agriculture,
forestry & fisheries

Department:
Agriculture, Forestry and Fisheries
REPUBLIC OF SOUTH AFRICA

REGISTRATION GUIDELINE FOR MINOR SPECIES

This guideline is intended to outline information and data requirements for minor species to applicants wishing to submit applications for the registration of Stock Remedies in South Africa in terms of the Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act, 1947 (Act 36 of 1947).

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DEFINITION OF TERMS

Generic drug/Stock Remedy
Generic drug is a product that contains active substance that have already been registered in terms of Act No. 36 of 1947

Limited market
A limited market for a stock remedy is a market that is limited in size due to its occurrence in minor species.

Major species
Major species are listed as food producing animals; cattle, sheep, pigs, chickens, salmon/catfish, horses, goats and non food producing animals such as dogs and cats. In South Africa, turkey, ostrich and some game animals are regarded as major species as they produce food for human consumption. All food producing animals will be regarded as major species.

Minor species
There is no internationally accepted definition of minor species. For the purpose of this document minor species refers to Cage birds, Racing pigeons and Ornamental fish.

Minor use
Minor use of stock remedies on major species is the use of medicine for the treatment or prevention of scarce diseases or diseases that are limited to small geographic areas and are indicated for smaller market sector.

New drug/Stock Remedy
New drug is a product containing an active pharmaceutical ingredient(s) that has not previously been assessed/ registered in South Africa for use in animals or a product with an active pharmaceutical ingredient(s) that has not been registered through Act No. 36 of 1947 but is listed in the Schedules of Act 101 of 1965.

1. INTRODUCTION

In South Africa there are a lot of unregistered stock remedies on the markets that are used on minor species. However, the safety, quality and efficacy of these medicines have not been established. This together with the welfare of animals makes this necessary to register and regulate these remedies.

Minor species is regarded as those domesticated animals other than major species. Major species are generally listed as food producing animals; cattle, sheep, pigs, chickens, salmon/catfish, horses, goats and non food producing animals such as dogs and cats. In South Africa, turkey, ostrich and some game animals are regarded as major species as they produce food for human consumption. Food producing animal will be regarded as major species. Therefore, for the purpose of this guideline minor species refers to cage birds, racing pigeons and ornamental fish.

The current registration requirements in terms of Act No. 36 of 1947 require that minor species remedies be registered with the same level of requirements as the orthodox medicine. These requirements do not provide incentives for companies to invest in developing products for registration purpose as the costs are high and it is often difficult to recover the costs due to limited markets. It is generally accepted that the problem is, in large part due to the costs of research and development being a disincentive to industry to bring such new products to the market place when the return on investment is likely to be small and certainly less than that resulting for mainstream products for major species. One major cause of the lack of authorised stock remedies seems to be also the limited economic value of some minor species and the fact that the animal owner has to bear the total cost of any treatment. Furthermore, the markets are much weaker and more fragmented than that of human health care and major species.

In 2009, the Registrar of Act No. 36 of 1947 issued a circular requesting all companies to submit a list of products used on minor species (cage birds, racing pigeon and ornamental fish) to the office to compile a register. Subsequently, the registrar requested the companies to prepare for registration which would begin after completion of guidelines for registration of stock remedies for minor species.

This guideline is for registration of stock remedies for minor species. Food producing animals are excluded. Minor use in major species will not be covered in this guideline.

2.1. Objectives

The objectives of this guideline are:

- to provide applicants with information on quality data requirements to support applications for authorisation of remedies intended for minor species;
- to provide applicants with information on quality, safety and efficacy data requirements to support applications for authorisation of stock remedies intended for minor species;

2.2. Scope of the guideline

The scope of this guideline is to provide data requirements for registration of;

- Registered stock remedies for use in a minor species.
- Medicines/remedies registered in other countries
- **New drug/Stock Remedy** for use in minor species.

This guideline is based on EU guidelines and policies on registration of Veterinary Medicines for minor species and minor use.

3. DATA REQUIREMENTS

The applicant should provide summary of information/motivation on:

- The product quality (e.g. active substance, finished product, mechanism of action, proposed indication and method of use);
- The status of the development of the product relevant for the classification for minor species;
- The target species and information on safety
- Prevalence of the condition in the in South Africa best available evidence for the incidence/prevalence of the disease including peer-reviewed published literature;
- Current and/or alternative approaches to therapy and available treatments;
- Severity of the condition and the need for this remedy;
- Potential zoonoses;
- Is the product indicated for a controlled animal disease in South Africa
- Registration in other countries/authorities

4. NEW DRUG APPLICATION AND GENERICS

For both New Drug Application and Generics that have not been registered under Act 36/1947, the application must be accompanied by a letter from Medicines Control Council of the Medicines and Related substances Control Act, 1965 (Act No 101 of 1965) granting the said product an exemption from scheduling under Act 101, so that the product can be registered under Act 36 of 1947.

5. PHARMACEUTICAL DATA

The following data as per stock remedies regulations (Regulations Relating to Stock Remedies, Regulation No. 2006) should be submitted:

- Chemistry
- Active Pharmaceutical Ingredient (API)
- Formulation and Manufacturing
- Stability data

Registered stock remedies for use in a minor species
In case of a registered stock remedy this will be regarded as line extension and no quality data will be required provided there are no changes on the active pharmaceutical ingredient, final formulation and packaging material. In case of changes occurring in the quality of the product, the applicant must substantiate and if necessary submit data as per stock remedies regulations (Regulations Relating to Stock Remedies, Regulation No. 2006).

Medicines registered in other countries for use in a minor species.
These will be regarded as new applications and full quality data (as per Regulations Relating to Stock Remedies, Regulation No. 2006) must be submitted with the application.

Entirely new medicine (new API) for use in a minor species.
Due to the costs of developing an entirely new medicine, it is considered that this category will only be encountered very rarely. Furthermore, the active substances in such medicines are likely to be substances that are: used in human or veterinary medicines or are used as pesticides. In such cases, a full supporting quality data package will be required and must be submitted (as per Regulations Relating to Stock Remedies, Regulation No. 2006).

6. EFFICACY DATA

6.1 Clinical studies

A rationale for the selected treatment regimen and duration of therapy should be provided. The proposed treatment regimen may be justified using:

- Specific dose determination/confirmation studies,
- and/or
- Pharmacokinetic and pharmacodynamic (e.g. MIC) data, and/or
- Literature data/results of pilot studies/clinical experience reports, and/or
- Extrapolation from another species for which the product is authorized
- In case a product is registered with other authorities the label should be submitted

In principle, a dose confirmation study and a field trial should be provided. Clinical studies should be conducted using the final formulation.

In the absence of specific dose determination studies, the efficacy of the product at the recommended dose regimen should be demonstrated in an adequate and controlled dose confirmation study in the target species. However, if a field study has been provided and the selected dose is justified (see section 5.1), dose confirmation studies might not be required. Where the efficacy of the test product has been evaluated in the minor species in dose determination and/or dose confirmation studies and where adequate data are available relating to target animal

safety, field studies may not be necessary for certain indications. In such cases, the absence of field studies must be justified.

The safety and efficacy of the product under evaluation should be investigated and demonstrated in the target species. Interspecies extrapolation of pre-clinical data will be accepted whenever scientifically justifiable. Extrapolation of data from a major to a minor species is most appropriate where the test product is authorised for the same or a similar indication in the major species, and where the pharmacology (both in terms of pharmacodynamics and pharmacokinetics) of the test product is likely to be comparable in both species.

Data to support the efficacy of the product for all proposed indications in the target species will be required.

Literature may be used to support the efficacy claim. Bibliographic data should originate from acknowledged scientific literature ideally from peer-reviewed journals and books. Should adequate documentation not exist in the literature, the efficacy of the product should be demonstrated in appropriately designed studies. The type and number of studies to be conducted will depend on the deficiencies in available data. It is recognized that existing studies may not satisfy current Good Clinical Practice (GCP) requirements. Such studies may be considered acceptable if the design is appropriate to the stated objective of the study. Ideally pivotal studies used to support applications for products intended for the treatment of infections or parasitic conditions should be conducted in South Africa in order to simulate South African conditions of use. Data from studies conducted outside of South Africa will be accepted if justifiable.

7. SAFETY DATA

7.1 Pre-clinical data

Data as per stock remedies regulations (Regulations Relating to Stock Remedies, Regulation No. 2006 should be submitted.

Preclinical data must be submitted for **New drug/Stock Remedy** for use in a minor species the following pre-clinical data must be submitted:

- Pharmacological (PD/PK)/ Metabolic
- Mammalian toxicity
- Occupational Health
- Ecotoxicity
- MSDS

Where justifiable interspecies extrapolation will be justifiable

For registered stock remedies for use in a minor species and medicines registered in terms of Act 101 of 1965 and those registered in other countries the applicant are not required to submit pre-clinical data.

The MSDS must be submitted with each application

7.2 Target animal safety

New drug/Stock Remedy for use in a minor species.

Target animal safety data must be submitted. The target animal safety data must include the margin of safety and tolerance study.

Registered stock remedies for use in a minor species and for medicines registered in terms of Act 101 of 1965 for use in a minor species and those registered in other countries

Tolerance study must be done. Additional information from bibliographic data will be accepted as supporting evidence for tolerance studies.

For all applications, appropriate data should be provided to characterise the tolerance of the target species to the test product following administration by the proposed route. Where no/limited data on the safety profile of the active substance in the target species are available, a basic controlled study demonstrating the safety of the (near) final formulation in the target species will be needed. In order to demonstrate a margin of safety in the target species, the study should be designed to investigate tolerance to the product when administered at doses in excess of the recommended treatment dose. The Applicant should justify the study design employed.

Where safety in breeding animals of another species is demonstrated, additional safety data in breeding animals of the target species might not be necessary. However, in the absence of adequate data, a restriction on use in breeding animals (e.g. use in accordance with the risk/benefit assessment of a veterinary surgeon) may be required.

8. RESIDUE DATA

Residue data is not applicable as these products are not for use in food producing animals. The label will have the warning," Not for use in food producing animals".

9. REFERENCES

1. Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act, 1947 (Act No. 36 of 1947)

2. Regulations Regarding Stock Remedies. Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act 1947 (Act 36 of 1947 as amended). Department of Agriculture. 2006

3. Guideline on the Quality data requirements for veterinary medicinal products intended for Minor Uses or Minor Species (EMEA/CVMP/QWP/128710/2004)

4. Guideline on Safety and Residue data requirements for veterinary medicinal products intended for Minor Uses or Minor Species (EMEA/CVMP/SWP/66781/2005)

5. Guideline on Efficacy and Target Animal Safety data requirements for veterinary medicinal products intended for Minor Uses or Minor Species (EMEA/CVMP/EWP/117899/2004)

6. Guidance on the classification of veterinary medicinal products indicated for minor use minor species (MUMS) / limited market (EMA/CVMP/388694/2014)

7. Regulations Regarding Stock Remedies. Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act 1947 (Act 36 of 1947 as amended). Department of Agriculture. 2006