

VETERINARY MEDICINAL PRODUCTS ADMINISTERED VIA THE TEAT DUCT TO LACTATING COWS FOR THE TREATMENT OF SUBCLINICAL MASTITIS

Guideline Title	Veterinary Medicinal Products Administered via the Teat Duct to Lactating Cows for the Treatment of Subclinical Mastitis.
Legislative Basis	Directive 81/852/EEC as amended
Date of First Adoption	November 1992
Date of Entry into Force	May 1993
Status	Last revised November 1992
Previous Titles	None
Other References	III/3173/92
Additional Notes	The objective of this document is to provide specific guidance in respect of the documentation of the efficacy of medicinal products developed for the treatment of subclinical mastitis. It should be read in conjunction with Directive 81/852/EEC as amended, and the note for guidance on <i>Good Clinical Practice for the Conduct of Clinical Trials on Veterinary Medicinal Products in the European Union</i> .

CONTENTS

1. OBJECTIVE
2. METHODS AND TREATMENTS
3. SELECTION OF ELIGIBLE HERDS AND ANIMALS
4. REPORTING
5. INTERPRETATION OF RESULTS
6. PRESENTATION OF DATA

VETERINARY MEDICINAL PRODUCTS ADMINISTERED VIA THE TEAT DUCT TO LACTATING COWS FOR THE TREATMENT OF SUBCLINICAL MASTITIS

1. OBJECTIVE

The objective of the trial is to assess the efficacy a medicinal product for the treatment of subclinical mastitis.

2. METHODS AND TREATMENTS

- 2.1 Where possible, comparative trials should be carried out on test and positive control products in two groups of animals:
- animals/quarters treated with the test product;
 - animals/quarters treated with an authorised control product. The control product must be authorised by the competent authorities and the choice of this product justified. Where no authorised product is available, a negative control group must be used.
- 2.2 The trial must be carried out on a sufficient number of herds and animals. Animals selected in each herd should not exceed 20% of the total number of cases treated in the complete study. The number of herds and animals should be justified.
- 2.3 Treatment should be allocated within each herd in a random manner using blinding as far as is practically possible. The balancing of the groups to include control and treated animals must be carried out at the individual herd level and on the total population.
- 2.4 The milk samplings and the microbiological investigation must be carried out in accordance with the methods recommended by the International Dairy Federation (IDF) (see Bulletin No 132, 1981).
- 2.5 Reference product
- Where possible, it is advisable to use a reference product with appropriate claims, approved in accordance with Directive 81/851/EEC as amended.
- 2.6 Test product
- The conditions of administration, dosage and frequency of administration should be described and should be those proposed.
- 2.7 Milk withdrawal period
- In a blinded study, the milk withdrawal period should be the same for each product (test + reference products) and correspond to the product with the longest withdrawal period. If blinding is not used, then the withdrawal period of the individual products should be observed.

2.8 Treatment unit

The treatment unit shall be the individual udder quarter. Where more than one quarter is affected within the same animal, the same treatment should be used.

3. SELECTION OF ELIGIBLE HERDS AND ANIMALS

3.1 Monitors should select animals from herds with:

- proper animal identification
- milking equipment of an acceptable standard.

3.2 All lactating cows of fifth lactation or less with subclinical mastitis as defined by the IDF (presence of pathogens in conjunction with a somatic cell count of $\geq 500\ 000$ /ml of milk. Bulletin No 211, 1987) and a daily milk yield in excess of 5 litres per day will be eligible for trial.

3.3 The population of animals must be described:

- animals which are to be excluded from the trial must be defined;
- animals which are to be included in the final analysis of data must also be defined.

3.4 The following animals are to be excluded from the trial:

- animals with intercurrent diseases,
- animals which were given systemic or intramammary anti-infectious and/or anti-inflammatory treatments within a 30-day period before the trial,
- animals with teat lesions.

3.5 Where possible, the history of the herd and animal must be recorded after the inclusion of an animal in the trial and before the commencement of the treatment.

Farm:

- name and address of herd owner;
- number of dairy cows;
- method of herd management/standard of milking machine/whether teat disinfection is practised or not;
- Cell counts of bulk milk samples in herds over the preceding 5 months (if available).

Animal:

- name and identification number;
- breed;
- number of lactations;
- date of calving;
- milk yield at time of treatment;
- individual somatic cell counts if available during preceding months;
- mastitis history if available;
- general condition.

4. REPORTING

4.1 Data required from each treated animal/quarter:

a) Clinical

- The animal will be examined by the trial investigator before and after treatment.

b) Milk

- Milk samples for bacteriological and cytological analysis will be collected before and after treatment.
- The number of samples and the time of sampling should be justified and be consistent for trials concerning a given product. The following sampling intervals: 7, 14 and 21 days after treatment, are recommended.

4.2 Animals or treated quarters to be omitted from final analysis of data:

- a) cases which are uninterpretable due to a lack or loss of information shall be listed in the final report and their distribution in each group shall be analysed;
- b) data collected from any sick or any animal which had to be treated with additional antibiotic or other supportive therapy during the course of the trial should not be included in the final data analysis. Details of all such cases should, however, be included in the final report.

5. INTERPRETATION OF RESULTS

5.1 The bacteriological cure must be evaluated for each treated infected quarter and must be based on total elimination of the pathogens which were present at the time of treatment. Response is usually measured at 14 and 21 days after treatment.

5.2 The cellular response must also be evaluated. A quarter will be considered to be cured subclinically if the SCC level is reduced to < 300 000/ml and the original pathogens are eliminated from the milk. Response is usually measured at 14 and 21 days after treatment.

5.3 Data should be expressed as numbers of quarters and number of cows cured.

5.4 The statistical methods used should be described and justified.

6. PRESENTATION OF DATA

A record form for each individual case should be presented in the final report. The data to be presented are described in the annex to Directive 81/852/EEC as amended by Directive 92/18/EEC.

In particular, the data on the bacteriological response for each organism and the subclinical response for each treated quarter must be summarised and tabulated.