Risk management of AMR in livestock sector in Japan

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Antimicrobial Veterinary Drugs for Livestock

- Legal base: The Pharmaceuticals and Medical Devices Law regulates approval, marketing, distribution and usage of the drugs to improve public health and hygiene.

- Main points:
  - Approved only after deliberation on quality, efficacy and safety by Pharmaceutical Affairs Council
  - Require diagnosis by a veterinarian before prescribing antimicrobials
  - Licensed retailers sell only to farmers with a prescription by a veterinarian
  - Should be used in accordance with regulations on the use based on the Law (e.g.) appropriate dosages, withdrawal periods, target animals, etc.
Antimicrobial Veterinary Drugs for Livestock

**Veterinarian**
Issue the prescription based on the result of diagnosis

**Licensed Retailer**
Order drug following prescription

**Livestock Farmer**
Sell drugs only to livestock farmers with prescriptions by veterinarians

Use in accordance with regulations on usage of drugs
Antimicrobial Feed Additives for Livestock

Legal base: The Law Concerning Safety Assurance and Quality Improvement of Feeds
⇒ promotes healthy development of livestock animals through the efficient use of nutritional ingredients in feed.

Main points:
○ Antimicrobial feed additives are designated after deliberation on effectiveness and safety for livestock animals by the Feed Council
○ A substance should not be designated as a feed additive if it could compromise the effectiveness of antimicrobial medicines to treat infectious diseases in humans
○ Should be used in accordance with the standards set by the Law e.g.) amount added, animal species, growth stage, etc.
○ Current status
  • 24 antimicrobial feed additives designated
  • 23 revoked due to the possibility of resistant bacteria or no sales prospect, etc.
    e.g.) Avoparcin (similar to Vancomycin in chemical structure)
Antimicrobial Feed Additives for Livestock

- Antimicrobial feed additives are used in a limited way under the MAFF regulation on amount in feed, target livestock species and growth stages etc., based on the Feed Safety Law.
- MAFF has revoked the designation of some antimicrobial feed additives due to possible risk of resistant bacteria or no sales prospect, etc. e.g.) Avoparcin (Antibiotics similar to Vancomycin in chemical structure)

Registered Manufacturer of feed additives ➔ Licensed Manufacturer of compounded feed (Feed Mill) ➔ Compounded Feed ➔ Registered Distributer ➔ Livestock Farmer

Use feed additives appropriately based on Feed Safety Law
MAFF requests FSC (Food Safety Commission) for risk assessment on the effect of food on human health regarding antimicrobial-resistant bacteria selected by antimicrobial use in livestock animals.

FSC established the assessment guideline for AMR: http://www.fsc.go.jp/senmon/hisiryou/taiseikin_hyoukasisin_english.pdf

FSC conducts risk assessment based on scientific findings in line with the guideline.
The result of risk assessment is described in qualitative terms, e.g.) “high”, “medium”, “low” or “negligible”

【Veterinary Drugs】
- Estimated as Medium (4 items)
  e.g.) Fluoroquinolones for cattle and swine
- Estimated as Low (3 items)
  e.g.) Pirlimycin for daily cow
- No need of risk assessments because those items are considered not to select resistant bacteria (1 item)
- In process (10 items)

【Feed additives】
- Estimated to be negligible (9 items)
  Monensin, Nosiheptide, Semduramisin, Lasalocid, Salinomycin, Narasin, Flavophospholipol, Avilamycin, Enramycin
- No need of risk assessments because those items are considered not to select resistant bacteria (4 items)
  Nicarbazin, Amprolium, Ethopabate, Morantel
- In process (11 items)
## Risk management for antimicrobials

Risk management measures based on the result of risk assessment by FSC

<table>
<thead>
<tr>
<th>Risk estimation</th>
<th>Examples of risk management</th>
<th>Veterinary drugs</th>
<th>Feed additives</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Revocation of approval</td>
<td>Revocation of designation</td>
<td></td>
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<tr>
<td></td>
<td>Temporary ban of use</td>
<td></td>
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<tr>
<td></td>
<td>Restriction of the usage</td>
<td>Restriction of target animal species</td>
<td></td>
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<tr>
<td>Medium</td>
<td>Shortening of applicable periods</td>
<td>Shortening of applicable periods</td>
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<td></td>
<td>Strict use as a second choice drug</td>
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<td></td>
<td>Enhancing monitoring (e.g. increasing number of samples)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>Continued monitoring</td>
<td>Continued monitoring</td>
<td></td>
</tr>
<tr>
<td>Negligible</td>
<td></td>
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</table>
The Use of Antimicrobials for animals (including food producing animals and companion animals)

Monitoring of the quantities of antimicrobials used in animal husbandry estimated on a basis of sales/production quantities.

- **Veterinary Drugs**: 1059 t (2001) to 796 t (2013)
- **Feed Additives**: 233 t (2001) to 235 t (2013)
- **Polyethers**: 235 t (2013), 58% of feed additives
The use of Antimicrobial Feed Additives by Risk Assessment Result (2013)

<table>
<thead>
<tr>
<th>The result of risk assessment</th>
<th>Quantities (t)</th>
<th>%</th>
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<tbody>
<tr>
<td>Negligible</td>
<td>164.4</td>
<td>69.9</td>
</tr>
<tr>
<td>Considered not to select resistant bacteria</td>
<td>34.6</td>
<td>14.7</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td><strong>199.0</strong></td>
<td><strong>84.6</strong></td>
</tr>
<tr>
<td>In process</td>
<td>36.1</td>
<td>15.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>235.1</strong></td>
<td><strong>100.0</strong></td>
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Monitoring System (JVARM)

Monitoring antimicrobial resistant bacteria since 1999 in the Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM)

- Target bacteria: Indicator (Escherichia coli, Enterococcus spp.), Zoonotic bacteria (Salmonella spp., Campylobacter spp.)

- **MAFF**
  - Design risk managements and provide the data for risk assessments to FSC

- **NVAL (National Veterinary Assay Laboratory)**
- **FAMIC (Food and Agricultural Materials Inspection Center)**
  - Analyze and evaluate data
  - Research into molecular epidemiology, resistance mechanism

- **Prefectural livestock Hygiene Service Center** (170 centers)
  - Collect feces on farms, isolate and identify bacteria, and measure MIC

- **Farms**

- **Samples**

- **Isolated bacteria, Data**

- **JVARM Report**

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JVARM has started collaboration with JANIS (Japan Nosocomial Infectious Surveillance: AMR surveillance for human health sector) in order to establish the integrated surveillance system recommended by WHO based on One Health Approach.

MAFF has added the monitoring of samples collected from slaughterhouses since 2012.
Main Points

ⅰ ) Prevent infection

It is essential to prevent infection by appropriate management of feeding, sanitation and vaccines.

ⅱ ) Definite diagnosis

Identify the cause of infection and determine treatment measures based on definite diagnosis by a veterinarian.

ⅲ ) Effective use of antimicrobials

・Choose effective antimicrobial drug with chemical sensitivity test.

・Fluoroquinolones, 3rd generation cephalosporins etc. should be used only as second choice drug, only if first choice drug has no effect.

ⅳ ) Share information

Share info about AMR bacteria among the relevant parties.
Conclusion

- AMR should be considered comprehensively with regard to human health, animal health, food hygiene, etc..

- It is important to decide the appropriate risk management strategy based on the scientific risk assessments.

- It is essential to evaluate the efficacy of each risk management option continuously after implementation and revise them if needed.
Thank you for your attention!

If you need more detailed information about JVARM, please refer to our website. http://www.maff.go.jp/nval/english/