Brief Introduction for Approval System of Antimicrobials in Japan

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Antimicrobials for animal use in Japan

1. Antimicrobial Veterinary Drugs
   ⇒ Under the Pharmaceutical and Medical Devices Act

2. Antimicrobial Feed Additives
   ⇒ Under the Law Concerning Safety Assurance and Quality Improvement of Feeds
Pharmaceutical and Medical Devices Act
(The Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics)
(Revision of Pharmaceutical Affairs Law)

• Objectives of this Act is
  - to regulate matters pertaining to drugs, quasi-drugs, cosmetics, medical devices, and regenerative and cellular therapy products.
  - to ensure their quality, efficacy and safety.
  - to regulate each stage of development, manufacturing /importing, marketing, retailing, and usage.

• The same Act regulates medicinal products for human use, and veterinary medicinal products (VMPs)
Veterinary Antimicrobial Control Systems

**<Before Manufacturing/Importing>**

1) **Marketing Approval System**
   - prohibit distribution of unapproved drug

2) **Prescription system**
   - prohibit selling drug without prescription of veterinarian

**<Usage of antimicrobials>**

3) **Restrictions for usage of antimicrobials in the food-producing animals**
   - establish usage standards of antimicrobials

**<At the retailing>**

Veterinarian
   - shall not prescribe without consultation (by The Veterinary Act)
2) Prescription system of Antimicrobials

① Issue the prescription based on the diagnosis/consultation

② Order drug following prescription

③ Sell drug only to livestock farmer with prescription

④ Use antimicrobials in accordance with regulations on usage of drugs
3) Restriction for usage of Antimicrobials in the food-producing animals

-Residual Aspect-

Standard on restriction for usage of veterinary drugs used for food-producing animals,
- Cattle, pigs, poultry, hourse, fish or bees,
- to assure the public health safety in administration of antimicrobials etc.
- to specify drugs that can be used in the target animals, with administration dosages and withdrawal times.
## Example of Standard of Restriction for usage of Veterinary drugs

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Target animal</th>
<th>Dosage</th>
<th>Prohibition period for use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin (in feed)</td>
<td>Cattle</td>
<td>Administration not more than 24mg /kg bw /day</td>
<td>For 5 day before killing for food</td>
</tr>
<tr>
<td></td>
<td>Pig</td>
<td>Administration not more than 24mg /kg bw/day</td>
<td>For 5 day before killing for food</td>
</tr>
<tr>
<td></td>
<td>Chicken</td>
<td>Administration not more than 40mg /kg bw/day</td>
<td>For 2 day before killing for food</td>
</tr>
</tbody>
</table>
A person intending to market a medicinal product, quasi-drug, or cosmetic shall, for each product, obtain marketing approval of the Minister with respect to its marketing.

- The approval shall not be granted when the drug;
  - does not possess effects indicated in the dossier,
  - has harmful action outweighing its effects,
  - does not have appropriate quality.

- Before providing an approval, the Minister shall seek the opinion of the Pharmaceutical Affairs and Food Sanitation Council (PAFSC).
Approval Process for Veterinary Medicinal Products (VMPs)

Applicant → MAFF (Minister of Agriculture, Forestry and Fisheries) → Application

MAFF (Minister of Agriculture, Forestry and Fisheries)

→ Food safety (ADI, Resistance)

FSC (Food Safety Commission)

Residue in food (MRL)

(Minister of Health, Labor and Welfare)

Pharmaceutical Affairs and Food Sanitation Council

Seek opinions

Efficacy Safety Quality

Seek opinions

*ADI, Acceptable Daily Intake;
*MRL, Maximum Residue Level
Data Required for application

1. Origin and background of the discovery
2. Physical and chemical properties (Incl. quality control methods) ⇐ GL27
3. Manufacturing protocol
4. Stability
5. Toxicity (GLP)
6. Target Animal Safety (GLP)
7. Pharmacological action (Efficacy) ⇐ GL27
8. Absorption, distribution, metabolism and excretion
9. Clinical trials (GCP)
10. Residue (GLP)
Marketing approval of VMPs

With these data

↓

* **Efficacy / Safety**
  (poisonous drugs, powerful drugs?, Prescription drug?)

* **Quality** (Shelf-life, Storage condition, Quality control methods)

* **Dosage, Administration route, Indications** (Target animals, Target diseases, dosing interval, restrictions (e.g. not for pregnancy) etc.)

* **Precautions**
  (Withdrawal time, adverse reactions etc.)