Veterinary Medicines Legislation and Maximum Residue Limits in the EU

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Outline

- Institutions of the European Union
- European Commission
- Development of the EU pharmaceutical legislation
- Legislative procedures
- Ongoing initiatives
The European Union

... a unique political and economic community
... with supranational and intergovernmental dimensions
... composed of 27 Member States with over 500 million citizens
Entities of the EU

- European Commission
- European Parliament
- Council of the European Union
- European Court of Justice
- Court of Auditors
Entities of the EU

- The President of the European Union
- High Representative of the Union for Foreign Affairs and Security Policy
- European Economic and Social Committee, Committee of the Regions, the European Central Bank, European Ombudsman
- European Agencies: EMA, EFSA, ECDC
The European Commission

College of Commissioners

- is currently composed of 27 commissioners, one from each Member State.
- The President of the Commission and all the other commissioners are nominated by the Council.
- The President and then the Commission in its entirety, need to be confirmed by Parliament.

The Services of the Commission

- Directorates-General (DGs) : “departments” or “ministries” covering a specific policy area or service
- headed by Director-General who is responsible to a Commissioner.
Legal framework for veterinary medicinal products - history

- 1981 - 2 directives establishing EU legal framework for veterinary medicines
- 1990: Regulation 2377/1990 introducing the concept of MRLs
- 2001: Codification exercise in 2001
- 2004: A major revision of the legal framework
- 2010: Implementing MRL regulation
## Legal instruments

<table>
<thead>
<tr>
<th>Instrument Type</th>
<th>Characteristics</th>
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</thead>
<tbody>
<tr>
<td>Regulation (general)</td>
<td>directly binding directly applicable in all MS</td>
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<tr>
<td>Directive</td>
<td>binding framework addressed to MS for implementation in national legislation</td>
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<tr>
<td>Decision (specific)</td>
<td>directly binding upon those addressed</td>
</tr>
<tr>
<td>Recommendations and opinions</td>
<td>no binding force</td>
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</tbody>
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Lisbon Treaty

- In force since 1 December 2009.
- Amends the current EU and European Commission Treaties without replacing them.
- A permanent Council President to chair EU summits.
- Representative of the EU for Foreign Affairs and Security Policy
- New provision on public health.
Lisbon Treaty – EU Health

- Shared competences with MS (Art. 4, TFEU), common safety concerns in public health matters.
- Competences to carry out actions to support, coordinate and supplement the actions of MS (Art. 6)
- Common agricultural policy (Art. 43, ex. Art. 37 TEC)
Lisbon Treaty – EU Health

- Internal market (Art. 114, ex. Art. 95 TEC)
- Measures in the veterinary and phytosanitary fields (Art. 168(4)(b))
- Setting high standards of quality and safety for medicinal products (Art. 168(4)(c))
Co-decision

- Co-decision procedure (Article 251 of the EC Treaty), allows the European Parliament to veto proposed legislation.
- Legislative procedure which is central to the Community's decision-making system.
- Established by the Maastricht Treaty.
- The roles shared by the three institutions (Council, European Parliament and Commission).
Co-decision

1. Proposal from the Commission
2. First reading by the EP - opinion
3. Amended proposal from the Commission
4. First reading by the Council
5. Council approves all the EP's amendments
6. Council can adopt the act as amended
7. EP has approved the proposal without amendments
8. Council can adopt the act
9. Common position of the Council
10. Communication from the Commission on common position
11. Second reading by the EP
12. EP approves common position or makes no comments
13. Act is deemed to be adopted
14. EP rejects common position
15. Act is deemed not to be adopted
16. EP proposes amendments to common position
17. Commission opinion on EP's amendments
18. Second reading by the Council
19. Council approves amended common position
20. Act adopted as amended
21. Council does not approve the amendments to the common position
22. Conciliation Committee is convened
23. Conciliation procedure
24. Conciliation Committee agrees on a joint text
25. Parliament and Council adopt the act concerned in accordance with the joint text
26. Act is adopted
27. Parliament and Council do not approve the joint text
28. Act is not adopted
29. Conciliation Committee does not agree on a joint text
30. Act is not adopted
Marketing authorisation

Main principle

• Ensuring consumer safety through authorisation of veterinary medicines
• Therefore, medicine is only allowed to be marketed and used in the EU if it has a valid marketing authorisation.
• No marketing authorisation if no MRL is established.
• Single EU market for pharmaceuticals
Marketing authorisation

– A medicinal product **may only be placed on the market** in the European Union when a marketing authorisation has been issued by the competent authority of a Member State for its own territory (a national authorisation) or when an authorisation has been granted for the entire Community (a Community authorisation).

– Authorisations are granted on the basis of the criteria of QUALITY, SAFETY and EFFICACY.

– For food producing species you need a Maximum Residue Limit for the relevant tissues.
The procedures available

CENTRALISED

- Applications made directly to the European Agency for the Evaluation of Medicinal Products (EMA)
- Leading to the grant of a Europe-wide marketing authorisation issued by the European Commission

DECENTRALISED and MUTUAL RECOGNITION

- Applications made to the MS selected by the applicant
- The procedure is based on mutual recognition of national marketing authorisations;
- Possible Community arbitration procedure
- Reference MS and concerned MS
“Referrals” – Community procedures regarding nationally authorised products

➢ Lack of agreement in mutual recognition
  - Refusal to recognise on grounds of “serious potential risk to human or animal health or to the environment”
  - Discussion in “Coordination Group”
  - If no agreement amongst MS: assessment EMA & Commission decision addressed to the MS
“Referrals” – Community procedures regarding nationally authorised products

- Harmonisation of marketing authorisations
- Community interest
- Urgent measures on pharmacovigilance grounds

In all cases: same procedure: Assessment EMA & Commission decision addressed to the MS
The Standing Committee

- In the area of medicinal products, the Commission is assisted by the Standing Committee on Medicinal Products for Human/Veterinary Use
- The Standing Committee is chaired by the Commission representative
- Referred to by Articles 87(3) of Regulation (EC) No 726/2004 and Article 89 of Directive 2001/82/EC
Overview MRLs

- Residues of medicines may end up in food; the safety of these residues needs to be ensured

Community rules

- Setting of safety levels of residues (MRLs)
- You need a MRL in order to obtain a marketing authorisation for a medicine
- Residue surveillance of imported products and foodstuffs produced in EU
Definitions

MRL

• The maximum concentration of a residue of a pharmacologically active substance which may be permitted in food of animal origin

Food-producing animal

• Animal kept, bred, raised, slaughtered or harvest for the purpose of producing food
Definitions

Hazard
• A situation that poses a level of threat

Risk
• Likelihood x seriousness of incident
MRLs as reference points

• For the establishment of withdrawal periods for medicines

• The withdrawal period is determined in the context of the marketing authorisation of the medicine

• The withdrawal period is set to ensure that residues in food will not exceed the MRL

• For the control of residues in food in the MS and at border inspection posts
Procedure for establishment of MRLs

- EU-procedure; one single assessment, valid for the whole EU; no national MRLs
- Requests for a MRL can be submitted to EMA by pharmaceutical industry, Commission, MS or an interested party
- Scientific opinion by EMA
Procedure for establishment of MRLs

- Risk analysis to ensure the safety of residues
- Adoption of Regulation on each MRL by Commission after agreement of MS
- MRL binding in all EU Member States
Principles for establishment of MRLs

- Establishment of ADI (toxicological effects, pharmacological effects, microbial effects)
- Residue studies
- Food basket
Classification of MRLs

- Permanent MRL
- Provisional MRL (incomplete data but no grounds for supposing a relevant risk)
- No MRL required (MRL not necessary for protection of public health)
- Prohibited substances (Where any residue can constitute a hazard)
Legal framework / history

- EU legislation on MRLs (No 2377/90) adopted in 1990, came into force on 1 January 1992

  Required MRLs for any new marketing authorisation

  Transition period for old products to 31.12.1999
Legal framework / history

- In 2009 new MRL regulation (No 470/2009)
  
  Defines the procedure for evaluation and the data requirements for the establishment of MRLs
Legal framework / history

- In 2010 implementing Commission regulation (No 37/2010); Annex contains classification of all evaluated active substances

- Up to now over 800 substances assessed by EMA
• Pharmacologically active substance must appear in Regulation 37/2010.
• If not, valid application for establishment of MRL prior to application for marketing authorisation
New provisions in MRL-Regulation

- Clarification of rules for extending existing MRLs for substances to other foodstuffs or species; extrapolation
- Establishment of MRLs for biocidal products
- Reference points of action for monitoring
- Adoption of international established MRLs (Codex) without a scientific opinion of EMA
Non legislative activities

- European Directorate for the Quality of Medicines (EDQM), e.g. monographs, biological standardisation programme
- International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH)
- OIE
- Codex, e.g. MRLs
- Confidentiality arrangements (e.g. USA, Canada, Japan)
- EU enlargement
Challenges

**Legislation**

- Filling regulatory gaps
- Adapting rules to changing environment
- Reduce burden for industry and competent authorities by increasing efficiency
Challenges

Implementation

- Clarity of legal interpretation
- Coherence between Member States
- Full implementation by all Member States
- Worksharing of all authorities
- Efficient communication in regulatory network
Conclusion

European Commission is committed, through its regulatory and non-regulatory initiatives:

1. to ensure a high level of public health protection,

2. contribute to the completion of internal market,

3. to create and stimulate environment for promoting competitiveness and innovation
Thank you
Policy context MRLs

• Ensure consumer safety through establishment of withdrawal periods and residue surveillance

• MRL procedure provides analytical method for surveillance by MS

• Facilitate trade through a science based MRL applicable in all MS