MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

MEDICINES CONTROL COUNCIL

VETERINARY ORPHAN PRODUCTS

This guideline is intended to provide recommendations to applicants wishing to submit applications for the registration of orphan products in veterinary medicines. It represents the Medicines Control Council's current thinking on the safety, quality and efficacy of Veterinary Orphan Products. It is not intended as an exclusive approach. Council 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 MCC is committed to ensure that all registered medicines will be of the required quality, safety and efficacy. It is important that applicants also adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.

Guidelines and application forms are available from the office of the Registrar of Medicines and the website.

Version 1: First publication released for implementation and comment	May 2012
Deadline for comment	29 June 2012

REGISTRAR OF MEDICINES

TABLE OF CONTENTS

1 INTRODUCTION

This guideline is intended to facilitate the evaluation and ~~a~~ registration of minor use medicines indicated for use in both minor and major species or medicines for use in a condition that is rare or occurs in limited geographical areas.

In recognition of the scarcity of approved veterinary medicines in RSA for minor use, special provisions in this guideline are included to facilitate evaluation and thereby the registration of Veterinary Orphan Products.

The registration process for Veterinary Orphan medicines includes evaluation of toxicity, target animal safety and withdrawal period data.

The applicant has to motivate the request for orphan product registration.

A registered veterinary orphan product may be marketed.

Periodic Safety Update Reports (PSUR) must be available on request.

Council may, at any time, request further information for registered products.

2 DEFINITIONS

2.1 Active Moiety/Ingredient

The moiety or that part of the molecule responsible for the physiological or pharmacological action of the veterinary medicine.

2.2 Consumer

Any person ingesting food of animal origin and therefore exposed to the potentially harmful veterinary medicine residues in animal products.

2.3 Exclusive approval

Means effective date of MCC approval as stated on the registration certificate of a designated orphan product, and applies to this product only.

2.4 Human food safety

Non clinical toxicology studies, total residue and metabolism studies, analytical method validation studies and tissue residue depletion studies.

2.5 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.

2.6 Maximum Residue Limit (MRL)

The maximum residue limit of a chemical allowed in food destined for human consumption. This value can be defined from the ADI or extrapolated according to current scientific knowledge, subject to approval by the Directorate: Food Control.

2.7 Minor Species

Any species other than those already named under major species.

2.8 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.

2 DEFINITIONS - continued

2.9 Orphan Product for veterinary use

Any veterinary medicine intended for sale in a minor species or intended for minor use in a major species.

2.10 Pharmaceutical Inspection and Co-operation Scheme (PIC/S) agreement

A co-operation agreement between participating medicine regulatory authorities in the field of inspections related to Manufacturers of medicines with the view to maintain mutual confidence and promoting the quality assurance of Good Manufacturing Practice inspections with the view to global harmonisation. Through the sharing of information on whether a particular manufacturing site is producing medicines in accordance with the GMP requirement, MCC may decide to waive or not to waive the requirement to perform an inspection. However, the MCC has the option of a follow up verification inspection, if necessary.

2.11 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.

2.12 Wildlife species

Those animals which live in an unconfined free-range environment and may or may not be in national, provincial or private conservation areas.
Such animals are not routinely ranch-raised for slaughter for human consumption.

2.13 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.

3 CONTENT AND FORMAT OF A SUBMISSION

A motivation for acceptance as a veterinary orphan product should be included in the covering letter and should address at least the following:

(i) A description of the disease or condition for which the medicine is proposed to be registered

(ii) The proposed species for use of such a medicine

(iii) Current regulatory status and the history of the medicine

(iv) Known marketing experience in other countries and or RSA

(v) The basis for concluding that the medicine is

- for minor use, and/or
- for a rare disease or condition

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

The current version of the MRF1 application form must be used.

The following PARTs must be submitted:

3 CONTENT AND FORMAT OF A SUBMISSION - continued

3.1 PARTs 1A 1B 1D

Complete the administrative information as required in these PARTs.

3.2 PART 1C a) and c) (PI and label) (No PIL)

3.3 PART 2A

Address the pharmaceutical issues in accordance with Pharmaceutical & Analytical guideline

3.4 PARTs 2B, 2D, 2E

Include either PART 2 B or PARTs 2D plus 2E.

Submit residue results of depletion studies and recommended withdrawal periods for veterinary medicines intended for food-producing animals.

Furthermore, the following aspects should be addressed:

3.4.1 A summary and analysis of available data on the pharmacological effects of the medicine. An explanation of how the data supports the rationale for use of the medicine in the rare disease or condition

3.4.2 A summary and analysis of available non-clinical and clinical data pertinent to the medicine and the disease and published reports. An explanation of how the data supports the rationale for use of the medicine in the rare disease or condition.

3.4.3 A definition of the population from which subjects will be identified for clinical trials, if known and proposed study design for establishing efficacy.

3.4.4 A detailed outline of any protocols under which the medicine has been or is being studied for the rare disease or condition and a summary of analysis of available data from such studies

3.4.5 Applicant's proposal as to the scope of non-clinical and clinical investigations needed to establish the safety and efficacy of the medicine (when applicable).

3.4.6 Target animal safety and human food safety information.

3.4.7 Data on user and environmental safety

3.4.8 Indication of the health risk to the patient/end–user/consumer and reported clinical problems. MCC determines that people will not be exposed to unsafe residues in their food as a result of the approved use. This is done by assessing the hazard and controlling exposure through the setting of tolerances and withdrawal periods. Minor use applications often derive benefit from interspecies data extrapolation when the drug product is already approved for use in major species and when such data already exists in the approved major species application.

3.4.9 Estimated prevalence of the disease or condition for which the product is intended to be used, together with a list of sources.

3.4.10 Confirmation that the product is of minor indication in a minor species.

3.4.11 An applicant may request orphan product designation of an already approved product for an unapproved use without regard to whether the prior marketing approval was for an orphan product.

3.5 PART 2 C and PART 3H

Exemption from submitting PART 2C may be requested if PART 3 H is submitted

3.6 PART 3

Full PART 3 to be submitted, in accordance with the requirements of the Pharmaceutical & Analytical and Stability guidelines.

3.7 PARTs 4 and 5

Exemption from these parts may be requested but the data should be available on request.

4 NAMES AND SCHEDULING

Proprietary names and scheduling status will be evaluated according to current guidelines.

5 UPDATE HISTORY

Date	Reason for update	Version & publication
Aug 2011	Version 1 prepared for comment	Version 1, May 2012
May 2012	Published for comment	
29 June 2012	Deadline for comment	