South African Health Products
Regulatory Authority
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26 June 2023

GUIDELINE FOR VETERINARY MEDICINES EXEMPTIONS FROM CERTAIN MEDICINE REGISTRATION REQUIREMENTS

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 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. The 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 all administrative requirements to avoid delays in the processing and evaluation of applications.

The guidelines and application forms are available from the SAHPRA website.

Document History

Final Version	Reason for Amendment	Effective Date [dd Month yyyy]
1	Final guideline for implementation	01 March 2020
2	– Administrative changes – Old document number 2.48 changed to SAHPGL-PEM-VET-01	05 August 2022

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Contents

Glossary

Abbreviation/ Term	Meaning
Well established APIs, API combinations and products	• When an active ingredient of a medicine has been used for more than 10 years and its efficacy and safety have been well established • has been widely used in a sufficiently large number of patients to permit the assumption that safety and efficacy are well known in the context of local disease patterns • have the same route of administration and strength, and the same or similar indications as in those countries that SAHPRA aligns with • undertake post-marketing monitoring • in such cases, registration may be based on results from the scientific literature
MUMS	Minor Use Minor Species
Major species	Cattle, Pigs, Sheep, Goats, Fowls, Ostriches, Horses, Dogs and Cats, i.e. either animals that contribute to a large extent to human food safety, or, animals of which a large number is treated.
Minor species	Any species other than those already named under major species.
Minor use	Either the use of a veterinary medicine in a minor species, or the use of a veterinary medicine in any animal species for an infrequently occurring or geographically limited disease.
Target animal safety study	Includes in vivo studies under controlled conditions which identify the toxicity syndrome(s) associated with the final formulation and the margin of safety of use of the product in the treated animal species for which approval is being sought.
Withdrawal period	The interval between the time of last administration of the veterinary medicine and the time when the animal can safely be slaughtered for food purposes.

1. INTRODUCTION

The Medicines and Related Substances Act (Act 101 of 1965) (hereinafter 'the Act') makes provision for the registration of medicines based on quality, safety, and efficacy. In addition, the registration process for veterinary medicines includes evaluation of toxicity, target animal safety, withdrawal period data, operator safety, and possible environmental impact.

1.1 Purpose

The purpose of this guideline is to clarify the provisions of the Act that allow for exemptions from certain requirements and to encourage applicants to register much-needed medicines for which the regulatory burden may be perceived as being too high e.g., minor use minor species.

1.2 Scope

This document describes the rationale on the development of guidance to applicants wishing to submit a dossier on quality, safety, and efficacy for veterinary medicinal products for minor use or minor species. It also covers certain exemptions to registration requirements where minimal data is available.

2. LEGAL PROVISION

Whilst the Act stipulates that only the quality, safety, and therapeutic efficacy of medicine may be considered to determine whether the registration or availability of medicine is in the public interest, the Act also makes provision for consideration of registration of medicines by exemption from certain registration requirements or exemption from registration in special circumstances.

The relevant legislation includes the following provisions:

2.1 The Act:

2.1.1 Section 1(3)

1.3 (a) In determining whether the registration or availability of medicine is in the public interest, regard shall be had only to the safety, quality, and therapeutic efficacy thereof in relation to its effect on the health of man or any animal.

2.1.2 Section 14(3)

(1) Save as provided in this section or sections 21 and 22A, no person shall sell any medicine, medical device, or IVD which is subject to registration by virtue of a declaration published in terms of subsection

(2) unless it is registered.

2.1.3 Section 36

Exclusion of any medicine, scheduled substance, medical device, or IVD from the operation of the Act

(1) The Minister may, on the recommendation of the Authority, by notice in the Gazette exclude, subject to such conditions as he or she may determine, any medicine, scheduled substance, medical device or IVD from the operation of any or all the provisions of this Act and may in like manner amend or withdraw any such notice.

2.2 Regulations made in terms of the Act:

The following General Regulations issued in terms of the Medicines Act enable the Authority to stipulate the technical requirements for the registration of medicines for both human and veterinary use and ensure continued compliance with the accepted standards and specifications.

2.2.1 Regulation 16 (6)

(6) A medicine, in respect of which an application for registration is made, must comply with the technical requirements as determined by the Authority.

2.2.2 Regulation 16 (9)

(9) The provisions of this regulation shall, with the necessary changes, apply to the application for the registration of veterinary medicines.

2.2.3 Regulation 53 (1)

Every medicine must continue to comply with the standards and specifications which were furnished to the Authority, and which have been accepted by the Authority with regards to such medicine.

Any proposed deviation from accepted standards and specifications referred to in sub-regulation (1) must be submitted to the Authority for prior approval and such deviation shall not be introduced before the said approval has been granted.

In recognition of the scarcity of approved veterinary medicines in South Africa for minor use including use in wildlife, special provisions in this guideline are included to facilitate the registration of such products.

3. General Requirements

All applications for exemptions from requirements must be addressed to the Authority.

3.1 Letter of application

3.1.1 Indicate clearly in the letter of application:

- the requirement(s) for which exemption is sought.
- justification for such exemption including the basis for concluding that alternative approaches may be used, or certain technical requirements waived and
- where the relevant justification is in the dossier.

3.1.2 Where information is available, at least the following should be addressed in the dossier:

(i) Details of registration or pending registration of the medicine with any other regulatory authority, and the history of the medicine.

(ii) Any sale in the Republic of South Africa.

(iii) Known marketing experience in other countries.

(iv) A description of the disease or condition for which the medicine is proposed to be used.

(v) The basis for concluding that the medicine is:

- in the interest of animal well-being; or
- for use in a pandemic or high impact situation.
- for animal welfare or clinical management, or unmet need or
- for a rare disease or condition.

(vi) The size and other demographic characteristics of the target population affected in RSA and the source of the information.

(vii) The proposed minor species for use or the proposed minor use in the case of veterinary medicine.

(viii) Data on user and environmental safety (if applicable)

(ix) Periodic Safety Update Reports (PSUR) to be monitored.

3.2 Application for registration

The application form has been upgraded to CTD format and it must be used for veterinary medicines.

4. Situations When Exemption from Certain Requirements may be considered

4.1 Transcription from MBR1/VMRF1 to CTD

Conversion of MBR1/ VMRF1 requires transcription of the currently approved information to the CTD format. Where information was not required at the time of submission of the original application, or for the registration of the medicine, or subsequent variations when these were applied for, it is not necessary to populate those sections of the CTD dossier (e.g., pharmaceutical development report). Resubmission of non-clinical and clinical data (Annexures 13, 14 & 15 / PARTs 4 & 5) in such cases is not required when transcribing from MBR1/VMRF1 to CTD.

4.2 Medicines where limited clinical data and safety are available

Promising medicines, based on 4.1.2 (v), with limited clinical data in support of safety and efficacy, may be considered if there is a prospective planned process and commitment by the applicant to gather further supporting evidence post marketing.

4.3 Medicines that are well established but the moiety has not previously been registered in South Africa

In such circumstances, literature-based evidence in support of safety and efficacy could be considered.

In such circumstances reliance can be applied, if the moiety has been registered in a Recognized Regulatory Authority, with full clinical data, currently still has an active marketing authorization and is under active post-marketing surveillance.

In terms of quality, Pharmacopoeial requirements, as well as compliance with the minimum requirements stipulated in the Quality guideline, could be considered.

The influence of the formulation on the release of the API may be demonstrated as no locally registered reference product would be available. Where a reference product can be obtained from a country which the Authority aligns, this product can be used for comparative studies. BE studies using the RRA reference product should be provided.

4.4 Medicines where the innovator product is no longer marketed in South Africa

In such circumstances, literature-based evidence in support of safety and efficacy could be considered. In terms of quality, Pharmacopoeial requirements, as well as compliance with the minimum requirements stipulated in the Quality guideline, could be considered. Previous registration with MCC or SAHPRA may be considered as evidence of safety and efficacy unless the innovator was withdrawn due to safety or efficacy concerns.

In terms of quality, Pharmacopoeial requirements, as well as compliance with the minimum requirements stipulated in the quality guideline could be considered.

The influence of the formulation on the release of the API may be demonstrated as no locally registered reference product would be available.

Where a reference product can be obtained from a country, the regulatory authority with which SAHPRA aligns, this product can be used for comparative studies.

4.5 Medicines where the innovator product is no longer marketed in South Africa but for which there are Pharmacopoeial monographs available

In such circumstances, literature-based evidence in support of safety and efficacy could be considered.

In terms of quality, Pharmacopoeial requirements, as well as compliance with the minimum requirements stipulated in the Quality guideline, could be considered.

The influence of the formulation on the release of the API may be demonstrated as no locally registered reference product would be available. Where a reference product can be obtained from a country, the regulatory authority with which SAHPRA aligns, this product can be used for comparative studies.

4.6 Specific veterinary medicines scenarios

4.6.1 Registered veterinary medicine for use in a minor species

Extrapolation of interspecies data of medicine already approved for use in a major species if relevant could be considered. If a commitment to collect safety and efficacy information as part of the post-marketing surveillance initiative is made, the motivation may be considered.

4.6.2 Registered veterinary medicine for a minor use

Extrapolation of the effect may be considered when the medicine is already approved for use in another species, and if relevant. If a commitment to collect safety and efficacy information as part of the post-marketing surveillance initiative is made, the motivation may be considered.

4.6.3 Entirely new medicine for use in a minor species or a minor use

In such circumstances, limited clinical data or literature-based evidence in support of safety and efficacy or extrapolation of data pertaining to a similar class medicine already approved, and/or if relevant a commitment to collect safety and efficacy information as part of the post-marketing surveillance initiative is made, the motivation may be considered.

4.6.4 Medicine registered for human use but not registered for use in a minor species or a minor use

In such circumstances limited clinical data or literature-based evidence in support of the safety and efficacy, or extrapolation of human data when adequately justified and/or and if relevant a commitment to collect safety and efficacy information as part of the post-marketing surveillance initiative is made, the motivation may be considered.

5 Module 4 and 5

5.1 Efficacy

The applicant is required to conduct pilot studies for proof of concept for minor use/minor species status designation. As an example, proof of efficacy in 1 to 5 of the target species with the following sample size is suggested: 1 species n = 6 to 10 animals and for 3 to 5 species n = 3.

The applicant needs to commit to collecting safety and efficacy information as part of the post-marketing surveillance initiative.

5.2 Withdrawal Periods

Submit results of residue depletion studies and recommended withdrawal period for veterinary medicines intended for use in food-producing animals. In the case of wildlife, a lot of products from immobilized animals end up in the food chain as 20% of meat consumed by the population is from wildlife. Where there are no MRLs yet, extrapolation from a major species (Refer to FDA and EMA MUMS guidelines) on a case-by-case basis using a worst-case scenario can be considered. In South Africa, a default withdrawal period of 90 days for conventional formulations is acceptable unless determined.

6 REFERENCES

The following related documents are referenced:

6.1 CVMP: Efficacy and target animal safety data requirements for veterinary medicinal products intended for minor uses or minor species.
6.2 CVMP: Quality data requirements for veterinary medicinal products intended for minor use or minor species (MUMS)/ limited market.
6.3 Safety and residue data requirements for veterinary medicinal products intended for minor use or minor species (MUMS)/ limited market.

7 VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces the old guideline for Veterinary Medicines Exemptions from Certain Medicine Registration Requirements (Document No. 2.48). It will be reviewed on this timeframe or as and when required.