Case study – nanotechnology

Phil Reeves | 5 November 2014
APVMA Advisory Board Futures Forum 2014
Outline of case study

Part 1: Regulating new technologies
- new technologies in veterinary medicine
- the importance of effectively regulating advanced technologies

Part 2: Individualized and targeted drug therapy
- what is the challenge?
- does nanotechnology offer a solution?
Technology-driven advances

Future drug developments in veterinary medicine

- continued advances in computer technology
- microfluidics
- nanotechnology
- high-throughput screening
- increased control and targeting of drug delivery
- increased knowledge of pharmacogenomics
The importance of effectively regulating advanced technologies

Is the regulatory framework developed for mid- and late-20th century drugs and technology appropriate for effectively regulating 21st century products?

The problem of regulating sophisticated materials

Andrew Maynard, Diana Bowman and Graeme Hodge

As complex new materials such as nanoparticles increasingly make their way into commercial products, regulatory frameworks need to overcome a number of key challenges to remain fit for purpose.
The most important single advance in veterinary pharmacology/therapeutics over the next 35 years

‘Improving the method by which regulatory agencies approve veterinary medications for animals, so that sponsors will be encouraged to bring more compounds forward to meet the needs of animals and the veterinarians who treat them’

Professor Mark Papich

‘Pharmacodynamics ........ provided that (a) companies consider research and innovation as their pivotal role; and (b) regulatory authorities do not apply the brake of precautionary principle but rather seek to understand and facilitate innovations.’

Professor Pierre Louis Toutain

The most important single advance in veterinary pharmacology/therapeutics over the next 35 years

‘Advances in nanotechnologies with novel and beneficial applications in veterinary medicine’

Phil Reeves

‘Individualized and targeted drug therapy across all species, using miniature sensing and delivery devices, some with embedded PK-PD algorithms or using nanodelivery platforms that provide local feedback on delivery mechanisms’

Professor Jim Riviere

Part 2: Individualized and targeted drug therapy

• what is the challenge?
• does nanotechnology offer a solution?
Meeting public health expectations in the 21\textsuperscript{st} century

There is a need to develop new antimicrobial drugs having minimal impact on gut flora and on environmental bacterial ecosystems.

This need might be met either by developing:

- new antimicrobial drugs; or
- new formulations of existing drugs to guarantee an appropriate pharmacokinetic (PK) profile and/or pharmacodynamic (PD) selectivity for target pathogens.
Appropriate pharmacokinetic profile

Salicylate half-life values:

<table>
<thead>
<tr>
<th>Animal</th>
<th>Half-life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goat</td>
<td>0.8 hours</td>
</tr>
<tr>
<td>Horse</td>
<td>1 hour</td>
</tr>
<tr>
<td>Pig</td>
<td>5.9 hours</td>
</tr>
<tr>
<td>Dog</td>
<td>8.6 hours</td>
</tr>
<tr>
<td>Cat</td>
<td>37.6 hours</td>
</tr>
</tbody>
</table>
Appropriate pharmacodynamic selectivity for target pathogens

Time-dependent effects

- time that plasma concentration > MIC for most of the dosing interval

Concentration-dependent effects

- do not need to maintain plasma concentration > MIC

Key: MIC = minimum inhibitory concentration
Pre-2014 – two of the nanomaterials used in drug delivery

Liposome

Dendrimer

Images copyright Russell Kightley
2014 – Report of a novel nanomaterial

Panel A: Amphiphilic Janos dendrimer depicted in 2-D

Panel B: Amphiphilic Janos dendrimer depicted in 3-D

Key: Hydrophilic and hydrophobic components are shown in blue and green, respectively.
Microfluidic device

• coupled to microcomputers containing pharmacokinetic (PK) algorithms to optimise dosage regimens, thereby facilitating individualization of therapeutics
Lotus effect
Release of drug by photo-triggering
Concluding thoughts

• regulations developed for mid- and late-20th century drugs and technology need updating and harmonising to effectively regulate 21st century products

• regulatory boundaries applicable to various combination products need to be clarified e.g. drug and delivery devices, implanted physiological feedback systems and nanoparticle drug carriers

• scientists with new perspectives and expertise need to be appointed while others with experience to integrate new technologies into the regulatory assessment systems should be retained
Thank you for your attention!