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ACVM REGISTRATION STANDARD AND GUIDELINE FOR EFFICACY OF ANTISPASMODIC PRODUCTS

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Endorsement:
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CONTENTS

ACVM REGISTRATION STANDARD AND GUIDELINE FOR EFFICACY OF ANTISPASMODIC PRODUCTS

1 INTRODUCTION

This document specifies the minimum study and reporting requirements, i.e. the standard, for efficacy studies submitted in support of an application to register an antispasmodic product, or to vary the conditions on a registered antispasmodic product. It also incorporates guidelines, which are intended to provide more detailed information and guidance to applicants to assist them in complying with the standard.

The requirements that form the standard are shown in this document in **bold font**, while the guidelines are in regular font.

Guidelines reflect principles commonly recognised by the scientific community as appropriate and necessary for collecting scientific data. It is recognised that there are acceptable methods, other than those described in these guidelines, that are capable of achieving the principles of this document.

The standard is compulsory in all cases where efficacy data are required to be provided for registration of antispasmodic products, unless a waiver has been granted by NZFSA.

Waivers may be granted to reduce the number of studies or type of data that an applicant must submit (e.g. by permitting cross-referencing to existing data held by NZFSA). *These waivers must be granted by NZFSA prior to the applicant submitting an application.* This standard will be reviewed periodically, and waivers incorporated if appropriate.

Applicants should note that they are responsible for providing all information required by the ACVM Group of NZFSA to make a decision on the application. Applications that do not contain the required information will not be assessed. If further advice is required, applicants are advised to contract the services of an appropriate consultant prior to submitting the application.

1.1 Scope

The standard must be followed by:

- all persons applying to register an antispasmodic product or to vary the conditions on a registered antispasmodic product;
- all persons accredited under the Agricultural Compounds and Veterinary Medicines Act 1997 to undertake a risk assessment of applications made to register an antispasmodic product or to vary the conditions on a registered antispasmodic product.

The standard provides specifications for:

- general efficacy requirements;
- clinical studies; and
- field studies.

1.2 Definition

Target species
The species of animal for which the test substance is intended for final use.

1.3 References

ACVM Research Standard
ACVM Registration Information Requirements for Veterinary Medicines in New Zealand

2 GENERAL REQUIREMENTS FOR EFFICACY STUDIES

2.1 Clinical requirements

2.1.1 All studies must be conducted in accordance with the *ACVM Research Standard.*

2.1.2 The efficacy of the product and/or its active ingredients must be investigated in the target species.

2.1.3 Product formulation used in studies must be identical to that being proposed for registration.

2.1.4 Experimental data must be confirmed by data obtained under practical field conditions.

2.1.5 Sample sizes must be adequate to detect differences among treatment groups with a statistical power of at least 80%.

2.1.6 Adequate statistical methods must be used and justified. A 5% or lesser probability level ($P \leq 0.05$) should be used in deciding whether to accept or reject the null hypothesis.

2.1.7 Where a dose range is stated on the label, efficacy studies must be undertaken using the lowest dose rate.

2.2 Documentation

2.2.1 Reports must be presented in accordance with the *ACVM Research Standard.*

2.2.2 The applicant must state the overseas licensing status of the remedy. A reason must be given where the remedy is not licensed for use in the country of origin.

3 SPECIFIC REQUIREMENTS FOR EFFICACY OF ANTISPASMODIC PRODUCTS

The following are minimum study and reporting requirements (with guidelines) for evaluating the efficacy of antispasmodic products. They are additional to the general efficacy requirements above.

Field studies using these products are usually less definitive than clinical studies because the parameters measured are often subjective. Therefore, clinical studies supported with solid *in vitro* evidence of efficacy are vital.

3.1 General

3.1.1 Claims for efficacy must be based on a demonstrated antispasmodic effect on a specific muscle type.

3.1.2 Pre-clinical studies must be reported, including the rationale for the selection of the active ingredient(s) and the dose(s) used. There must be definitive evidence of an antispasmodic effect *in vitro*.

3.2 Clinical studies

3.2.1 Study animals must be free of disease that could affect the outcome of the study.

The animals used should be subject to similar feeding, anthelmintic and vaccination regimens.

Acclimatisation to the study environment, including any monitoring devices, is appropriate.

3.2.2 A negative control group must be included.

A crossover design is suitable for these studies with each animal acting as its own control. The washout period between treatments in a crossover study should take into account the known pharmacokinetics of the antispasmodic used. Saline is a suitable control substance.

3.2.3 The method of measuring the antispasmodic effect must be fully described.

Contractions may be measured directly (e.g. pressure tracings, electrical activity) or indirectly (e.g. pain relief, ingesta flow). Where indirect measurements are made, the correlation between the parameters measured and the antispasmodic activity of the product should be clearly explained.

3.2.4 The following parameters must be reported for each animal:

- **the lag time from drug administration to the start of the antispasmodic effect;**
- **the duration of the antispasmodic effect; and**
- **subjective observations of the investigator(s).**

3.2.5 The experimental design should monitor other significant clinical effects of the drug where indicated by the pharmacology of the product, e.g. cardiovascular, CNS.

3.3 Field studies

3.3.1 The method of measuring the antispasmodic effect must be fully described.

Where indirect measurements are made, the correlation between the parameters measured and the antispasmodic activity of the product should be clearly explained.

3.3.2 The following parameters must be reported for each animal:

- **the lag time from drug administration to the start of the antispasmodic effect;**
- **the duration of the antispasmodic effect; and**
- **subjective observations of the investigator(s).**