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ACVM REGISTRATION STANDARD AND GUIDELINE FOR EFFICACY OF ANTIHISTAMINE PRODUCTS

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CONTENTS

- 1 INTRODUCTION
 - 1.1 Scope
 - 1.2 Definitions
 - 1.3 References

- 2 GENERAL REQUIREMENTS FOR EFFICACY STUDIES
 - 2.1 Clinical requirements
 - 2.2 Documentation

- 3 SPECIFIC REQUIREMENTS FOR EFFICACY OF ANTIHISTAMINE PRODUCTS
 - 3.1 General
 - 3.2 Clinical studies
 - 3.3 Field studies

ACVM REGISTRATION STANDARD AND GUIDELINE FOR EFFICACY OF ANTIHISTAMINE 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 antihistamine product, or to vary the conditions on a registered antihistamine 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 is required to be provided for registration of an antihistamine product, 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 antihistamine product or to vary the conditions on a registered antihistamine product;
- all persons accredited under the Agricultural Compounds and Veterinary Medicines Act 1997 to undertake a risk assessment of applications made to register an antihistamine product or to vary the conditions on a registered antihistamine 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 ANTIHISTAMINE PRODUCTS

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

3.1 General

- 3.1.1 Claims for efficacy must be based on a known antihistamine effect demonstrated by *in vitro* studies.**
- 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.**
- 3.1.3 Studies must show that the antihistamine is efficacious in the treatment of the specific disease syndrome in the target species, e.g. bovine asthma, canine atopic dermatitis, etc.**

3.2 Clinical studies

- 3.2.1 The method of measuring the antihistamine effect must be fully described.**

Effects may be measured directly or indirectly. Where indirect measures are made, the correlation between the parameters measured and the antihistamine activity of the product should be clearly explained.

- 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 antihistamine used.

- 3.2.3 The method of diagnosing the disease condition of study animals must be fully described.**

This should include steps taken to rule out other causes of the disease, e.g. blood chemistry, ectoparasiticide treatment. If a grading system is used for diagnosis, it should be reported.

- 3.2.4 Study animals must be free of the effects of medication that may interfere with study results (e.g. corticosteroids).**

Hypoallergenic diets may be continued provided both the treated and control animals are on the same diet. Nutrients used as treatment, e.g. essential fatty acids, should be discontinued for the duration of the study.

3.2.5 The following parameters must be reported for each animal:

- **the lag time from drug administration to the start of the antihistamine effect;**
- **the duration of the antihistamine effect;**
- **the extent to which the antihistamine was effective; and**
- **subjective observations of the investigator(s), including side effects.**

If a grading system is used to determine the extent of efficacy, the grades used should be explained in terms of clinical recovery. Where practicable, observations should be made by the same person.

3.3 Field studies

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

Effects may be measured directly or indirectly. Where indirect measures are made, the correlation between the parameters measured and the antihistamine activity of the product should be clearly explained.

3.3.2 The method of diagnosing the disease condition of study animals must be fully described.

This should include steps taken to rule out other causes of the disease, e.g. blood chemistry, ectoparasiticide treatment. If a grading system is used for diagnosis, it should be reported.

3.3.3 Study animals must be free of the effects of medication that may interfere with study results (e.g. corticosteroids).

Hypoallergenic diets may be continued provided both the treated and control animals are on the same diet. Nutrients used as treatment, e.g. essential fatty acids, should be discontinued for the duration of the study.

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- **the extent to which the antihistamine was effective; and**
- **subjective observations of the investigator(s), including side effects.**

If a grading system is used to determine the extent of efficacy, the grades used should be explained in terms of clinical recovery. Where practicable, observations should be made by the same person. If not, it should be clearly stated by whom observations were made.