



1 20 January 2021
2 EMA/CVMP/IWP/671155/2020
3 Committee for Medicinal Products for Veterinary Use (CVMP)

4 **Concept paper on the provision of field efficacy studies in**
5 **support of marketing authorisation applications for**
6 **immunological veterinary medicinal products and on**
7 **indications for veterinary vaccines**

8
9

| | |
|--|------------------|
| Agreed by Immunologicals Working Party | 17 December 2020 |
| Adopted by CVMP for release for consultation | 20 January 2021 |
| Start of public consultation | 29 January 2021 |
| End of consultation (deadline for comments) | 31 March 2021 |

10
11 The proposed guidelines will replace the 'Note for guidance – Field trials' with veterinary vaccines'
12 (EMA/CVMP/852/99-FINAL) and the 'Revised position paper on indications for veterinary vaccines'
13 (EMA/CVMP/042/97-Rev.1-FINAL)

14
15 Comments should be provided using this [template](#). The completed comments form should be sent to
Vet-guidelines@ema.europa.eu

16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100
101
102
103
104
105
106
107
108
109
110
111
112
113
114
115
116
117
118
119
120
121
122
123
124
125
126
127
128
129
130
131
132
133
134
135
136
137
138
139
140
141
142
143
144
145
146
147
148
149
150
151
152
153
154
155
156
157
158
159
160
161
162
163
164
165
166
167
168
169
170
171
172
173
174
175
176
177
178
179
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199
200
201
202
203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228
229
230
231
232
233
234
235
236
237
238
239
240
241
242
243
244
245
246
247
248
249
250
251
252
253
254
255
256
257
258
259
260
261
262
263
264
265
266
267
268
269
270
271
272
273
274
275
276
277
278
279
280
281
282
283
284
285
286
287
288
289
290
291
292
293
294
295
296
297
298
299
300
301
302
303
304
305
306
307
308
309
310
311
312
313
314
315
316
317
318
319
320
321
322
323
324
325
326
327
328
329
330
331
332
333
334
335
336
337
338
339
340
341
342
343
344
345
346
347
348
349
350
351
352
353
354
355
356
357
358
359
360
361
362
363
364
365
366
367
368
369
370
371
372
373
374
375
376
377
378
379
380
381
382
383
384
385
386
387
388
389
390
391
392
393
394
395
396
397
398
399
400
401
402
403
404
405
406
407
408
409
410
411
412
413
414
415
416
417
418
419
420
421
422
423
424
425
426
427
428
429
430
431
432
433
434
435
436
437
438
439
440
441
442
443
444
445
446
447
448
449
450
451
452
453
454
455
456
457
458
459
460
461
462
463
464
465
466
467
468
469
470
471
472
473
474
475
476
477
478
479
480
481
482
483
484
485
486
487
488
489
490
491
492
493
494
495
496
497
498
499
500
501
502
503
504
505
506
507
508
509
510
511
512
513
514
515
516
517
518
519
520
521
522
523
524
525
526
527
528
529
530
531
532
533
534
535
536
537
538
539
540
541
542
543
544
545
546
547
548
549
550
551
552
553
554
555
556
557
558
559
560
561
562
563
564
565
566
567
568
569
570
571
572
573
574
575
576
577
578
579
580
581
582
583
584
585
586
587
588
589
590
591
592
593
594
595
596
597
598
599
600
601
602
603
604
605
606
607
608
609
610
611
612
613
614
615
616
617
618
619
620
621
622
623
624
625
626
627
628
629
630
631
632
633
634
635
636
637
638
639
640
641
642
643
644
645
646
647
648
649
650
651
652
653
654
655
656
657
658
659
660
661
662
663
664
665
666
667
668
669
670
671
672
673
674
675
676
677
678
679
680
681
682
683
684
685
686
687
688
689
690
691
692
693
694
695
696
697
698
699
700
701
702
703
704
705
706
707
708
709
710
711
712
713
714
715
716
717
718
719
720
721
722
723
724
725
726
727
728
729
730
731
732
733
734
735
736
737
738
739
740
741
742
743
744
745
746
747
748
749
750
751
752
753
754
755
756
757
758
759
760
761
762
763
764
765
766
767
768
769
770
771
772
773
774
775
776
777
778
779
780
781
782
783
784
785
786
787
788
789
790
791
792
793
794
795
796
797
798
799
800
801
802
803
804
805
806
807
808
809
810
811
812
813
814
815
816
817
818
819
820
821
822
823
824
825
826
827
828
829
830
831
832
833
834
835
836
837
838
839
840
841
842
843
844
845
846
847
848
849
850
851
852
853
854
855
856
857
858
859
860
861
862
863
864
865
866
867
868
869
870
871
872
873
874
875
876
877
878
879
880
881
882
883
884
885
886
887
888
889
890
891
892
893
894
895
896
897
898
899
900
901
902
903
904
905
906
907
908
909
910
911
912
913
914
915
916
917
918
919
920
921
922
923
924
925
926
927
928
929
930
931
932
933
934
935
936
937
938
939
940
941
942
943
944
945
946
947
948
949
950
951
952
953
954
955
956
957
958
959
960
961
962
963
964
965
966
967
968
969
970
971
972
973
974
975
976
977
978
979
980
981
982
983
984
985
986
987
988
989
990
991
992
993
994
995
996
997
998
999
1000

| | |
|----------|--|
| Keywords | Field efficacy, indications, veterinary vaccines |
|----------|--|



18 **1. Introduction**

19 To date, field efficacy data is generally expected to be provided in support of a marketing authorisation
20 application for a vaccine. This requirement is based on existing legislation. However, currently the draft
21 Annex to the Commission Delegated Regulation amending Annex II to Regulation (EC) 2019/6 (still to
22 be adopted or endorsed by the European Commission) states in section IIIb, Requirements for
23 Immunological Veterinary Medicinal Products:

24 *"In general, pre-clinical studies shall be supported by trials carried out in field conditions.*

25 *When pre-clinical studies fully support the claims made in the summary of product characteristics,*
26 *trials carried out in field conditions are not required.*

27 *Unless otherwise justified, results from pre-clinical studies shall be supplemented with data from*
28 *clinical trials, using batches representative of the manufacturing process described in the marketing*
29 *authorisation application. Both safety and efficacy may be investigated in the same clinical trials."*

30 The existing "Note for Guidance - Field trials with Veterinary Vaccines" EMEA/CVMP/852/99-FINAL lists
31 a number of situations when the omission of field efficacy data may be accepted. In particular,
32 vaccines against notifiable and/or exotic diseases, vaccines against rare or sporadic diseases and
33 vaccines for minor species are listed.

34 Assuming Annex II to Regulation (EU) 2019/6 comes into force as it is drafted today, further vaccine
35 types or indications may be considered exempt from the requirement for field efficacy data, in addition
36 to those currently listed in the existing guideline. This would lessen the administrative and practical
37 burden placed on applicants to complete a marketing authorisation dossier.

38 Absence of field efficacy data may have implications for the description of indications for veterinary
39 vaccines in product literature, for this reason the position paper on indications for veterinary vaccines
40 may need to be updated.

41 The Immunologicals Working Party has been tasked to reflect on the requirement to provide efficacy
42 clinical trials in support of marketing authorisation applications for veterinary vaccines and to review
43 the already existing guidance on this issue.

44 **2. Problem statement**

45 A Joint European Medicines Agency (EMA)/Heads of Medicines Agencies (HMA) focus group meeting
46 with invited stakeholders was held in June 2017 to examine the relevance of efficacy clinical trials in
47 the context of an EU authorisation for veterinary vaccines. Based on the outcome of the Focus Group
48 meeting the joint EMA/HMA Steering Group on veterinary vaccine availability recommended that CVMP
49 consider how best to provide predictability to applicants as to those situations in which a justification to
50 omit field efficacy data will be accepted by regulators and how best to reflect in the SPC of veterinary
51 vaccines the efficacy data that have been provided.

52 As stated in the introduction, Annex II to Regulation (EU) 2019/6 has now been drafted to include a
53 statement that field efficacy data may be omitted under particular conditions (*"When pre-clinical*
54 *studies fully support the claims made in the summary of product characteristics, trials carried out in*
55 *field conditions are not required."*).

56 Currently, the guideline "Field trials with Veterinary Vaccines" EMEA/CVMP/852/99-FINAL includes a
57 section on 'deviations from the basic principle'. However, this section lists only a few exceptional
58 circumstances when field efficacy data are not required (Minor Use Minor Species products, vaccines

59 against notifiable diseases, vaccines against sporadic diseases). In order to provide clarity and
60 predictability on the need for provision of field efficacy data, also in light of the statements on clinical
61 trials in Annex II to Regulation (EU) 2019/6, a revision of the guideline is proposed.

62 The revised guideline should be updated to include further guidance on the type of products that would
63 or would not require field efficacy data.

64 The position paper on indications for veterinary vaccines may need to be updated as a consequence of
65 changes to the guideline on field trials with veterinary vaccines. This update should provide clear
66 guidance on how efficacy data is to be reflected in the SPC.

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

68 At the focus group meeting in 2017, preliminary data from a review of immunological products
69 authorised via the centralised route were presented. The findings suggest that, for some vaccines, field
70 efficacy trials were pivotal in defining some indications and, in addition, field studies may provide data
71 that increases understanding of the appropriate use of a vaccine and informs other sections of the SPC.
72 However, for the majority of immunological products considered in the review, field data appeared to
73 be of limited value from an efficacy perspective and was only generally supportive to the claims.

74 Veterinary vaccines represent a very wide range of products, all having specific properties with regard
75 to safety and efficacy. In general, it is difficult to cover all the vaccine types using a limited set of
76 criteria. In addition, it is challenging to list all vaccines for veterinary use, including future solutions.
77 This makes it difficult to define upfront those vaccines for which field efficacy data would not be
78 required, either by defining a set of criteria or by providing a list.

79 The introduction of uncertainties concerning data requirements should be avoided as much as possible.
80 It may therefore be possible to approach the problem described above by defining or describing both
81 the types of vaccines for which field efficacy data would not be required, as well as those for which
82 field efficacy data would be required. In this way, it may not be possible to cover all future veterinary
83 vaccines, but it would provide clarity in many cases. For any vaccines falling outside these categories,
84 there is always the option to request scientific advice.

85 The revision of the guideline should encompass the following:

- 86 • To provide guidance for which vaccines/indications omission of efficacy clinical trials may be
87 justified.
- 88 • To provide guidance for which vaccines/indications field efficacy data should be provided and
89 the type of data required.

90 The revision of the position paper on indications for veterinary vaccines should provide clear guidance
91 on how efficacy data, generated in the laboratory and/or in the field, is to be reflected in the product
92 literature.

93 **4. Recommendation**

94 The Committee for Medicinal Products for Veterinary use (CVMP) recommends the Immunologicals
95 Working Party (IWP) to revise the Note for guidance on field trials with veterinary vaccines, taking into
96 account the issues identified above.

97 The guidance should be updated to clarify for which vaccines/indications applicants could be exempted
98 from providing clinical efficacy data, apart from those vaccine types already exempted in the current

99 guidance. In addition, it is foreseen that guidance should be included for which vaccine indications
100 clinical efficacy data would be required. In addition, the format of the guidance needs to be updated to
101 the current standard e.g. guideline.

102 The Committee for Medicinal Products for Veterinary use (CVMP) also recommends the Immunologicals
103 Working Party (IWP) to revise the position paper on indications for veterinary vaccines, following the
104 update of the guidance on field trials with veterinary vaccines. The position paper should be updated to
105 provide guidance on how efficacy data (in the presence or in the absence of field efficacy data) is to be
106 reflected in the product literature. In addition, the format needs to be updated to a current standard
107 (e.g. guideline, reflection paper) that needs to be defined.

108 **5. Proposed timetable**

| | | |
|-----|-----------------|--|
| 109 | 29 January 2021 | Concept paper released for consultation |
| 110 | 31 March 2021 | Deadline for comments from stakeholders |
| 111 | May 2021 | Discussion in IWP |
| 112 | July 2021 | Adoption of the draft guideline by CVMP and release for consultation |
| 113 | October 2021 | Expected end of consultation |
| 114 | January 2022 | Expected date for adoption by CVMP and publication of the guideline |

115 It is expected that the guideline will come into operation earlier than six months after adoption,
116 coinciding with the date of application of the veterinary medicines Regulation (EU) 2019/6
117 (28 January 2022).

118 **6. Resource requirements for preparation**

119 The revision of each of the existing guidance will involve the IWP (including a drafting group composed
120 of rapporteur, co-rapporteur and 1-2 IWP members).

121 The IWP drafting group/s will meet virtually as required (e.g. 2-3 virtual meetings). Discussion is
122 foreseen at 1-2 IWP plenary meetings.

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

124 It is anticipated that the guideline would provide clarity and predictability to both industry and
125 regulators on the need to perform efficacy clinical trials. It would result in a more consistent
126 assessment of efficacy data. The guidance should result in reduction of requirements and thereby
127 reduce the use of resources for industry and contribute to the enhanced availability of vaccines.

128 **8. Interested parties**

129 Veterinary pharmaceutical industry and consultants.

130 EU Regulatory authorities involved in assessment of marketing authorisation applications for
131 immunological veterinary medicinal products.

132

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

134 Annex to the Commission Delegated Regulation amending Annex II to Regulation (EC) No 2019/6 of
135 the European Parliament and of the Council (draft published on 10 November 2020).

136 Note for Guidance on field trials with veterinary vaccines (EMA/CVMP/852/00-FINAL).

137 Revised Position paper on indications for veterinary vaccines for veterinary vaccines
138 (EMA/CVMP/042/97-Rev.1-FINAL).

139 Report on the Focus Group meeting with invited stakeholders on field efficacy trials in the context of an
140 EU authorisation for veterinary vaccines (EMA/405642/2017).