



1 26 July 2024
2 EMA/CVMP/EWP/247519/2024
3 Committee for Veterinary Medicinal Products (CVMP)

4 **Concept paper on the revision of the guideline on**
5 **veterinary medicinal products controlling *Varroa***
6 ***destructor* parasitosis in bees**
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Agreed by Efficacy Working Party (EWP-V)	June 2024
Adopted by CVMP for release for consultation	18 July 2024
Start of public consultation	26 July 2024
End of consultation (deadline for comments)	31 October 2024

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9 The proposed guideline will replace the current "Guideline on veterinary medicinal products controlling
10 *Varroa destructor* parasitosis in bees" (EMA/CVMP/EWP/459883/2008-Rev.1).

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12 Comments should be provided using this [template](#). The completed comments form should be sent to
vet-guidelines@ema.europa.eu.

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Keywords	<i>Varroosis, honeybees, efficacy, veterinary medicinal products, capped brood.</i>
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14 **1. Introduction**

15 The CVMP guideline on veterinary medicinal products controlling *Varroa destructor* parasitosis in bees
16 (EMA/CVMP/EWP/459883/2008) was initially adopted in July 2008, with the last revision (Rev.1) carried
17 out in July 2021 to implement administrative changes in order to align the guideline to Regulation (EU)
18 2019/6.

19 This concept paper addresses the need for a comprehensive revision of the guideline. The revision will be
20 based on points for improvement raised by a stakeholder contemplating the development of new veterinary
21 medicinal products (VMPs) for the treatment of varroosis, but also more generally, on other points
22 reviewed in the light of current scientific knowledge in the field and on regulatory experience.

23 In general, due to the efficacy of new active substances or VMPs with different mechanisms of action
24 and/or physico-chemical properties, it is necessary to address methods and special considerations when
25 designing study protocols that are better suited to the modes of action of these substances or VMPs. In
26 addition, owing to the risk of emergence of resistance to existing substances, it is considered appropriate to
27 support potential new substances or products to obtain a marketing authorisation.

28 **2. Problem statement**

29 This guideline aims to provide general guidance on aspects that should be considered or addressed when
30 designing and conducting studies aimed at demonstrating efficacy and target animal safety for VMPs
31 intended for varroosis control in honey bees.

32 The assessment of the efficacy in the current guideline is mainly focused on products targeting dispersal-
33 phase mites and on the mortality of *Varroa* based on the count of mite fall as part of a critical test. Thus,
34 the efficacy and safety of VMPs with particular physical properties, such as vaporous acaricides that may
35 penetrate below brood cappings, or products which have a longer-term impact on the dynamics of mite
36 populations (e.g. products interfering with reproduction) may not be adequately addressed. Therefore, the
37 revision of the guideline in order to include additional methods taking into account these properties to
38 assess the efficacy should be considered.

39 In addition, some sections of the guideline should be updated in order to incorporate the information
40 included in the Q&A document (EMA/CVMP/EWP/77872/2018) on the follow-up treatment and the
41 evaluation of safety in queens. Moreover, certain other sections of the guideline could be revised, e.g. to
42 better explain the function of negative control colonies in the evaluation of the efficacy.

43 Finally, as several other related guidelines have been recently developed, e.g. Guideline on efficacy and
44 target animal safety data requirements for applications for non-immunological veterinary medicinal
45 products intended for limited markets submitted under Article 23 of the Regulation (EU) 2019/6
46 (EMA/CVMP/52665/2020) or Guideline on efficacy and target animal safety data requirements for
47 applications for non-immunological veterinary medicinal products intended for limited markets but not
48 eligible for authorisation under Article 23 of Regulation (EU) 2019/6 (EMA/CVMP/EWP/231668/2022), it
49 should be ensured that the guideline on VMPs controlling *Varroa destructor* parasitosis in bees is in line
50 with those other linked guidance documents.

51 **3. Discussion (on the problem statement)**

52 The lack of different and more flexible approaches in certain sections of the current guideline may lead to
53 challenges in inadequate assessment of target animal safety and efficacy for some VMPs. For example,
54 historically, varroacides have been products targeting dispersal-phase mites. Vaporious acaricides, such as

55 formic acid and thymol, have physical properties distinct from contact chemicals, and these may require
56 special consideration when designing study protocols.

57 In particular, the following points should be noted:

- 58 • Vaporous acaricides depend on the maintenance of a minimum dose of active substance inside the
59 hive to be effective. However, unlike for contact chemicals, airflow through the hive can alter the
60 dose of vaporous acaricides. Thus, airflow through hive during efficacy testing should be in
61 accordance with the intended instructions for use.
- 62 • The current guideline includes only one means of determining product efficacy: mortality of *Varroa*
63 based on mite fall on bottom boards. It may be useful to also include supplementary methods, such
64 as those based on estimating infestation rates in adult bees before and after treatment (e.g.
65 ethanol washes or powdered sugar shakes) to support product authorisation.
- 66 • Moreover, some active substances like vaporous acaricides may be effective in capped brood,
67 killing reproductive-phase as well as dispersal-phase *Varroa* [1]. The guideline currently does not
68 contain a recognised method for assessing efficacy of varroacides causing mortality within capped
69 brood cells. This could be important as, according to some references, a significant percentage of
70 the *Varroa* population within a colony may be located within capped brood cells [2].
- 71 • Additionally, in certain cases it could be useful to understand longer-term impact of acaricides in
72 honeybee colonies, e.g. those interfering with the reproductive capacity of the mites. Although the
73 guideline includes guidance on conducting long-term monitoring of colony strength parameters, it
74 does not currently include methods of assessing long-term effects of treatments on *Varroa*
75 population dynamics.
- 76 • In the current guideline, it is not clearly explained how the control colonies should be used in the
77 efficacy assessment at the different stages of clinical product development, taking into account
78 that, basically, the efficacy percent is calculated only for the treated colonies using the follow-up
79 treatment.
- 80 • The guideline should also be in alignment with current recommendation for 3Rs principles and
81 animal welfare testing approaches.

82 Consequently, the following items should be considered in the current revision of the guideline:

- 83 • Consider the need to highlight the importance of tightly-fitting equipment when conducting efficacy
84 testing on vaporous acaricides and airflow through the hive as it can alter the dose of these
85 products.
- 86 • Consider the need to include in the current guideline supplementary methods to evaluate the
87 efficacy, such as methods based on estimating infestation rates in adult bees [3] before and after
88 treatment, methods to assess the efficacy in capped brood, or methods to evaluate the long-term
89 effects [4] of acaricides on *Varroa* population dynamics.
- 90 • Consider the role of the control colonies at different stages of clinical product development and the
91 efficacy calculates.
- 92 • Reconsider the current recommendations regarding efficacy thresholds (minimum percentages of
93 mite count reduction), which might not be adapted anymore to the range of new substances,
94 products or indications that are or will be developed.
- 95 • Align the guideline with current scientific and regulatory requirements, including 3Rs principles and
96 animal welfare.

97 Furthermore, considering the current scientific knowledge, other sections of the current guideline could be
98 open to revision, if appropriate.

99 **4. Recommendation**

100 The CVMP recommends the revision of the existing guideline on veterinary medicinal products controlling
101 *Varroa destructor* parasitosis in bees in order to provide clearer guidance and to align the guideline with
102 current scientific and regulatory requirements, taking into account the issues identified above.

103 **5. Proposed timetable**

104	July 2024	Concept paper released for public consultation
105	31 October 2024	Deadline for comments from interested parties
106	Q2 2025	Expected date for adoption of the draft revised guideline by CVMP for release for 107 consultation
108	Q4 2025	Expected end of consultation on the draft revised guideline
109	Q2 2026	Expected date for adoption by CVMP and publication of the revised guideline

110 **6. Resource requirements for preparation**

111 Revision of the guideline will involve one EWP-V rapporteur and three co-rapporteurs.

112 The preparation of the draft revised guideline will require discussion at several EWP-V plenary meetings.
113 Drafting group meetings (virtual) will be organised, as needed.

114 **7. Impact assessment (anticipated)**

115 The revision of the guideline is expected to improve the guidance for applicants as well as for regulatory
116 authorities. It is not intended to increase the requirements for marketing authorisation applications for such
117 veterinary medicinal products.

118 **8. Interested parties**

- 119 • Veterinary pharmaceutical industry and consultants;
- 120 • EU regulatory authorities involved in the assessment of marketing authorisation applications for
121 veterinary medicinal products;
- 122 • Veterinary organisations and professional bodies;
- 123 • Scientific veterinary associations.

124 **9. References to literature, guidelines, etc.**

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