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ACVM REGISTRATION STANDARD AND GUIDELINE FOR EFFICACY OF TEAT SANITISERS

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Endorsement:
Date:

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1 INTRODUCTION

Efficacy of a veterinary medicine is understood to be the degree to which the medicinal claims made by the applicant have been justified and are likely to be attained under practical field conditions within New Zealand. The need for an efficacy standard arises from section 4 of the ACVM Act 1997, which provides for prevention or management of risks associated with the use of agricultural compounds:

- risks to trade in primary produce; and
- risks to animal welfare; and
- risks to agricultural security.

Risks to animal welfare can arise if the use of a compound, or its failure to achieve product claims, could result in unnecessary pain or distress in the target animal. Efficacy data is the verification that the trade name product will prevent or treat diseases characterised by unnecessary pain or distress. Any claim for these diseases must be soundly supported by scientific evidence consistent with these standards.

This document specifies the minimum study and reporting requirements, i.e. the standard, for efficacy studies submitted in support of an application to register a teat sanitiser or to vary the conditions on a registered teat sanitiser. 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 a teat sanitiser, 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 a teat sanitiser or to vary the conditions on a registered teat sanitiser;
- all persons conducting a data assessment on applications made to register a teat sanitiser or to vary the conditions on a registered teat sanitiser.

The standard provides specifications for:

- general efficacy requirements;
- experimental design;
- field studies.

1.2 Definitions and abbreviations

cfu
Colony forming units.

Good Research Practice (GRP)
A standard for the design, conduct, recording and reporting of studies that provides assurance that the data and reported results are complete, correct and accurate.

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

1.3 References

ACVM Research Standard
Current version of VICH Harmonised Guidance for Good Clinical Practice

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 and use patterns used in studies must be identical to those being proposed for registration.

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

2.1.5 In the case of fixed combination products, it must be demonstrated that all active ingredients produce their expected effect(s).

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

2.1.7 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.

2.1.8 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 veterinary medicine. A reason must be given where the veterinary medicine is not licensed for use in the country of origin.

3 SPECIFIC REQUIREMENTS FOR EFFICACY OF TEAT SANITISERS

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

3.1 General

3.1.1 Efficacy data must be collected on each pathogen for which a claim is made.

3.1.2 The inoculum used in pre-clinical studies must be recent field isolates of specified species relevant to New Zealand.

3.1.3 Efficacy is judged on the results of bacteriological cultures from treated and untreated quarters.

3.1.4 It must be demonstrated that concentrated drug products are not inactivated by acidic or hard water.

3.1.5 All pre-clinical studies conducted in the target animal must be reported.

3.1.6 *In vitro* studies cannot be used as sole claims of efficacy unless an information waiver is granted.

3.1.7 The results of all clinical and microbiological examinations must be reported.

3.2 Experimental design

3.2.1 The experimental unit is the individual teat and its associated quarter.

A suitable protocol for pre-clinical testing of efficacy of teat sanitisers using excised teats is previously known as 'Protocol A' and is detailed in *Journal of Dairy Science 61* (7) 951, 1978.

3.2.2 Damaged teats must be recorded and excluded before and during the study.

3.2.3 A negative control group must be used.

The study environment should be as uniform as possible for all experimental groups in the study.

3.3 Field studies

3.3.1 The length of the study required to demonstrate efficacy of a teat dip will depend on the number of uninfected quarters available initially, on the rate of new infection in the control group, and on the percentage reduction in infections in the treated group.

Animal numbers per experimental group depend upon differences expected.

It is recommended that herds with a high incidence of mastitis are used in these studies if possible. It is assumed that such a herd will have a high rate of new infection, and that the effects of the teat sanitiser will be determined efficiently.

Treatment groups should be balanced for age, stage of lactation and infection status.

An acceptable protocol to follow for field trials to show the efficacy of teat sanitisers is the American National Mastitis Council's *Recommended Protocol for Determining Efficacy of a Postmilking Barrier Teat Dip Based on Reduction of Naturally Occurring New Intramammary Infections*.

3.3.2 Any concurrent antibiotic or non-antibiotic therapy administered to a study animal or herd must be fully described.

3.3.3 A pre-study culture/somatic cell survey must be undertaken in order to establish the baseline incidence of mastitis in the herd. This must include milk samples from all lactating quarters on all animals in the herd. This survey must take place within one week prior to the initiation of the study.

3.3.4 The following data is required for each herd:

- **herd size;**
- **number of animals currently lactating;**
- **percentage of lactating animals affected by mastitis;**
- **approximate age of each animal;**
- **stage of lactation;**
- **vaccination history.**

Tail or foot banding is an appropriate method of identifying animals to be treated.

3.3.5 The test substance must be applied immediately after the milking machine is removed.

Teats should be completely covered by the test substance when it is applied.

A split herd design may be used. Under this design, all teats of half of the animals are treated at milking with the test substance, with the remaining half serving as untreated controls. Determine the number of new infections that occur in all quarters of all animals, both treated and control quarters.

3.3.6 Culture quarter milk samples monthly (single sample) or bimonthly (duplicate samples) during the study. Milk must be grossly examined at the time of sampling for signs of clinical mastitis.

3.3.7 The number of new infections that occur in both treated and untreated quarters must be determined and reported.

An individual quarter is eligible for only one infection during a lactation. When a new infection is confirmed, the quarter may be treated, but that quarter is excluded from the trial during the remainder of the lactation. Quarters infected in one lactation may be included in the trial in the subsequent lactation if it is determined that the infection was eliminated during the dry period either spontaneously or as a result of therapy.

3.3.8 A new intramammary infection is diagnosed in a previously uninfected quarter when the same bacterial species is isolated from:

- **two consecutive samples, usually monthly samples, during the study (³500 cfu/ml);**
- **a single sample from a quarter with clinical mastitis (³100 cfu/ml);**
- **three consecutive samples during the study (³100 cfu/ml).**

3.3.9 Any study animals that die must have a postmortem examination, including udder histopathology, carried out and reported.

3.3.10 Where different herds/investigators are used, statistical analysis must be conducted using methods for discrete data that accounts for differences due to herds and investigators.

3.3.11 The following information must be included in the final study report:

- **duration of the study;**
- **numbers of quarters in the study at the onset and on the date of each sampling;**
- **numbers of new intramammary infections, categorised by bacterial species or type, that occurred in control and treated groups;**
- **percentage reduction in new infection in the treated group for each bacterial species against which efficacy is claimed.**

3.3.12 For specific types of infectious mastitis with known aetiologies, adequate efficacy will be demonstrated when incidence of new intramammary infections is reduced by 50%.