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Committee for Medicinal Products for Veterinary Use (CVMP)

Concept paper for the development of a guideline on data requirements for authorisation of immunological veterinary medicinal products under exceptional circumstances

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

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

Keywords	Immunological veterinary medicinal products, veterinary vaccines, exceptional circumstances, new veterinary regulation[1]

[1] To be identified here during preparation of the concept paper - keywords represent an internet search tool - Rapporteurs to propose and Working Party/Committee to adopt.

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1. Introduction

In the EU, marketing authorisations for veterinary medicinal products (VMPs) will be based on the requirements of Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products (repealing Directive 2001/82/EC), Article 8 whereby the respective data requirements are set out in Annex II (the date of application of Regulation (EU) 2019/6 is 28 January 2022).

The concept of a marketing authorisation under exceptional circumstances related to animal or public health included in Articles 25, 26 and 27 of Regulation (EU) 2019/6 allows for the issuing of marketing authorisations based on a reduced data set regarding quality, safety and efficacy in case of a concurrent lack of suitable authorised VMPs. However, it needs to be demonstrated that for objective and verifiable reasons certain quality, safety or efficacy documentation required in accordance with Annex II cannot be provided. It has to be stated clearly in the summary of product characteristics that based on the lack of comprehensive data only a limited assessment of quality, safety of efficacy has been conducted.

The scope of Articles 25, 26 and 27 of Regulation (EU) 2019/6 (marketing authorisations in exceptional circumstances) applies to VMPs generally. However, Immunological VMPs (IVMP), in particular vaccines, can be considered the main type of VMPs for which the provision is likely to apply, in situations where there is (the risk of) an outbreak of a new infectious disease in Europe that has the potential for severe impact on animal or public health. In this scenario, the immediate availability of a vaccine on the market and the possibility for rapid vaccination may be critical for outbreak control and/or disease eradication.

The Immunologicals Working Party has been tasked with the preparation of guidance on data requirements for the authorisation of immunological veterinary medicinal products (IVMPs) under exceptional circumstances. This guideline can also be seen as contributing to the Network action plan on availability of vaccines.

2. Problem statement

While in an emergency situation the use of unauthorised vaccines is in principle possible, there are risks associated with such use that must be taken into consideration. As outlined in the "CVMP reflection paper on the risks that should be considered prior to the use of unauthorised vaccines in emergency situations" (EMA/CVMP/IWP/49593/2013), there is a clear preference to use vaccines with a valid marketing authorisation.

The challenges of developing, manufacturing and authorising vaccines to enable a rapid response in the event of an emergency / outbreak have to be considered in the context of the current EU regulatory framework. On this point, it is recognised that such vaccines may be manufactured by companies outside the EU or by small and medium-sized enterprises (SMEs) having no or limited experience with this regulatory framework, data requirements for applications for marketing authorisation and the activities expected from applicants before, during and after the authorisation procedures. Therefore, clear guidance is needed to put the risks of having only an incomplete data set and the possibility of rapid establishment of a vaccination program in balance.

The purpose of the guideline proposed for development is to provide clear advice for applicants and assessors to define the minimum data requirements for all relevant parts of the application dossier for a marketing authorisation of IVMPs in exceptional circumstances. Clear guidance on data requirements will allow for an appropriate benefit–risk assessment where the risks of having an incomplete data set

can be balanced against the possibility of rapid establishment of a vaccination program and the resulting animal, public health and economic benefits. The particular risks in case of significant data gaps, and how these should be viewed in the context of the overall benefit-risk evaluation, will be dependent on the type of disease and the type of vaccine and will have to be considered individually on a case-by-case basis.

Because the marketing authorisation may be granted subject to one or more requirements for the marketing authorisation holder (such as introduction of conditions or restrictions, notification of adverse events to the competent authority or the conduct of post authorisation studies), it should be considered in which cases these requirements are an appropriate substitute for the absence of certain data normally submitted pre-authorisation.

Furthermore, the guideline may include recommendations for standard wording for inclusion in the product information to provide the user with clear information on the nature of the missing data and a justification for its absence.

Once a new guidance document is finalised, it is intended that existing related guidelines ("Guideline on requirements for an authorisation under exceptional circumstances for vaccines for emergency use against bluetongue" (EMEA/CVMP/IWP/37267/2008) and the "Guideline on requirements for an authorisation under exceptional circumstances for vaccines for use in birds against avian influenza (EMEA/CVMP/IWP/222624/2006)) will be withdrawn.

3. Discussion (on the problem statement)

The heterogeneity of IVMPs will make it necessary to define data requirements for a marketing authorisation of IVMPs in exceptional circumstances at a high-level focussing on those aspects for which the absence of data would pose the most significant risks. However, once work on the guideline commences, consideration will be given to defining additional requirements for certain specific vaccines, as appropriate.

While the draft Annex II of Regulation (EU) 2019/6 lays down the general requirements for applications for MA for vaccines, the full data set required for a normal marketing authorisation will not be submitted with applications for marketing authorisations under exceptional circumstances. The most critical elements of the data package submitted in support of a MA application for an IVMP are outlined below. Absence of sufficient data or information on these critical elements could make it substantially difficult or impossible to perform an appropriate benefit–risk assessment. Requirements for documentation to address each of these points are therefore considered an essential part of the guideline.

- Quality
    - qualitative particulars of all the constituents - vaccine ingredients.
    - information on the manufacturing process.
    - validated inactivation process for inactivated vaccines.
    - management of extraneous agents including TSE.
    - relevant and validated batch potency test.
    - sterility and/or purity issues.
- Safety

- basic safety tests with regard to the verification of potential unacceptable adverse events relating to the use of the vaccine and the impact on animal health.
- reversion to virulence and spread of the vaccine strain to other susceptible animals (for live attenuated vaccines).
- user safety (self-injection, human transmission of vaccine strain).
- study of residues and food safety considerations from vaccine components (e.g. preservatives, adjuvants, zoonotic vaccine strains).
- assessment for GMO vaccines.

- Efficacy
  - information regarding immunogenicity and relevance of the vaccine strain to the current epidemiological situation in the field, to verify the protection of the vaccinated animal and therefore benefit of the vaccine.
  - proposal for a vaccination schedule (primary vaccination, vaccination of particular groups, e.g. pregnant animals).

The granting of a marketing authorisation under exceptional circumstances may be conditional on certain restrictions on use, notification of adverse events to the competent authority or the generation of data post authorisation.

A yearly re–examination of the authorisation under exceptional circumstances is foreseen according to Article 27 of Regulation (EU) 2019/6. If the benefit-risk balance remains positive, the competent authority or the Commission, as applicable, shall extend the validity of the marketing authorisation for one year. The marketing authorisation may be granted for an unlimited period of time provided that the marketing authorisation holder submits the missing data on quality, safety or efficacy referred to in Article 25 of Regulation (EU) 2019/6. In this case, the full data set has to be in accordance with the requirements as laid down in Annex II.

It should be noted that procedural aspects including the approach to re-examination of MAs and/or extending the validity of MAs in accordance with Article 27 are not in the scope of the proposed guideline. These procedural aspects will be elaborated as a separate exercise by the Agency.

4. Recommendation

The Committee for Medicinal Products for Veterinary Use (CVMP) recommends the Immunologicals Working Party (IWP) to draft a guideline on minimum data requirements concerning quality, safety and efficacy for a marketing authorisation under exceptional circumstances for IVMPs to facilitate rapid authorisation in the interest of animal or public health in the event of an outbreak of a new infectious disease or a disease for which no IVMP is authorised.

The aim of the guideline should be provision of clear advice to applicants and assessors regarding the essential data sets required for such an application and to detail the risks associated with the absence of certain data that would normally be provided in support of a marketing authorisation application submitted in accordance with Article 8 of Regulation (EU) 2019/6.

5. Proposed timetable

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

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

6. Resource requirements for preparation

The development of the new guideline will involve the IWP (including a drafting group composed of rapporteur, co-rapporteur and one IWP member).

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

7. Impact assessment (anticipated)

It is anticipated that the guideline would have an essential impact on animal and public health and also an economical benefit for the farming industry in case of outbreaks of emerging or new infectious diseases. The advice given to applicants and regulatory authorities regarding the essential data sets to be provided/assessed would facilitate both vaccine development and the subsequent authorisation procedure and, consequently, pave the way to quicker availability of vaccines in an emergency situation.

8. Interested parties

Veterinary pharmaceutical industry and consultants.

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

EU competent authorities responsible for animal disease control.

9. References to literature, guidelines, etc.

Directive 2001/82/EC of the European Parliament and the Council of 6 November 2001 on the Community Code relating to Veterinary Medicinal Products as amended.

Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC.

Annex to the Commission Delegated Regulation amending Annex II to Regulation (EU) No 2019/6 of the European Parliament and of the Council (draft published for feedback, 10 November 2020).

175 Reflection paper on the risks that should be considered prior to the use of unauthorised vaccines in
176 emergency situations (EMA/CVMP/IWP/49593/2013).

177 Guideline on requirements for an authorisation under exceptional circumstances for vaccines for
178 emergency use against bluetongue (EMEA/CVMP/IWP/37267/2008).

179 Guideline on requirements for an authorisation under exceptional circumstances for vaccines for use in
180 birds against avian influenza (EMEA/CVMP/IWP/222624/2006).