

Veterinary regulatory writing in Europe

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Abstract

Regulatory writing for the veterinary pharmaceutical industry is in many ways similar to other types of regulatory writing, but there are also clear differences. This article outlines the veterinary regulatory structure in Europe and, in particular, dossier content, competent regulatory authorities, as well as registration procedures. Adjacent fields of regulatory writing are addressed and an overview of typical documents is given. Furthermore, specific veterinary regulatory information sources for medical writers are provided.

Keywords: Veterinary medicinal product, Regulatory affairs

Writing for the veterinary pharmaceutical industry is like being a 'minor species' among medical writers. Most colleagues work for the human pharmaceutical industry and most seminars or workshops deal with topics specific for human medicinal products, such as the Clinical Trials Directive or the Common Technical Document (CTD) format for regulatory submissions. Many aspects of writing for the animal health industry are, of course, similar to other areas of medical writing, but there are also very specific topics to consider.

In veterinary medical writing, there is, for example, not only a patient to consider, as in all clinical studies, but also the owner of the patient. Furthermore, for veterinary health products, a considerable part of the registration dossier deals with human food safety because livestock animals produce food for human consumption, an aspect that medical writers or regulatory affairs professionals for human pharma do not touch. Another example is the importance of environmental safety testing because animals may be kept on pastures and may expose the environment directly to substances that present a potential hazard for the environment. This is a minor aspect

to be considered in registration dossiers for human medicinal products.

The product dossier for veterinary medicinal products

Veterinary registration dossiers follow the Notice to Applicants (NtA) structure as laid out in Eudralex volume 6B,¹ and do not yet follow the CTD structure. It is, in general, acceptable to use the CTD format, but in this case, a correlation table to the NtA structure must be provided. Also, it is possible to have a hybrid dossier consisting of an NtA structure for most parts and, for example, a CTD module for the quality documentation. The exact format of the dossier should be discussed in a pre-submission meeting with the competent regulatory authority.

When it comes to details of the content of the dossier, there are some differences between pharmaceutical and immunological veterinary medicinal products. However, the general dossier structure for both is as follows:

- Part 1: Administrative information and summary of the dossier.
- Part 2: Quality documentation.
- Part 3: Safety documentation (for pharmaceutical products, this comprises also residues documentation).
- Part 4: Efficacy documentation.

Part 1

Important documents in part 1 of the dossier, for which the regulatory affairs department might seek the help of a medical writer, are the detailed and critical summaries (expert reports) of the quality, safety, and efficacy documentation; the summary of product characteristics; and the product information literature (labelling and package leaflet). Specific aspects to consider when writing the latter for veterinary medicinal products were addressed in an earlier article.²

Dossier parts 2, 3, and 4 may each have a written introduction, but this is not mandatory in the age of e-submissions. The parts can consist only of the individual study reports or literature references.

Part 2

Part 2 of the dossier deals with the physicochemical, biological, or microbiological documentation for the individual components and the finished product. This is usually the part of the dossier that contains the most sensitive information with regard to protecting intellectual property.

Part 3

Part 3 of a pharmaceutical (i.e. a non-immunological) product covers the safety of the product to the user, the consumer (of foodstuffs produced by animals), and the environment. It contains mainly the toxicological studies performed in laboratory animals, especially the no-observed-effect levels. Based on these studies, a user risk assessment is performed and, for products intended for food-producing animals, an acceptable daily intake of potential residues in edible tissues is calculated.

Based on the acceptable daily intake, maximum residue levels for the active substance and its metabolites are determined for each relevant food commodity (e.g. edible tissues and milk from cattle or edible tissues and eggs from poultry). Such a setting of maximum residue levels follows a separate registration procedure and has a separate dossier.

Dossiers for products intended for use in food-producing animals have an additional Part 3B, which contains residue depletion studies in the target animal species. This is used to determine the time that needs to elapse between administration of the veterinary medicinal product to the animal and slaughter or milking of the animal, the so-called withdrawal period. This is the time between administration of the active substance to the animal and the decline of any potential residues in foodstuffs of animal origin below the respective maximum residue levels.

Furthermore, an environmental risk assessment is performed, which can be based on an extensive set of studies, especially for livestock animals that are kept on pasture or for fish that are kept in open water.

The focus of part 3 of an immunological product is the assessment of the potential risks that may result from the exposure of human beings to the veterinary medicinal product, for example during its administration to the animal. When such products consist of live organisms, especially those

that could be shed by vaccinated animals, the potential risk to unvaccinated animals must be evaluated. On the other hand, residue depletion studies are not normally necessary, except when certain adjuvants or preservatives are used.

Part 4

Part 4 describes the efficacy of the product in the target animal species (i.e. patient). This can be companion animals such as dogs or cats and livestock animals such as cattle, pigs, horses, and poultry. For immunological as well as pharmaceutical products, the focus is confirming the clinical dose through laboratory studies and field trials. For pharmaceutical products, part 4 furthermore includes pharmacological information such as the mode of action, potential resistance of antimicrobial or antiparasitic substances, pharmacokinetic particulars, the tolerance in the target animal species, and the determination of the clinical dose.

Competent regulatory authorities

Depending on the European country, the competent regulatory authority for the assessment of veterinary dossiers can be the same as for human medicinal products, or it can be a separate authority. The EMA, for example, has departments for human as well as veterinary medicinal products (covering immunologicals and pharmaceuticals). In Germany, however, veterinary pharmaceutical products are regulated nationally through the Federal Office of Consumer Protection and Food Safety, whereas the competent regulatory authority for veterinary (as well as human) immunological products is the Paul Ehrlich Institute. For environmental safety aspects, the German regulatory authority consults the Federal Office for the Environment.

There are also Member States of the European Union (EU) that differentiate between topical antiparasitic veterinary medicinal products, which are regulated through agricultural agencies, and other veterinary medicinal products, which are handled by either the competent regulatory authority for human medicinal products or a specific veterinary one.

Registration procedures

The registration procedures for veterinary medicinal products are, in general, the same as for human medicinal products. Small companies that focus on the local market in a certain country sometimes still choose the national registration procedure, namely application and product licence only in one EU country. Larger companies usually use the

European registration procedures, namely the mutual recognition procedure, the decentralised procedure, or the centralised procedure:

- *Mutual recognition procedure:* Many products that are currently on the market were registered years or decades ago when there were only national registration procedures in individual countries. The mutual recognition procedure must be used when a marketing authorisation holder now wants to extend such an existing product licence to other EU countries. A so-called Reference Member State is nominated which will evaluate the registration dossier and this assessment will then be accepted by the so-called Concerned Member States of the procedure.
- *Decentralised procedure:* Where a company intends to licence a new product in more than one European country, the decentralised procedure is usually chosen. The system of Reference Member States and Concerned Member States applies for this procedure, too, but the application is sent simultaneously to all involved countries.
- *Centralised procedure:* Applications for the centralised procedure are submitted to the EMA. There are some products that fall under the mandatory scope of the centralised procedure, such as veterinary medicinal products developed using certain biotechnological processes. Others fall under the optional scope, such as products containing new active substances. A marketing authorisation following the centralised procedure is granted by the European Commission and is valid for the entire Community market.

For veterinary medicinal products, generic (pharmaceutical) or biosimilar (immunological)

products can be registered and bibliographic applications (i.e. most of the dossier is based on literature references) can be made.

Areas adjacent to veterinary medical writing

There are some adjacent fields of regulatory writing for veterinary medicinal products, such as writing for pesticidal products, biocidal products, or medical devices.

The words pesticide and biocide are often used incorrectly as synonyms. From a regulatory point of view, pesticides are used to protect plants or crops from pests and diseases or control weeds. Biocides are used to control harmful or unwanted organisms through chemical or biological means either in the surroundings (houses, stables) by impregnating clothes or parasite barrier nets, or by direct application on human skin. Common examples of such products are disinfectants, wood preservatives, and insect repellents. Both fields are regulated by separate European legislation.

There is a grey area between veterinary biocidal products and antiparasitic products or disinfectants used on animals or in animal husbandry. For certain products, there is a choice whether to register a product through the animal health or the biocides regulations. Here, it often depends on the focus of the company that wants to register the product and on the expertise of their regulatory affairs department.

The term 'medical device' is not established for veterinary use in the EU and there is no European registration procedure for such products. In the USA, these products are known as 'veterinary devices' and are regulated by the Food and Drug Administration.

Table 1: Information sources for veterinary regulatory writing

Source	Description
Volume 5 of Eudralex ¹ ('The rules governing medicinal products in the European Union')	The main piece of European legislation with regard to applications for marketing authorisation for veterinary medicinal products, Directive 2001/82/EC ³ as amended, is published on this website of the European Commission in all official European languages
Volume 6 of Eudralex ¹	The registration procedures as well as the presentation and content of the dossier are described here
Volume 7 of Eudralex ¹ and the EMA's website ⁴ and the VICH website ⁵	The scientific guidelines prepared by the EMA's Committee for Medicinal Products for Veterinary Use are no longer directly published on the European Commission's Eudralex website ¹ (formerly in Volume 7) but on the EMA's website. The EMA's website also covers the guidelines established by the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) ⁵
Volume 8 of Eudralex ¹	The legal framework for the establishment of maximum residue limits for medicinal products for veterinary use is provided here
Volume 9 of Eudralex ¹ IFAH-Europe ⁶	The pharmacovigilance guidelines are published here International Federation for Animal Health (IFAH) Europe represents manufacturers of veterinary medicines, vaccines, and other animal health products in Europe (veterinary industry association)

A further adjacent field of veterinary regulatory writing is preparing pharmacovigilance documents. Pharmacovigilance may be part of the regulatory affairs department, but it can also be self-standing or integrated into the clinical development department.

Information sources for veterinary regulatory writing

For someone who is new to veterinary regulatory writing, it is essential to have a good overview of the regulatory structure, legislation, and guidance documents. Table 1 lists the main information sources for veterinary regulatory writing.

Conclusion

Veterinary medical writing is a diverse field with some parallels to medical writing for human pharmaceuticals and other adjacent fields. However, focused training is limited, so a background in veterinary medicine, biology, or agricultural science is valuable, especially for understanding the specific

diseases, treatment routines, animal husbandry systems, and terminology.

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3. Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products, as amended.
4. European Medicines Agency Website. Veterinary regulatory, scientific guidelines. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000173.jsp&mid=WC0b01ac058002d89a.
5. International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) website: <http://www.vichsec.org/>.
6. International Federation for Animal Health Europe (IFAH-Europe) website: <http://www.ifaheurope.org/>.

Author information

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