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Veterinary Medicines and Inspections

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COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

CONCEPT PAPER ON THE REVISION OF THE GUIDELINE FOR DEMONSTRATION EFFICACY OF VETERINARY MEDICINAL PRODUCT CONTROLLING VARROA DESTRUCTOR AND ACARAPIS WOODI PARASITOSIS IN HONEY BEES (III/9283/90)

AGREED BY EFFICACY WORKING PARTY (EWP-V)	July 2007
ADOPTION BY CVMP FOR RELEASE FOR CONSULTATION	13 September 2007
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 March 2008

The proposed guideline will replace guideline "Veterinary medicinal products controlling *Varroa jacobsoni* and *Acarapis woodi* parasitosis in bees" (7AE16a, Volume 7)

Comments should be provided electronically to vet-guidelines@emea.europa.eu

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KEYWORDS	Guideline, veterinary medicinal product, bee, medicines, *Varroa destructor*

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1. INTRODUCTION

Beekeeping is an economic activity with significant impact on rural areas. Bees contribute to the pollination of plants and add to the biodiversity. From the perspective of a relevant organic farming activity, bee keeping has also received attention with respect to disease prevention and veterinary treatments (*Council Regulation (EU) 1804/1999; Annex I, Chapter C).*

The Guideline for demonstration of efficacy of veterinary medicinal products controlling *Varroa Destructor* and *Acarapis Woodi* parasitosis in honey bees came into effect in March 1992 and has been in force since, without being revised.

In the last 10 years there is increasing concern about the lack of availability of veterinary medicinal products (VMP) to treat certain pathologies that can affect bee colonies.

Applications for products on *Varroa* control have been authorised following national procedures and Mutual Recognition Procedures. However, the current situation on the availability of products to control *Varroa* infestations is not satisfactory and widening of the product range is desirable. In doing so, the possibility of certain active substances ending up in brood, honey and/or wax should be acknowledged . It should also be considered that environmental conditions can have a significant impact on the health of bee colonies as well as on the effectiveness of products. All these factors may limit the range of possible new substances and should be taken into account.

The honey bee is considered as a minor species and the revised guideline should take into account the relevant MUMS-Guideline. The majority of beekeepers are non-professionals and the involvement of veterinarians in *Varroa* control is minimal. Beekeepers can purchase commercially available products or even prepare their own products for treating varroosis in their own colonies. Although sold for *Varroa* control, not all of these products are authorised veterinary medicinal products.

2. PROBLEM STATEMENT

To beekeepers the occurrence of resistance is a major concern. Due to, amongst others, the inappropriate use of (authorised veterinary medicinal) products, resistance of *Varroa* mites to active substances, such as fluvalinate, has increased to such a level that some products have become inefficacious.

Considering the differences in bee keeping throughout the EU as well as the variation in climatic conditions, the Guideline should focus on the level of control that can be achieved in relation to the qualities of substances/products with respect to e.g. temperature range (inside and outside the hive), bee strains and activity, type of beehive, season, level of infestation, etc. Beekeepers should be able to effectively control *Varroa* under various conditions on the basis of such information of available products.

The original Guideline concerns *Varroa destructor* and *Acarapis woodi. Varroa destructor* has been renamed *Varroa destructor* and the Guideline should be amended accordingly. Also the prevalence of *Acarapis woodi* is almost negligible in most countries. Considering the differences in biology between both parasite species as well as the difference in importance of infestations between *Varroa destructor* and *Acarapis Woodi,* the Guidance document should only focus on a single parasite species, i.e. *Varroa destructor*.

3. DISCUSSION

A number of issues have been identified that should be addressed or changed in the current guideline. The following sections could be revised:

General comment:

- Leaving out the tracheal mite *Acarapis woodi* as a target parasite from the revised guideline.

Assessment of efficacy

- Section 2.1: The need of an *in vitro* study for the efficacy of the active compound or a calculation of the ED_{50} and ED_{100} should not appear as being compulsory and might be omitted, as such studies are difficult to carry out .

- Sections 2.2 and 2.3: The protocols for the assesment of efficacy in dose confirmation studies and clinical trials should be specified and brought into conformity as much as posible (see http://www.alp.admin.ch/themen/00502/00567/00573/index.html?lang=en).

Amongst others, the following requirements should be considered:

- Collection of dead *Varroa* mites in hives should be done with a sticky sheet on a movable tray at the botom of the hive.
- Numbers of fallen mites should be counted at regular intervals before, during and after treatment, and the frequency of counting and for how long should depend on the mode of action of the acaricide studied.
- Instead of killing bee colonies to determine the number of remaining mites, a standard control treatment with a chemically not related product with proven efficacy should be applied.
- The natural mortality of *Varroa* mites in hives should be calculated and taken into account, specially in long-term treatment studies.

- Section 3: Safety for bees

- The tolerance of bees for a substance should be tested in several European bee strains.
- The natural mortality of bees in hives should be taken into account, especially in safety studies.
- Recommendations for long term efficacy and safety studies (sections 3.2 and 3.3) are very demanding and difficult to carry out and should be brought into line with the practical situation.

- Section 2.5: Statistics

Statistical analysis should be appropriate for the bee keeping practice, taking into account the "unit of analysis" problems in relation to group treatments. Studies should be designed to allow for generalised conclusions although the difficulties connected to the inclusion of a representative sample (including relevant co-variators) is acknowledged, due to the fact that beekeping is a relatively small scale activity. The guideline should adress the issue of appropriate evaluation of small samples.

- Section 2.6: Resistance pattern

Data regarding the resistance of *Varroa* mites against a substance should be based on observations, as development of resistance includes many factors, being problematical to reproduce experimentally.

RECOMMENDATION

The Working Party recommends to revise the Guideline on Veterinary Medicinal Products controlling *Varroa destructor* and *Acarapis woodi* parasitosis in Bees.

The guideline, currently in force, was prepared in the 1990s when the control of *Varroa* was more promising. Only a few veterinary medicinal products have been authorised for the treatment of varroosis in honey bees. Some of them have appeared to become less efficacious because the increasing level of resistances to these approved molecules. Experience from recent years indicate that a revision of methods and standards as mentioned in the current Guideline is desirable considering the design of studies and the subsequent safety and efficacy assessment of products for the control of *Varroa destructor*.

The objective of the proposed revision is to bring guidance into conformity with methods currently regarded as valid.

5. PROPOSED TIMETABLE

September 2007	Concept paper to be adopted by CVMP
March 2008	End of public consultation
2 Q 2008	Discussion of comments in EWP
3 Q 2008	First draft guideline to be discussed in EWP
2-3 Q 2009	Expected date for adoption by EWP
2-3 Q 2009	Draft guideline for discussion and adoption to CVMP

6. RESOURCE REQUIREMENTS FOR PREPARATION

Member States to provide input via EWP.
Rapporteurs to prepare the draft guideline.

7. IMPACT ASSESSMENT (Anticipated)

It is anticipated that a revised Guideline will improve quality of data produced by industry, recommendation on use and hence the effectiveness of product under practical conditions. Product data will be more uniform, facilitating the assessment.

8. INTERESTED PARTIES

Pharmaceutical industry.
Regulatory authorities.
Scientific associations (EU-Group for integrated *Varroa* control).

National institutions involved in varroa control.

Honey bee keepers; honey producers

9. REFERENCES TO LITERATURE, GUIDELINES ETC

"Technical guidelines for evaluation of treatments for control of *Varroa* mites in honey bee colonies"; the European Working Group for the co-ordination of research on integrated varroa control.

Guideline On efficacy and target animal safety data requirements for veterinary medicinal products intended for minor uses or minor species (EMEA/CVMP/EWP/117899/2004)

Council Regulation (EU) 1804/1999; Annex I, Chapter C