EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

The Director General

Brussels,
SANTE/E5/CS/mcd 379717
Sent by e-mail only

Dear Prof Rasi,

Subject: Annex II to Regulation (EU) 2019/6 on veterinary medicinal products[1]

On 7th January 2019 the new Regulation on veterinary medicinal products ('VMP Regulation') was published.

In accordance with its Article 160, it will start applying 3 years from its entry into force, i.e. on 28th January 2022.

In the course of negotiations of the text of the VMP Regulation, the co-legislators agreed that there is a need to adjust the requirements for the technical documentation to demonstrate the quality, safety and efficacy of veterinary medicinal products when applying for a marketing authorisations (currently set out in Annex I to Directive 2001/82/EC and transferred as Annex II to the VMP Regulation).

It is acknowledged that the existing requirements regarding the technical documentation on the quality, safety and efficacy of veterinary medicinal products presented when applying for a marketing authorisation as set out in Annex I to Directive 2001/82/EC work sufficiently well in practice and that there is no urgent need, therefore, to substantially change those requirements.

However, there is a need to align the requirements of the current Annex II with the new provisions of the VMP Regulation and in particular to develop specific requirements for biological and novel therapy veterinary medicinal products as well as to respond to the identified discrepancies with the international scientific progress or latest developments,

[1] 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, OJ L 4, 7.1.2019, p. 43.

Prof Guido Rasi
Executive Director
European Medicines Agency
30 Churchill Place
Canary Wharf
London E14 5EU
United Kingdom

including guidance from VICH, WHO, OIE as well as OECD and European Pharmacopeia standards.

In this respect, according to Article 146(2) of the VMP Regulation, the Commission shall adopt a delegated act amending Annex II in order to achieve a sufficient level of detail that ensures legal certainty and harmonisation, as well as any necessary updating.

In accordance with Article 153(3), that delegated act shall be adopted at the latest by 12 months before the date of application of the VMP Regulation.

In this context, we would like to ask you to provide us with the Agency's scientific advice regarding the technical data to be provided by the applicants for marketing authorisations of veterinary medicinal products. In particular, and taking into account that the type of the veterinary medicinal product should be decisive for the composition of the application dossier, we would like to have your scientific advice on the technical documentation necessary for demonstrating the quality, safety and efficacy for the following types of products:

- technical requirements for a full dossier for a marketing authorisation in accordance with Article 8 of the VMP Regulation:

    - data set requirements for quality, safety and efficacy for veterinary medicinal products other than biologicals, including any particular requirements for antimicrobial veterinary medicinal products;

    - data set requirements for quality, safety and efficacy for biological veterinary medicinal products, including any particular requirements for:

        (i) immunological veterinary medicinal products,
        (ii) biological veterinary medicinal products other than immunologicals,

    - data set requirements for novel therapy veterinary medicinal products, including products designed for gene therapy, regenerative medicine, tissue engineering, blood product therapy, phage therapy, products issued from nanotechnologies, or any other therapy which is considered as a nascent field in veterinary medicine;

- specific requirements for:

    - generic veterinary medicinal products, including similar biological veterinary medicinal products,
    - hybrid veterinary medicinal products,
    - combination veterinary medicinal products,
    - application based on informed consent,
    - application based on bibliographic data,
    - applications for limited markets,
    - applications in exceptional circumstances.

Where possible, when elaborating on the above, we would appreciate if you could take account of the order of the presentation of the data as prescribed in the Notice to Applicants (Volume 6B).

Where possible, when elaborating on the above, the conclusions of the work conducted by the Task Force on availability for vaccines, and particularly specific requirement for Vaccine Antigen Master File or technological Platform, should be taken into account.

Relevant excerpts from the VMP Regulation are included in Annex I for your convenience.

We would kindly ask for your advice by the end of August 2019. We would also ask that the Agency update our services on the main progress of its work on a monthly basis.

We would like to thank you for your collaboration.

Yours sincerely,

Anne Bucher

Encl. : Annex I

Annex I

Relevant excerpts from the VMP Regulation.

Recitals:

(92) It is generally accepted that the existing requirements regarding the technical documentation on the quality, safety and efficacy of veterinary medicinal products presented when applying for a marketing authorisation in Annex I to Directive 2001/82/EC as last amended by Commission Directive 2009/9/EC1 work sufficiently well in practice. There is no urgent need, therefore, to substantially change those requirements. However, there is a need to adjust those requirements in order to respond to the identified discrepancies with the international scientific progress or latest developments, including guidance from VICH, WHO, the Organisation for Economic Co-operation and Development (OECD) standards, and taking into account also the need to develop specific requirements for novel therapy veterinary medicinal products while avoiding major overhaul of the current provisions, in particular not altering their structure.

(93) In order to, inter alia, adapt this Regulation to the scientific developments of the sector, to exercise the supervisory powers of the Commission effectively, and to introduce harmonised standards within the Union, the power to adopt acts in accordance with Article 290 TFEU should be delegated to the Commission in respect of establishing the criteria for the designation of the antimicrobials which are to be reserved for treatment of certain infections in humans; establishing the requirements for collection of data as regards the antimicrobial medicinal products, rules on the methods of collection and quality assurance; establishing the rules to ensure the effective and safe use of veterinary medicinal products authorised and prescribed for oral administration via routes other than medicated feed; providing details on content and format of the information as regards equine species in the single lifetime identification document; amending the rules on withdrawal period in the light of new scientific evidence; providing the necessary detailed rules on the application, by operators in third countries, of the provisions on the prohibition of the use of antimicrobial medicinal products in animals for the purpose of promoting growth or increase yield and the prohibition of the use of designated antimicrobials; laying down the procedure for the imposition of fines or periodic penalty payments as well as the conditions and methods for their collection; and amending Annex II in order to (i) adapt the requirements regarding the technical documentation on the quality, safety and efficacy of veterinary medicinal products to technical and scientific progress and (ii) achieve a sufficient level of detail that ensures legal certainty and harmonisation as well as any necessary updating. It is of particular importance that the Commission carry out appropriate consultations during its preparatory work, including at expert level, and that those consultations be conducted in accordance with the principles laid down in the Interinstitutional Agreement of 13 April 2016 on Better Law-Making1. In particular, to ensure equal participation in the preparation of delegated acts, the European Parliament and the Council receive all documents at the same time as Member States' experts, and their experts systematically have access to meetings of Commission expert groups dealing with the preparation of delegated acts.

Articles:

Article 8
Data to be submitted with the application

1. An application for a marketing authorisation shall contain the following:

(a) the information set out in Annex I;

(b) technical documentation necessary for demonstrating the quality, safety and efficacy of the veterinary medicinal product in accordance with the requirements set out in Annex II;

(c) a summary of the pharmacovigilance system master file.

Article 18
Generic veterinary medicinal products

1. By way of derogation from point (b) of Article 8(1), it shall not be required that an application for a marketing authorisation for a generic veterinary medicinal product contain the documentation on safety and efficacy if all the following conditions are fulfilled:

(a) bioavailability studies have demonstrated bioequivalence of a generic veterinary medicinal product with the reference veterinary medicinal product or a justification is provided as to why such studies were not performed;

(b) the application satisfies the requirements set out in Annex II;

(c) the applicant demonstrates that the application concerns a generic veterinary medicinal product of a reference veterinary medicinal product for which the period of protection of the technical documentation laid down in Articles 39 and 40 has elapsed or is due to elapse in less than two years.

Article 19
Hybrid veterinary medicinal products

1. By way of derogation from Article 18(1), the results of appropriate pre-clinical studies or clinical trials shall be required when the veterinary medicinal product does not meet all the characteristics of a generic veterinary medicinal product because of one or more of the following reasons:

(a) there are changes in the active substance or substances, indications for use, strength, pharmaceutical form or route of administration of the generic veterinary medicinal product compared to the reference veterinary medicinal product;

(b) bioavailability studies cannot be used to demonstrate bioequivalence with the reference veterinary medicinal product; or

(c) there are differences relating to raw materials or in manufacturing processes of the biological veterinary medicinal product and the reference biological veterinary medicinal product.

Article 20
Combination veterinary medicinal products

By way of derogation from point (b) of Article 8(1), in the case of veterinary medicinal products containing active substances used in the composition of authorised veterinary medicinal products it shall not be required to provide safety and efficacy data relating to each individual active substance.

Article 21
Application based on informed consent

By way of derogation from point (b) of Article 8(1), an applicant for a marketing authorisation for a veterinary medicinal product shall not be required to provide the technical documentation on quality, safety and efficacy if that applicant demonstrates permission, in the form of a letter of access, to use such documentation submitted in respect of the already authorised veterinary medicinal product.

Article 22
Application based on bibliographic data

1. By way of derogation from point (b) of Article 8(1), the applicant shall not be required to provide the documentation on safety and efficacy if that applicant demonstrates that the active substances of the veterinary medicinal product have been in well-established veterinary use within the Union for at least 10 years, that their efficacy is documented and that they provide an acceptable level of safety.

2. The application shall satisfy the requirements set out in Annex II.

Article 23
Applications for limited markets

1. By way of derogation from point (b) of Article 8(1), the applicant shall not be required to provide the comprehensive safety or efficacy documentation required in accordance with Annex II, if all of the following conditions are met:

(a) the benefit of the availability on the market of the veterinary medicinal product to the animal or public health outweighs the risk inherent in the fact that certain documentation has not been provided;

(b) the applicant provides the evidence that the veterinary medicinal product is intended for a limited market.

Article 25
Applications in exceptional circumstances

By way of derogation from point (b) of Article 8(1), in exceptional circumstances related to animal or public health, an applicant may submit an application which does not meet all requirements of that point, for which the benefit of the immediate availability on the market of the veterinary medicinal product concerned to the animal or public health outweighs the risk inherent in the fact that certain quality, safety or efficacy documentation has not been provided. In such a case, the applicant shall be required to demonstrate that for objective and verifiable reasons certain quality, safety or efficacy documentation required in accordance with Annex II cannot be provided.

Article 146
Amendments to Annex II

1. The Commission is empowered to adopt delegated acts in accordance with Article 147(2) in order to amend Annex II by adapting the requirements regarding the technical documentation on the quality, safety and efficacy of veterinary medicinal products to technical and scientific progress.

2. The Commission shall adopt delegated acts in accordance with Article 147(3) amending Annex II in order to achieve a sufficient level of detail that ensures legal certainty and harmonisation as well as any necessary updating, while avoiding unnecessary disruption with Annex II, including as regards the introduction of specific requirements for novel therapy veterinary medicinal products. When adopting those delegated acts, the Commission shall have due regard to animal and public health and environmental considerations.