

Sustainable use of Antimicrobials in Animal Health – a view from the Industry

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Sustainable use of antimicrobials In Animal Health – a view from the industry

- Presentation is not focused on data.
 - Data is relatively sparse for sustainable use
 - Data is often open to multiple / selective (!) interpretations
 - Issue is complex and multidimensional
- Intention is to invite thought and look at the issue from a different point of view
- At the moment there is not a therapeutic crisis in veterinary medicine for target pathogens: the antimicrobial resistance 'issue' is about resistant genes / bacteria transmissible to humans

Antimicrobials are used in farm animals to treat life threatening and other significant diseases: a range of factors drive use levels and will be important when implementing control measures

Factors increasing Use:

- Animal movements
- Few diseases have really effective vaccines
- Larger production units
- Poor management
- Genetic selection of animals for production
- Drug patent expiry

Factors reducing use:

- Growth promoters banned in EU
- Effective vaccines exist for some pathogens but not diseases
- No health service for vets and medicines - economics of farm animal production

- Companion Animal use more closely mimics human use
- Antimicrobial resistance does not kill people or animals, diseases do: the first consideration should therefore be good medicine and the second, minimising antimicrobial resistance

Responsible prescription by veterinarians and use by animal owners is part of a comprehensive solution

- Improve management practices (housing, nutrition, biosecurity etc)
- Improving compliance and implementation of prescriptions by animal owners is important to optimise efficacy (and thereby reduce need for retreatments)
- The development of improved diagnostics may help target the right choice of antimicrobial in the future (but only if timely results and cost effective)
- Off-label / Extra-label use will remain essential
- Responsible Use Guidelines need to be realistic and flexible for implementation by veterinarians:

Pfizer Animal Health EuAfME Responsible Use Guidelines: Criteria to be considered in decision making

- (1) Efficacy or maximising the effect**
- Pathogens
 - Severity of the disease
 - Suitable classes of antimicrobial
 - Product availability
 - Formulation
- (2) Safety or minimising the risk:**
- Target animal safety
 - Consumer safety (food producing animals)
 - Antimicrobial safety (is this where generic-based formularies can provide useful advice?)
 - User safety
 - Environmental safety
- (3) Affordability:**
- This factor will be taken into account but it must always be less important
 - Farming is a business
 - Companion Animal owners
- (4) Additional steps which should be taken in all cases:**
- All use of antimicrobials should be accompanied by advice, further diagnostic steps (as necessary) and implementation of other non-antimicrobial disease control measures.

A number of solutions will require continued investments in research but may play a role in the longer term

- Addressing the current resistance reservoirs in animal and human health is going to be challenging
 - Novel technologies will be needed especially if (some) resistant strains appear fitter than wild strains [Silva et al 2011 PLoS Genetics]
- Improvements in animal genetics (reduce susceptibility to disease / pathogen)
 - However, economic pressures have focused genetic improvement on production parameters: little progress as yet on reduced susceptibility to disease
- Reduce impact of pathogens (more and better vaccines)
 - ‘Low hanging fruit’ have been plucked (ie high need x high volume x high feasibility)
 - Future vaccine developments are going to be harder and may need novel sources of funding

Minimising spread (between animals, from animals to man) is critical but may require challenging changes in behaviour

- The use of antimicrobials 'causes' antimicrobial resistance... (in animals or man)
- BUT how relatively important are antimicrobials in the spread of resistant organisms or resistance genes? ie what is the main source of
 - MRSA in dogs / cats
 - MRSA CC398 in pigs? [Boens 2011 Preventative Veterinary Medicine]
 - ESBLs in Poultry? [EFSA 2011]
- Freedom to purchase, to sell, to trade are all much harder targets than antimicrobial use in animals. But is sufficient focus being placed on these issues?
- Similarly for humans, the freedoms to import food, to vacation abroad are all likely to be considered basic 'rights' but are important in the arrival and spread of resistant bacteria
- Is sufficient emphasis being currently placed on preventing spread of resistant organisms or resistance genes within the livestock sector?

Outright Bans Of Specific Classes Or Blanket Reduction Targets Of Antimicrobials Are Attractive Targets, But Will They Solve The Problem?

- 'Easy' / 'political' broad brush approaches to a complex situation, however, not necessarily appropriate for all resistance reservoirs
 - Problems of co-resistance and cross resistance confound the situation eg other beta-lactams and 3rd / 4th generation cephalosporins
 - Linked resistance genes lead to co-selection
- Reductions in overall volume of antimicrobial are likely to be only be achieved with significant reductions in older antimicrobials eg tetracyclines
 - But tetracyclines are not currently a class of particular focus
 - May lead to switching to other, more potent, classes
- Unless there is significant end-user 'buy in' there is the risk that stringent measures will lead to cheating or illegal use

Continued Availability Of Effective Antimicrobial Treatments And New Antimicrobial Classes Will Remain Essential For Veterinary Medicine

- Risk management (risk vs reward) starts very early in veterinary and human discovery programs
 - Companies prioritise competing areas of discovery investment
 - As regulatory hurdles get higher and market values erode, investment is less likely
- The end is a stringent regulatory review by EMA/CVMP or national agencies
 - Agencies review current science and all generated data (and can ask for more): decide whether to approve or not, and final label indications, warnings etc
- With increasing restrictions and without continued investment in new classes, how likely is it that in the future animal health mirror the human medicine therapeutic crisis?
- Generics are driven by Intellectual Property and EU regulatory legislation (but note this is principally human legislation supporting reducing healthcare costs)
 - Evidence in humans that generic introductions, by reducing cost and increasing use, can increase resistance rates [Jensen 2010 J Antimicrobial Chemotherapy]
 - Is the current approach to generics appropriate for veterinary antimicrobials or would extended exclusivity periods be more appropriate?

Sustainable use of antimicrobials in Animal Health is a complex issue which will require appropriate and proportional responses

- Reducing unnecessary use of antimicrobials, with support from veterinarians and farmers, is achievable
- Reducing spread between animals should have an increased focus and improvements are achievable
- Concern about whether blanket bans or broad reduction targets are going to have any meaningful impact and may have unintended consequences
- Encouraging innovation in new classes of antimicrobials for veterinary (or human) medicine is achievable, but with increased regulation and restriction on use, extended exclusivity periods will be necessary

Thank you for your attention

