LEGISLATION, REGISTRATION AND CONTROL PROCEDURES FOR VETERINARY MEDICINAL PRODUCTS IN NORTHERN AFRICA

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Session 2: Legislation, registration and control for veterinary medicinal products
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Summary

The central part of the Maghreb region in North Africa comprises Morocco, Algeria and Tunisia.

It forms a homogeneous entity, in which livestock production plays a leading role and makes a major contribution to agricultural GDP.

More than 43 million sheep and 5 million cattle are raised in this region, which also has an extensive modern poultry industry with an estimated annual production of nearly 600 million broiler chicks.

These national livestock populations have naturally led to the development of the veterinary drug market, a market that was worth 91 million Euros in 2006 and is steadily growing.

Given the size of this market, in terms of both local production and imports, the authorities in these three countries have rapidly introduced specific legislation and the market is now highly regulated. Thus, procedures now exist for the registration, distribution and control of these highly sensitive products.

While these procedures are globally very similar from one country to another, there are some specific features, which we shall be highlighting.

These regulatory aspects are constantly evolving in response to the never-ending technical and technological changes affecting this strategically important product for the development of livestock farming in the countries of the Maghreb.
I. Introduction

Private veterinary medicine has undergone remarkable growth in the past decade in the Maghreb countries (Morocco, Tunisia and Algeria) due to the importance and potential of livestock production in the region.

The existence of a major network of veterinary practitioners has gone hand in hand with remarkable growth in the market for veterinary medicinal products, framed by copious legislation that covers aspects ranging from local production, importation, registration and distribution, to controlling the products that are placed on the market.

These three countries have set up an animal health accreditation mandate (mandat sanitaire) that allows practitioners to participate in major prevention campaigns and therefore become actively involved in epidemiological surveillance, as well as bringing them into close contact with livestock producers and allowing them to pass on healthcare practices (Ref. 2.b; 3.f; 4.j).

II. Animal production and veterinary medicinal products

1. Ecological zones and livestock production systems

Livestock production in the Maghreb is basically extensive for small ruminants, whilst dairy and meat cattle are found in the high plateau regions and around the large towns and cities in the north. Large poultry units and modern hatcheries are also found in the north and around urban centres where poultry consumption is high. This activity can only grow, given the development of mass retailing and fast food chains. As a result, we expect to see greater use of medicinal products in this sector, which is already reflected in rising turnover in recent years.

2. Veterinary medicinal product market

The market for veterinary medicinal products is worth around 91 million euros (excluding the Premix market).

Over the past 10 years, this market has grown steadily at an estimated 5% a year. This growth is driven by:

- Greater use of veterinary medicinal products, with increasing numbers of practitioners in rural areas.
- Major development of poultry production.
- Growing demand from dairy farmers for regular medical care.
- Tighter veterinary control for sheep production.

The products used are mainly for ruminants (43 million sheep, 10 million goats and more than 5 million cattle) and poultry (almost 600 million chickens).
The very small market for companion animals is expected to grow in line with rising living standards, especially in the large urban centres.

Table 1: Livestock populations in the Maghreb

<table>
<thead>
<tr>
<th></th>
<th>Morocco</th>
<th>Algeria</th>
<th>Tunisia</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruminants</td>
<td>24,500,000</td>
<td>24,500,000</td>
<td>8,150,000</td>
<td>57,150,000</td>
</tr>
<tr>
<td>Poultry</td>
<td>259,130,000</td>
<td>243,700,000</td>
<td>74,345,000</td>
<td>577,175,000</td>
</tr>
</tbody>
</table>

Table 2: Market turnover

<table>
<thead>
<tr>
<th>Millions of euros</th>
<th>Morocco</th>
<th>Algeria</th>
<th>Tunisia</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruminant market</td>
<td>20.00</td>
<td>19.40</td>
<td>5.00</td>
<td>44.40</td>
</tr>
<tr>
<td>Poultry market</td>
<td>18.00</td>
<td>18.00</td>
<td>5.46</td>
<td>41.46</td>
</tr>
<tr>
<td>Total</td>
<td>38.00</td>
<td>37.40</td>
<td>10.46</td>
<td>85.86</td>
</tr>
<tr>
<td>Total market</td>
<td>40.00</td>
<td>40.60</td>
<td>11.36</td>
<td>91.96</td>
</tr>
</tbody>
</table>

Pie charts of the Maghreb market for veterinary medicinal products:

Figure 1
An essentially Maghreb market

Figure 2
Distribution by country for poultry and ruminants

Figure 3
Distribution by country and by species

Figure 4
Distribution by country and by species

Figure 5
Distribution by country and by species
3. **Origin of veterinary medicinal products**

Morocco, Algeria and Tunisia all have an expanding pharmaceutical industry that is starting to make significant inroads into the market.

These units manufacture and package biologicals (vaccines, sera), antibiotics and anti-parasitic drugs.

The remaining medicinal products are imported, mainly from Europe.

The market is currently dominated by recognised international firms. Three laboratories (Merial, Ceva and Intervet) represent more than 50% of turnover, with Ceva the only firm to have a manufacturing unit in each of the three Maghreb countries, supporting and working in partnership with local producers.

4. **Market configuration and therapeutic classes**

An analysis of therapeutic classes shows that the Maghreb market is dominated by anti-infectious drugs (35-40%) and anti-parasitic drugs (20-23%), followed by vaccines (15-19%) and vitamins (12-14%).

**Table 3: Distribution by therapeutic class**

<table>
<thead>
<tr>
<th></th>
<th>Anti-infectious drugs</th>
<th>Anti-parasitic drugs</th>
<th>Vaccines</th>
<th>Vitamins</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morocco</td>
<td>39%</td>
<td>23%</td>
<td>17%</td>
<td>13%</td>
<td>8%</td>
</tr>
<tr>
<td>Algeria</td>
<td>38%</td>
<td>22%</td>
<td>15%</td>
<td>12%</td>
<td>13%</td>
</tr>
<tr>
<td>Tunisia</td>
<td>35%</td>
<td>22%</td>
<td>19%</td>
<td>14%</td>
<td>10%</td>
</tr>
</tbody>
</table>

III. **Distribution of veterinary medicinal products**

All three countries have a distribution network that is made up of private importers and distributors in Morocco and Algeria, whilst in Tunisia, the role of importer still falls to public institutions (Pharmacie Centrale, Institut Pasteur and Institut de Recherche Vétérinaire), although there are also wholesaler/distributors run by pharmacists. Under international commitments adopted by Tunisia, this monopoly is set to be eliminated in 2010-2011. (Ref. 2.a; 2.e; 3.b; 3.g; 3.h; 4.a; 4.b; 4.c; 4.d).
All importers and distributors must of course be approved by the ministry responsible for managing and controlling veterinary medicinal products, following the advice of specialist inter-ministerial commissions.

An important point is that all importers and distributors must come under the technical direction of a veterinarian or pharmacist.

Moreover, veterinary practitioners are dispensers in all three countries, although in Tunisia they can obtain supplies only from the Pharmacie Centrale or the Institut Pasteur, based on nomenclature drawn up by the competent authorities. (Ref. 2.d; 3.b; 3.e; 3.g; 3.i; 4.b; 4.c; 4.e; 4.j).

IV. Registration process

The countries have an obligation to guarantee the efficacy and safety of drugs to users by means of proper legislation and regulations governing the market for veterinary medicinal products, the different stakeholders involved, their roles, the inspection and control mechanism and punitive action against offenders.

The primary task of the authorities responsible for controlling veterinary medicinal products is therefore to ensure that, at the time of registration, the manufacturer applying for approval meets the requirements at every stage of the process.

This process appears to be properly codified in the regulatory texts of Morocco, Algeria and Tunisia and the marketing authorisation (MA) is the final process, after which the authority gives its consent to the marketing of the veterinary medicinal product concerned by the application (Ref. 2.a; 2.c; 2.e; 3.b; 3.c; 3.g; 3.j; 4.b; 4.c; 4.d; 4.f; 4.g).

1. Registration aspects common to all three countries

   ➢ Administrative aspects:

   An application for approval of a pharmaceutical speciality must be sent to the minister responsible for the central veterinary pharmacy department.

   This application must mention:

   1. The names, forenames, positions and company name of the manufacturer (or the importer).

   2. The number and date of the licence to practice of the pharmacist or veterinarian responsible for manufacture (or importer).

   3. The special name, either a fanciful name, or a common scientific name followed by the name of the manufacturer or trademark, and the name and address of the person responsible for placing it on the market.

   4. The pharmaceutical form, the content or the number of therapeutic units.
5. The formula for preparing the speciality and the composition.

6. Administration methods and routes, therapeutic medications, precautions to be taken during administration, normal dosage, contra-indications and secondary effects.

7. The presumed stability date, in particular the expiration date, which must appear on the internal and external packaging.

8. An indication of the places of manufacture, control, packaging and distribution.

9. An attestation that the manufacturer is authorised to produce pharmaceutical specialities in its own country and that the speciality concerned is authorised and marketed in the country of origin (MA).

10. The nature or composition of the container with the packaging plan.

11. Sales samples of the speciality concerned.

➢ Technical aspects:

All MA applications must be accompanied by a technical dossier containing:

1. A description of the method and conditions under which the medicinal product is manufactured.

2. A description of the methods for the control of raw materials and finished products, and if necessary during the manufacturing process, as well as an indication of the results obtained from these methods.

3. Pharmaco-toxicological test reports.

4. Clinical studies and the conclusions concerning:
   
   a) The animal species concerned.
   
   b) The safety of the medicinal product under normal conditions of use and its therapeutic effect.
   
   c) The dosage and duration of treatment and the observation period.
   
   d) Indications, contra-indications and undesirable secondary effects; any interactions identified with other medicinal products.
   
   e) Normal and special conditions for prescription, administration and use.
   
   f) The clinical risks of an overdose.

The control techniques used for raw materials and finished products, as well as for the pharmaco-toxicological and clinical studies presented by manufacturing laboratories, must be performed, where necessary, by experts appointed by the minister responsible for the veterinary pharmacy.

2. Differences identified

The main difference between the three countries is the ministry responsible for signing the MA.
It is the responsibility of the ministries of public health and agriculture in Morocco, the ministry of agriculture in Algeria, and the ministry of public health in Tunisia.

In addition to requiring the permit for the manufacturer to produce and market a medicinal product in the country of origin, just like the other countries, Algeria requires the MA obtained in another country.

Finally, Morocco and Tunisia have a policy for fixing prices in their country, whilst prices can be set completely freely in Algeria.
Figure 8: Registration procedures in Morocco

- Submission of dossier + Samples
- Ministry of Public Health
- National Control Laboratory for Pharmaceutical Products
- Inter-ministerial Commission
- Feasibility study by the Control Laboratory or the Institut Pasteur of Algeria
- Inter-ministerial Commission
- “Presentation + study of dossier”
- Opinion “Dossier conforms”
- Granted
- Rejected
- Reserved
- Analyses + Results
- Opinion “Satisfactory results”
- Favourable opinion
- MA signed by the Minister for Agriculture
- MA signed by the Minister for Public Health
- MA signed by the two Ministers

Figure 9: Registration procedures in Algeria

- Submission of technical administrative dossier + Samples
- Ministry of Agriculture
- National Control Laboratory for Pharmaceutical Products
- Feasibility study by the Control Laboratory or the Institut Pasteur of Algeria
- Inter-ministerial Commission
- “Presentation + study of dossier”
- Opinion “Dossier conforms”
- Granted
- Rejected
- Reserved
- Analyses + Results
- Opinion “Satisfactory results”
- Favourable opinion
- MA signed by the Minister for Agriculture
V. Control procedures

There are inspection and control procedures in all three countries at different stages in the process.

1. At the time of MA application

It is mandatory to supply samples of the product for which an MA application is being made and this forms part of the regulatory procedures. All aspects of the samples are analysed by the national control laboratories for pharmaceutical products within the three countries, and a favourable result is vital for obtaining the MA, notwithstanding the other technical and administrative aspects. (Ref. 2.f; 3.c; 4.d)

There is a national control laboratory for pharmaceutical products in Morocco and Tunisia, whilst in Algeria there are two public entities (SAIDAL and DIGROMED) that analyse veterinary medicinal products on behalf of the agriculture ministry.
Note that Algeria also has a national control laboratory for pharmaceutical products approved by the WHO and the European Pharmacopoeia, where the ministry of agriculture sits on the Board of Management. It currently controls pharmaceutical products for human use, and new agreements will soon enable it to control veterinary medicinal products. The Institut Pasteur of Algeria controls biological products for both human and veterinary use.

2. **At the time of importation**

There are control procedures at border posts permanently manned by veterinary inspectors.

This control includes checking the MA and a physical control of products (identification, expiration date, cold chain and transport conditions). The control may also involve random sampling for laboratory analysis.

3. **At the time of distribution**

Distributors and private practitioners may be subjected to spot-checks to inspect the storage conditions of medicinal products, the absence of out-of-date products – seizing them where appropriate – and the absence of non-approved products, as well as checking the cold chain for biological products.

4. **Pharmacovigilance**

Algeria has set up a pharmacovigilance network with private practitioners; they use a data sheet to identify any anomaly or undesirable effect of a medicinal product during use, which they must return to the central office.

VI. **Conclusion**

The central region of the Maghreb has successfully established a regulatory framework for veterinary medicinal products and has a pharmaceutical industry with significant turnover, which even exports some products (worth 5 to 6 million euros a year).

It is now time to implement good manufacturing practices and good distribution practices that are understood and used by all stakeholders in the sector.

Monitoring technological innovations and technical progress should be the watchword at all levels.

In addition, integration within the Arab Maghreb Union (UMA), as recommended by the “Convention on veterinary medicine and cooperation in the field of animal health between member states of the Arab Maghreb Union” of 9 and 10 March 1991, in particular article 2 point 5, could help to boost this fast-growing market (Ref. 1).
References

1. Convention on veterinary medicine and cooperation in the field of animal health between member states of the Arab Maghreb Union (Convention relative à la médecine vétérinaire et à la coopération dans le domaine de la santé animale entre les États membres de l’Union du Maghreb Arabe).

2. Moroccan legislation:
   a. Law no. 17-04 concerning drugs and the pharmacy (Official Bulletin of 07/12/2006).
   b. Dahir no. 1-80-340 of 25 December 1980 promulgating Law no. 21-80 concerning the private practice of veterinary medicine, veterinary surgery and veterinary pharmacy.
   d. Decree no. 2-82-541 of 15 March 1983 implementing law no. 21-80 of 25 December 1980 concerning the private practice of veterinary medicine, veterinary surgery and veterinary pharmacy.
   e. Decree no. 2-76-266 of 6 May 1977 concerning the approval, authorisation to supply pharmaceutical specialities and the advertising of medical specialities to pharmaceutical dispensaries.
   f. Decree no. 2-72-373 of 24 April 1974 concerning the creation of a national control laboratory for medicinal products and pharmaceutical specialities.

3. Algerian legislation:
   a. Law 85-05 of 16 February 1985, concerning health protection and promotion.
   b. Law 88-08 du 26 January 1988, concerning veterinary medicine and animal health protection – Algeria.
   c. Executive decree 90-240 of 04 August 1990 laying down the conditions for the manufacture, marketing and control of veterinary medicinal products – Algeria.
   d. Executive decree no. 02-216 of 20 June 2002 defining pharmaceutical products for veterinary use that are subject to 7% value added tax.
   e. Executive decree no. 06-118 of 12 March 2006, extending executive decree no. 88-252 of 31 December 1988 laying down the conditions for the private practice of veterinary medicine and animal surgery.
   f. Order of 14 July 2005 amending and extending the order of 30 November 2003, laying down the procedures for granting the animal health accreditation mandate to private veterinary practitioners for carrying out animal disease prevention and eradication programmes ordered by the national veterinary authority.
   g. Inter-ministerial order no. 204 SPM of 10 April 1994 concerning the composition and operating conditions of the commission referred to in article 3 of executive decree no. 90-240 of 04 August 1990 laying down the conditions for the manufacture, marketing and control of veterinary medicinal products.
h. Order of 28 March 2006 defining the provisions for the conditions for the delivery of a health permit to establishments responsible for the production, packaging and storage of animal feed.

i. Decision no. 03 SPM of 27 January 1996, appointing the members of the inter-ministerial commission responsible for the preliminary examination of requests for agreements and administrative authorisations for establishments responsible for the manufacture and wholesale distribution of veterinary medicinal products.

j. Decision no. 557 of 31 May 2004, defining the list of experts approved by the inter-ministerial commission responsible for deciding on marketing authorisations for veterinary medicinal products.

4. Tunisian legislation:
   a. Law no. 69-54 of 26 July 1969 regulating poisonous substances.
   b. Law no. 73-55 of 3 August 1973, organising the pharmaceutical professions.
   c. Law no. 78-23 of 8 March 1978 organising the veterinary pharmacy.
   d. Law no. 85-91 of 22 November 1985, regulating the manufacture and registration of medicinal products for human use.
   e. Law no. 92/75 of August 1992, organising the dispensing of medicinal products by veterinarians.
   f. Decree no. 79-831 of 28 September 1979, defining the rules of good manufacturing practice veterinary medicinal products and their quality control, packaging, labelling and denomination, as well as approval application procedures.
   g. Order of the Minister of Public Health of 10 September 1996, defining procedures for the granting, renewal and assignment of a marketing authorisation for medicinal products for human use.
   h. Order of the Minister of Public Health of 15 October 2002, defining the composition and operating procedures of the technical committee for pharmaceutical specialities with a view to marketing authorisation.
   j. Inter-ministerial order of 12 February 2000, defining the conditions for supplying veterinarians with pharmaceutical and biological products for veterinary use.
   k. Ministerial order of 28 July 2004 defining the procedures for granting an animal health accreditation mandate.