Clarification on the naming of a VMP and the use of standard terms

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Keywords

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Abstract

This article provides insight into what constitutes the name of a veterinary medicinal product (VMP), and the use of standard terms of European Pharmacopoeia during the mutual recognition and decentralised procedures.

It is clear that, over the years, national competent authorities (NCAs) and applicants have developed different interpretations on the use of standard terms. The importance of standardisation can be seen at the level of correct use of products, market surveillance and free movement of VMPs across Europe.

The Coordination Group for Mutual Recognition and Decentralised Procedures – veterinary (CMDv) offers clarification and advice for the correct naming of the VMP, and the use of standard terms.

Introduction

For two decades, the Working Group on Quality Review of Documents (QRD)[1] and, more specifically, the veterinary subgroup has been working on the product specific review for VMPs, aiming at linguistic adherence and consistency in terminology. Guidance is issued with the annotated QRDvet template for product information, providing reference to terminology and standard statements. No less important is the work done by the European Directorate for the Quality of Medicines & Healthcare (EDQM). It provides standardised nomenclatures and quality of standards for medicinal substances and products. A list of standard terms[2] was initially drawn up by the European Pharmacopoeia Commission further to the request by the EU Commission for use in marketing authorisation applications (MAAs).

Standard terms have the dual purpose of bringing accurate information to the veterinarian and animal owner/keeper, and distinguishing VMPs having the same tradename.

In recent years, the CMDv has noted that applicants do not always adhere to the use of standard terms during MAAs. Both NCAs and applicants may have different interpretations of the EDQM standard terms for pharmaceutical forms and routes of administration, the use of controlled terms for target species and expression of the active substance in the product information. The CMDv is exploring ways to ensure greater standardisation in terminology in order to avoid discrepancies in the mutual recognition and decentralised procedures (MRPs/DCPs).

What constitutes a VMP name?

Definitions. According to Article 1(22) of Directive 2001/82/EC as amended,[3] it should be noted that the name of a VMP may be either "an invented name not liable to confusion with the common name, or a common or scientific name accompanied by a trademark or the name of the marketing authorisation holder".

It is also understood by the Directive that a common name, according to Article 1(23) is the "international non-proprietary name recommended by the World Health Organisation, or, if one does not exist, the usual common name."

The invented or common name by itself is not sufficient to unambiguously identify the VMP. For identification purposes the strength, pharmaceutical form and possibly the target species would be required. The combination of the product name with these qualifiers is referred to as "full (information) name". However, the term "full name" is not provided in any legislation but is understood to mean the name of the product, followed by the strength, pharmaceutical form and the target species. In some cases the strength is not relevant, eg, for vaccines. It should be noted that the "full name" is not the actual name of the product, unless this has been specifically applied for and approved during the procedure. In such cases, the product name is not to be translated and the strength, pharmaceutical form and target species must still be stated in the national language, following the product name, even if the product name contains information such as the pharmaceutical form or target species.

The target species should be added only if necessary, in order to avoid any confusion over different presentations of the VMP (eg, the same active substance and invented name) in different formulations for different target species.

The CMDv released a clarification paper[4] in November 2013 to determine what constitutes a product name.

Application form for marketing authorisation. When completing the electronic application form for an MAA (http://esubmission.ema.europa.eu/eaf), the applicant is requested to state "product (invented) name" (the name in the reference member state) in the "declaration and signature" section, along with dedicated fields for the pharmaceutical form and strength/units.

The user guide for the electronic application form for a marketing authorisation (veterinary)[5] states under the "Administrative Data – Product (Invented)" name: "In the case of an application under the

mutual recognition or decentralised procedure the product name used in the reference member state should be listed. Here should be quoted only the product or invented name in the box and not the *full* name of the product."

A list of the different proposed invented names and marketing authorisation holders in the concerned member states should be appended to the application form in Annex 5.18.

Agreement of a product name in MRP and DCP. Ideally, the invented name would be identical in all the EU member states involved in the procedure. This would enable the applicant to facilitate multilingual packages shared between member states, helping to address availability and bringing products to small markets. It is, however, still possible to have an invented name which is different in some member states.

Reaching agreement over the product name is a national issue, and is a decision for each NCA. It is, however, mandatory to include all invented names with the corresponding member state (in brackets) in Section 1 of the summary of product characteristics (SPC) approved at the end of the procedure. To aid this process, the CMDv has drafted a clarification paper[6] on how to agree on the product name in the DCP. The procedure is meant to maximise the use of the clock stop period, effectively bringing the product name discussions between applicant and NCAs forward. This paper only applies to the DCP, because the timeframe involved for the MRP (90 days) is too restrictive. Nevertheless the reference member state (RMS), concerned member states (CMSs) and the applicant should try their utmost to reach agreement on an approvable name before the end of the procedure.

Summary of product characteristics, labelling and package leaflet. According to Directive 2001/82/EC, as amended, the name of the VMP must be stated, followed by its qualifiers (strength and pharmaceutical form, etc), in the SPC (Article 14), in the labelling text (Article 58), and in the package leaflet (Article 61). When drafting the SPC, labelling and leaflet, companies should refer to the guidance in the annotated QRD veterinary product information template.[7]

Use of standard terms during MRPs/DCPs

Pharmaceutical form – route of administration. The standard terms for pharmaceutical forms and routes of administration are contained in the "List of standard terms for pharmaceutical dosage forms, routes of administration and containers", kept up to date by the EDQM. In the Notice to Applicants (NtA), Volume 6C, Summary of Product Characteristics, SPC Pharmaceuticals (July 2006),[8] the following is stated: "The pharmaceutical form should be described by the European Pharmacopoeia full standard term. If an appropriate standard term does not exist, a new term may be constructed from a combination of standard terms."

The user guide for the electronic application form for a marketing authorisation states clearly under "Administrative data – Pharmaceutical Form": "The pharmaceutical form should be selected in the drop-down list, which includes the pharmaceutical forms described in the Standard terms published in the European Pharmacopoeia that provides standardised nomenclatures and quality standards for medicinal substances and products. Only the full term should be mentioned (not the short term)."

The value for "pharmaceutical form" is noted in the "declaration and signature" section of the application form, from where subsequent fields are populated automatically.

Finally, at the level of pharmaceutical form and route of administration, the annotated QRD template again refers to the "standard terms" from the EDQM.

An example of this is an application relating to "lyophilisate for oculonasal suspension". The applicant proposed the following pharmaceutical form in an application for a marketing authorisation: "Live freeze-dried vaccine pellet to be reconstituted with water for an aerosol suspension". The applicant's explanation relied on the fact that this term had been accepted previously in some EEA member states. According the EDQM, however, the term "live freeze-dried vaccine pellet to be reconstituted with water for an aerosol suspension" is not valid and therefore could not be approved. The EDQM Standard Terms Database indicates that the term "lyophilisate for oculonasal suspension" should be used. Its definition is a "solid preparation consisting of a freeze-dried powder intended to be dispersed in the specified liquid to create a suspension for oculonasal use". The applicant did not agree and preferred "lyophilisate for aerosol suspension" in order to be consistent with the pharmaceutical form stated in the SPC of other recently authorised live avian viral vaccines to be applied via different routes of administration. The RMS and the CMSs reached a consensus on the use of "lyophilisate for suspension" as the pharmaceutical form.

Active substance. In compliance with the NtA Volume 6C, SPC-Pharmaceuticals, and according to the QRD annotated template, full details of the qualitative and quantitative composition in terms of active substance(s) should be stated, as follows:

- Qualitative composition. A hierarchy in nomenclature is defined in the NtA Vol 6C SPC: The international non-proprietary name (INN) should be used, accompanied by its salt, derivative or hydrate form if relevant. If no INN exists, the European Pharmacopoeia name should be used, or failing this, one of the Pharmacopoeia of the member states. If the substance is not in the Pharmacopoeia, the usual common name should be used. In the absence of a common name, the exact scientific designation should be given.
- Quantitative expression. The quantity of the active substance should be expressed per dosage unit or according to the form of administration for a given volume or weight, using their INN or common names. This means that the expression should be relevant for the use of the product, and should therefore be consistent with the posology. In many cases the quantity of the active substance is presented as a salt form, eg, "amoxicillin trihydrate y mg". According to the guidance, it should be presented as: "Amoxicillin x mg equivalent to y mg amoxicillin trihydrate".

The CMDv would like to reiterate the importance of adding the quantity of INN to the SPC Section 2 (corresponding package leaflet and labelling sections) in order to be compliant with the reference documents. Deviation can cause problems and dosing errors (especially at the level of the amount to be administered) since the amount of the active substance is not easily comparable and understood.

Target species. Both the user guide for the electronic application form for a marketing authorisation (veterinary) and the annotated QRD template require the section to be completed in accordance with the target species "Controlled Term List" on the European Union Telematics Controlled Terms (EUTCT) website,[9] including any sub-category. However, applicants sometimes misinterpret this guidance and provide the target species as sub-categories without quoting the species. For example, an entry might read: "Broilers (broiler

breeders)", where the correct expression according to EUTCT would be: "Chickens (broiler breeders)". Similarly, an entry stating: "Piglets (at age of 3 to 5 days)", should read: "Pigs (piglets at age of 3 to 5 days)".

Deviation from the guidance can cause availability problems, as it is difficult to search for products in the databases or by use of search engines when the standard term target species have not been used.

Conclusion

Standard terms are vital aspects in MAs for VMPs, market surveillance, and free movement of VMPs across Europe. The CMDv holds the opinion that: (1) when appropriate standard terms have been established, they should be utilised; (2) standardisation of terms is a key principle in veterinary MAAs, and the product literature of VMPs; (3) member states can request changes for any addition of a new term, or the revision or suppression of an existing term to the Standard Terms Database, to be addressed to the EDQM.

Further information relating to the CMDv, its activities, Best Practice Guides and guidance can be found on its webpages on the HMA website (www.hma.eu/159.html). The CMDv would also encourage use of the RSS feed option to ensure alerts to newly posted documents are received.

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