EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 13 March 2014
2 EMA/CVMP/SWP/92311/2014
3 Committee for Medicinal Products for Veterinary Use (CVMP)

4 Concept paper for a guideline on user safety of topically 5 administered products

Agreed by Safety Working Party	February 2014
Adopted by CVMP for release for consultation	13 March 2014
Start of public consultation	24 March 2014
End of consultation (deadline for comments)	30 June 2014

6 The proposed guideline will supplement the existing "User Safety Guideline" (EMA/CVMP/543/03-
7 Rev.1).

Comments should be provided using this template. The completed comments form should be sent to vet-guidelines@ema.europa.eu

8

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

1. Introduction

This concept paper addresses the need for a specific user safety guideline for topically administered products. The CVMP adopted the revised general User Safety Guideline for pharmaceutical veterinary medicinal products (EMA/CVMP/543/03-Rev.1) in March 2010. This document provides general guidance on how user risk assessment should be conducted and reported. It does not provide specific guidance on how exposure from topically administered products should be assessed.

The increase in the number of applications for topically administered products in recent years highlighted the need for a coherent and common approach on how exposure from such products should be assessed. Both industry and regulatory agencies have developed their own approaches for addressing the issue and this has resulted in divergent conclusions. This concept paper describes and discusses the basis for the need for a new guideline to supplement the existing user safety guideline.

2. Problem statement

The current User Safety Guideline for pharmaceutical veterinary medicinal products does not include guidance on the approach or methodology to be applied when conducting a user risk assessment for topically administered products. There are no agreed EU guidelines on this topic but some member state agencies and the US Environmental Protection Agency (EPA) have published methodologies to be used. Furthermore, there does not appear to be a standardised test system for estimating the amount of residues dislodged onto the hands following stroking of an animal after it has been administered a topical product. This has created a situation where studies are conducted differently and regulatory authorities use different methodologies for evaluating the risk to the user, resulting in divergent conclusions.

3. Discussion (on the problem statement)

There has been an increase in the number of topically administered products to pet animals for the treatment of flea and other infestations. The existing user safety guideline provides guidance on how user risk assessments should be conducted and reported but does not address specific aspects relevant for topically administered products (e.g. collar, spot-on, pour-on). As a result, different companies and regulatory authorities apply different approaches in assessing the risk to the user from such products.

When conducting user risk assessments for topically administered products, other than direct exposure to the product from the container (accidental spillage), additional exposure is also possible when owners or other household members including children come into contact with the animals after administration of a topical product. The resulting exposure depends on the physico-chemical properties of the product as well as the nature and state of the fur and the vigorousness of the contact. In many cases worst case exposure can be estimated based on conservative default assumptions. Exposure can be divided into acute/sub-chronic exposure covering short term and long term scenarios. Agreeing the exposure scenarios and the assumptions would be an aim of the proposed guideline.

More accurate estimations of exposure can be achieved through the generation of experimental data. In particular, the amount of residue dislodged from a treated animal onto the user is often investigated by means of the so called ‘wipe test’. However, there is no standardised ‘wipe test’ and as a result, the values obtained can vary significantly depending on the way it was conducted and evaluated. Providing recommendations for the conduct of wipe tests would be a further aim of the proposed guideline.

Existing guidance on user risk assessments for topically applied products is available in the form of a US EPA guideline (2012) as well as in guidance developed by some individual EU member states but a harmonised approach acceptable across Europe has not been agreed. A number of national agencies have now acquired valuable experience by assessing the risk to users from topically administered products. Based on the experience gained and on the available guidance on the matter, a commonly agreed approach can now be developed that will allow applicants and regulatory agencies to assess the risk to users in a coherent, consistent and transparent manner.

4. Recommendation

The Safety Working Party recommends that a new guideline be prepared to address the problems identified above. The new guideline should provide formulas and assumptions/default values for use in estimating exposure and the margin of exposure, and provide recommendations on the conduct of 'wipe tests'.

This additional guideline is not intended to introduce new requirements.

5. Proposed timetable

February 2014 – Concept paper endorsed by SWP.

March 2014 – adoption of concept paper for release for consultation by CVMP.

June 2014 – end of consultation period.

Timelines for development of the guideline will be determined following review of comments received on the concept paper.

6. Resource requirements for preparation

The new guideline will involve the SWP, SWP secretariat and the CVMP. The SWP should appoint a group of at least 3 rapporteurs from amongst its members and/or national experts.

It is anticipated that development of a draft guideline would require two physical drafting group meetings as well as 3 additional virtual meetings and discussion time during scheduled SWP meetings.

7. Impact assessment (anticipated)

The guidance will clarify requirements for regulators and industry with respect to methodologies and data to be used in estimating exposure and so will encourage consistent and predictable decisions.

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

8. Interested parties

Pharmaceutical Industry, EU Competent Authorities, Consultants

9. References to literature, guidelines, etc.

1. CVMP guideline on user safety for pharmaceutical veterinary medicinal products (EMA/CVMP/543/03-Rev.1), available at http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/03/WC500077971.pdf
2. Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on the results of the user safety assessment of antiparasiticides collars for companion animals concerned by a withdrawal of marketing authorization (2012)
3. RIVM (2007) - Oral exposure of children to chemicals via hand-to-mouth contact (RIVM report 320005004/2007), available at http://www.rivm.nl/bibliotheek/rapporten/320005004.pdf
4. US EPA (1997) - Standard Operating Procedures (SOPs) for Residential Exposure Assessments, available at http://www.epa.gov/oppfead1/trac/science/trac6a05.pdf
5. US EPA (2012) - Standard Operating Procedures for Residential Pesticide Exposure Assessment, available at http://www.epa.gov/pesticides/science/USEPA-OPP-HED_Residential%20SOPs_Oct2012.pdf
6. OECD (2004) - Guidance Document for the conduct of skin absorption studies. OECD series on testing and assessment Number 28. ENV/JM/MONO(2004)2, available at http://search.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono(2004)2&doclanguage=en
7. EC (2004) - Guidance Document on Dermal Absorption. Sanco/222/2000 rev. 7. 19 March 2004, available at http://ec.europa.eu/food/plant/protection/evaluation/guidance/wrkdoc20_rev_en.pdf
8. EFSA Scientific Opinion (2012) Guidance on dermal absorption, EFSA Panel on Plant Protection Products and their Residues (PPR). EFSA Journal 10(4): 2665, available at http://www.efsa.europa.eu/en/efsajournal/doc/2665.pdf