Do innovative solutions require novel regulatory paradigms?

Dr Trish Logie MRCVS
Advisor Global Regulatory Innovation
Elanco Animal Health
15th December 2016
Veterinary Medicinal Products Today

- Livestock production and animal health face dynamic challenges
- Responsible use plays a significant role in AM stewardship
- Existing methods of addressing these challenges are sometimes insufficient
  - Antimicrobial resistance
  - Anthelmintic resistance
  - Changing geographical disease patterns
  - Increased focus on animal welfare in the face of increased production needs
- Regulation of veterinary medicines has evolved over years
  - Antimicrobial risk assessment
  - Environmental risk assessment
  - More robust user and consumer safety assessment
  - New clinical trial methodologies
  - Quality by Design in manufacturing
  - Pharmacovigilance
- The “One Health” philosophy is essential to human and animal wellbeing and continued access to effective antimicrobials
One Health to Sustainable Animal Care

- **Healthy Animals**: Healthy animals produce more protein with less resources.
- **Healthy People**: Human health starts with good nutrition. Limits hidden hunger, obesity, diabetes.
- **Healthy Planet**: Decreasing resource use helps sustain growing population.

- Environmentally sound
- Economically viable
- Socially responsible

Sustainable livestock farming
The Future

• Stewardship of existing AM molecules, while essential, is not enough
• Need to find new and creative solutions
  • New antimicrobials
  • New alternatives to antimicrobials
  • New husbandry / breeding techniques
  • Combination practices / therapies

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.
Total Number of New Antibacterial Agents

- 1983-1987
- 1988-1992
- 1993-1997
- 1998-2002
- 2003-2007
- 2008-2012

ANTIBIOTIC DEVELOPMENT IS DWINDLING


©2015, Elanco Animal Health, a division of Eli Lilly and Company
Opportunities

There are a wide range of novel approaches becoming available to try to manage the risks associated with emerging antimicrobial resistance:

- Immune-modulators (e.g. Imrestor)
- Lytic enzymes
- Vaccines
- Antibodies
- Phage therapies
- Pre / probiotics
- Heavy metals
- Others

How will we treat novel classes of antimicrobials vs alternatives to antimicrobials?
Questions

• Are the current practices surrounding review and regulation of VMPs still appropriate for all of these new molecules?

• Are existing regulatory practices at risk of preventing valuable new alternatives to antimicrobials from reaching the market?

• Do we have a unique opportunity in the revision of Directive 2001/82/EC to take a broader view and enable creative solutions to today’s problems?

• Does 21CFR part 514.4 permit creative solutions?
Quality

- Quality – a reliable manufacturing process underpins any consistent product and remains the keystone for an approvable product

- Quality by Design is emerging as an efficient way to manage manufacturing development of the lifecycle of the product

- Recently used successfully for complete QbD Part 2 / CMC technical sections in the EU and US for Imrestor

- EMA / CVM support was invaluable as was the expertise of reviewers specialised in this area

- Already proving valuable in the lifecycle of Imrestor
Safety

- Are there possibilities for waivers / reduced data? For example ICH Guideline (S6)
  - Mutagenicity
  - Carcinogenicity
- Immunogenicity – standardisation?
- Allergenicity – when is it needed? The role of in silico data?
- Other studies – case by case still appropriate, but can we give specific guidance for novel technologies?
- Residues – for molecules where there is no oral bioavailability can we make the MRL / HFS technical section process more simple & efficient?
- Environmental safety –
  - many unknowns around phages, pro/pre biotics,
  - heavy metals have significant risks
- Resistance testing and surveillance: what does this look like for phages, lytic enzymes, heavy metals etc?
Efficacy

• Degree of efficacy
  – What level of efficacy is appropriate?
  – Do we need a “cure” or is a reduction in bacterial load / risk enough?
  – Can the efficacy be lower than traditional antimicrobials?
  – How can we gauge clinical significance of effect?
  – How can we measure the effectiveness of preventative products better?
  – For products in food animal species, should production losses be taken into account within degree of efficacy?
  – How do we assess contribution of such products to a health management strategy?
  – How can we write indications and labels for products where different combinations of health and husbandry techniques can act synergistically to reduce use of traditional antimicrobials?
Efficacy

- Field trial challenges
  - Smaller effects require larger number of animals to conclusively demonstrate efficacy
  - Larger numbers = larger investment
  - Larger numbers can = longer duration of study = increased variables

- Provisional approvals could allow field based data to be gathered to later convert to a full approval?

- Incentivise review process for novel alternatives to antimicrobials? A MUMS type pre-determination of eligibility could lead to:
  - Reduced data
  - Reduced review time
  - Reduced fees
  - Reduced reporting
  - Increased data protection
Communication

• Global development plans
• Regulatory communication – ITFs and early information meetings
• Scientific Advice / pre-submission meetings
• Regulatory communication between Agencies: EMA / CVM / VDD / APVMA etc.
• Joint advice meetings (harmonised advice!)
• Work sharing on review of novel therapies?
  Legally challenging……but could help to spread knowledge globally
Legislation

- New classes of antimicrobials can be reserved for human only use
- New classes / molecules only suitable for animal use – can any reassurance be given?
- Surveillance and monitoring
  - Could reduction in the use of traditional AMs have a place on the label for alternatives?
  - Could ‘animal only’ AMs have different reporting requirements than shared class?
Conclusion

- Alternatives to existing AMs are essential
- Maintaining an open and flexible regulatory environment is also essential
- Existing pipeline opportunities could be brought forward faster / more easily with incentives around:
  - Increased clarity on data needs
  - Data packages (MUMS style)
  - Review time
  - Reduced fees
  - Reporting needs
  - Increased global information sharing
  - Increased data protection
“The thoughtless person playing with penicillin is morally responsible for the death of the man who succumbs to infection with the penicillin resistant organism”

Sir Alexander Fleming
Questions?