidelines. The document should be read in conjunction with the Regulations and relevant VICH/SAHPRA/RRA guidelines.

The confidentiality of information submitted to SAHPRA is governed by Section 34 of the Act. The Authority, advisory committee members and 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.

1.2 Scope

Legislation requires that SAHPRA shall register every medicine before it may be sold / marketed. It is a legal requirement that data submitted for evaluation should substantiate all claims and should meet technical requirements of quality, safety, and efficacy for the purposes for which it is intended. The only exception to this rule is if a Section 21 exemption is granted by SAHPRA for an unregistered medicine in terms of the Act for certain purposes.

1.3 GENERAL: Applicant / PHCR/ HRC

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.

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 the Authority.

The application submitted should be signed by the pharmacist authorised to communicate with the Authority. This pharmacist should be in full-time employment 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.

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 53/1974;

• 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 SAHPGL-INSP-04. For subsequent applications, reference to the allocated SMF number will suffice.

2. LEGAL PROVISION

2.1.1 Where and how to send applications

Applications should be addressed to the Chief Executive Officer and should be clearly coded. Also refer to the Variations Addendum: Document SAHPGL-HPA-06 for variations codes.

The medium for submitting the CTD and e-Submission related submissions to the authority is through the online upload utility (refer to the SAHPGL-ICT-01_File Transfer Protocol (FTP) User Guide for Files/Dossier Submission). A request for the File Transfer Protocol (FTP) User Guide for Files/Dossier Submission should be sent to vetmedicines@sahpra.org.za. An applicant seeking access to the FPT should submit a request, with their license number.

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

2.1.2 Language

In terms of Regulation 16 (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.

2.1 When a veterinary product should be registered

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

2.1.1 Any of the ingredients of the veterinary product is listed in one of the Schedules to the Act;

2.1.2 The product is a veterinary medicine by virtue of the definition of a veterinary medicine in the Act.

The Act defines a medicine as:

a) means any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in:-

(i) the diagnosis, treatment, mitigation, modification, or prevention of disease, abnormal physical or mental state or the symptoms thereof in humans; or

(ii) restoring, correcting, or modifying any somatic or psychic or organic function in humans, and

b) includes any veterinary medicine

2.1.3 If the product falls under any of the pharmacological classifications as specified Annexure to the Regulations.

2.1.4 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.

NOTE: All scheduled substances are registerable under Act 101 of 1965, unless they are specifically exempted from the requirements of the schedules in terms of Section 36 of the Act.

2.2 Types of Veterinary Medicine Applications

Medicine applications for registration for animal use are divided into the following types:

2.2.1 New chemical entity applications that include pre-clinical (including food safety, environmental toxicity, and user safety) and clinical information in support of the efficacy and safety of the formulation/dosage form, indication/s per species and dosage regimen. This includes clones to the NCE.

2.2.2 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.

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

2.2.4 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

2.2.5 Veterinary biological applications

- May include but not limited to the following: (i) Plasma-derived products and (ii) Biotechnology-derived medicinal products e.g., monoclonal antibodies

2.2.6 Post-registration variations concerning quality control for example change of FPRC or a Pharmaceutical / Analytical Change must be submitted in the CTD.

2.3 Evaluation Pathways

Veterinary medicines applications for new registrations and variations in South Africa will follow one of three evaluation / review pathways:

a) Full review

b) Abridged review

c) Verified review

2.3.1 Recognition

Review types (b), (c) (d) and (e) represent reliance pathways, which SAHPRA will be implementing to reduce evaluation times. To qualify for a reliance pathway, an application must have received prior approval from the reference recognised regulatory authority. The World Health Organisation defines reliance as "The act whereby the regulatory authority in one jurisdiction may consider and give significant weight to (i.e., totally or partially) 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) to reduce evaluation times.

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 clinical and quality 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 collaborative agreement.

Note: SAHPRA is currently in the process of negotiating recognition agreements with RRAs. The guiding principle is that applications approved by RRAs with which SAHPRA shares a recognition agreement may not need to be fully evaluated separately by SAHPRA.

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 structure and BMR document. Evaluators may still need to review data in the dossier as required (even when presented with un-redacted reports).

2.3.2 SAHPRA's Recognised Regulatory Authorities for Registration of Veterinary Medicines

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:

US-FDA (CVM),

EMA (CVMP),

Japan Ministry of Agriculture, Forestry and Fisheries (JMAFF),

Health Canada (VDD),

Australia, (APVMA),

UK (VMD),

Swissmedic

New Zealand.

2.3.3 Application for reliance and expedited reviews

A given application often differs in complexity for clinical versus quality aspects and between various species. Reliance pathways are applied independently for clinical and quality sections based on the quality of documents submitted. This approach widens the use of reliance, by not limiting an application to the same pathway / reference RRA throughout. For further guidance, please refer to the Vet Clinical Guideline (document no 3.14) and the EMA/VICH guidelines.

2.3.3.1 Expedited review process: Refer to the latest version of HPA03-202223 Priority Review Requests Communication.

2.3.3.2 Medicines for Use in a Public Health Emergency (PHE): Refer to the latest version of the guideline - SAHPGL-PEM-01 Availability of medicines for use in a PHE.

2.3.4 Technical screening of applications

Applicants are to provide SAHPRA with the intended evaluation pathways for quality and clinical evaluation, along with a brief motivation. Providing the intended pathways prevents unnecessary screening for reliance documentation in instances where a full review is intended by the applicant. Request for a review pathway must be included in the letter of request for an application number.

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 technical screening queries with applicants regarding insufficient reliance documentation to ensure that as many applications as possible qualify for abridged and verified reviews. Applications will default to a full review in the absence of a suitable reliance pathway.

2.3.5 Un-redacted/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 an RRA. The following requirements apply:

- Un-redacted assessment / evaluation reports should at least include all aspects of safety, environmental toxicity (if applicable) 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, officially 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 (see appendix for a template) included in the application (appended to the letter of application). This letter should be sent to the Unit at the point of request of an application number to allow the unit ample time to obtain the documentation from the RRA However, SAHPRA does not guarantee that these reports will be obtained. For a single given RRA, only one letter should be signed covering both quality and clinical access to the un-redacted reports. The Letter of Access must also be signed by the MAH in the associated RRA country.

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

3. REQUIREMENT AND PREPARATION OF AN APPLICATION

3.1 Requirements

Please note: The VMRF1 format is no longer acceptable since 31 December 2021.

3.1.1 For ZA CTD (Common Technical Document for South Africa) format submissions please refer to the Guidance for the Submission of the South African CTD / eCTD General & Module 1.

For e-Submissions, PDFs will be accepted for a period to be determined by SAHPRA. All veterinary medicines applicants need to request for an application number before submission of a registration dossier.

3.1.2 **For Inspectorate-Veterinary medicines variations**, that involve replacement or addition of a manufacturing site/packaging site/ batch control or testing site, the applicant is required to submit the Veterinary Medicines Unit Approval letter to the DVP as part of the supporting documents.

3.2 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)

4. MANUFACTURING REQUIREMENTS

The following related documents are referenced:

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 (RSA guide to GMP) (latest edition: SAHPGL-INSP-02)

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 upfront for applications of registration of imported medicines. When acceptable evidence of GMP compliance is not available, overseas manufacturers are inspected by the South African GMP Inspectorate before registration of the medicine is approved.

5. SAMPLES

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

6. CODING OF SUBMISSIONS and SPECIAL CONDITIONS

6A. Coding of applications / submissions / correspondence facilitates distribution, processing, and tracking.

The codes should be placed on the **first page of each letter of application in bold lettering** 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 as well as the code. All supporting documentation must be included with the letter of application.

Submission codes

CODE	SUBJECT
ANA	All new-registration applications (including extension applications)
AGC	General enquires and correspondence – Health Product Authorisation
RGC	General enquires and correspondence – Veterinary Medicines Unit
PGC	General enquires and correspondence – Pharmaceutical Evaluation and Registration (PE&R)
SGC	General correspondence involving enquiries on policy issues and changes that are not product-specific
VPA	All variation applications
BGC	Inspectorate and Regulatory Compliance

6B. Variations Permitted during the Registration Process

All applications for registration in terms of Section 15 of the Act 101 are required to be complete in terms of the CTD and data requirements and no variations during the registration process are permissible except for the following:

- Transfer of Applicancy with motivation in exceptional circumstances
- Urgent restriction safety updates as requested by or as deemed necessary by SAHPRA or the applicant following consultation with SAHPRA

- Updated reliance documentation, e.g., where an RRA approval is obtained for the product after the application was submitted to SAHPRA

6C. Permissible review response rounds and period for response submissions

- SAHPRA's review process for new medicines and variations will permit for all units a maximum number of three response rounds. If the applicant fails to address the queries adequately by the third query round, the application will be tabled for rejection from the respective unit.

- Each response timeframe should be no longer than 30 working days from the date sent to the Applicant

- Applicants may submit a *written request for one extension of timeline for a response per response round and which may not exceed a further 30 working days. Requests will only be considered by the Authority if the applicant provides appropriate scientific justification.

Note: If an applicant does not respond to the queries and does not communicate any request for extension, their application will be tabled for rejection.

6D Renewals

Refer to the latest version of the following documents:

• SAHPGL-HPA-04 Renewal of Human and Veterinary Medicines Requirements and Process

• Communication on Medicines Registration Renewals Implementation Framework

• Renewals Frequently Asked Questions (FAQs)

6E. Responsibilities of Relevant Units

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

Pharmaceutical Evaluation and Management (PEM)

It comprises the following sub-units: Veterinary medicines, Complementary medicines, Human Biologicals, Human quality and bioequivalence assessments pre and post registration.

Veterinary medicines unit

The Veterinary Medicines Unit is responsible for:

a) evaluation of clinical and pre-clinical data including clinical aspects of the Professional Information and relevant changes to veterinary medicines.

b) evaluation of clinical trial protocols and clinical trial amendments;

c) reporting of adverse events arising from a clinical trials and use of registered veterinary medicine

d) authorisation of use of unregistered medicines for named patience and for clinical trial purposes.

e) Quality evaluation of the drug substance (API) and drug product (finished pharmaceutical

product);

f) Bioequivalence evaluation of generic veterinary medicines

Inspectorate and Regulatory Compliance

The Inspectorate and Regulatory Compliance 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 prior to issuing a license;

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;

Please note: Evaluation of proprietary names and changes thereto have now been moved to the Clinical Unit (CEM).

6.1 Health Product Authorisation

The Health Products Authorisation Unit 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

e) tracking of new applications and variations to registered medicines

6.2 Fees

6.2.1 The fees payable are published in the Government Gazette (document no 42474) also available on the website.

6.2.2 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.

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

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

6.3 Cancellation or withdrawal of applications

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

6.3.1 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.

6.3.2 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.

6.3.3 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.

7. REFERENCES

The following related documents are referenced:

7.1 SAHPGL-PEM-VET-03_v2 Guideline for Veterinary Medicines Exemptions from Certain Medicine Registration Requirements

7.2 SAHPGL-PEM-VET-02_v2 VETERINARY MEDICINES CLINICAL GUIDELINE

7.3 2020.12.22 Fees payable GG No 44026, no 1379

7.4 SAHPGL-INSP-02 Guideline for Good Manufacturing Practice

7.5 17.05 Payment Guideline

7.6 5.08 Reliance Guideline

7.7 SAHPGL-HPA-04 Renewal of Human and Veterinary Medicines Requirements and processes

7.8 SAHPGL-PEM-01 Availability of medicines in a Public Health Emergency (PHE)

7.9 SAHPGL-HPA-06 Variations Addendum For Human And Veterinary Medicines

8. VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces a guideline for General Information for Registration of Veterinary Medicines, old document number 3.01. It will be reviewed on this timeframe or as and when required.

9. ADDENDA

9.1 Addendum A: 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
7.1 Each individual dosage form of a particular medicine		X
7.2 Variations of the active ingredient of a product		X
7.3Tablets 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
7.4 Syrups/Liquids/Solutions (excluding parenteral) /Creams/Ointments		
a) Different container sizes of the same strength and formulation.	X	
b) The same container size of different strengths and formulations.		X
2.7.5 **Ampoules and Vials and Large Volume Parenterals**	**Same**	**Separate**
a) Ampoules containing identical solutions of the same strength (provided the dose remains constant) but of different volumes.		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	
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 of the same formulation if the single-dose ampoule corresponds to the dose indicated for the multi-dose 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
	r) Applications containing the same active ingredient(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
7.5	Same formulation with different proprietary names whether of the same or different applicants		X

The following table guides the veterinary medicines applicants which documents should be compiled for CTD submission:

DOSSIER CTD MODULES FOR REGISTRATION OF A VETERINARY MEDICINE

Section	MODULE	COMMENTS
2.1	**MODULE 1: ADMINISTRATIVE INFORMATION**	
2.1.1	**Cover letter**	

	2.1.2	**Comprehensive Table of Contents**	A complete list of all documents provided in the product dossier by module
	2.1.3	**Completed, signed, and dated application form**	
	2.1.4	**Declaration by applicant**	
	2.1.5	**Screening checklist**	
	2.1.6	**Proof of payment of appropriate fees**	
	2.1.7	**Manufacturing and Marketing Authorization(s)**	
	2.1.8	**Summary of Product Characteristics (SmPC) and Proposed Package Insert**	
	2.1.9	**Labelling**	
2.2		**MODULE 2**	
	2.2.1?	**Quality Overall Summary – Product Dossiers (QOS – PD)**	
	2.2.2?	**Quality Information summary/SCoRE doc**	
3		**MODULE 3**	
		Table of Contents of Module 3	
3.2.S		**ACTIVE PHARMACEUTICAL INGREDIENT (API)**	
	3.1	**Approved API source(s)**	
		DMF[1]	
		CEP[2] with annexes	
	3.2.S.1	**General Information**	
	3.2.S.1.1	Nomenclature	
	3.2.S.1.2	Chemical Structure	
	3.2.S.1.3	Physicochemical Properties	
	3.2.S.1.4	Physical Description	
	3.2.S1..5	Solubility/Quantitative Aqueous pH Solubility Profile	
	3.2.S.1.6	Polymorphs	
	3.2.S.1.7	Particle Size Distribution	
	3.2.S.2	**Manufacture**	
	3.2.S.2.1	Manufacturer(s) name and address	
	3.2.S.2.2	Description of Manufacturing Process and Process Controls	
	3.2.S.2.3	Control of Materials	
	3.2.S.2.4	Controls of Critical Steps and Intermediates	
	3.2.S.2.5	Process Validation and/or Evaluation ~ Must be submitted for sterile APIs and NCEs	
		For applications with DMF, sections S2.3, S2.4, S2.5 and S2.6 are included in the closed part of DMF	
3.2.S.3		**CHARACTERISATION**	
Section		**Documents**	

	3.2.S.3.1	Elucidation of Structure and other Characteristics	
	3.2.S.3.2	Impurities	
3.2.S.4		**CONTROL OF DRUG SUBSTANCE**	
	3.2.S.4.1	API Specifications	
	3.2.S.4.2	Analytical Procedures	
	3.2.S.4.3	Validation of Analytical Procedures	
	3.2.S.4.4	Batch Analysis	
	3.2.S.4.5	Justification of Specification	
3.2.S.5		**REFERENCE STANDARDS**	
3.2.S.6		**CONTAINER CLOSURE SYSTEM**	
		Specifications and Test Methods	
3.2.S.7		**Stability**	
3.2.S.7.1		Forced degradation (stress) studies	
3.2.S.7.2.1		Accelerated and Long-term studies	
3.2.S.7.2.2		Drug substances intended for storage in a refrigerator	
3.2.S.7.2.3		Drug substances intended for storage in a freezer	
3.2.S.7.2.4		Drug substances intended for storage -20 ^{0}C	
3.2.S.7.3		**Proposed storage conditions and re-test period**	
3.2.P		**FINISHED PHARMACEUTICAL PRODUCT (FPP)**	
3.2.P.1		**Description of the Drug Product**	
3.2.P.2		**Pharmaceutical Development**	
3.2.P.2.1		Formulation and Process Development	
3.2.P.2.2		Physicochemical Characteristics of the Drug Substance	
3.2.P.2.3		Compatibility	
3.2.P.2.4		Physicochemical Characteristics of the Drug Product Relevant to Performance	
3.2.P.2.5		Microbiological Attributes	
3.2.P.2.6		Container Closure System	
3.2.P.3		**Manufacture**	
	3.2.P.3.1	**Manufacturer(s)**	
	3.2.P.3.2	**Formulae**	
	3.2.P.3.2.1	Unit Formula	
	3.2.P.3.2.2	Batch Formula	
	3.2.P.3.3	**Manufacturing Process**	
	3.2.P.3.4	**Process validation** ~For three consecutive batches	
	3.2.P.3.4.1	Sterile Products	
	3.2.P.3.4.2	Non-sterile Products	
3.2.P.4		**Control of Excipients**	
	3.2.P.4.1	**Specifications**	
	3.2.P.4.2	Analytical Procedures and Validation	
	3.2.P.4.3	Justification of Specifications	
	3.2.P.4.4	**Excipients of Human or Animal Origin**	

		*: BSE / TSE free certification	
	3.2.P.4.5	**Novel excipients** ***:** Provide information provided as per full API Section	
3.2.P.5		**Control of FPP**	
	3.2.P.5.1	**Finished Product Specifications**	
	3.2.P.5.2	**Analytical Procedures**	
	3.2.P.5.3	**Validation of Analytical Procedures**	
	3.2.P.5.4	**Batch Analysis**	
	3.2.P.5.5	Justification of Specification	
3.2.P.6		**Reference Standards**	
3.2.P.7		**Packaging/Container Closure System**	
	3.2.P.7.1	**Specifications and Test Methods**	
3.2.P.8		**Stability**	
3.2.P.8.1		Accelerated and Long-term Studies (General Case)	
3.2.P.8.1.1		Medicinal substances intended for storage in a refrigerator	
3.2.P.8.1.2		Medicinal substances intended for storage in a freezer	
3.2.P.8.1.3		Medicinal substances intended for storage below -20 ^{0}C	
3.2.P.8.2		**Proposed Storage Conditions and Shelf-life**	
3.2.P.8.3		**Stability Commitment**	
3.2.8		Additional Information	
3.2.8		Stability of Medicated Feeds	
3.2.8		**Mixing Studies**	
3.2.8		Premixes Proposed for Concurrent Use	
3.2.8		Feed Assay Validation	
3.2.8		*Samples*	
3.2.R		**REGIONAL INFORMATION/ REQUIREMENTS**	
	3.2.R.1	**Production documentation**	
	3.2.R.1.1	**Master production documentation**	
	3.2.R.1.2	**Executed production documentation**	
Section		**DOCUMENTS**	
4.1		**MODULE 4** **NON-CLINICAL PHARMACO-TOXICOLOGICAL DATA**	A must for new pharmaceutical active ingredients
4.2		**Data presentation**	Involves initial studies in laboratory animals and later pre-clinical studies in the target species, which should take into consideration the following: 1. Pharmacology 2. Toxicology 3. Discussions and conclusions 4. Expert report
4.3		**Pharmacodynamics**	Tests performed to establish the pharmacological actions that are relevant to the proposed indication(s) of the API and mechanisms of action
4.4		**Other actions (desired/undesired)**	Summary of action(s) other than those of therapeutic use. E.g. significant adverse reactions
4.5		**Pharmacodynamic interactions**	
4.6		**Pharmacokinetics**	Pharmacokinetics studies should be made with single dose by various routes.
4.7		**Absorption**	
4.8		**Distribution of API and metabolites**	

4.9	**Biotransformation**	
4.10	**Pharmacokinetic interactions**	
4.11	**Excretion**	
4.12	**Toxicological studies**	Should be described in relation to the proposed clinical use.
4.13	**General toxicity studies**	
4.14	**Acute, sub-acute and long-term toxicity studies**	
4.15	**Safety to users**	Studies on potential harmful effects to exposure by various routes, e.g. inhalation, topical contact, oral ingestion, performed on laboratory animals
4.16	**Risk assessment of veterinary medicines residues in food of animal origin**	**4.16 RESIDUE STUDIES** **4.16.1** Situations and conditions when the residue data requirements could be waived **4.16.2** Situations and conditions when the residue data requirement cannot be waived **4.16.3** Residue depletion study **4.16.4** Comprehensive residue depletion study **4.16.5** Analytical methodology
4.17	**Toxicity to the environment**	Products requiring environmental assessment include: (a) Antibiotics in poultry, pig, and fish feeds (b) Anthelmintics in large animals (c) Expired medicines from veterinary hospitals/clinics, co-ops and manufacturing plants
4.18	**Presentation of safety studies**	
5.1	**MODULE 5** **EFFICACY DATA**	Applicable to new chemical entities and bioequivalence studies. A summary of well presented, controlled blinded clinical trials conducted in target animals investigating the pharmacological and therapeutic properties, and adverse reactions is required. GCP compliant studies.
	Registration details	
	List of countries where product is registered	
	Proof of registration countries with stringent regulation (VICH founding and standing members)	
	Sample of FPP	
5.2	**Pharmacodynamic studies (target animals)**	
5.3	**Pharmacokinetics and bioavailability of the medicine in target animals**	
5.4	**Efficacy clinical end point studies in target species**	

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