HMA statement on the review of veterinary medicinal product legislation

The Heads of Medicines Agencies (HMA) welcome the new proposal for a regulation on veterinary medicinal products by the European Commission as an attempt to tackle the specificities of the veterinary pharmaceutical sector by addressing long-standing problems of medicines availability, administrative burden, competitiveness, functioning of the internal market as well as the growing public health risk of antimicrobial resistance (AMR). However, the HMA believe that the proposal would result in some unintended and unacceptable consequences, and create new risks, while certain significant opportunities have been missed in the framing of the new legislation. The HMA would like to highlight its key concerns, in the hope that amendments can be made to the proposal during the process of adoption, for the benefit of public health, animal health and the environment, while at the same time aiming for the aforementioned goals.

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Chairman of the HMA Management Group

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Background

The HMA represent a network of national competent authorities (NCAs) responsible for the authorisation and monitoring of human and veterinary medicinal products in the European Economic Area. The HMA have been in existence for many years and have contributed to discussions on veterinary medicines availability in Europe over the last decade. In 2008, the HMA initiated a reflection process regarding the review of the veterinary medicinal products framework through its "HMA Task Force on improvement of veterinary legislation".

As part of the reflection, the HMA held consultations with stakeholders, and, in 2010, partook in the formal European Commission (EC) consultation regarding the ‘better regulation’ of veterinary pharmaceuticals. Arising from this exercise, the HMA sent three letters to the Commission between 2011 and 2014 in order to help the Commission develop its proposal on improvement of veterinary legislation.

On 10 September 2014, the European Commission adopted a package of three legislative proposals, including one on veterinary medicinal products, one on medicated feeds and an amendment to Regulation (EC) No 726/2004. The HMA welcome the proposals as an attempt to address long-standing challenges set out by the Commission. The HMA regret however that no opportunity has been provided to them for commenting on the draft legislation before the final adoption by the Commission. During the recent plenary meetings of the HMA in Rome and Riga, the HMA considered how best to input their views and decided to send this statement expressing a majority view to the relevant Council Working Group and the European Parliament, so that these views can be considered during the negotiations. This analysis is made having regard to the previous HMA letters to the European Commission, expressing the majority view of the HMA.

The HMA have restricted their input to key issues in this statement.

1. Changes to improve the regulatory systems for veterinary medicines

The HMA fully support, in principle, the need for a simplified, efficient and proportionate authorisation process. Appreciating that the scope of the centralised procedure is to be expanded, the HMA have particular concerns in relation to the proposed fundamental changes in the authorisation procedures for mutual recognition (MRP) and the decentralised procedure (DCP) as follows:

a. Unlike the current situation where all Concerned Member States (CMSs) receive the application dossier for a new veterinary medicine being presented for a national market authorisation [together with the assessment report of the Reference Member State (RMS)], in the proposal only the RMS would receive the dossier. As each NCA must be able to stand over the marketing authorisations on its national market, it is the right of the NCA to be able to consult the dossier in order to verify technical aspects (e.g. that the withdrawal period is adequate and that the residue studies underpinning it have been conducted

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2 HMA letter to EC regarding the review of veterinary medicinal product legislation, July 18th 2011; HMA-V ideas for improvement of the veterinary legislation, June 28th 2012; HMA letter to the European Commission regarding autogenous vaccines for veterinary use, April 9th 2014.
in accordance with EU requirements). Moreover, the NCAs consider the added value of peer review of the evaluation to be necessary in order to ensure a robust assessment (similar to the co-rapporteur and peer-reviewers roles in the centralised assessment procedure), which also helps to ensure public confidence in the evaluation system. It is suggested that the dossier should be deposited in a central location, accessible to any NCA who wishes to consult it. This could be easily facilitated by an appropriate IT system. This is particularly important as in a repeat use of the MRP/DCP the proposed procedure is an administrative procedure only, with no opportunity for the new CMSs to comment or raise objections to the previous evaluation (the CMSs being required to accept a product without the dossier and not being allowed to query the assessment carried out originally).

b. The draft proposal also foresees that the co-ordinating group involved in the MRP and DCP, i.e. the CMDv will, de facto, become a risk management body, with voting on applications taking place by a simple majority of those present (whether or not the product is intended for their national market). It should be considered whether this is a legally viable mechanism for decisions on applications which affect not only the Member States concerned and present for the vote, but all other Member States.

c. The proposal for harmonisation of so-called ‘legacy’ products\(^4\) is seen as ambitious but seriously problematic. Under the proposal, certain products would be grouped and be harmonised either by a scientific or an administrative procedure. Under the latter procedure, the proposal defines that the harmonised authorisation shall include all species and all therapeutic indications mentioned in any existing authorisation for ‘similar products’ in any Member State. Also, the shortest withdrawal period (of those applied in any of the Member States where a similar product has a marketing authorisation) shall apply. Experience in the referral procedure before the European Medicines Agency\(^5\) demonstrates that such a rigid and legal requirement could compromise consumer safety [e.g. if newer residue data are available for a veterinary product which demonstrate that the shortest withdrawal period is inadequate and therefore unsafe] and that a more nuanced but essentially scientific approach is needed (e.g. one based on a proposal from the marketing authorisation holder based on the technical content of the product dossier). Moreover, this harmonisation should not be limited to products authorised before 2004 (as envisaged in the proposal) but also include products authorised after 2004 that are based on reference products authorised before 2004. This proposal should allow that the authorisation for any such product be updated according to the outcome of the harmonisation for the reference products so that the harmonisation might be maintained into the future (e.g. by transfer of the products concerned to the MRP/DCP).

Finally, the HMA support the creation of a legal provision for conditional approval for veterinary medicines, as already exists in the legislation relating to the authorisation of human medicines. The HMA regret that this approval route was not part of the draft regulation as it is a means to allow early access to needed medicines.

2. Risks in changing the tools available to monitor and regulate veterinary medicines

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\(^4\) Legacy products are veterinary medicines that have been authorised nationally in Member States over the years. Even if they are manufactured by the same pharmaceutical company, the indications, warnings, dosage and withdrawal periods may differ in some respects between Member States. The lack of harmonisation might also result in discrepancies between the particulars of the originator and the generic product on the same national market.

\(^5\) Opinions on referral procedures are formulated by the Committee of Medicinal Products for Veterinary Use (CVMP) under the aegis of the European Medicines Agency (EMA)
Under the proposal, the responsibility for monitoring veterinary medicinal products on the market appears to shift from the marketing authorisation holders to the regulatory authorities (e.g. certain existing regulatory mechanisms such as renewal of marketing authorisations and periodic safety update reports (PSURs) on adverse reactions are to be abolished). The HMA support the goal to simplify the pharmacovigilance system with a tailored approach for veterinary medicines but believe that the responsibility for product safety and efficacy should always remain with the marketing authorisation holder. The proposal also foresees that the surveillance of pharmacovigilance be reduced mainly to signal detection of adverse events. The HMA believe that this is not sufficient and that a continuous system for benefit / risk analysis purposes should be maintained.

The HMA would also urge that the concept of Good Veterinary Pharmacovigilance be included in the new proposal.

3. Changes to stimulate innovation

The HMA are concerned about the adequacy of the proposed increases in the data protection periods being afforded in the proposal, and would like to point out that the concept of the global marketing authorisation (already enshrined in the current legislation) has negatively influenced the development of products currently. If the ‘global’ authorisation system continues as before, it is expected to negate the proposed benefits of any increase in the protection periods set out (animal health companies [including both originator and generic companies] have indicated that they will not develop new additional product presentations which will not be given data protection).

The regulatory framework should be in a position to address possible new therapeutic advances in veterinary medicines in the future. HMA would wish to see an enabling provision in the legislation which will allow adaptation of the regulatory requirements to the specific needs of such products. Therefore the HMA wish to see that provision is made for the regulation of advanced therapies, as well as an enabling clause to cater for other possible innovations in the future.

The HMA believe that there remains a need to regulate inactivated autogenous vaccines, and ban the use of live autogenous vaccines. Such products currently represent a growing market involving largely unauthorised veterinary medicines that pose a potentially significant threat to the spread of animal diseases. The HMA support also a clarification of the definition of autogenous vaccines.

In the new proposal for the ‘cascade’, which governs the choice of an alternative medicine where there is no suitable authorised veterinary medicine, the existing hierarchy is removed, making it easier to use human medicines directly. The HMA have concerns about the impact of this measure, as it might act as a strong disincentive to industry to develop veterinary products (as veterinarians potentially choose cheaper human medicine alternatives that have no efficacy data in animals over an existing authorised veterinary product). The

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6 In this context, ‘global’ refers to the initial authorised product, together with any extensions thereof, including additional presentations of the drug (e.g. tables, injectables, premixes, pour-ons), and also including any additional strengths, indications, etc.

7 Today, once a company has a medicine containing an active substance authorised, any additional species, pharmaceutical form or different route of administration subsequently authorised for that company for a product containing that active substance belongs to the same ‘global’ marketing authorisation. The data protection period begins with the first authorisation.

8 The ‘cascade’ refers to the current legal provision in Directive 2001/82/EC as amended that allows veterinary practitioners to prescribe and use unauthorised medicines that would not otherwise be permitted.
HMA believe that the modification of the cascade legislation should not lead to greater use of human medicines in the first instance.

The HMA support the need for an environmental risk assessment (ERA) for veterinary medicines. However, the proposal does not resolve the problems for applicants of generic medicines who have to provide an ERA even though one is available for the originator medicine. The HMA consider it necessary to put in place a system that avoids the need for conducting repeated ERA studies. One possibility could be the use of an ERA monograph system on active substances and worksharing of assessments.

The HMA are concerned by the omission of any reference to Good Manufacturing Practice (GMP) as a requirement for veterinary medicines. The HMA would urge that the GMP concept be explicitly retained in the manufacture of veterinary medicines.

4. **Antimicrobial resistance (AMR)**

The HMA expect that the availability of new regulatory tools outlined in the proposal will help address the threat of AMR. The HMA strongly support the legal tools for the evaluation of benefit/risk balance taking into account the risk of AMR, as well as the specific provision for refusing the use of veterinary antibiotics. The HMA request that a definition of the terms ‘antimicrobial’ and ‘prevention/metaphylaxis’ be included in the proposed legislation as these terms are often used incorrectly, leading to misunderstandings.

5. **Other aspects**

The HMA have restricted their comments to the key parameters. However, HMA have conducted a substantive review of the proposal and are available to provide additional and detailed comments, if requested.

**Conclusion**

The HMA are mindful that the proposal for the new legislation has been a long time in preparation and represents considerable effort by the European Commission to address the specificities of the veterinary pharmaceutical sector. The HMA believe that the proposal would benefit from the further structured input of the NCAs. The HMA are willing to engage constructively with the relevant Council Working Party and European Parliament to achieve this aim and would welcome the opportunity to do so.