



European Medicines Agency
Veterinary Medicines and Inspections

London, 15 December 2006
EMEA/CVMP/QWP/434665/2006

COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

CONCEPT PAPER ON THE DEVELOPMENT OF A GUIDELINE ON THE QUALITY ASPECTS OF SINGLE-DOSE VETERINARY SPOT-ON PRODUCTS
--

AGREED BY QUALITY WORKING PARTY	November 2006
ADOPTION BY CVMP FOR RELEASE FOR CONSULTATION	13 December 2006
END OF CONSULTATION (DEADLINE FOR COMMENTS)	13 March 2007

Comments should be provided to QWP@emea.europa.eu

Fax +44 20 7418 8447

KEYWORDS	Spot-on, veterinary, single dose
-----------------	----------------------------------

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 and they are now widespread throughout the EU. They have been authorised by national, mutual recognition and centralised procedures.

2. PROBLEM STATEMENT

Although single-dose veterinary spot-on products have been authorised for many years there is no guidance available within the EU on matters such as finished product quality control (active substance content versus declared levels), selection of excipients (in particular solvents), filling overages, residual volumes on expression, and stability under low temperature conditions.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

No guidance is currently available within the EU concerning finished product quality control, filling overages, residual volumes on expression, and stability under low temperature conditions for single-dose veterinary spot-on products. There is a monograph in the European Pharmacopoeia for liquid preparations for cutaneous application but this gives no guidance on single-dose spot-on products.

The absence of a guideline leads to anomalies, for example two single-dose spot-on products recently authorised by the centralised route had different bases for the calculation of the content of active substance, resulting in unusually wide (particularly upper) limits for uniformity of dose.

At the outset of the development of spot-on products a number of companies are tending to define the strength as % w/w or % w/v and then set fill volume limits for the single dose containers. When the expression of strength is revised, for example during the registration process, to mg per dose this tends to lead to the situation where the assay results are skewed above the declared concentration in mg per dose. The alternative approach is to define from the outset the desired dose in mg per container of average extractable mass. Fill volume limits are then defined based on process validation data and the residual volume of product in the containers after expression of the dose. In this way, assay results are centred on the declared concentration in mg.

Difficulties are created for companies if they have to change their approach to the expression of strength and determination of assay during the development/registration of a product. If clear guidance is available at the outset on the approach to take, difficulties later on can be avoided.

The absence of guidance leads to excessive numbers of questions during mutual recognition procedures.

4. RECOMMENDATION

In the absence of clear guidance on the quality aspects of single-dose veterinary spot-on products, the CVMP recommends that the Quality Working Party (QWP) produces a guideline.

Points that will be addressed should include finished product quality control, filling overages, residual volumes on expression and stability under low temperature conditions.

It is not expected that the guideline will apply to medicinal products already authorised. It is also likely that, when defining an implementation date, due account will need to be taken of spot-on products which are already advanced in their development and nearing registration.

The scope of such guidance would be restricted to veterinary medicinal products which are not of immunological, biotechnological or biological origin.

5. PROPOSED TIMETABLE

It is expected that the guideline will come into operation six months after adoption.

It is anticipated that a draft guideline could be available 6 months after adoption of the concept paper, and that this would then be released for external consultation for 6 months before its finalisation within another 6 months.

6. RESOURCE REQUIREMENTS FOR PREPARATION

QWP to appoint Rapporteur. CVMP to consider concept paper. QWP Rapporteur to prepare the draft Guideline. Member States to provide input via their QWP Members. CVMP to review and comment on the draft guideline prior to its release for consultation. QWP Rapporteur to revise the draft following consultation. QWP to approve revised draft. Adoption by CVMP.

7. IMPACT ASSESSMENT (ANTICIPATED)

No adverse impact on industry with respect to either resources or costs is foreseen.

The guidance will clarify requirements for regulators and industry (applicants for marketing authorisations and also product manufacturers). Assessment times should be reduced resulting in products reaching the market more quickly. The numbers of questions during mutual recognition, decentralised and centralised procedures should be reduced.

8. INTERESTED PARTIES

Veterinary pharmaceutical industry

IFAH-Europe

EDQM

9. REFERENCES TO LITERATURE, GUIDELINES ETC

None