Monitoring on quality of veterinary medicinal products (post-marketing surveillance)

Chinese Taipei
Bureau of Animal and Plant Health Inspection and Quarantine,
Council of Agriculture, Executive Yuan
Animal Health Inspection Division
Veterinary Medicinal Products Section
Dr. Wenyuan Yang
Regulatory framework

1. Policy making and legislation
2. VMPs registration
3. License management

1. Post-marketing surveillance
2. Management of VMPs manufacturers, wholesalers, and retailers
3. Inspection of VMPs manufacturing plants

Council of Agriculture; COA
(Competent authority)

ANIMAL HEALTH RESEARCH INSTITUTE; AHRI
(Competent authority)

Bureau of Animal and Plant Health Inspection and Quarantine; BAPHIQ
(Competent authority)

Municipality government
(Local authorities)

County government
(Local authorities)

Animal Drug Inspection Branch; ADIB

Sample testing and analysis

6 LADIAS
(Enforcing authorities)

16 LADIAS
(Enforcing authorities)

Local Animal Disease Inspection Authority (LADIAS)
Regulatory framework

- BAPHIQ-VMPs
  - Animal Health Inspection Division
    - VMPs registration
    - License management
    - Management of manufacturing, wholesales, and retailers
    - Post-marketing surveillance
    - AMU and AMR surveillance
    - Residue monitoring
Regulatory framework

- AHRI
- ADIB
  - Sample testing and analysis
- 22 LADIAs
  - Post-marketing surveillance
  - Management of VMPs manufacturers, wholesalers, and retailers
  - Inspection of VMPs manufacturing plants
Regulatory framework

- Legislation & Guidelines

Veterinary Drugs Control Act: **VDCA**

- Enforcement Rules of Veterinary Drugs Control Act
- Establishment requirements for VMPs Manufacturing Factories
- Regulation for VMPs GMP
- Testing Standards for VMPs
- Regulations for Registration of VMPs
- Regulations Managing VMPs Sales
- Guideline for Use of Veterinary Medicines
- Sale, Utilization, and Management of Prescription Drugs by the Veterinarian (or Veterinarian Aides)

Manufacturing & testing
- Licensing
- Management of VMPs sale
- Management of use

Veterinary Drugs Control Act (VDCA)
Approval process of VMPs registration

Apply

Review of dossier

Pilot production

Sample analysis

Review of technical documents by committee (Proposal of field trial, results of assays and trials)

Authorization

Issuing license (validity: 5 year)
Information of VMPs industry

• Manufacturing plants/ factories:
  • Pharmaceuticals: 34
  • Biologicals: 8

• VMPs Wholesalers and Retailers: 2,099

• VMP licenses:

<table>
<thead>
<tr>
<th>Category</th>
<th>Valid licenses (No.)</th>
<th>Subtotal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Manufacturing</td>
<td>Import</td>
</tr>
<tr>
<td>APIs</td>
<td>9</td>
<td>70</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td>3,292</td>
<td>528</td>
</tr>
<tr>
<td>Biologicals</td>
<td>230</td>
<td>309</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

API: active pharmaceutical ingredient
Post-marketing surveillance of VMPs

- **Annual projects**
- **Random sampling**
  - Pharmaceuticals: 135 products/yr
  - Biologicals: 55 products/yr
- **Qualification based on Testing Standards for VMPs**
  - Pharmaceuticals: API content test
  - Biologicals: quality tests
Scheme of VMPs post-marketing surveillance

Sampling from the market by LACIAs

Send to ADIB for quality tests

Non-compliant

Back to manufacturing factory or importer depository to test same batch VMPs

Non-compliant

Compliant

Closed

Fine manufacturer or importer NT$60,000 to 300,000

Compliant

Fine person handling substandard VMPs NT$30,000 to 150,000
Penalties for substandard VMPs

• VDCA Article 30.3
  • Regarding the entity that deals with (manufactures, imports or repackages; displays or stockpiles to sell or intent to sell substandard drugs, the municipal competent authority is to publicize the (1) name and address of the entity, (2) name and address of the person in charge, (3) names of the drugs and (4) specifics of the offense. Regarding a major or repeat offender, the original license-issuing agency may annul each specific veterinary drug license or dealership license.
Penalties for substandard VMPs

• VDCA Article 36
  • 36.1 The person manufacturing or importing substandard veterinary drugs is subject to a fine of NT$60,000 to NT$300,000.
  • 36.2 The person handling substandard veterinary drugs – repacking, selling, transporting, holding for oneself or others, brokering, assigning to a third party, or displaying/caching with intent to sell – is subject to a fine of NT$30,000 to NT$150,000.
## Results of pharmaceutical post-marketing surveillance

<table>
<thead>
<tr>
<th>Pharmaceuticals</th>
<th>API</th>
<th>Sampling products</th>
<th>Non-compliant products</th>
<th>Compliant rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td></td>
<td>83</td>
<td>4</td>
<td>95.18%</td>
</tr>
<tr>
<td></td>
<td>Penicillin G</td>
<td></td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Doxycycline</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td>285</td>
<td>3</td>
<td>98.95%</td>
</tr>
<tr>
<td></td>
<td>Oxytocin</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Disinfectant</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>368</strong></td>
<td><strong>7</strong></td>
<td><strong>98.10%</strong></td>
</tr>
</tbody>
</table>

Reference period: Jan 1\(^{\text{st}}\) to Dec 31\(^{\text{th}}\), 2019
Composition of antibiotic samples

Reference period: Jan 1st to Dec 31st, 2019

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Others</td>
<td>16</td>
</tr>
<tr>
<td>Lincomycin</td>
<td>13</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>10</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>9</td>
</tr>
<tr>
<td>Ceftiofur</td>
<td>8</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>8</td>
</tr>
<tr>
<td>Tylosin tartrate</td>
<td>4</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>4</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>5</td>
</tr>
<tr>
<td>Oxytetracycline</td>
<td>6</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>4</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>5</td>
</tr>
<tr>
<td>Oxytetracycline</td>
<td>6</td>
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<td>Enrofloxacin</td>
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<td>Penicillin G</td>
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<td>Lincomycin</td>
<td>13</td>
</tr>
<tr>
<td>Others</td>
<td>16</td>
</tr>
</tbody>
</table>

Others

Kanamycin: 3
Trimethoprim: 3
Cephalexin: 2
Erythromycin: 2
Florfenicol: 2
Ampicillin: 1
Colistin: 1
Tiamulin: 1
Tilmicosin: 1
# Non-compliant pharmaceuticals

<table>
<thead>
<tr>
<th>License No.</th>
<th>API</th>
<th>Batch No.</th>
<th>Dosage</th>
<th>Non-compliant cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>00146</td>
<td>Penicillin G</td>
<td>75P716</td>
<td>Suspended injection</td>
<td>API &lt;90% labeled content</td>
</tr>
<tr>
<td>00146</td>
<td>Penicillin G</td>
<td>Y03-0011</td>
<td>Suspended injection</td>
<td>API &lt;95% labeled content</td>
</tr>
<tr>
<td>05564</td>
<td>Penicillin G</td>
<td>8230912</td>
<td>Suspended injection</td>
<td>API &lt;95% labeled content</td>
</tr>
<tr>
<td>07934</td>
<td>Doxycycline</td>
<td>JAC005P</td>
<td>Powder</td>
<td>API &lt;95% labeled content</td>
</tr>
<tr>
<td>06240</td>
<td>Oxytocin</td>
<td>801019</td>
<td>Injection</td>
<td>No API</td>
</tr>
<tr>
<td>02455</td>
<td>Disinfectant</td>
<td>194001</td>
<td>Solution</td>
<td>pH value &lt; specification</td>
</tr>
<tr>
<td>02455</td>
<td>Disinfectant</td>
<td>194002</td>
<td>Solution</td>
<td>pH value &lt; specification</td>
</tr>
</tbody>
</table>

Reference period: Jan 1\(^{st}\) to Dec 31\(^{th}\), 2019
Non-compliant pharmaceuticals

• Products in violation of the regulations were sent to the LADIA for further investigations and/or legal actions.
Results of biological post-marketing surveillance

<table>
<thead>
<tr>
<th>Assays/vaccines</th>
<th>Livestock</th>
<th>Poultry</th>
<th>Compliant rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>13</td>
<td>2</td>
<td>100%</td>
</tr>
<tr>
<td>Antigen content</td>
<td>12</td>
<td>26</td>
<td>100%</td>
</tr>
<tr>
<td>Live cell count (bacteria)</td>
<td>0</td>
<td>2</td>
<td>100%</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>30</td>
<td>100%</td>
</tr>
</tbody>
</table>

Reference period: Jan 1\(^{st}\) to Dec 31\(^{th}\), 2019
Interventions for substandard VMPs

- VDCA Article 29
  - (1) if it is made **domestically** and – upon inspection – can be modified and made usable, the municipal competent authority shall send personnel to supervise the original manufacturer to **modify the drug** before a set deadline;
  - (2) if it is **imported** with approval, the authority shall have it sealed and put in custody while the central competent authority orders the importer to **initiate a goods-for-return process** with the original overseas manufacturer.
Interventions for substandard VMPs

• VDCA Article 43
  • Substandard veterinary drugs uncovered under this Act – if not modified or returned by a deadline set according to Article 29 – may be confiscated for destruction.
Summary

• Regular inspections of VMPs manufacturing plants are conducted to secure the quality control for production.

• Post-marketing surveillance is implemented to ensure VMPs quality in the market and continuously supported by annual projects.

• Manufactured and imported biologicals are requested for batch-by-batch sample testing, guaranteeing 100% compliant rate of biologicals in the market.
Questions