

Animal Health Companies Experience

Medicines for bees

What the EMEA can do to increase availability

14th December 2009, London



Which? February 2006...



Concerns about **HONEY**

Honey should be a natural, pure and minimally processed food – but recent checks have detected traces of antibiotics

Last October the Food Standards Agency (FSA) notified trading standards officers (TSOs) around the country of a product recall for Natural Choice Pure Clear Honey. Tests carried out by TSOs in Hull detected residues of the antibiotics chloramphenicol and sulphonamide after a consumer complained to them that it tasted odd.

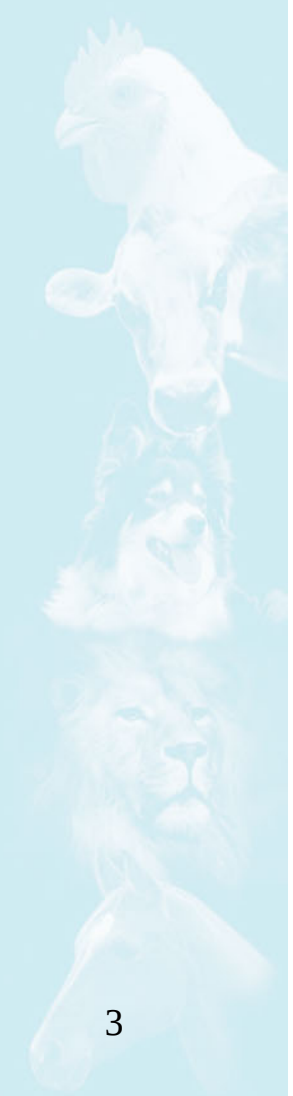
Antibiotics are used to treat bees for various diseases, such as the devastating European foul brood disease, which weakens and eventually wipes out entire bee colonies. In the UK, antibiotics can be used only with a vet's prescription, and any honey from a treated beehive can't be used for human food. However, outside Europe, controls can vary. The Natural Choice Pure Clear Honey wasn't

shouldn't be there. The FSA told us that it has been aware of tylosin residues in honey since early 2005, and tests carried out in several EU countries over the past two years have also found tylosin at low levels. Brian Butcher, who chairs the Honey Association, told us: 'Residues in honey are a worldwide problem, and the industry is working very hard to eliminate them. In non-EU countries, it can be easier to obtain veterinary medicines, and beekeepers in some countries tend not to be the wealthiest of people. So the temptations to use antibiotics to protect their livelihood are enormous.'

A spokesman from the Veterinary Medicines Directorate (VMD), a government agency that oversees the use of veterinary medicines, told

Is there a willingness from our side?

- Beekeepers are confronted with many challenges
- Diseases and the lack of therapeutic options is a major concern
- R&D based Animal Health Companies do recognize that concern,
 - And share the concern from the society as a whole
 - And see the value for the beekeepers
- but are confronted with several issues
 - Market is relatively small
 - Need for MRLs without any data protection
 - Most of the suitable medicines are old and therefore equally not eligible for data protection



Three case-stories to illustrate...

- Oxalic acid (Ceva Santé Animale)
Got the registration, but no sales...
- Fumagillin (Ceva Santé Animale)
MRL is a major obstacle
- Tylosin tartrate (Elanco Animal Health)
Lack of data protection kills the ROI

Oxalic acid

- MUMS symposium Madrid 26th June 2003
- December 2003 Oxalic acid MRL
 - Develop by a consortium ?
- 2004 Meet with Spanish bees Keepers
 - Definition of the product
- 2005 meeting with AEMV
 - Definition of the MUMS dossier
 - Launch of the development
- June 2007 MA in Spain – ECOXAL

Oxalic acid

- 2007 Launch of the product
 - Low sales
- 2008 – 2009
 - Demand from UK, BE, FR, EL for an MRP
 - Proposition of cascade system first
 - Not used
- August 2009 – VMD give an import permit
 - No sales
- Oxalic acid use is unauthorised raw material

Oxalic acid - conclusion

- Good collaboration industry - NCA
- No Return On Investment for industry
 - Difficulties to convince the board to continue
- No possibility to invest and to comply with commitment
 - Loss of the MA ?
- At the end - **a failure story**

Fumagillin uses

Fumagillin and honeybees

- Fumagillin DCH (Fumidil B) on the UE market since 1970
- Prevention and treatment of nosema disease, caused by a microsporidian parasite of the gut (*Nosema Apis*)

Fumagillin and trout

- Fumaqua developed in 1995 Never on the market (lack of MRL)
- Preventive treatment of Proliferative Kidney Disease (PKD) after detection of the parasite

Fumagillin MRL

- **1994 – 1999** Development of an MRL dossier
 - “Old substances procedure” Reg 2377/70
- **1999** - The CVMP concluded that an MRL for fumagillin could not be recommended.
- Inclusion of Fumagillin in the list of essential substances for veterinary medicine (EMEA/CVMP/411-00)

Fumagillin MRL

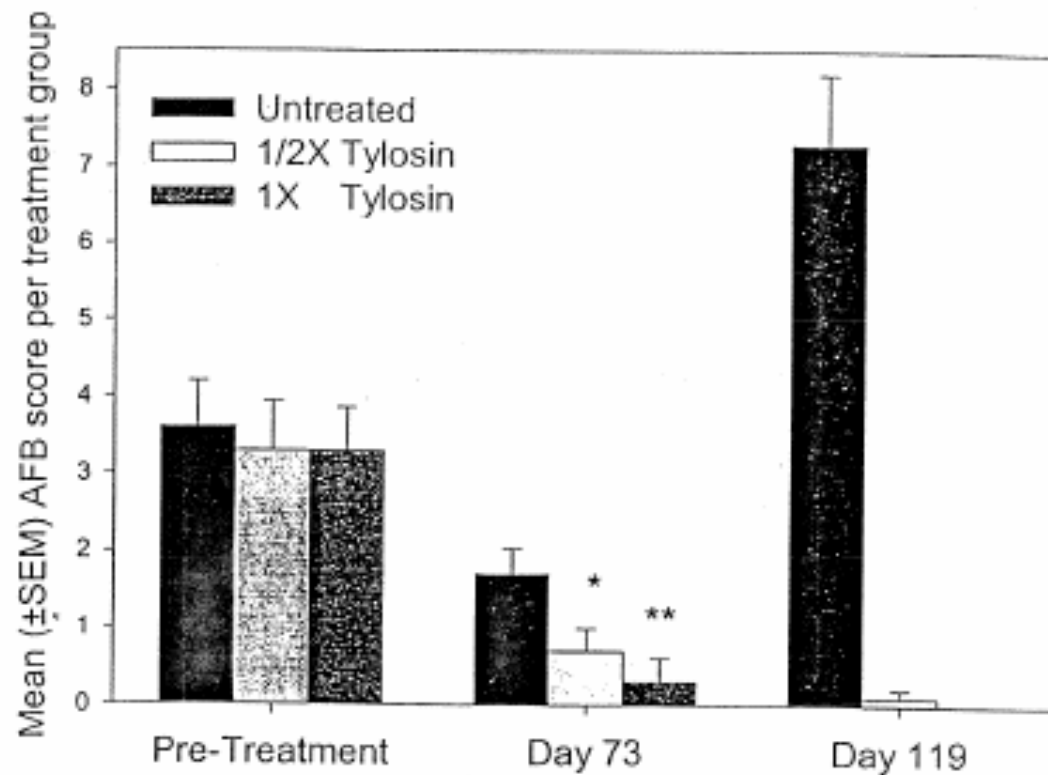
- **2004 New regulatory context**
 - Note for guidance for the establishment of MRL for minor animal species
 - Position paper regarding availability of VMP for MUMS (EMA/477/03)
 - Free scientific advice to support research and development of VMP for MUMS (May 2004)
- **2005 Free Scientific Advice**
 - Mutagenesis studies
 - Repeated toxicity study
 - Reproductive toxicity studies

Tylan soluble

- Has been used in bee-keeping globally
- Has received approval in the USA from FDA upon dossier in which USDA and Industry (Elanco Animal Health) have worked together
- Registered claim for the treatment of American foulbrood (*Paenobacillus larvae*) in honeybees
- 200 mg per hive weekly for 3 weeks, mixed with sugar and dusted into hive
- Efficacy study : all colonies disease-free
- Safety study in bees : no adverse events
- Residue depletion study: withdrawal time suggested of four weeks before the honey flow

Tylan soluble

Figure 1. Mean disease ratings of fowlbrood-infected colonies treated with tylosin.¹



¹Ratings and treatments as described in Table 1. Asterisks indicate significant differences when compared to "untreated" (sugar controls): * P = 0.05; ** P = 0.01 (Wilcoxon Rank Sums test).

EU situation ?

- MRL?
 - Tylosin obtained all food producing species
 - 80% of microbiological ADI filled
 - Honey excluded so far, but room available
- Data on efficacy and safety answered by US dossier
- Request from beekeepers association (UK)
- Company in principle positive towards claim, ...

Company in principle positive towards claim in EU, ...

- But concerns over what questions might still come up for the MRL dossier (experiences with other minor species dossiers eg on rabbits)
- But concerns over further data requirements, even for the minor species and the minor use (also previous experience)
- But Directive 2004/28 created Global Marketing Authorisation, preventing data protection for the dossier: therefore any work done by the Company would immediately be available for the generic competition
- Therefore the biggest but, the lack of data protection prevents any return on investment

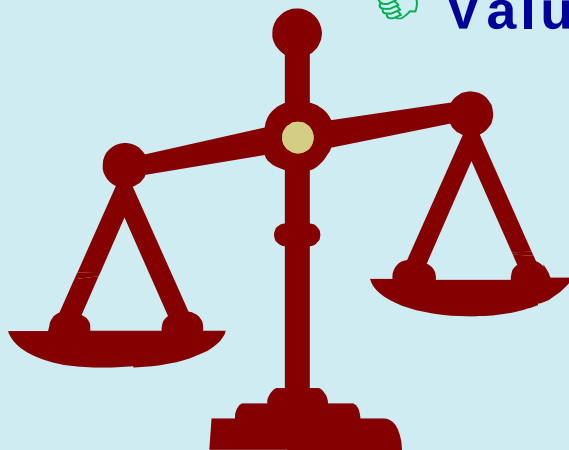
So overall, the balance, right now



Interest for the society



Value for the bees keepers



Lack of MRL data protection

(and cost of data production)



Lack of dossier data protection

(and cost of data production)



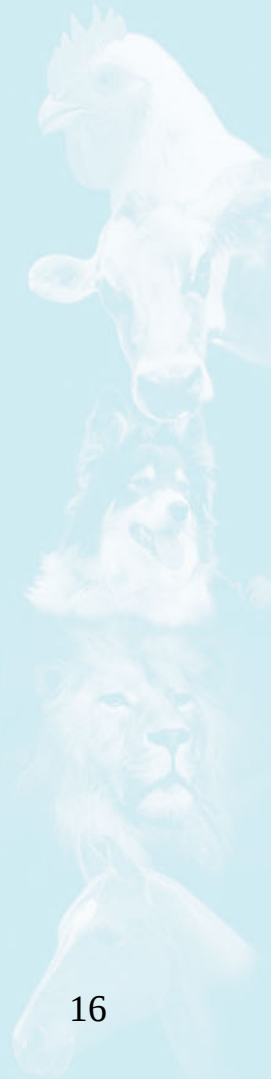
Market size



no R O I

Still we have hope,...

- If needs of honeybees and their keepers would be seen as critical for agriculture and society
- If benefit-risk analysis would allow to advance on appropriate data
- If data protection could be provided...



Thank you for your attention