Risk to public health from using of pleuromutilin in pigs

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Risk to public health from using of pleuromutilin in pigs

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The Danish Authorities provide guidelines to private veterinarians on selection of antimicrobials for use in animals. One of the components in the guidelines is the level of risk posed to public health from antimicrobial resistance formation, when using the drug. The recommendations are based on risk assessments. This poster presents the risk assessment carried out to assess the risk to public health from using pleuromutilin in pigs.

METHODOLOGY:
Qualitative risk assessment following the OIE framework was carried out: RISK = RELEASE*EXPOSURE*CONSEQUENCES. Scale used: Very low, low, medium, high. A guideline developed by European Medical Agency (EMA) was used for inspiration and a risk pathway was developed to ensure a systematic and comprehensive approach to hazard identification and assessment.

HAZARDS:
Pleuromutilin consumption
In animals: Pigs use 99.9 % of all pleuromutilin prescribed in Denmark, which amounts to 10 % of total consumption of all antimicrobials in pigs. Only used for oral (group) short-term treatments. Consumption is low in comparison with other European countries. In humans: Pleuromutilins are not used for humans in Denmark. Cross-resistance to Linezolid may occur from pleuromutilin usage. Linezolid is a last line drug for highly resistant Gram positive infections and is hardly ever used/needed in Denmark.

Hazards of relevance:
- Pleuromutilin or Linezolid-resistant MRSA CC398
- Pleuromutilin or Linezolid-resistant Enterococcus

RESULTS:

<table>
<thead>
<tr>
<th>Hazard ID</th>
<th>Release</th>
<th>Exposure</th>
<th>Consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA CC398:</td>
<td>Low risk (medium uncertainty)</td>
<td>Enterococcus: Low risk (high uncertainty)</td>
<td></td>
</tr>
<tr>
<td>MRSA CC398:</td>
<td>High</td>
<td>General public: Very low (low uncertainty)</td>
<td>Foodborne exposure: Unknown probability (high uncertainty)</td>
</tr>
<tr>
<td>Enterococcus:</td>
<td>Low</td>
<td>Vulnerable groups: high</td>
<td>Enterococcus: Low (high uncertainty)</td>
</tr>
<tr>
<td>Direct exposure</td>
<td>Occupational exposure: High</td>
<td>General public: Very low (low uncertainty)</td>
<td>Vulnerable groups: high</td>
</tr>
</tbody>
</table>

DISCUSSION OF RESULTS
- The risk estimate increased from Very Low to Low since 2010
- The risk estimate applies to today’s situation only and assessment should be repeated if:
  - Pleuromutilin consumption increases substantially in pigs
  - A new pleuromutilin is developed for use in humans
  - Increasing prevalence of mobile, easily transmissible resistance mechanisms
  - Public health need for Linezolid increases

Relevant data gaps
- C. difficile was identified as a possible hazard but excluded because of insufficient knowledge and Linezolid is not used for treatment
- Resistance to pleuromutilin is not monitored in Denmark
- MRSA CC398 resistance to Linezolid is not monitored
- The public health relevance of Enterococcus spp. originating from pigs is uncertain

DISCUSSION OF METHODOLOGY
- Issues with risk assessment of antimicrobial resistance:
  - Risk (antimicrobial consumption) is not limited to one species or one source
  - Current frameworks struggle to handle cross-resistance and co-resistance
  - Relevance to public health of resistance genes in the environment is unknown
  - Risk question is paramount and must be precise, detailed, comprehensive and agreed
  - Antimicrobial consumption levels in the present has long-term effects on resistance
  - Surveillance of mobile resistant elements is usually limited to within specific bacterial species

RECOMMENDATIONS
Prudent use of antimicrobials is paramount – even low risk antimicrobials
Guidelines for usage of antimicrobials should be based on risk assessments for the actual situation, where the guidelines apply.
Development of risk assessment frameworks reflecting the biology of antimicrobial resistance is needed