Implications for the United States drawn from European Union experiences with antimicrobial use, policy, and resistance

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Introduction
Spurred on by heavy antimicrobial use in healthcare systems worldwide, antimicrobial resistance (AMR) is a preeminent global health crisis. Antimicrobials are also economically important as antimicrobial growth-promotants (AGPs) for food animals. Due to connections between antimicrobial use in food animals and increased AMR arising in zoonotic pathogens, many governments worldwide have enacted or proposed legislation intended to curb veterinary antimicrobial use. We reviewed this information to propose possible implications of the recent AGP regulations in the United States.

Possible United States impacts
Animal medicine and health:
• Increased therapeutic use of livestock antimicrobials
• Increased use of antimicrobial alternatives (vaccination programs, antimicrobial peptides, biosecurity measures, etc.)
• Increase in weanling pig mortality
• Decrease in some AMR prevalence

Human Health:
• Negligible effect on continually-increasing AMR prevalence

Economic Impacts:
• Protection against negative trade impacts caused by anti-AGP food import markets
• Increase appeal to niche AGP free markets
• Slightly (~1-3%) increased prices of food animal products5

Recommendations
• Continue advancing science-based judicious antimicrobial usage in both animals and humans
• Define comparisons between human and animal antimicrobial doses
• Expand and standardize monitoring and surveillance infrastructures for antimicrobial usage and resistance prevalence in both humans and animals. Do not exclude companion animals
• Continue to invest in new antimicrobials and alternatives

FDA Guidelines/Regulations4
FDA Guidelines:
• non-binding statements of the FDA’s stance on an issue

Veterinary Feed Directive:
• A category of regulatory control created by the Animal Drug Availability Act in 1996. For certain drugs that are used in animal feeds, it requires veterinary approval before the sale of certain drugs used in animal feed. Approval is not a prescription. “medically important” antimicrobials were moved to this designation on January 1, 2017, and had growth promotion uses removed from their indication label. “Off-label” use is illegal.

2003 - Guidance 152:
• Outlines three process to assess the risk of AMR from animal antimicrobial use.

2012 - Guidance 209:
• Advocates for the requirement of VFD approval for human-use “medically important” antimicrobials

2013 - Guidance 213:
• Describes the process for how drug manufacturers can remove growth promotion claims from labels and how to add prevention and therapeutic claims.

Observe Effects of EU Ban
Table 1. Food animal antimicrobial regulations within the European Union1

<table>
<thead>
<tr>
<th>Year</th>
<th>Regulation</th>
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<tbody>
<tr>
<td>1972</td>
<td>EU bans on tetracycline, penicillin, and streptomycin as</td>
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<tr>
<td>1974</td>
<td>AGPs</td>
</tr>
<tr>
<td>1986</td>
<td>Swedish ban on all AGPs</td>
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<tr>
<td>1995</td>
<td>Danish ban on avoparcin</td>
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<tr>
<td>1996</td>
<td>German ban on avoparcin use in food animals</td>
</tr>
<tr>
<td>1997</td>
<td>EU ban on food animal avoparcin use, Dutch ban on olaguindox and carbadox use in food animals</td>
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<tr>
<td>1998</td>
<td>Danish ban on virginiamycin use in food animals</td>
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<tr>
<td>1999</td>
<td>EU ban on olaguindox, carbadox, bacitracin, tylosin, spiramycin, and virginiamycin</td>
</tr>
<tr>
<td>2006</td>
<td>EU-wide ban on all AGPs</td>
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</tbody>
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Animal medicine and health:
• Apparent overall decreases in antimicrobial use per lb. biomass
• Increase in therapeutic use of food animal antimicrobials
• Noted decreases in some AMR prevalence

Human Health:
• Negligible effect on continually-increasing AMR prevalence, with possible exception of vancomycin

Economic Impacts:
• Lower overall production in some countries (~1%) and increase in domestic meat price (~1%)2
• Increase need to import in some countries

References