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Oversight Group on Product Classification (CVMP)

Questions and answers on classification of veterinary medicinal products

Final

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Background

The Annex I of the now obsolete Directive 2001/82/EC recognised two classes of veterinary medicinal products (VMPs): (1) VMPs other than immunological VMPs and (2) immunological VMPs. The Directive defined an immunological VMP but did not have a definition of a biological VMP, as the field virtually did not exist at the time of adopting the Directive. The immunological VMPs developed previously could relatively easily fit into the broad sub-categories of vaccines and immunosera.

The scientific development in the field of VMPs necessitated an update of the regulatory framework, and this was brought about by Regulation (EU) 2019/6, as amended. Regulation (EU) 2019/6 introduces the definition of a biological substance and a biological VMP. The accelerating progress in the development of novel VMP types has also been recognised: the concept of a *novel therapy veterinary medicinal product* has also been introduced. Commission Delegated Regulation (EU) 2021/805, which amends Annex II to Regulation (EU) 2019/6, specifies the requirements for technical information on (1) VMPs other than biological VMPs, (2) biological VMPs other than immunological VMPs and (3) immunological VMPs, and, among other requirements, also the specific data requirements for novel therapy VMPs.

Experience shows that, for some of the veterinary medicinal products, allocation into one of the three product categories may not be straightforward. This is especially the case for some biological products, where there may be uncertainty whether they are an *immunological VMP* or a *biological VMP other than immunological VMP*. An appropriate understanding of the data requirements is crucial for the

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developers of VMPs, which was reflected in an increased number of classification requests to CVMP over the past two years.

This Q&A document has been developed by CVMP and EMA to address uncertainties in terms of product classification by providing guidance and clarity to stakeholders from the viewpoint of 1) whether a VMP is a non-biological VMP, biological VMP other than immunological VMP, or immunological VMP and 2) whether a VMP is a novel therapy product. The guiding principle is to ensure that the dossier contains information that will allow for adequate assessment of the product. The classification is based first and foremost on the definitions provided by the Regulation (EU) 2019/6 and takes into account scientific (such as mode of action) and regulatory aspects (such as data requirements influenced by the use and properties of the product). The scope of this Q&A paper are only the products that fall within the scope of Regulation (EU) 2019/6.

1. Is a product a non-biological, biological non-immunological, or immunological VMP?

If an active substance initiates or mediates an antigen-specific immune response in the target animal, the product is considered an immunological VMP because it acts via an activation of the adaptive immune system (e.g. a vaccine). This is regardless of whether the antigen-specific adaptive immune response is targeting an exogenous or endogenous antigen.

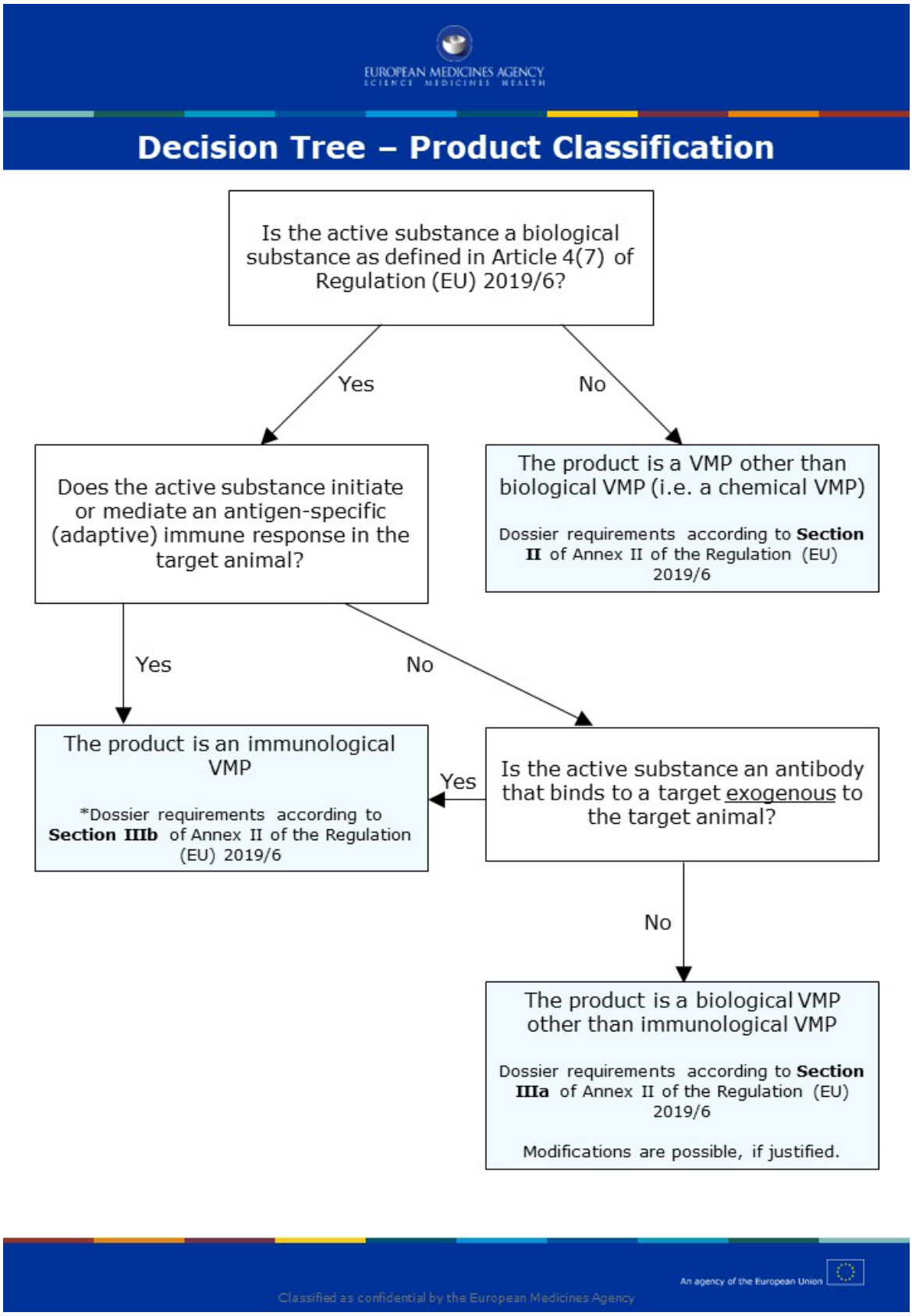
If an active substance interacts with the immune system but does not initiate a specific response via the adaptive immune system (e.g. it has a general, modifying effect on the function of the immune system), the product is not considered an immunological VMP, but a biological non-immunological VMP because its action does not contribute directly toward elimination/neutralisation of a specific target.

If an active substance is an antibody (i.e. uses an immunological mechanism) which binds to a specific exogenous target (e.g. antibodies against bacterial or viral pathogens), the product is considered an immunological VMP, because its action contributes directly toward elimination/neutralisation of such a target.

Lastly, if an active substance acts on a specific endogenous target via an immunological mechanism (e.g. monoclonal antibodies specific for a growth factor), the product is not considered an immunological VMP, but a biological non-immunological VMP. Regulatory dossier requirements are influenced by this situation because the safety assessment of such a product acting against target animal's own target(s) has some specificities compared to that of an immunological VMP.

These principles have been summarised in the decision tree below.

NB: The terms 'immunological VMP' and 'veterinary vaccine' are not synonyms. That is, the term 'immunological VMP' encompasses not only veterinary vaccines, but also e.g. antibodies that target specific exogenous targets via an immunological mechanism, or any other active substances that interact with target animal's immune system and lead to a specific immune response.



* Please note that for products classified as immunological VMPs that act via stimulation of generation of antibodies by the target animal which are then targeting self-antigens ("vaccine-like against endogenous protein"), the possible risk to the consumer will need to be addressed as part of the assessment of the marketing authorisation application.

2. Is a product a *novel therapy product*?

It is important that VMP developers have clarity early in the development process on whether their product is considered a novel therapy or not, because specific data requirements might apply, additional to the standard requirements for evaluation of quality, safety, and efficacy, as listed in Section V of Annex II of the Regulation (EU) 2019/6.

Article 4(43) and section V of Annex II of Regulation (EU) 2019/6 provide an indication what is considered a novel therapy veterinary medicinal product. The table below reflects this and provides an overview of veterinary medicinal products that are considered to be novel therapy products:

Type of a VMP	**Novel therapy product (Y/N)?**
Gene therapy	Y
Regenerative medicine	Y
Tissue engineering and cell therapy	Y
Blood product therapy	Y
Phage therapy	Y
Issued from nanotechnologies	Y
RNA antisense and RNA interference therapy	Y
Any other therapy which is considered as a nascent field in veterinary medicine	Apply for CVMP recommendation

One of the options for a product to be recognised as a novel therapy VMP is to satisfy the condition under Article 4(43)(c), i.e. to be considered as belonging to a *nascent field* in veterinary medicine. Given that the term "nascent" indicates that what is considered nascent will change with time, if an applicant needs a clarification whether their product belongs to a nascent field or not, consultation of the CVMP is advised. Recommendations will be made on a case-by-case basis.