Legislation, Registration and Control Procedures for Veterinary Medicinal Products in the European Union

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Presentation

- Legal Framework
- Medicines control within the EU
- Networking model of medicines regulation in the European Union
- Activities of the network
- Lessons learnt and prospects for the future

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Medicines Regulation in the EU

• Summary description
  – Chapter I.1.9, Section 2 of the 'OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals'

• Key websites
  – European Commission DG Enterprise
    • EudraLex: The Rules Governing Medicinal Products in the European Union
      • http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/index.htm
  – EMEA Veterinary Medicines Webpage
    • http://www.ema.europa.eu/index/indexv1.htm
    • To become
    • http://www.ema.europa.eu/index/indexv1.htm
Medicines Regulation in the EU

• Key websites cont.
  – Heads of Medicines Agencies (EU)
    • http://www.hma.eu/
  – European Directorate for the Quality of Medicines
    • Home of the European Pharmacopoeia
      • http://www.edqm.eu/site/Homepage-628.html
  – VICH – International Cooperation on Harmonisation of the Technical Requirements for Registration of Veterinary Products
    • http://www.vichsec.org/
Legal Framework

- Harmonised legal framework covering pharmaceutical products as part of the Acquis Communautaire

- Key legal instruments
Legal Framework

• Key legal instruments
Regulatory Activities in the EU

• Control of **manufacture**
  – Manufacturing authorisation

• Control of **placing on the market**
  – Establishment of **Maximum Residue Limits (MRLs)**
  – Marketing authorisation

• **Monitoring of products** on the market
  – Pharmacovigilance (monitoring adverse drug reactions)
  – Sampling and testing
  – Inspection of facilities
Requirements for manufacture

- Manufacturing authorisation issued by national competent authority
  - Recognition of compliance with requirements of GMP in line with Directive 91/412/EEC
- Facility inspection
- Product related inspection
- “Qualified Person” certifies compliance of each batch with terms of marketing authorisation
Routes to authorisation

• Any veterinary medicinal product placed on the EU market must have a marketing authorisation ('Product Licence')

• Four routes to authorisation
  – National
  – Mutual Recognition
  – Decentralised Procedure
  – Centralised Procedure

• Same technical requirements for all procedures defined in Annex 1 to Directive 2001/82/EC, as amended
## Routes to Authorisation

<table>
<thead>
<tr>
<th>Type of Authorisation</th>
<th>National</th>
<th>Mutual Recognition</th>
<th>Decentralised</th>
<th>Centralised</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Issued by</strong></td>
<td>National Authority</td>
<td>National Authority through CMDv</td>
<td>National Authority through CMDv</td>
<td>European Commission through EMEA/CVMP</td>
</tr>
<tr>
<td><strong>Validity</strong></td>
<td>One Member State</td>
<td>Several Member States</td>
<td>Several Member States</td>
<td>All Member States</td>
</tr>
<tr>
<td><strong>Time to authorisation (standard)</strong></td>
<td>210 days</td>
<td>210 days</td>
<td>210 days</td>
<td>210 days</td>
</tr>
<tr>
<td><strong>Appeal &amp;/or arbitration</strong></td>
<td>National appeal systems</td>
<td>Appeal to CMDv then arbitration by CVMP</td>
<td>Appeal to CMDv then arbitration by CVMP</td>
<td>Re-examination by CVMP</td>
</tr>
<tr>
<td><strong>Types of product</strong></td>
<td>Conventional, novel actives and generics</td>
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<td>Novel, biotech, GMO and generics of CAPs</td>
</tr>
</tbody>
</table>
Control of products on the EU market

- Pharmacovigilance requirements
  - Urgent reporting of serious Suspected Adverse Reactions (SARs)
  - Periodic Safety Update Reports (PSURs)
  - Pharmacovigilance inspections
  - Development of Eudravigilance Veterinary Database for electronic reporting

- One renewal at 5 years
  - Option for further renewals based on pharmacovigilance
Control of products on the EU market

- Rapid Alerts
  - Pharmacovigilance
  - Quality defects

- Sampling and testing by network of Official Medicines Control Laboratories (OMCLs)
  - Coordinated by EDQM
    - Network of OMCLs
    - Testing of centrally authorised products

- Periodic inspections to maintain GMP accreditation of manufacturers
The European Medicines Regulatory Networking Model

- Elements of the network
  - National Competent Authorities coordinated by Heads of Medicines Agencies (HMA)
    - Human/Joint Agencies/Authorities
    - Veterinary Agencies/Authorities
    - Inspection Agencies/Authorities
      - 42 agencies, including EEA
  - European Medicines Agency (EMEA)
  - European Commission
  - European Directorate for the Quality of Medicines & Healthcare (EDQM)
  - Network of Official Medicines Control Laboratories
  - MRA partners
The European Medicines Regulatory Networking Model

- NCA-EEA
- NCA-MS
- CMDv
- CVMP
- EMEA
- EDQM
- European Commission

- IT Systems
- OMCL Network
- Heads of Medicines Agency
- Referrals & Arbitration
- Rapid Alert Systems
The European Medicines Regulatory Networking Model

- Committees of the network
  - Coordination Group for Mutual Recognition and Decentralised Procedures – veterinary (CMD-v)
  - Committee for Medicinal Products for Veterinary Use (CVMP), and its
    - Working Parties and Scientific Advisory Groups
  - Standing Committee on Veterinary Medicinal Products
    - Veterinary Pharmaceutical Committee
Committee for Medicinal Products for Veterinary Use - CVMP

• Composition of the CVMP
  – Chairman (Dr Moulin, FR)
  – Vice-chair (Dr Holm, DK)
  – 1 Member for each EU Member State
  – 1 Member from each EEA Country
  – 5 Members co-opted according to their expertise
CVMP - Scientific Committees

Pharmacovigilance Working Party
Secretary: Raquel Gopal

Environmental Risk Assessment WP
Secretary: Jordi Torren

Efficacy WP
Secretary: Barbara Cyrus

Scientific Advice Working Party
Secretary: Karen Quigley

Joint CHMP/CVMP Quality WP
Vet Secretary: Teresa Potter

Antimicrobial Scientific Advisory Group
Secretary: Jordi Torren

Safety WP
Secretary: Nicholas Jarrett

Immunologicals WP
Secretary: Nikolaus Križ

CVMP
Secretary: Fia Westerholm

CMDv
Secretary: Emily Drury
The European Medicines Regulatory Networking Model

- Activities of the CVMP
  - Establishment of Maximum Residue Limits (MRLs)
  - Authorisation of products
  - Referral and arbitration
  - Production of guidance documents
  - Production of scientific strategy documents
  - Comment on legislative proposals
  - Post-authorisation activities
    - Pharmacovigilance
      - including Eudravigilance Veterinary
    - Sampling and testing
  - Inspection of manufacture

Pharmacovigilance

Sampling and testing
The European Medicines Regulatory Networking Model

• Essential components for an effective network
  – Harmonised legal and technical requirements
  – An effective infrastructure for coordination and cooperation
    • Buildings and physical facilities
    • Coordinatory body
    • Established and agreed procedures
  – Effective IT systems
    • EU Telematics programme
      – e.g. http://eudrapharm.eu/eudrapharm/welcome.do
  – A common language
  – Mutual trust and transparency
  – Interest in work sharing
The European Medicines Regulatory Networking Model

- Lessons learnt during building of European Regulatory Network
  - Sharing of resources can be effective and efficient
  - Mutual trust and transparency are essential and increase with experience
  - Gains to industry and competitiveness can be considerable
    - Time
    - Resource
    - 'Level playing field'
    - Predictability
  - Resource constraints drive ever greater efficiency
The European Medicines Regulatory Networking Model

• Prospects for the future
  – Harmonised interpretation of requirements is a continuous challenge
  – ‘Old’ products particularly difficult
  – Compulsory arbitration and referral leading to greater harmonisation and predictability
  – Emphasis and drive for improved IT systems
The European Medicines Regulatory Networking Model

- Prospects for the future
  - increasing trend for 'Centres of Excellence'
  - increase in worksharing
  - emphasis on training and cooperation
  - European Commission is currently reviewing the legislation to assess the need for
    - simplification
    - ensuring a proportionate regulatory burden
    - adapting to the needs of the veterinary sector
The End

• Thank you for your attention
Details of authorisation procedures
National Marketing Authorisation

• Issued by national competent authority
• Permits marketing in one Member State only
• Assessment procedure lasts a maximum of 210 days (not including 'clock stops' for industry)
• May form the basis for mutual recognition
Mutual Recognition Procedure

- Based on 'mutual recognition' of national marketing authorisation
- National authority of original Member State as the 'Reference Member State' for the product
- Between 1 and 26 'Concerned Member States' plus EEA countries (Norway, Iceland and Lichtenstein)
- Coordinated through the Coordination Group for Mutual Recognition and Decentralised Procedures – Veterinary (CMDv)
Mutual Recognition Procedure

• Preparation/Updating of assessment report within 90 days
• Mutual Recognition Procedure of 90 days with 60 more days for referral if no agreement
• Arbitration by the Committee for Medicinal Products for Veterinary Use (CVMP)
• Veterinary Mutual Recognition Index
  – http://www.hma.eu/vmri.html
Decentralised Procedure

- For products not already authorised in EU
- One Reference Member State
- 1 to 26 Concerned Member States
- 210 day procedure with 60 day referral period if no agreement can be reached
- Arbitration by CVMP
Centralised Procedure

• Authorisation issued by European Commission which is valid throughout the EU and EEA

• Scope
  – Compulsory for products based on biotechnology, genetically modified organisms (GMO) and growth promoters
  – Optional for products containing new active substances or which are innovative
  – Details in Annex to Regulation 726/2004
Centralised Procedure

- Application coordinated by EMEA through the CVMP using expertise of the national authorities
- 210 day procedure with 60 day appeal if necessary
- European Public Assessment Report (EPAR) published on EMEA website