LEGISLATION REQUIREMENTS FOR CONTROL OVER VETERINARY PRODUCTS IN SOUTH AMERICA

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Legislation requirements for control over veterinary products in South America

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Abstract

The importance of the measures applied to control the importation, export, registration, supply, sale and use of veterinary medicines, biologicals and diagnostic reagents is based on their relevance to the animal and public health, through the prevention of zoonoses and its impact on food safety.

South America plays a major role in the production and exportation of products of animal origin, thus the availability of safe and effective veterinary products is mandatory.

The evolution of the regulatory framework and the different regional approaches towards the harmonisation of the requirements for the registration and control of veterinary products are presented, and the activities and outcomes of the Americas Committee of Veterinary Medicines, CAMEVET are described.
I. Introduction

The availability of quality veterinary products is an essential issue related to the prevention and control of animal and zoonotic diseases, and the improvement of animal productivity and food safety.

Registration and control of veterinary products is an unavoidable responsibility for the Veterinary Services, since the market authorisations must ensure the adequate quality and purity, efficacy and safety of products, and even assure that treated animals prove no harm for the consumers.

A special consideration is usually taken for biological products, since the lack of adequacy on the approval process and further quality controls may leave the animal and human population in a risk situation. Besides that, pharmacological products have also to be considered as an important matter, thus they constitute the only barrier available for the control of many animal diseases, specially those which cannot be prevented by vaccination, and also provide numerous effects in benefit of animal productivity and human health.

South America plays an important role in the production and exportation of animal products. According to OIE World Animal Health Information Database (WAHID)[1], South American animal population in 2006 ranged 149 million bovines, 5448 million birds and 41 million swine.

Data provided by the International Federation for Animal Health (IFAH) [2] shows that the animal health market in Latin America represents the 11.6% share of the global volume of veterinary products commercialised, for a value of 1.870 million dollars in 2006 and showing a 10 percent growth related to 2005.

The livestock population and animal density is related to the technological development of the animal productive systems. These variables also defining the industrial production of veterinary medicines and biologicals in individual countries. The manufacture of veterinary products could then be considered as an essential industry providing the tools required for the animal health, welfare, and human public health.

According to the OIE Terrestrial Animal Health Code, Veterinary Authorities should be able to demonstrate their capacity to exert control over all the matters involving animal health. This broad definition includes the assessment for the application of measures by the Veterinary Authorities, which should be able to demonstrate the existence of effective controls applied on the importation, export, registration, supply, sale and use of veterinary medicines, biologicals and diagnostic reagents, as described on Article 1.3.4.9. [3]

Another point specified in the Terrestrial Code with direct influence on the registration and control measures for veterinary pharmacological products is detailed on the Annex 3.9.3 [3],
which applies to the guidelines for the responsible and prudent use of antimicrobial agents in veterinary medicine.

Although these recommendations are particular for antimicrobials, most of the general aspects can be considered for the majority of pharmacological products, since part of the guidelines refer to the aspects of the product licensing, covering the need of guarantees for quality, safety and efficacy.

Based on the special productive characteristics of South America and the actual international requirements for the animal production and livestock trade, the need for active registration and control systems for veterinary products becomes an unavoidable issue for the Veterinary Authorities.

II. The registration and control for veterinary products: 25 years ago

For comparison, during the 1980 decade many countries in South America lacked an active evaluation process for the authorisation and control of veterinary products, and in some cases market approvals did not include any evaluation or control [4].

The increase in the marketing of veterinary products, associated with the evolution of the livestock production, made official services face many difficulties regarding the control activities, due to insufficient regulatory frameworks and resources. The absence of requisites for the manufacture and control of veterinary products had the consequence on the irregular quality in the products available, coupled to the lack of enforcement actions.

From the side of the industrial sector, and under the absence of sound regulatory requirements, the manufacture and commercialisation of veterinary products acted as a non-regulated market, in which several product qualities coexisted, and in many cases the industry itself did not guarantee the efficacy and safety of the products. The situation seemed favourable for the promotion and sale of products which did not meet the minimum quality requirements, and the existence of fraudulent market procedures.

In the case of the farmers, the situation was endorsed by the absence of demand in the quality of products, even also the evident lack of efficacy, safety and economical losses for the producers.

Another deficiency showed at the official regulatory areas was related to the access to information, where the availability of publications from reference international organisations was limited.

Related to the scarce availability of updated information, there was no communication between regulatory bodies from the countries, resulting in great divergences in registration requisites and the measures taken in response to arising problems.
From the point of view of the human health and trade of animal products, the uncontrolled use of veterinary products and the absence of residue avoidance and control plans in many countries resulted in a risk situation, with potential harmful effects on human health, and posed a problem for the export of animal products.

### III. The initiatives for harmonisation in South America

The globalisation in economy and commerce and the development of transport and communication systems have transformed the Veterinary Services into parts of active networks, demanding their activities beyond their geographical barriers, so the creation and application of common procedures becomes an unavoidable topic, considering the particular situation of South America [5].

Harmonisation initiatives have been linked to the creation of Regional Trade Agreements, and principally associated to the establishment of common sanitary trade measures and the objective of the promotion of fair competition in the marketing of veterinary products.

**Mercosur** (Mercado Común del Sur - South common market [6]) was founded in 1991 among Argentina, Brasil, Paraguay and Uruguay, under the Treaty of Asuncion, and updated by the 1994 Treaty of Ouro Preto, incorporating Venezuela as a full member in 2006.

Based on the purpose of the promotion of free trade, one of the issues was related to the registration and commercialisation of veterinary products. This led to the organisation and harmonisation of the regulatory framework for its member countries, through the creation of the Veterinary Products Commission in 1992.

The activities of the Commission resulted in the production from 1992 to 1997 of many Decisions covering the registration and control of veterinary products, and are listed on Table 1.

The proposed harmonisation system was based on the regulatory equivalence of the approval requisites in member countries, and provided the mutual recognition for the registration of those products which were compliant on harmonised technical outlines, containing the quality requirements and basic product characteristics, and identified under a common classification system.

**Andean Community** trade bloc (Comunidad Andina [7]) was formed under the Cartagena Agreement signed in 1969, by Bolivia, Colombia, Ecuador and Peru, incorporating Chile as an associated member in 2006. One of the purposes included in the Agreement was related to the establishment and execution of common provisions and programs on plant and animal health.
Under this agreement, member countries signed the Decision 483 in year 2000[7], covering the common rules for the registration, control, marketing and use of veterinary products, including the procedures for the mutual recognition for the registration of products.

The mutual recognition system for products previously registered in one country was based on the voluntary extension of the approval certificate to the other member countries, through the submission and evaluation by the registration areas from each country.

For both Trade Agreements, the objective of establishing equivalent regulatory measures for veterinary products could be fulfilled, since the implementation and application of common approval and control systems could not be put in action.

Currently, Andean Community and Mercosur countries act as associated members, and published a joint letter of intention for future negotiations towards the complete integration of South America under the Union of South American Nations (UNASUR).

Central American Customs Union (Unión Aduanera Centroamericana [8]) is a trade agreement signed in 1960 by Costa Rica, El Salvador, Guatemala, Honduras and Nicaragua under the General Treatise for Economical Integration. This treatise was revised under the Guatemala Protocol in 1993, which included the need for the harmonisation of regulations regarding veterinary products.

As a result of the work carried out by the Sanitary and Phytosanitary Measures Group, member countries approved in 2008 the Central American Technical Regulation on veterinary products [9], covering the aspects for the registration, manufacture and control of veterinary products, and the procedure for the mutual recognition of registered products in member countries.

This rule comprises many of the concepts used in the Mercosur Resolutions, and is mainly based on the harmonised guidelines developed by the Americas Committee of Veterinary Medicines.

The system for the product approval in member countries is based in two systems, a Common Sanitary Registration for the registration on individual countries through the evaluation of the technical information in each country, and a Simplified Sanitary Registration, which applies for products included in a Harmonised List of Products (based on the compliance on harmonised technical outlines), for which the approval process in member countries is done through a simplified evaluation.

CAMEVET (Comité Americano de Medicamentos Veterinarios - Americas Committee of Veterinary Medicines)[10] is a technical working group based on the OIE Regional Representation for the Americas, composed by the representatives of the veterinary products
regulatory agencies from American OIE member countries, and the associations of veterinary products industries as collaborating members.

The goals of the Committee are the coordination of the technical information for the registration and control of veterinary products, with the purpose to harmonise the technical requirements, and to develop quality and commercial exchange between countries.

Another objective is the share of information on the rules governing registration, control, manufacture and marketing of veterinary medicines, aiming to assure the quality, efficacy and safety of products, in order to reach regulatory homologation in member countries.

Through annual meetings since 1992, the initial work focused on the harmonisation of the contents of technical outlines on biological and pharmacological products, linked with the Mercosur activities.

Following seminars, guidelines on Good Manufacturing Practices (including guides for conducting audits), templates for international approval certificates, and the organisation of the requirements for the registration of pharmaceutical and biological products under specific application forms, were produced.

Another important document produced by the Committee refers to the labelling for veterinary products, for which the inclusion of the harmonised guideline in the OIE Terrestrial Code is actually under analysis.

Currently, a reference document on good practices on use of veterinary medicines is being developed, related to the proposal for the extension of the OIE guidelines for the responsible and prudent use of antimicrobial agents to the whole spectrum of veterinary products.

As CAMEVET is a technical workgroup, harmonised documents act as guidelines for the regulatory and industrial areas from member countries, which can adopt and include them into their local regulations.

IV. The evolution and the actual requirements in South America

Linked to the advancement of the livestock production and commerce, regulatory areas from South American countries could adapt to the growth in the veterinary market and establish the legal basis to regulate and control their activities.

This notable adaptation was associated to the harmonisation initiatives, which posed an opportunity for the modernisation of the approval and control requisites, since the common work led to the application of regulations adapted to the special cultural, social and economical situation of each sub region.
Another advantage which produced a revolution on the interaction between regulatory bodies was related to the availability of information originated on international reference organisations, and the creation of networks formed by the registration areas, mainly through their interaction under the CAMEVET.

The increase in the exportation of animal products also posed a challenge for the Veterinary Authorities, due to the need for the existence of residue avoidance and control plans, mainly associated to the approval and control systems for veterinary products.

Since that, a general description of the requisites for the approval of veterinary products could be outlined under three broad areas.

- The first area refers to the facilities intended for the manufacture of veterinary products, whereas all of the regulations include general installation requisites.
- Related to this, the homogeneous application of Good Manufacture Practices is still an unaccomplished issue, since the exigencies may vary from different countries, and in few cases are actually not required.
- The second group relates to the product registration, where the requisites and the contents of the registration forms are similar, existing differences on special topics, such as the evaluation of efficacy, requisites for stability testing, and even the exigencies for the products labelling.
- The last area refers to the control activities led by each country on the marketed products, where the exigencies of the pharmacovigilance and control systems vary completely between countries, from the complete control by official authorities of every batch produced to the reliance on the controls made by the producers and periodic quality audits.

Under that broad description of the differences, it is mandatory that regional harmonisation initiatives remove all of the discrepancies and establish common approval and control procedures, taking in account the different structural realities in South America.

V. Conclusion

South American countries have adopted different approaches for the establishment of the legal requisites for the market authorisation and control for veterinary products, coupled to the harmonisation initiatives, which were closely related in time, and sharing similar rationales. Besides that, the complete task could not be fulfilled in most of the cases, principally due to the lack of continuity in the homologation process.

The notable differences in the productive structure and economy in South American countries pose a major difficulty for the complete harmonisation and mutual recognition procedures, one of the objectives of the Americas Committee of Veterinary Medicines.
Currently, the Committee is the only discussion and proposal forum which responds to the needs and capabilities of Southern American veterinary products registration offices.

Even that, the inclusion of the technical CAMEVET guidelines in the regulations of member countries can be considered as an unfinished task, since their application is partial and difficult, for which the inclusion of harmonized guidelines of the OIE Standards could become a feasible alternative for the complete harmonization of the rules governing the registration and control of veterinary medicines.

This is a process which will face many difficulties but will result in benefits for all of the participants.

References

4. Gimeno, EJ Vilches AM Benefits to be derived from establishing a veterinary product approval process in developing countries Rev sci tech Off int Epiz 1984, 3 (4) 883-894
5. Gimeno, EJ The organisation and future development of Veterinary Services in Latin America Rev sci tech Off int Epiz 2003, 22 (2) 449-461
Appendix

Table 1: List of MERCOSUR Resolutions (Identified as MERCOSUR/GMC/RES)

<table>
<thead>
<tr>
<th>Resolution</th>
<th>Title</th>
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<tr>
<td>29/92</td>
<td>Creation of the Veterinary Products Commission</td>
</tr>
<tr>
<td>3/93</td>
<td>Proposal for the harmonised registration and control system for veterinary products</td>
</tr>
<tr>
<td>11/93</td>
<td>Regulatory Framework for veterinary products</td>
</tr>
<tr>
<td>29/93</td>
<td>Homologation system for registration certificates</td>
</tr>
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<td>44/93</td>
<td>Registration formularies for pharmacological, biological and medicated feedstuffs. Products classification tables</td>
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<td>39/96</td>
<td>Annex for the regulatory framework for veterinary products</td>
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<td>40/96</td>
<td>Registration for the veterinary products harmonisation system</td>
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<td>76/96</td>
<td>Technical requisites on registration for antiparasitary products</td>
</tr>
<tr>
<td>2/97</td>
<td>Contents for product technical outlines and classification table</td>
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<tr>
<td>3/97</td>
<td>Technical regulation on registration of antimicrobial products</td>
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<tr>
<td>4/97</td>
<td>Technical regulation on production and control of vaccines, antigens and diluents for aviculture</td>
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Table 2: List of CAMEVET harmonised guidelines

<table>
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<tr>
<th>Seminar - Year of approval</th>
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<tbody>
<tr>
<td>IX Seminar (2003)</td>
<td>CAMEVET template for Free Sale Certificates</td>
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<tr>
<td>IX Seminar (2003)</td>
<td>CAMEVET template for Exportation Certificates</td>
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<tr>
<td>X Seminar (2004)</td>
<td>Registration form for pharmacological and biological products</td>
</tr>
<tr>
<td>XII Seminar (2005)</td>
<td>Labelling for veterinary products</td>
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