Veterinary regulations and the use of treatments

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Workshop on medicines for bees - What the Agency can do to increase availability

COUNCIL REGULATION (EEC) No 2309/93 of 22 July 1993
laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products

of 31 March 2004
laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

TITLE IV
THE EUROPEAN MEDICINES AGENCY — RESPONSIBILITIES AND ADMINISTRATIVE STRUCTURE

……
(b) the Committee for Medicinal Products for Veterinary Use, which shall be responsible for preparing the opinion of the Agency on any question relating to the evaluation of medicinal products for veterinary use;

http://www.ema.europa.eu/ema
Veterinary regulations

Veterinary regulations

Veterinary regulations

The National Procedure
The product can then only be sold in that particular EU country.

The Mutual Recognition Procedure
Mutual recognition means that EU countries may approve the decision made about a medicinal product by another EU country.

..... CMD(v) (Coordination Group for mutual recognition and Decentralised procedures (veterinary)

The Decentralised Procedure
The decentralised procedure should be used for products that have not yet received authorisation in an EU country.

The Centralised Procedure
An approval for a medicinal product intended for use in all EU countries may be obtained by applying to the EMA (European Medicines Agency) in London.
What a veterinary medicinal product is?

2. *Veterinary medicinal product*:

(a) any substance or combination of substances presented as having properties for treating or preventing disease in animals; or

(b) any substance or combination of substances which may be used in or administered to animals with a view either to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis;
What withdrawal period is?

9. Withdrawal period:

The period necessary between the last administration of the veterinary medicinal product to animals, under normal conditions of use and in accordance with the provisions of this Directive, and the production of foodstuffs from such animals, in order to protect public health by ensuring that such foodstuffs do not contain residues in quantities in excess of the maximum residue limits for active substances laid down pursuant to Regulation (EEC) No 2377/90.
What a veterinary prescription is?

21. **Veterinary prescription:**

Any prescription for a veterinary medicinal product issued by a professional person qualified to do so in accordance with applicable national law.
What a marketing authorisation is?

Article 5

1. No veterinary medicinal product may be placed on the market of a Member State unless a marketing authorisation has been granted by the competent authorities of that Member State in accordance with this Directive (2004/28/EC) or a marketing authorisation has been granted in accordance with Regulation (EC) No 726/2004.
What a MRL is?

**Article 6**

1. A veterinary medicinal product may not be the subject of a **marketing authorisation** for the purpose of administering it to one or more **food-producing species** unless the **pharmacologically active substances** which it contains appear in Annexes I, II or III to Regulation (EEC) No 2377/90.

**COMMISSION REGULATION (EC) No 470/2009**

**COMMISSION REGULATION (EU) No 37/2010**

of 22 December 2009
COMMISSION REGULATION (EU) No 37/2010
of 22 December 2009
on pharmacologically active substances and their
classification regarding maximum residue limits in
foodstuffs of animal origin

Having regard to Regulation (EC) No 470/2009 of the European Parliament and of
the Council of 6 May 2009 laying down Community procedures for the
establishment of residue limits of pharmacologically active substances in
foodstuffs of animal origin, repealing Council Regulation (EEC) No 2377/90 and
and Regulation (EC) No 726/2004 of the European Parliament and of the
Council(1), and in particular Article 27(1) thereof,

In order to protect public health, pharmacologically active substances, on the
basis of the scientific assessment of the safety of those substances, were
classified in four Annexes to Council Regulation (EEC) No 2377/90 of 26 June
1990 laying down a Community procedure for the establishment of maximum
residue limits of veterinary medicinal products in foodstuffs of animal origin.
Veterinary regulations

For reasons of ease of use, all pharmacologically active substances should be listed in one Annex in alphabetical order.

For reasons of clarity, **two separate tables** should be established: one for **allowed substances**, listed in Annexes I, II and III of Regulation (EEC) No 2377/90, and one for **prohibited substances**, listed on Annex IV to that Regulation.

The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Veterinary Medicinal Products,
### Veterinary regulations

#### Table 1

**Allowed substances**

<table>
<thead>
<tr>
<th>Pharmacologically active Substance</th>
<th>Marker residue</th>
<th>Animal Species</th>
<th>MRL</th>
<th>Target Tissues</th>
<th>Other Provisions (according to Article 14(7) of Regulation (EC) No 470/2009)</th>
<th>Therapeutic Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitraz</td>
<td>Sum of amitraz and all metabolites containing the 2,4-DMA moiety, expressed as amitraz</td>
<td>Bees</td>
<td>200 µg/kg</td>
<td>Honey</td>
<td>NO ENTRY</td>
<td>Antiparasitic agents/Anti-parasites against ectoparasites</td>
</tr>
<tr>
<td>Camphor</td>
<td>NOT APPLICABLE</td>
<td>All food producing species</td>
<td>No MRL required</td>
<td>NOT APPLICABLE</td>
<td>External use only</td>
<td>NO ENTRY</td>
</tr>
<tr>
<td>Coumafos</td>
<td>Coumafos</td>
<td>Bees</td>
<td>100 µg/kg</td>
<td>Honey</td>
<td>NO ENTRY</td>
<td>Antiparasitic agents/Anti-parasites against ectoparasites</td>
</tr>
<tr>
<td>Eucalyptol</td>
<td>NOT APPLICABLE</td>
<td>All food producing species</td>
<td>No MRL required</td>
<td>NOT APPLICABLE</td>
<td>NO ENTRY</td>
<td>NO ENTRY</td>
</tr>
<tr>
<td>Flumethrin</td>
<td>NOT APPLICABLE</td>
<td>Bees</td>
<td>No MRL required</td>
<td>NO ENTRY</td>
<td>Antiparasitic agents/Anti-parasites against ectoparasites</td>
<td>NO ENTRY</td>
</tr>
<tr>
<td>Formic acid</td>
<td>NOT APPLICABLE</td>
<td>All food producing species</td>
<td>No MRL required</td>
<td>NOT APPLICABLE</td>
<td>NO ENTRY</td>
<td>NO ENTRY</td>
</tr>
<tr>
<td>Menthol</td>
<td>NOT APPLICABLE</td>
<td>All food producing species</td>
<td>No MRL required</td>
<td>NOT APPLICABLE</td>
<td>NO ENTRY</td>
<td>NO ENTRY</td>
</tr>
<tr>
<td>Oxalic acid</td>
<td>NOT APPLICABLE</td>
<td>Bees</td>
<td>No MRL required</td>
<td>NOT APPLICABLE</td>
<td>NO ENTRY</td>
<td>Anti-infectious agent</td>
</tr>
<tr>
<td>Tau fluvalinate</td>
<td>NOT APPLICABLE</td>
<td>Bees</td>
<td>No MRL required</td>
<td>NO ENTRY</td>
<td>NO ENTRY</td>
<td>NO ENTRY</td>
</tr>
<tr>
<td>Thymol</td>
<td>NOT APPLICABLE</td>
<td>All food producing species</td>
<td>No MRL required</td>
<td>NOT APPLICABLE</td>
<td>NO ENTRY</td>
<td>NO ENTRY</td>
</tr>
</tbody>
</table>
### Veterinary regulations

#### Table 2

**Prohibited substances**

<table>
<thead>
<tr>
<th>Pharmacologically active substance</th>
<th>MRL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aristolochia spp. and preparations thereof</strong></td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td><strong>Chloramphenicol</strong></td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Chloroform</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Colchicine</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Dapsone</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Dimetridazole</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td><strong>Nitrofurans (including furazolidone)</strong></td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Ronidazole</td>
<td>MRL cannot be established</td>
</tr>
</tbody>
</table>
Veterinary regulations

Article 11

1. Member States shall take the necessary measures to ensure that, if there is no authorised veterinary medicinal product in a Member State for a condition affecting a food-producing species, by way of exception, the veterinarian responsible may, under his direct personal responsibility and in particular to avoid causing unacceptable suffering, treat the animals concerned on a particular holding with:

To use medicines off-label within strict limits. This procedure is called "the cascade"
Veterinary regulations

(a) a veterinary medicinal product authorised in the Member State concerned under this Directive or under Regulation (EC) No 726/2004 for use with another animal species, or for another condition in the same species; or

(b) if there is no product as referred to in point (a), either:
   (i) a medicinal product for human use authorised in the Member State concerned in accordance with Directive 2001/83/EC or under Regulation (EC) No 726/2004, or
   (ii) a veterinary medicinal product authorised in another Member State in accordance with this Directive for use in the same species or in another food-producing species for the condition in question or for another condition; or

(c) if there is no product as referred to in subparagraph (b), and within the limits of the law of the Member State concerned, a veterinary medicinal product prepared extemporaneously by a person authorised to do so under national legislation in accordance with the terms of a veterinary prescription.
COUNCIL REGULATION (EC) No 1804/1999
of 19 July 1999
supplementing Regulation (EEC) No 2092/91 on organic production of agricultural products and indications referring thereto on agricultural products and foodstuffs to include livestock production
6. Disease prevention and veterinary treatments

6.3. The use of veterinary medicinal products in beekeeping which complies with this Regulation shall respect the following principles:

(a) they can be used in so far as the corresponding use is authorised in the Member State in accordance with the relevant Community provisions or national provisions in conformity with Community law;
(b) phytotherapeutic and homeopathic products shall be used in preference to allopathic products chemically synthesised, provided that their therapeutic effect is effective for the condition for which the treatment is intended;
(c) if the use of the abovementioned products should prove or is unlikely to be effective to eradicate a disease or infestation which risks destroying colonies, allopathic chemically synthesised medicinal products may be used under the responsibility of a veterinarian, or other persons authorised by the Member State, without prejudice to the principles laid down in paragraphs (a) and (b) above;
(d) the use of allopathic chemically synthesised medicinal products for preventive treatments is prohibited;
(e) without prejudice to the principle in (a) above formic acid, lactic acid, acetic acid and oxalic acid and the following substances: menthol, thymol, eucalyptol or camphor can be used in cases of infestation with Varroa jacobsoni.
COMMISSION DIRECTIVE 2006/130/EC
of 11 December 2006
implementing Directive 2001/82/EC of the European Parliament and of the Council as regards the establishment of criteria for exempting certain veterinary medicinal products for food-producing animals from the requirement of a veterinary prescription
Veterinary medicinal products for food-producing animals may be exempted from the requirement to be dispensed only against veterinary prescription, if all of the following criteria are satisfied:

(a) the administration of veterinary medicinal products is restricted to formulations requiring no particular knowledge or skill in using the products;
(b) the veterinary medicinal product does not present a direct or indirect risk, even if administered incorrectly, to the animal or animals treated, to the person administering the product or to the environment;
(c) the summary of product characteristics of the veterinary medicinal product does not contain any warnings of potential serious side effects deriving from its correct use;
(d) neither the veterinary medicinal product nor any other product containing the same active substance has previously been the subject of frequent serious adverse reaction reporting;
(e) the summary of product characteristics does not refer to contraindications related to other veterinary medicinal products commonly used without prescription;
(f) the veterinary medicinal product is not subject to special storage conditions;
(g) there is no risk for consumer safety as regards residues in food obtained from treated animals even where the veterinary medicinal products are used incorrectly;
(h) there is no risk to human or animal health as regards the development of resistance to antimicrobials or anthelmintic substances even where the veterinary medicinal products containing those substances are used incorrectly.
Article 50

Rapid alert system

1. A rapid alert system for the notification of a direct or indirect risk to human health deriving from food or feed is hereby established as a network. It shall involve the Member States, the Commission and the Authority. The Member States, the Commission and the Authority shall each designate a contact point, which shall be a member of the network. The Commission shall be responsible for managing the network.

http://ec.europa.eu/food/food/rapidalert/index_en.htm
Food control regulations


REGULATION (EC) No 882/2004 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 29 April 2004 on official controls performed to ensure the verification of compliance with feed and food law, animal health and animal welfare rules
Varroa destructor/Tropilaelaps spp./Acarapis woodi

- Several veterinary medicines authorised
- Concern for the future due to observed resistance against synthetic medicines
- Temporary authorisation in some EU country
- Uncertainty of effectiveness of “natural” medicines
Nosema spp.

- No authorised medicines are available
- Other control measures and feed integrators are applied
- Exceptions do exist within EU countries (UK, fumagillin)
- Temporary authorisation in some EU country (e.g., UK, Spain, Slovenia)
Foulbrood

✓ For the American and European Foulbrood no authorised medicines are available

✓ Some antibiotics show efficacy against the bacteria in the larvae, however not against the spores, these can only be destroyed by eradication (e.g. burning)

✓ Exceptions do exist within EU countries (UK, tetracycline for EFB)
SUMMARY OPINION* OF THE COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE ON THE ESTABLISHMENT OF MAXIMUM RESIDUE LIMITS

OXYTETRACYCLINE
(Extension to honey bees)

On 19 April 2006 the Committee for Medicinal Products for Veterinary Use adopted an Opinion** recommending the amendment of the existing Annex I entry for oxytetracycline in Council Regulation (EEC) No 2377/90, to include an MRL for honey, as follows:

<table>
<thead>
<tr>
<th>Pharmacologically active substance(s)</th>
<th>Market residue sum of parent drug and its 4-chlorohydrin</th>
<th>Annual species</th>
<th>MRLs</th>
<th>Target tissue</th>
<th>Other provisions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxytetracycline</td>
<td></td>
<td>All food producing species</td>
<td>100 μg/kg, 300 μg/kg, 600 μg/kg, 100 μg/kg, 200 μg/kg</td>
<td>Muscle, Liver, Kidney, Milk, Eggs</td>
<td>25 μg/kg</td>
</tr>
</tbody>
</table>
Aethina tumida

Coumafos-based medicine authorised in some EU countries
Perspectives

- Authorisation of bee medicines should be made easier
- Better harmonised across Europe
- More attention to "minor uses/minor species" (MUMS)
- Innovative developments should be encouraged
- Draft proposal for the European Union Animal Health Law (Veterinary medicines not included)
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Honeybee Health