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Veterinary Medicines in Europe: The Big News for 2013?....Wait until 2014!

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At the time of writing this review, the European Commission's proposal (COM Proposal) for the new legislation governing Veterinary Medicinal Products (VMPs) in Europe is approximately one year later than expected. **Will Drury** of **Cyton Biosciences** and **Hope Baird** from sister **Knoell business Shotwell & Carr** outline what the proposals may contain.

The year 2013 for the VMP industry has been defined by the wait for the COM Proposal and the many discussions which have attempted to identify what the new legislation might look like. The Commission has given away very little except that the hallowed 1-1-1 principle (1 dossier, 1 scientific assessment, 1 decision for marketing authorisation) will not be a feature of the new legislation.

With the COM proposal (hopefully) arriving in early 2014, the best estimates of when the new legislation could come into force is now somewhere around Q2, 2017. With that timeline in mind, all parties have seen the need to make improvements to the current system, as far as Directive 2001/82 will allow, through the "soft" legislation (eg guidelines).

Therefore, 2013 has also seen the publication of many new guidelines, recommendations, best practice guides and so forth; these indicate the big issues of the moment and those issues which we would anticipate will feature in the COM Proposal.

Antimicrobial resistance

Tighter regulation of the use of antimicrobials within the veterinary sector is likely to be built into the COM Proposal. If ever there was a need for the 1-1-1 principle, the authorisation of the antimicrobial VMPs highlights this need in technicolor. You need only look at the CVMP monthly meeting minutes or the CMDv reports to see the enormous disharmony in the approved conditions of use of antimicrobials across the various EU member states.

The referrals being tackled by the CVMP and CMDv make use of the combined data, experience and expertise of the member states to allow the most scientifically justified decisions to be made. However, these referrals are extremely time-consuming and as soon as one is concluded new ones are continually being triggered.

It is, therefore, not hard to foresee the harmonization of marketing authorizations (MA) for antibiotics being addressed in the COM Proposal. Could the scope of the Centralised Procedure be extended to include all new antibiotic products as the mandatory route of authorization? Will there be a formalised timeline and schedule for the harmonization of already-approved active substances? Despite the very limited scientific substantiation, it seems likely that political pressure will push the regulation of antimicrobials to the top of the agenda for the COM proposal.

Meanwhile, the issue of antibiotic resistance is also influencing animal health policy in the US. The FDA published in late 2013 the Guidance for Industry (GFI) 209 and 213, which will begin to phase out growth promotion uses of antibiotic compounds that are important for human use. The intention is that these antibiotics will gradually be restricted to use only for therapeutic purposes in animals. The US response, focusing only on antimicrobials important for human health, falls short of the EU's 2006 total ban on antimicrobials for growth promotion. At that time, EU producers felt they were placed at a competitive disadvantage in the global meat markets while many experts thought the ban of substances such as monensin, salinomycin, avilamycin and flavophospholipol had little impact on resistance levels to antimicrobials important for human medicine – some even claiming the total ban on growth promoters may actually have resulted in increased therapeutic use. It remains to be seen if political pressure in the US is now satisfied, or if it too will seek a complete ban.

Innovation

Whilst the details of the COM Proposal remain almost entirely unknown outside the senior members of the regulators, it has been acknowledged by all parties that innovation in VMPs has been stifled by the current legislation. In response to this, the CVMP has endorsed an update to the mandate of the Innovation Task Force (ITF) so that VMPs (and borderline products) may also benefit from this free advice.

In the ongoing battle between innovators and generics, it is anticipated that the COM Proposal will introduce measures to improve data protection for innovators, which is likely to make life more difficult for the generic companies. Furthermore, it has also been indicated that there should not be any expectation that the environmental data requirements for generics will be reduced. However, the move towards favouring innovator companies may not be helped by the European Medicines Agency (EMA)'s move towards greater transparency. It was recently announced that the EMA will, in 2014, continue to publish and provide access to (human) clinical trials data. This move is part of the overall policy of access to documents which allows public access to all business-related documents, including redacted parts of MA application dossiers.

The facility for access to documents has been extensively used by the human medicines industry but to a much lesser extent in the veterinary sector; nearly 700,000 pages relating to human medicines were released in 2012 compared to approximately 5,000 pages relating to VMPs.

The Mutual Recognition and Decentralised Procedure

With referrals introducing unwanted uncertainty for industry and occupying such a significant proportion of time for the CVMP and CMDv, it is good news that there will soon be a new Mutual Recognition and Decentralised Procedure Improvement Working Group (a subgroup of the CMDv). This working group has been formed in recognition of the time it will take before the new legislation will come into force. Whilst the mandate of the Working Group has yet to be published (but is expected imminently) it can be hoped that 2014 will begin to see improvements in the Mutual Recognition Procedure and Decentralised Procedure and perhaps an increase in the number of referrals which are resolved at CMDv, before arbitration is necessary by the CVMP.

Other challenges

There are many other areas of VMP legislation which are likely to be changed under the COM Proposal. Some areas, such as pharmacovigilance, where all parties recognise the disproportionate administrative burden will hopefully be improved. Other areas, such as the various exemptions applicable to medicines for horses, could become less favourable, following the scandal of mislabelled horsemeat and the discovery of drug residues in the meat which are prohibited from entry into the food chain. Debate continues between industry and the regulators on the subject of product labelling and packaging, one of the most significant areas of administrative burden for industry. Addressing the need for less complex multi-lingual packaging, there are ongoing discussions on the acceptability of pictograms and the development of a catalogue of standard pictograms. Further developments are expected for this area in 2014 and in the COM Proposal. Whilst there has been no confirmation from the European Commission about changes to the regulation of fixed combination VMPs, it has been suggested that these products will be more tightly controlled. This would not be unexpected in the context of concerns about development of antimicrobial resistance, but could greater justification be required for the approval of VMPs in other therapeutic groups which are frequently put into combination products?

Given the recent surge in marketing authorizations for new combinations of ecto and endoparasiticides (Ceva's Vectra 3D; Merial's Broadline and Certifect; Elanco's Trifexis) any changes in the requirements for approval of fixed combination products would have important implications for the development of new products.

Conclusions

The last year has seen many developments in the regulation of VMPs in the EU, but the most eagerly anticipated announcement has been a no-show. In 2014 it would be a great surprise if we didn't finally see the COM Proposal, but beyond that, nothing in the COM Proposal should be expected.

To a greater or lesser degree, all of the areas of interest from 2013 are likely to be affected by the COM Proposal: antibiotic resistance; function of the MRP / DCP and activities of the CMDv; handling of referrals; data protection and generics; environmental impact assessment; product labelling; pharmacovigilance. Cyton will be watching these developments closely and keeping our clients informed of their implications for industry.

You can follow all of the latest news in the regulations of Veterinary Medicines in Europe and the rest of the world at the Cyton website: www.cyton.com/news.