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DRAFT

GUIDELINE ON THE QUALITY ASPECTS OF SINGLE-DOSE VETERINARY SPOT-ON PRODUCTS

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GUIDELINE ON THE QUALITY ASPECTS OF SINGLE-DOSE VETERINARY SPOT-ON PRODUCTS

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EXECUTIVE SUMMARY

This guideline is intended to point out to both pharmaceutical companies and regulators some of the factors that should be considered when developing veterinary single-dose spot-on products and how these might best be addressed.

1. INTRODUCTION

Veterinary spot-on products are low-volume liquids applied topically, usually for the control of ectoparasites and/or endoparasites. The European Pharmacopoeia standard terms for the pharmaceutical form are spot-on solution, spot-on emulsion and spot-on suspension and the route of administration is spot-on use, a sub-route of cutaneous use. Spot-on products are generally applied between the shoulder blades and/or to the back of the animal. The first spot-on product was authorised in Europe as a multidose product in the 1980s.

Veterinary spot-on products are often presented as single-dose liquids, usually solutions, for the treatment of cats and dogs. The first single dose spot-on product authorised in Europe was in the early 1990s. They are now widespread throughout the EU and have been authorised by national, mutual recognition and centralised procedures.

Although there is a monograph in the European Pharmacopoeia for liquid preparations for cutaneous application, this gives no guidance on single-dose spot-on products.

This guideline sets out the quality data requirements that are specific to single-dose veterinary spot-on products.

2. SCOPE

The guideline applies to pharmaceutical veterinary medicinal products presented as single-dose liquids, which are administered topically to individual animals. It applies to all single-dose spot-on products, whether applied at one or several spots. The types of pharmaceutical forms that are taken into account in this guideline include: spot-on solution, spot-on emulsion and spot-on suspension.

Veterinary medicinal products which are of immunological, biotechnological or biological origin are excluded from its scope.

The guideline provides recommendations regarding matters such as finished product quality control, selection of excipients (in particular solvents), filling overages, residual volumes on expression, and stability. The guideline is intended to give guidance on aspects specific to single-dose veterinary spot-on products and is not intended to replace general guidance given in existing VICH/CVMP Quality guidelines.

The guideline does not apply to medicinal products already authorised.

3. LEGAL BASIS

This guideline should be read in conjunction with Directive 2001/82/EC as amended by Directive 2004/28/EC.

4. MAIN GUIDELINE TEXT

4.1 Part IIA Composition

Development Pharmaceutics

The fundamental principle to be applied to these products is that they are single dose products akin to tablets or capsules and should be designed, manufactured and controlled as such. At the outset of product development, the desired dose in mg per container of average extractable mass should be defined. The fill volume for the single dose containers should take into consideration aspects such as the concentration of the bulk product, the volume expressed and the residual volume of product in the container after expression of the dose. Results of studies designed to determine the residual volume of product in each size of container after expression of the dose should be provided. Assay limits in the finished product specification should be centred on the declared concentration in mg per container of average delivered mass as this represents the amount that will be applied to the animal. If necessary for weights and measures purposes, the total volume may be recorded but it must be clearly stated that this will include the residual portion.

There are no special requirements for excipients, which are usually non-aqueous solvents with antioxidants or other stabilisers. These are selected during clinical development and quality is demonstrated in the same way as for any other pharmaceutical excipient in any other drug product.

4.2 Part IIB Method of manufacture

The target fill volume for any particular batch should be based upon the assay of the specific batch of bulk product and the previously determined residual volume that will remain in the containers after expression of the dose. (However, this method should not be used to compensate for active contents outside the normal $\pm$5% deviation from target in the bulk solution.) This will ensure that a container of average extractable mass will deliver the claimed dose of active substance.

Fill volume limits should be defined based on process validation data. Consideration should be given to the requirement for the finished dosage form to meet the requirements of European Pharmacopoeia general text 2.9.40, Uniformity of dosage units.

4.3 Part IIF Control of the finished product

As indicated above, the assay should be expressed in terms of the quantity by mass of the active substance in a container of average delivered mass or volume. Limits of 95 – 105 % of the declared content should be applied to this parameter. This should preferably be determined by expressing a specified number of dosage units in a manner likely to be used by the person treating the animal, bulking the resultant contents, determining the assay on a concentration basis and calculating the quantity by mass of the active substance in a container of average delivered mass or volume.

A test for uniformity of delivered dose should be applied in accordance with the European Pharmacopoeia general text 2.9.40, Uniformity of dosage units. This should be determined by expressing the required number of dosage units in a manner likely to be used by the person treating the animal.

Microbiological aspects should be considered in the same manner as for any other drug product, bearing in mind that spot-on products are sometimes applied to damaged skin.

4.4 Part IIG Stability

Stability testing should include determination of the mass of individual containers. Assay results should be expressed in terms of mass of active substance per container of average extractable mass and on a concentration basis. The possibility of water uptake or solvent loss through the containers should be considered.

4.5 SPC and Product Literature

In the SPC and product literature (labelling and package insert), the product name should include the pharmaceutical form, spot-on solution, spot-on emulsion or spot-on suspension as appropriate. The strength should be expressed in terms of delivered mass of active substance per container, not as concentration within the solution or suspension or per unit volume or mass.

A warning should be included concerning the possibility of splashing during opening of the packs, together with instructions on how to avoid this.