ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Deltanil 100 mg Spot-on Solution for cattle

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0425/001/DC
Name, strength and pharmaceutical form	Deltanil 100 mg Spot-on Solution for cattle
Applicant	Virbac S.A. 1ere Avenue, 2065m – LID 06516 Carros Cedex France
Active substance(s)	Deltamethrin
ATC Vetcode	QP53AC11
Target species	Cattle
Indication for use	As a topical application for the treatment and prevention of infestations by lice and flies on cattle. For the treatment and prevention of infestations by both sucking and biting lice, including *Bovicola bovis*, *Solenopotes capillatus*, *Linognathus vituli* and *Haematopinus eurysternus*. Also as an aid in the treatment and prevention of infestations by both biting and nuisance flies including *Haematobia irritans*, Stomoxys calcitrans, *Musca* species and *Hydrotaea irritans*.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic hybrid application in accordance with Article 13 (3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	7th October 2013
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Belgium, France, Germany, The Netherlands

I. SCIENTIFIC OVERVIEW

Deltanil Spot-on Solution for cattle is an ectoparasiticide containing deltamethrin, a synthetic pyrethroid. The product has been developed as a generic hybrid of Pfizer Spot On Insecticide 1% Cutaneous Solution. Bioequivalence is claimed with Pfizer Spot On Insecticide 1% Cutaneous Solution. The product is applied topically to cattle at a dose rate of 10 ml per animal.

The product is indicated for the treatment and prevention of infestations by lice and flies on cattle. The product should not be used in animals with known hypersensitivity to the active substance or any of the excipients and is also contraindicated for use in sick or convalescent animals.

The product is produced and controlled using validated methods and text which ensure the consistency of the product released on the market. It has been shown that the product can be used safely in the target species; the slight reactions observed are indicated in the SPC[1].

The product is safe for the end user, the consumer of foodstuffs from treated animals and for the environment when used as recommended. Suitable warnings and precautions are indicated in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

[1] SPC – Summary of Product Characteristics

II. QUALITY ASPECTS

A. Composition

The product contains deltamethrin as the active substance and triglycerides, medium chain as the excipient.

The container / closure system consists of a cardboard carton containing ten 10 ml high-density polyethylene (HDPE) tubes. The particulars of the container and controls performed are provided and conform to regulation. The choice of formulation and the absence of preservative are justified.

The product is established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. Process validation data on the product have been presented in accordance with the relevant European guidelines. The product is manufactured by mixing the excipients with the active substance until dissolution is complete and then filling the container.

C. Control of Starting Materials

The active substance is deltamethrin, an established active substance described in the British Veterinary Pharmacopoeia. Data on the active substance was supplied in the form of an Active Substance Master File (ASMF) from one manufacturer and an in-house specification was provided for the other active substance manufacturer. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

The excipient complies with the relevant Ph. Eur. monograph and batch analysis data have been provided for one batch of the excipient.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

E. Control on intermediate products

Not applicable.

F. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product. The tests include identification of the active substance, identification of impurities, visual appearance and microbial purity.

Satisfactory validation data for the analytical methods have been provided.
Batch analytical data from the proposed production sites have been provided demonstrating compliance with the specification.

G. Stability

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. A retest period of 12 months has been established for both manufacturers of the active substance.

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions. Data were provided for batches stored at 25°C/60%RH and 40°C/75%RH for 6 months. A shelf life of 24 months is supported.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Shelf life of the finished product as packaged for sale: 36 months.
Store in tightly closed original container away from food, drink and animal feeding stuffs.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

As this is a generic application according to Article 13 (3) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of pharmacological studies are not required.

Toxicological Studies

As this is a generic application according to Article 13 (3) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of pharmacological studies are not required.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which describes the various means by which deltamethrin may come into contact with the user, including exposure of the skin and / or eyes. Warnings and precautions as listed in the product literature are adequate to ensure safety to users of the product:

- Wear protective clothing including waterproof apron and boots and impervious gloves when either applying the product or handling recently treated animals.
- Remove heavily contaminated clothing immediately and wash before re-use.
- Wash splashes from skin immediately with soap and plenty of water.
- Wash hands and exposed skin after handling this product and before meals.
- In case of contact with eyes, rinse immediately with plenty of clean, running water and seek medical advice.
- In case of accidental ingestion, wash out mouth immediately with plenty of water, seek medical advice and show the package leaflet to the physician.
- Do not smoke, drink or eat while handling the product.
- This product contains deltamethrin which may produce tingling, itchiness and blotchy redness on exposed skin. If you feel unwell after working with this product, consult your doctor and show this label.

Ecotoxicity

The applicant provided a Phase I environmental risk assessment in compliance with the relevant guideline which showed that further assessment was required

for cattle raised on pasture because the product is an ectoparasiticide. A Phase II environmental risk assessment was provided.

The assessment concluded that deltamethrin would not pose a risk to the environment when used as recommended. It is reported that up to 50% of deltamethrin topically applied to cattle was absorbed through the skin and later excreted almost exclusively in faeces. The PEC[2] values for soil, groundwater and surface water are 1.267 µg/l, 0.00113 µg/l and 0.00038 µg/l respectively for beef cattle. These values indicate that the product is not expected to pose a risk to the environment when used as directed. Data have been provided on the toxicity of deltamethrin to dung insects and the risk quotient (RQ) is > 100. As such appropriate warnings are included in the product literature advising on the frequency of re-treatments and the duration of deltamethrin excretion:

- Deltamethrin is toxic to dung insects. The risk to dung fauna can be reduced by avoiding too frequent and repeated use of deltamethrin (and other synthetic pyrethroids) in cattle, e.g. by using a single treatment per year on the same pasture.
- Deltamethrin has the potential to adversely affect non-target organisms. Following treatment, deltamethrin is excreted in faeces. Deltamethrin excretion may take place over a period of 2 to 4 weeks. Faeces containing deltamethrin excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms.

Deltamethrin is highly toxic to aquatic organisms and honey bees. The following warnings are therefore present on the product literature:

- Deltamethrin is toxic to aquatic organisms and honey bees and may accumulate in sediment.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

Residue depletion studies for meat withdrawal periods were not conducted because the product has been shown to be the same as the reference product and the applicant proposed the same meat withdrawal period for cattle.

The applicant has provided a milk residue depletion study for cattle. The study showed the withdrawal period of zero days as per the reference product is acceptable.

[2] PEC – Predicted Environmental Concentration

Withdrawal Periods

Meat and offal: 17 days
Milk: Zero hours

IV CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application according to Article 13 (3) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of pharmacological studies are not required.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13 (3) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of studies on the tolerance in the target species are not required.

Resistance

The bibliography provided indicates there is resistance to many classes of ectoparasiticides, some of which may be indicated for the treatment of ticks, lice and blowfly. The applicant has provided references that suggest there is resistance to deltamethrin in some species of tick. Adequate warnings and precautions appear on the product literature:

- To avoid resistance, the product should only be used if the susceptibility of the local fly population to the active substance is assured.
- Cases of resistance to deltamethrin have been reported in stinging and nuisance flies in cattle.
- Care should be taken to avoid the following practices because they increase the risk of development of resistance and could ultimately result in ineffective therapy:
  - too frequent and repeated use of ectoparasiticides from the same class over an extended period of time
  - underdosing which may be due to underestimation of bodyweight, misadministration of the product.
- The product will reduce the number of flies resting directly on the animal but it is not expected to eliminate all flies on the farm. The strategic use of the product should, therefore, be based on local and regional epidemiological information about the susceptibility of parasites, and used in association with other pest management methods.

IV.B Clinical Studies

Laboratory Trials

As this is a generic application according to Article 13 (3) of Directive 2001/82/EC as amended and bioequivalence with the reference product can be assumed because of the nature of the product, results of laboratory trials are not required.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the benefit/risk profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

This section contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

•	06 November 2014	To add an additional site responsible for quality control of the finished product. To extend the shelf-life of the finished product as packaged for sale, from 24 months to 36 months.
•	20 March 2014	Change in test procedures for the finished product.