Better regulation of veterinary pharmaceuticals: how to put in place a simpler legal framework, safeguarding public and animal health while increasing the competitiveness of companies

1. ABOUT THE CONSULTATION

1.1. What is the purpose of this consultation?

In the context of co-decision procedure concerning the proposal for a Regulation on residue limits of pharmaceutical products in foodstuffs the Commission made the following declaration1:

"The Commission is aware of concerns expressed by citizens, veterinarians, Member States and the animal health industry as regards the directive laying down the rules for the authorization of veterinary medicinal products, in particular the importance of addressing existing problems linked to the availability of veterinary medicinal products and the use of medicinal products in species for which they are not authorized and any disproportionate regulatory burden hampering innovation, whilst ensuring a high level of consumer safety with respect to food or animal origin. The Commission points out those positive steps are being taken in this direction such as the simplification of the rules on variations of veterinary medicinal products and this review of the legislation on maximum residue limits in food. In addition, in order to address the objectives of consumer safety and animal health protection, competitiveness of the veterinary industry including SMEs and reduction of administrative burden, the Commission will present in 2010 an assessment of the problems in the application of the veterinary medicinal products directive with a view to making, where appropriate, legal proposals".

By means of this public consultation, the Directorate General for Health and Consumers (DG Health and Consumers) intends to consult all stakeholders on their views on the strengths and weaknesses of the current legal framework for veterinary medicinal products and how it could be improved. Your comments will help DG Health and Consumers to draft the impact assessment on a revision of the veterinary legal framework and, where appropriate, to draft proposals to change the legal framework. It is emphasised that the public consultation relates to the current legal framework for veterinary medicinal products. Therefore the scope of the public consultation includes Directive 2001/82/EC, Regulation (EC) No 726/2004 and all other legislation directly relating to veterinary medicines. Veterinary medicines cover also biologicals, for example vaccines.

It is important that any contribution should be supported, where possible, by detailed evidence. In particular, we would like to receive as many quantitative data, studies and evaluations as possible which will allow us to better describe the current situation and to analyse the impact of potential changes. However, if you have only descriptive information this can still be very useful to us.

It needs to be emphasised that the purpose of this consultation paper is not to outline detailed legal amendments. The paper provides a basis for discussion on key issues and key items where a need and/or possible amendments of the legal framework have already been identified by stakeholders (see sections 3 and 4). However, stakeholders are asked to comment on all issues related to the current legal framework for veterinary medicinal products, and to submit any general or detailed comment or proposal to change the legal framework. We would especially like to specially invite contributions from stakeholders on the key issues set out in this consultation paper.

The consultation paper is structured as follows:

- Section 1 relates to the consultation (explaining how and by when to submit consultation responses and the next steps).
- Section 2 provides a brief guide to the legal framework for veterinary medicinal products, as well as a summary of strengths and weaknesses of the current framework as pointed out by stakeholders.
Section 3 sets out the main objectives and options for a review of the legal framework in relation to the Commission’s declaration.

Section 4 presents the key issues where possible amendments of the legal framework have been already identified by stakeholders.

Section 5 relates to the general information as requested of submitting parties.

Through this public consultation, DG Health and Consumers is committed to ensure that all stakeholders can make their views known on this important issue.

This document does not represent an official position of the European Commission. Based on the results of the public consultation, among others, DG Health and Consumers will prepare a report of the impact assessment on a revision of the veterinary legal framework.

1.2. Who is consulted?

Contributions are invited from all stakeholders and interested parties dealing with medicines for veterinary use. Stakeholders who are not established within the European Union are likewise invited to comment. Comments from Small and Medium-sized Enterprises (SMEs) involved in the pharmaceutical sector are especially welcomed.

1.3. How can I contribute?

Submitting parties should indicate whether they are a citizen (name, telephone number, email address, Member State / country), non-business organisation, business organisation, enterprise or a public authority. In the case of a business organisation or enterprise, please indicate the type of stakeholder (farmer, veterinarian, manufacturer, wholesaler, pharmaceutical industry, importer, researcher, other) and which countries your enterprise or organisation covers. In the case of business organisation or enterprise, please indicate the yearly turnover and number of employees in order to determine whether your business organisation or enterprise falls within the Community definition of a small and medium-sized enterprise (i.e., <50m EUR yearly turnover and, cumulatively, <250 employees).

An acknowledgement of receipt will be issued for each contribution received, within five working days. Contributions will be made publicly available on the ‘Pharmaceuticals’ website of the Commission* once the consultation period is over. If you do not wish your contribution to be made public, please indicate this clearly and specifically in your submission. In this case, only an indication of the contributor will be disclosed. Professional organisations are invited to register in the Commission’s Register for Interest Representatives (http://ec.europa.eu/transparency/regrin/) set up as part of the European Transparency Initiative in order to provide the Commission and the public at large with information about the objectives, funding and structures of interest representatives.

1.4. What will happen next?

All contributions will be carefully analysed. A summary of the outcome of the consultation will be published on the ‘Pharmaceuticals’ website of the European Commission and also sent directly to all contributors. The results of the consultation will be utilised for the impact assessment report on a revision of the legal framework for veterinary medicinal products.

For regularly updated information on the next steps of the impact assessment exercise, please consult the webpage of SANCO Pharmaceuticals.
2 LEGAL FRAMEWORK FOR VETERINARY MEDICINAL PRODUCTS: A BRIEF DESCRIPTION AND THE PERCEIVED STRENGTHS AND WEAKNESSES

2.1 Context

Within the European Union veterinary medicinal products are regulated by legislation throughout their entire lifetime on the basis of scientific expertise. The primary objective of this legislation is to protect public and animal health on the basis of scientific evaluation. A secondary objective is the completion of the internal market for pharmaceutical products.

In order to ensure the quality, safety and efficacy of medicines, a veterinary medicinal product may only be placed on the market in the Community when a marketing authorisation has been issued. Throughout the lifetime of veterinary medicinal products, animal health companies are subject to harmonised pharmacovigilance requirements to monitor adverse reactions to a medicine and/or new side effects. The legal framework provides a special, simplified registration procedure for homeopathic medicinal products. This procedure takes into account the particular characteristics of homeopathic products, such as the very low level of active substances they contain and the difficulty of applying to them the conventional statistical methods. Comments are welcome on this specific procedure for homeopathic products.

For almost 20 years, veterinary medicinal products in the EU were regulated under Directive 81/851/EEC and Directive 81/852/EEC. In 1990, Regulation (EC) No 2377/1990 entered into force, introducing the concept of maximum residue limits. The Directive 81/851/EEC and Directive 81/852/EEC were supplemented in 1993 by Regulation (EEC) No 2309/93, which established the European Medicines Evaluation Agency (EMEA) and the centralised Community procedure for both human and veterinary medicines. The Directive 81/851/EEC and Directive 81/852/EEC were merged in the Community code of Directive 2001/82/EC which provided the legal environment for the authorisation, manufacturing, marketing, distribution and use of veterinary medicinal products. A major revision of this framework was carried out in 2004 by Regulation (EC) No 726/2004 and Directive 2004/28/EC. Subsequently, parts of the legal environment were further amended: this included the data to be submitted in order to obtain marketing authorisation for a veterinary medicinal product and the procedure for amendments in relation to authorised products. The Commission also decided to assist small and medium-sized enterprises in promoting innovation and the development of new veterinary products. A last major revision was introduced in 2009 by Regulation (EC) No 470/2009 replacing Regulation (EC) No 2377/1990 on maximum residue limits. This new regulation was developed with a view to increasing the availability of veterinary medical products.

The EU regulatory legal frameworks for veterinary and human medicines have developed in parallel over the years and have much in common. This provides a number of advantages in terms of ease of understanding and adoption, interpretation and case-law. However, the nature or the needs of the veterinary context may require a different approach to be adopted than for human medicines. For example, for veterinary medicines administered to food producing animals the regulatory environment must ensure that residues of veterinary medicines do not pose a risk to consumers.

The spread of antimicrobial resistance is a major threat to both public health and animal health. This issue is currently being debated at various levels. Any result that has relevance for this review should be introduced in the process for implementing the Commission’s declaration. In the public consultation this horizontal issue is included as part of several key issues.

2.2 General strengths and weaknesses of the legal framework as perceived by stakeholders

The regulatory framework is considered to have helped to enhance the quality, efficacy and safety of the medicines to animals, consumers of foodstuffs, users of medicines and the environment. It has also played an essential role in establishing consumer confidence in veterinary pharmaceutical products and making progress towards a single market for veterinary medicines.
However, the framework is perceived by stakeholders to have become complex with its mixture of centralised, decentralised and national authorisations procedures and responsibilities plus the consequent increase in the time, cost and uncertainty of developing new veterinary medicinal products. Companies indicate that they spend considerable sums of money to keep existing products on the market and continue to raise concerns over unnecessary regulatory burdens, e.g. those which are caused by requirements and conditions in the legal framework that are seen as unnecessary or - while a harmonised regulatory environment exists for the authorisation and placing on the market of veterinary medicinal products - divergences in the implementation of Community legislation by Member States.

Companies also point out that there are not enough incentives in place for extending the scope of existing medicinal products on the market and also for developing new products. The general view is that the regulatory framework has not delivered the positive impact on the availability of authorised veterinary medicinal products where possible and as required. The problem is particularly striking where the market is small and the expected return on investment for companies is low. First, small markets exist for those disease conditions which are rarely encountered. Second, small markets exist for those species where the number of animals, birds, fish or insects (bees) is comparatively small and insufficient in the EU or in specific geographical areas to justify the costs for the development and authorisation of veterinarian medicines. Other terms often used to describe these small markets are "minor species" and "minor uses". For some specific animal species and diseases the possibilities of treatment with authorised medicines are limited. This poses significant problems for animal owners, farmers, producers of aquatic food and veterinarians. For producers of foodstuffs, the risks of the production process increase. Veterinarians are faced with situations where there is no authorised veterinary medicine available and they may consider resorting to off-label use of medicines in order to treat the disease. The shortage of authorised medicines may also have implications for public health either through the inability to control zoonotic diseases in animals, through the off-label use of veterinary medicines or the use of illegal substances with the attendant risks of exposing consumers to potentially harmful drug residues in foodstuffs.

Another issue is the incorrect functioning of the internal market. For most of the authorised veterinary medicinal products marketing authorisations seem to have been granted by national authorities, and the existing mechanism for recognizing the assessment of veterinary medicinal products by other Member States (mutual recognition procedure) has been only partially successful. Delays are identified by stakeholders in the assessment process due to shortcoming and backlogs in national approval systems and discrepancies are perceived with regard to the national implementation of the EU regulatory framework in the individual Member States. Therefore, despite the review of the legislation in 2004 and other initiatives undertaken, in practice a genuine single market for veterinary medicinal products does not seem to be a reality. Lastly, stakeholders raised concerns that the particular characteristics of the veterinary sector are not sufficiently integrated in the framework and that it does not contain enough incentives to stimulate innovation, in particular incentives to stimulate the development of new veterinary medicinal products.

3 SCOPE, MAIN OBJECTIVES AND OPTIONS OF A REVISION OF THE LEGAL FRAMEWORK FOR VETERINARY MEDICINAL PRODUCTS

The Commission's declaration (see paragraph 1.1) states that an assessment has to be provided of the problems in the application of the veterinary medicinal products directive. The scope of this public consultation and the review will be the regulatory framework (the veterinary directive and all other relevant regulatory documents) concerning veterinary medicinal products. This will enable the Commission with the possibility to receive the information and to make, where appropriate, legal proposals for addressing the concerns expressed by citizens, non-governmental organizations, veterinarians, enterprises active in the food chain, Member States, the animal health industry and other interested parties in relation to the legal framework for veterinary medicinal products.

The objectives of the review of the legal framework are, without compromising public and animal health, as follows: (1) to increase the availability of veterinary medicinal products, (2) to decrease administrative burden and (3) to improve the functioning of the internal market for veterinary medicinal products. The policy options
are structured into three demarcation fields: specific features of the veterinary sector, administrative burden and single market (see table 1). It should be noted that a combination of various options will be probably required in order to adequately address the weaknesses and problems of the current legal framework (see paragraph 2.2).

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On the basis of these objectives and options DG Health and Consumers is preparing an assessment of the possible impacts. This includes an analysis of the likely impacts of the main options and an examination of possible synergies and trade-offs. The results of the public consultation, as indicated earlier, will be carefully considered and included in the report of the impact assessment.

4 KEY ISSUES TO BE DISCUSSED

It is important to emphasise the difference between key issues and the three demarcation fields as included in Part Three of this public consultation. The demarcation fields are used to structure the policy options. The key issues in this fourth part of the public consultation are subjects on which the Commission specifically invites interested parties to provide a contribution and which may fall within the scope of one or more policy options
as included in Table 1. Therefore, the information provided in the contribution could be applied for more than one policy option.

4.1 Key issue N° 1: Data exclusivity

4.1.1 The issue
Regulatory authorities require pharmaceutical companies to submit extensive data establishing the safety, quality and efficacy of a new drug before they approve it for sale. These data are the result of many years of research and clinical trials and are expensive to produce. In the current legal framework, an applicant shall not be required to provide the results of a safety and residue test or of the pre-clinical and clinical trials if it can be demonstrated that the medicinal products is a generic of a reference medicinal product. Therefore, a generic company can rely on the data of a reference medicinal product (original product) for the marketing authorisation. However, tests assessing the potential risks posed by medicinal product for the environment also have to be provided by the generic applicant.

When a company has a medicine containing an active substance that is 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 period of exclusivity (including the extension of this period to another food-producing species) begins with the first authorisation. Thus, the period of exclusivity for any additional investment is directly linked to the granting of the initial authorisation.

Currently the term of exclusivity is ten years (13 years in the case of medicinal products for fish or bees). The ten-year period is extended by one year for each extension of the marketing authorisation to another food-producing species (with a maximum of 13 years). This extension to another food-producing species has to take place within the five years following the granting of the initial marketing authorisation. As indicated above, the term of exclusivity is currently 13 years in the case of medicinal products for fish or bees. For other minor food-producing species it was expected that veterinary medicinal products would be derived from existing medicinal products for major food-producing species, and consequently an additional year of exclusivity was included in the legal framework.

Data exclusivity as provided by pharmaceutical legislation is one way to reward successful product research and development. In general the patent system is regarded the primary mechanism to reward and protect innovation, and the pharmaceutical sector relies heavily on patents to protect inventions. Stakeholders point out that the current framework of data exclusivity does not provide sufficient incentives for innovation in the animal health sector. In particular it has been pointed out that the current additional period of data exclusivity for each extension of the authorisation to another food-producing species does not provide a sufficient return on investment. Although the investment in an additional species may be smaller than for the first species, the commercial target market of the additional species will also be smaller and thus it would take longer to obtain a return on investment.

National marketing authorisations of veterinary medicinal products with the same active pharmaceutical ingredient have often different terms in Member States. Companies can choose which reference products to depend on. This implies that the Summary of Product Characteristics (SPC) for a generic product being marketed in Member States may differ significantly from the originator product already authorised in a given Member State.

4.1.2 Consequences
Data exclusivity prevents originator companies from having to face competition from generics during the period of exclusivity and gives an opportunity to benefit financially from the innovation. This provides an incentive for innovation, for example to develop products for small markets. Generic medicines contain well-known substances. Therefore applicants can depend for the marketing authorisation partially on existing data and there is no need to repeat (animal) testing and trials. It could be argued that competition of generics should be promoted for the interest of the users of medicines in obtaining low price medicinal products. On the other hand data exclusivity provides companies an incentive for innovation. The issue is to balance the goal
of improving access to low-cost veterinary medicinal products while preserving sufficient incentives needed for innovation. An exclusivity period that is too long might involve unnecessary high costs for medicines, while too short a period might involve an inappropriate incentive for innovation and consequently lead to less development of new medicines.

For older reference products the existing data may not be fulfilling the expectations of recent evaluation standards. This means that Member States may have to authorise a generic product on another basis than the current original one. This situation could result in harmonisation across Member States of the SPC of the generic but also in disharmony within a given Member State between the generic SPC and the SPC of the original product. Some interested parties consider that this situation may create a risk that veterinary products not being used appropriately and, consequently, it may have an impact on animal or public health. It must be emphasised, however, that the reference veterinary medicinal products have been assessed in the past and were found to be safe and efficacious at the time.

4.1.3 Options to address this issue
Exclusivity conditions could be adjusted to provide the appropriate incentives. This could be done across the board in order to provide a better incentive for innovation or specifically for small markets. Longer periods of exclusivity could be provided in the case of markets for which there is no reasonable expectation of the pharmaceutical companies recovering research and development costs.

Tests assessing the potential risks posed by medicinal products for the environment must also be provided by the generic applicant. Potential environmental risks posed by medicinal products mostly apply to a range of authorised products. Therefore it could be efficient to generate these data as part of a non-individual approach and the use of a monograph system could be evaluated. Another option could be to no longer differentiate between the tests for environmental risks and other data. This would imply that for all data the same data exclusivity rules would apply.

Do you agree with the description of the issue
Yes

Please indicate your satisfaction with the level of data protection provided by the current legal framework
Very unsatisfactory

Do you have quantitative or qualitative data showing the impact of the current data exclusivity period on innovation
Yes

If so please provide estimate of impact
Data exclusivity is extremely important for the development of veterinary medicinal products to reward successful product research and protect innovation. After taking account project failures, capital cost and the time needed to complete the development cycle (10 years) the financial investment for a major new product amounts to more than 60 million Euros. This sum must be recovered from sales over time. Without data exclusivity price competition increases and will not allow revenues for reinvestment into research. This will have a negative impact on availability of new products long term.

Type II variations of the marketing authorisation in order to include another farm animal species is unique compared to human medicines and are very expensive. We need almost 3 years to complete such a project and calculate cost of more than 30 million Euro for that. However the legally protected additional period of data exclusivity (1 year and only if the licence is granted within 5 years of the life of the product) does by far not provide sufficient return on investment. The lack of data protection has an important impact on the availability of medicines and on off label use. Since the returns are lower in small markets/use with fewer sales opportunities, the impacts are even more seriously.

The principle of the “Global Marketing Authorisation” for the animal health sector does not at all reflect the specifics and is totally inappropriate applied.
Furthermore variations for an additional therapeutic indication for the same species are getting more and more expensive. The development costs for Farm Animals amount 2 Mio. Euro - without any data protection granted for that.

The current regulatory environment for veterinary medicines in the EU favours generic medicines and creates a negative environment for the development of new and innovative medicinal products. For example innovator companies are often asked by the regulatory authorities to provide new additional data when a new safety issue arises, while existing generic products are not. This creates an unlevel playing field and reduces the available budget for investment in new products.

Do you have data on effective protection periods of originator products calculated from the authorisation of the originator until the first authorisation of a generic?

No

If so, please provide data.

Do you agree that generic companies provide for a competitive market within the veterinary pharmaceutical industry that is reflected in the pricing structure of veterinary medicines which is passed on to the end user?

Agree

Do you consider that the current data exclusivity period in the legal framework strikes the appropriate balance between innovation and competition?

Very unsatisfactory

Please substantiate your reply.
The global reference product system completely disregards the specificities of veterinary medicinal products. In animal health there is more than 1 species, creating fragmented markets and necessitating major investments in line extensions. The development effort required for adding an animal species, major new indication or pharmaceutical dosage form to an existing product label is substantial and requires extra data protection. Additionally, the current data exclusivity period is also not long enough as an incentive to develop products for MUMS.

Would you agree to increase the general period of data protection of 10 years?

Strongly agree

Do you consider the current additional data exclusivity period of one year for each extension of the authorisation to another food-producing species appropriate?

Very unsatisfactory

Please substantiate your reply.
One year data exclusivity is not enough to allow a company to obtain an appropriate return on the investment and recover the extensive costs it takes to develop products for further companion animal as well as food producing animal species. Usually the new markets are important for vets, owners, producers and animals but of limited size.

By means of the global marketing authorisation all different product developments using the same active pharmaceutical ingredient are regarded as a single one, not taking into consideration the extra innovation investment it takes to extent the authorisation. Rather than having 10 years regulatory protection for a whole number of different product developments, 10 years should be allocated to each species developed. Also the time window within which the marketing authorization for a new species development needs to be obtained should be extended from 5 to 8 years to make it a realistic development scenario.

Do you consider that in data protection rules there are particular burdens in relation to the features of SMEs?

No
Would you be in favour of major product developments (for example extending the authorisation to additional animal species, new formulations of the substance) being subject to their own period of exclusivity (i.e. not being part of the global marketing authorisation for the product containing that active substance)?

Favour very much

Do you consider the current general market exclusivity period of 13 years for fish and bees appropriate?

Yes

Please substantiate your reply

Medicines availability is a major issue for all small market like fish and bees. In order to stimulate innovation for these minor markets additional measures are necessary.

Should the data exclusivity period of 13 years for bees and fish be extended to other species?

Very satisfactory

If so, please indicate the species which in your opinion require the same approach as bees and fish. Please substantiate your reply, in particular providing the reasons to include new types of species. The exclusivity period should be extended to all minor species.

Would you be in favour of amending the condition that only in a time period of five years following the granting of the initial marketing authorisation an extension of the period of market exclusivity can be obtained?

Favour not at all

Should specific intellectual property incentives be developed for small markets?

Yes

If so, how would you define small markets?

Small market should
- include minor species
- include products for minor indications
- include products with a limited geographical distribution

If the 1-1-1 Concept will have been realised in future a many more products will be available throughout the EU (true single market) and there should be less “small markets”. Moreover, if the labelling requirements were improved in line with the proposals presented below in this consultation paper, it would become profitable for the industry to market products in smaller markets and part of the current problems would be resolved.

Do you have concrete proposals (to amend the legal framework) concerning intellectual property rights?

1. 10 years Data Protection (DP) granted for new products for each species. The separate DP periods for each species are not cumulative and not being part of the global marketing authorisation for the product containing that active substance.

2. An additional 1 year’s DP (i.e. 10+1) granted for additional therapeutic indications for that species if it is authorised in the first 8 years of the life of the product.

3. 6 months DP for additional sub populations (c.f. paediatrics in human medicine).

4. DP granted to the company that generates the data (e.g. any company, not necessarily the first company, could develop the additional data).

5. A data protection period of 13 years for all minor species – not just fish & bees.
6. 5 years data protection granted to any studies required by the regulatory authorities outside of the data protection period of the original product.

Do you agree that generics increase the availability of veterinary medicines (e.g. in smaller Member States in which the original product was not marketed)?
Strongly disagree

Do you have data to substantiate that generics improve availability of veterinary medicinal products?
No

Do you think an applicant should be allowed to use the data in relation the potential risks posed by medicinal product for the environment (like for the results of safety and residue test or of the pre-clinical and clinical trials)?
Yes

Would you favour a monograph system for environmental risks?
Favour not at all

Generic veterinary products may be based on reference products that have been on the market for a long time, and the approval of these reference products will have taken place not according to current requirements. Do you consider that generic veterinary products based on these "old" reference products could pose a risk for public or animal health?
No

Do you have concrete proposals (to amend the legal framework) in relation to generics?
The same requirements for all authorisation holders are essential for fair competition. If additional experimental data are required outside the data protection period by the regulatory authorities, the authorities should provide these requirements for all approved products - originator and generic products alike. In an appropriate transitional period (5 years) data protection is necessary. Under this general condition, the environmental risk assessment (ERA) data can be changed during the review so that in future ERA datasets can be treated the same as other safety data. The only reason for the establishment of the special environmental data protection in the legislation of 2004 was to prevent unfair distortion of the market. Without this data protection only originator companies would have been asked to generate the expensive environmental safety packets freely available for the generic companies.

4.2 Key issue N° 2: Authorisation procedure

4.2.1 The issue
There are several procedures for authorisation in the EU. The centralised procedure results in a single marketing authorisation (called a 'Community marketing authorisation') that is valid across the EU; the European Medicines Agency (EMA) is responsible for the scientific assessment of the application. The centralised procedure is compulsory for certain categories of medicines (for example medicines derived from biotechnology processes). National marketing authorisations result in a marketing authorisation only for the Member State concerned or they can be valid for several Member States under a mutual recognition procedure or a decentralised procedure. In these procedures the marketing authorization in one Member State will be recognised by the other Member States. The applicant must submit an application in all Member States concerned. Scientific assessment and management decisions are made by national authorities.

Although there is a harmonised regulatory environment in the EU for the authorisation and placing on the market of veterinary medicinal products, differences between Member States in interpreting the legislative framework for veterinary medicinal products, as well as the existence of numerous national requirements for authorisation, result in a situation where enterprises are confronted by different rules and interpretations in different countries. However, animals treated with veterinary medicines and their foodstuffs can move
unhindered within the internal market even if the veterinary products themselves cannot. It should also be noted that the authorisation systems have become very complex. It is important to note that during the last 8 years the decentralised procedure appears to have become more attractive for companies, as there has been a substantial increase in the number of applications for this procedure. In general, interest in a centralised procedure is limited. This is probably due to the fact that, for the most part, the animal health industry is not interested in launching its product on all national European markets. Thus, the various, parallel authorisation procedures seem to cater for specific needs of companies by offering various routes to obtain marketing authorisation.

Under the current legal framework the authorisation of a medicine shall be refused if it is clear that the balance of risks and benefits is unfavourable. A risk is defined as any risk relating to the quality, safety and efficacy of the veterinary medicinal product as regards animal or human health. However, the current legislation does not lay down any requirement to perform a risk-benefit assessment which also takes into consideration the indirect risks related to the development of antimicrobial resistance. Neither does the legal framework contain a clear basis for refusing a marketing application and/or certain indications where authorisation of an antimicrobial might pose an indirect risk to animal or human health, such as risks relating to the development and/or the prevalence of antimicrobial resistance. Nor does the legal framework provide a specific legal basis to restrict the use of certain antimicrobials in veterinary medicines which are critical in human medicine.

4.2.2 Consequences
Enterprises consider the authorisation procedure as time consuming and involving a high administrative burden, which leads to relatively high costs. The procedure is also considered unpredictable in some cases. This may deter companies from investing in innovation. The different opinions of competent authorities on whether a marketing authorisation can be granted, or on the details of the marketing authorisation, also create a barrier to the free movement of veterinary products within the Community.

4.2.3 Options to address this issue
The authorisation system could be amended in order to achieve a genuine internal market for veterinary medicinal products. A more centralised risk assessment and authorisation procedure could streamline and increase efficiency and predictability, and speed up decision making. The resources gained could be invested in improving the quality of the system.

More or less centralised systems of authorisation and levels of co-operation will be assessed in the assessment:

- The first option is an optimal use of the current authorisation procedures for veterinary medicinal products at national and Community level (option 1: best use of current procedures). Competent authorities could put in place a system of enhanced co-operation with the aim of pooling the existing resources better at EU level, for example by points of excellence, pooling the best available expertise in the EU, assessing and/or authorising products for several Member States (assessment and authorisation of the application could be carried out by different bodies). Given that this option would make use of current authorisation procedures, each concerned Member State would have to give prior confirmation of its agreement to participate in this procedure.

- Each authorisation of a veterinary medicinal product, regardless of the procedure under which the medicine has been authorised and regardless of the authority involved, will be valid throughout the EU (option 2: each authority decides for all). This could apply to all products authorised after a specified date.

- Some Member States can decide to work together more and, by giving up the possibility to object to a decision, to automatically recognise a decision of another Member State (option 3: voluntary automatic recognition). The decision of the competent authority of one Member State will be valid and binding on the territory of the Member State(s) that co-operate within this structure.

- One body in the EU will authorise all types of veterinary medicinal products in the EU by means of a single authorisation procedure. The outcome would be binding on all Member States (option 4: centralised system); in this option a specific body would assess all future applications starting from a specified date.

The options are not mutually exclusive, as some of their features could be combined to create a new option. DG Health and Consumers is aware that the options provisionally selected take account of a limited series of
factors and that they do not exhaust the full range of political choices that could be offered to the Commission. However, DG Health and Consumers takes the view that the three options selected represent the main political choices. Stakeholders are invited not only to evaluate the options, but also to enrich them and help to assess their feasibility and possible impact. In their replies stakeholders could refer to the effects of the option concerning efficiency, effectiveness, predictability, administrative burden and time-to-approval.

How do you rank your satisfaction with the current authorisation procedures?
Dissatisfied

How do you rank your satisfaction with the current centralised procedure?
Dissatisfied

How do you rank your satisfaction with the current decentralised and mutual recognition procedure?
Dissatisfied

What are your criteria for selecting the reference Member State in the decentralised procedure?
Previous favourable experience
Reputation for scientific expertise

What are in your opinion the advantages, strengths, flaws and weakness of the current range of procedures for the authorisation of veterinary medicines?
Advantages and Strength:
Determined costs; respecting of prescribed timelines;

Flaws and weakness:
Mutual recognition Procedure (MRP) and Decentralised Procedure (DCP):
Lack of a real mutual recognition spirit
National specific interpretation of guidelines and national requirements (less acceptance of electronic dossier, dossier contents, translation in many languages)
Due to the required unanimity within the CMDv only one member can provoke a CVMP referral. For now 27 Member States we believe this voting procedure is not appropriate for any longer.

Centralised Procedure (CP):
It is incomprehensible that CVMP and CMDv come in parts to diametrically opposite decisions on the same data, even with the same experts. Furthermore it is regrettable that communication possibilities between the applicant and the rapporteur of the CVMP have not been improved.

Furthermore there is a lack of an independent expert group in case of a reexamination.

Would you favour extending the scope of the Community procedure (extending the type of products that could be authorised by the Community procedure)?
Favour clearly

Do you think a conditional authorisation, similar to the one included in the legal framework for human medicines, would help to mitigate the availability problem?
Agree

Do you consider that there is a need for several authorisation procedures in the EU?
No
Do you consider it necessary that the number of authorisation procedures should be simplified by reducing it to only one?
Strongly agree
Which of the above options described in paragraph 4.2.3 would you prefer? Would you prefer another option? Please explain your choice and try to specify in particular which economic, social and environmental effects you expect from your choice, giving as much as possible quantitative information as possible.

In view of the negative experience with the current system we do not believe that a system whereby one national authority decides for all member States would work (option 2). However in order to pool the best available expertise resources for the risk assessment we would appreciate an enhanced cooperation within the national authorities, where determined expert teams evaluate determined products or product classes. This evaluation should be binding for all member states and enable the Marketing Authorisation throughout the EU.

According to IFAH Europe’s 1-1-1 concept which Bayer supports we think that

- only one single application should be necessary with no translations and even worse national specific needs;
- only one scientific assessment should be conducted a single time by a team of experts recruited from the different Member States for the specific procedure in question and providing the best available expertise;
- the product evaluation should be valid for all EU Member States;
- in case of a favourable outcome a marketing authorisation should be granted by the authorities without reassessment

Such a procedure has many advantages as more efficiency, less administrative burden, more science based risk assessments and last but not least a harmonised and predictable application of the regulation and guidelines within the EU.

In the current regulatory system there are too many repetitions of "scientific evaluation/decisions", e.g. CMDv, CVMP, referrals. Furthermore, some evaluations and subsequent decisions seem to be undermined by political agendas rather than science. In a new system it should be ensured that committee/working group mandates match their composition. It appears the need to differentiate between decision-making committees which require Member State representation and scientific groups/advisory committees which could follow the expert model. The "One system" with the backbone of the national agencies providing for a best network of expertise for scientific evaluation plus a decision making committee as mentioned above would have a considerable potential to reduce the existing double, triple, and parallel work in the existing system as well as to provide for a uniform interpretation of the existing regulatory rules.

An example of different outcomes apparently depending on the procedures is our experience in the case of the Cevazuril referral. While for Cevazuril - a generic product of Baycox swine - a phase II Environmental Risk Assessment (ERA) was not required by CVMP, Bayer Animal Health in the former renewal, new line extension applications for all species as well as CMDv and CVMP referrals was always asked to deliver expensive datasets for the ERA. By means of the additional tests and research for delivering the data Bayer had to bear additional cost amounting 1 Million Euro. Such an unlevel playing field destroys markets and impeaches the credibility of a science based authorisation procedure.

What, in your experience, are the necessary conditions for a successful authorisation procedure, and what are the main obstacles?

First of all it is necessary to have a clear, transparent and binding procedure that is independent of political and local preferences balancing the benefits with the risks in appropriate and harmonised way. In order to performing such high quality scientific assessments professional staff should be recruited from the Member States. Furthermore in order to save time and increase the availability of MUMS products within the EU market access to all MS should be granted after a single assessment of a dossier.

The main obstacle is the lack of real mutual recognition spirit and the lack of harmonised interpretation of legislation and guidelines leading to disagreement between Member States.

What could be done to improve the current authorisation procedures?
In order to create a true single market for veterinary pharmaceuticals a change of the registration system is unavoidable.

Do you consider that there are parts in the authorisation procedures in particular burdensome for SMEs?
No

Would you favour including in the legal framework a requirement to perform a risk-benefit assessment which also takes into account indirect risks related to the use of the veterinary medicine, for example the development of antimicrobial resistance?
Favour not at all

The first marketing authorisation is valid for five years (Article 28 of Directive 2001/82/EC,) and the authorisation may be renewed on the basis of a re-evaluation. Do you consider this system of renewal appropriate if an effective pharmacovigilance system and variations system existed for veterinary medicinal products?
Strongly disagree

Would you favour including in the legal framework a clear basis for restricting a marketing application and/or providing certain indications in cases where authorisation of the specific veterinary medicine would pose an indirect risk to animal or human health?
Favour not at all

Would you favour that the legal framework provides a specific legal basis to restrict the use of antimicrobials which are critical for human medicine?
Favour not at all

4.3 Key issue N° 3: Packaging and labelling

4.3.1 The issue
Packaging and labelling requirements provide information to users and improve consumer protection. However, the costs to meet the requirements, particularly in terms of additional national requirements, may lead to a reduction in the range of products authorised for species and indications in smaller markets. Stakeholders take the view that the necessary costs to develop national packaging and labelling constitute a substantial obstacle to the development of products.

4.3.2 Consequences
There appears to be considerable scope for reducing the administrative burden related to packaging and labelling and thereby contributing to the objectives of this review.

4.3.3 Options to address this issue
One possible option could be to consider packaging and labelling requirements as being the responsibility of the marketing authorisation holder. Also the potential to simplify the requirements could be assessed, for example by taking the view that language requirements are the responsibility of the Member States, who would therefore decide on the languages to be used in their country. Finally, the quantity of compulsory key information could be reduced by optimal use of abbreviations, pictograms and leaflets and references to information available on line.

Do you consider EU - packaging and labelling requirements essential in terms of providing appropriate information to the users of veterinary medicines?
Clearly essential
Would you be in favour of fewer packaging and labelling requirements, or none at all, in the EU legal framework?
Favour very much

Would you favour Member States being allowed to decide which language is to be used for labelling and packaging?
Favour clearly (allow MSs to permit the use of a non-national language on labelling and packaging)

Can you agree to have specific requirements for small packs (small packaging would include ampoules, blister packs and other immediate packs of relative small size), e.g. information being given on the outer packaging of small packs?
Strongly agree

Would you be in favour of reducing the information on the label as much as possible and to making it easier for labels to be used in a number of Member States?
Favour very much

Do you have any concrete proposals to amend the legal framework?
In order to increase product availability in the European market packaging and labelling requirements should be reduced to a minimum (i.e. Product name, Dosage, Quantity/Volume and possibility to use official pictograms for other information). Further required specifics can be provided in local language on a multilingual leaflet. Furthermore Member States should be given the flexibility to permit the use of a non-national language on labelling and packaging.

4.4 Key issue N° 4: Pharmacovigilance and monitoring

4.4.1 The issue
Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem. The existing legal framework for veterinary pharmacovigilance mirrors human pharmacovigilance. This has led to equally complex requirements in both veterinary and human pharmacovigilance. Stakeholders generally consider that veterinary pharmacovigilance is too heavy and burdensome. They point out that, when the current requirements were established, it was assumed that the needs for human patients applied equally to veterinary medicines and, consequently, no specific consideration was given to the actual needs and expectations of veterinarians and animal owners. However, it is important to stress that stakeholders do not question the need for adequate surveillance. Furthermore, stakeholders report a lack of harmony in the implementation of the EU legal framework for pharmacovigilance in Member States.

At the moment no monitoring system exists that delivers standardized and reliable data on usage of antimicrobials in food-producing species and companion animals in the EU.

4.4.2 Consequences
Pharmacovigilance that is too heavy and burdensome is just as damaging as an unnecessary administrative burden.

No comparable and reliable data are available on usage of antimicrobials in food-producing species and companion animals in the EU. Reliable data would provide a tool for risk profiling, risk-benefit analysis and to assess the impact of measures taken in relation to the prudent use of antimicrobials.

4.4.3 Options to address this issue
There appears to be considerable scope for reducing the administrative burden related to veterinary pharmacovigilance. The question is how to simplify the pharmacovigilance without compromising adequate
surveillance. For this it seems required that the fundamental principles and needs underlying the requirements for conducting veterinary pharmacovigilance must be reconsidered. At the end of 2008 the Commission submitted proposals for legislation on pharmacovigilance. Their aim is to strengthen and rationalize the EU pharmacovigilance system for human medicinal products but they do not cover the veterinary sector. Aspects of these Commission proposals could be used to improve the veterinary pharmacovigilance system. However, first of all it appears necessary to evaluate whether the needs and expectations relating to the safety of veterinary medicines should differ from those of human medicines, and - if so - how this should be reflected in the veterinary pharmacovigilance rules. Two specific aspects of the Commission proposal in relation to pharmacovigilance for human medicines are highlighted.

Directive 2001/82/EC requires that a detailed description of the pharmacovigilance system is provided in the marketing authorisation dossier. By introducing the concept of a "pharmacovigilance master file" it would be possible to avoid the duplication of much of the information that is common to all products from the same company, because it would allow the applicant to provide the common information of the pharmacovigilance dossier once only. A decision could be taken to limit reporting to serious adverse reactions and also to restrict the submission of Periodic Safety Update Reports (PSURs) to serious situations (and to abolish the periodic submission of PSURs).

A general legal base could be introduced in the legal framework to enable EU harmonised systems for data collection on the sales and uses of veterinary medicinal products to be set up in the Member States.

Do you consider that the needs and expectations concerning the safety level of veterinary pharmacovigilance could be different for human pharmacovigilance?

Agree

If so, please substantiate your reply.

Veterinary industry is much smaller than the human pharmaceutical industry and it is necessary to balance the administrative burden on the Marketing Authorisation Holder and authorities with the benefit to the animals. Unlike human pharmacovigilance veterinary pharmacovigilance provides rarely a direct impact on human safety. Additionally, unlike majority of human medicines all of the clinical safety efficacy studies for veterinary studies are done in the target species. This leads to a different level of expectation for veterinary pharmacovigilance.

Which measures would you like to propose to amend veterinary pharmacovigilance?

In order to optimize the resources without decreasing the safety level we support a harmonised pharmacovigilance system in line with an international approach (VICH) avoiding additional national requirements. Furthermore Marketing Authority Holders should send all reports of adverse events directly to the European Database. On basis of these data only one assessment should be made by product formulation and or active ingredient.

Considering the high number of products the administrative burden can tremendously be reduced by reducing the frequency of the Periodic Safety Update Reports.

The adoption of a pharmacovigilance master file system for all the products marketed by a company would additionally reduce the administrative burden. This would allow the detailed description of the pharmacovigilance system to be submitted just once and updated just once per occasion instead of per product.

Would you favour the introduction of a masterfile for pharmacovigilance or any other means of reducing the regulatory burden of authorisation holders?

Favour very much
Do you think that there are particular problems in the legislation for pharmacovigilance for SMEs?
No

Would you favour the introduction of a specific legal base for establishing harmonised systems for data collection on the sales and use of medicines in the EU?
Favour somewhat

4.5 Key issue № 5: The distribution channel

4.5.1 The issue
Member States made use of the latitude for national implementation in the legal framework with regard to the veterinary pharmaceutical supply chain. This resulted in divergent requirements for operators in Europe. Some stakeholders indicate that, in order to build a genuine single market for veterinary medicinal products, it is not sufficient to harmonise the authorisation of veterinary medicines. The conditions for companies and practitioners to operate in the whole pharmaceutical supply chain (manufacturers, importers, wholesalers, distributors, retailers, veterinarians and farmers) should also be standardised and harmonised in the EU as well. For example, different rules exist in Member States for the prescription of veterinary medicines. This leads to different standards as regards the use of medicines. In the context of the control of residues in food of animal origin the way in which veterinary medicines are being used is an important issue. According to some stakeholders the legal framework should also be updated to include new methods of distribution such as electronic prescription, internet trade, internet pharmacies and mail order selling. It is also questioned whether the current legal framework is properly designed to respond to the situation of parallel imports.\(^{18}\)

Counterfeit\(^{19}\) medicines may present a threat to animal health through lack of therapeutic effect and/or through inherent toxicity. The most harmful consequences of counterfeit veterinary medicinal products on human health could be the non-respect of maximum residue limits of veterinary substances in foodstuffs and the occurrence of toxic materials in the counterfeit medicines in foodstuffs. The discovery of counterfeit medicines damages also the image of industry that complies with the rules. At EU level no specific rules exist on counterfeiting of veterinary medicinal products. In 2008 the Commission adopted a proposal to amend Directive 2001/83/EC for medicinal products for human use as regards the prevention of the entry into the legal supply chain of medicinal products which are falsified in relation to their identity, history or source\(^{20}\), which foresees specific measures to address the increased risk in the legal supply chain.

4.5.2 Consequences
Stakeholders indicate that a genuine single market for veterinary medicinal products will not develop as long the conditions for companies to operate in the pharmaceutical supply chain of veterinary medicines would not be better standardised and better harmonised. For example, Article 70 of Directive 2001/82/EC allows veterinarians to provide services in another Member State on a very restrictive basis. However, these cross-border veterinarian activities are regulated both by divergent rules of the Member State in which his veterinarian practice is situated and the host Member State in which he is active at that moment, resulting in a complex and unclear legal environment.

Counterfeiting is difficult to detect, to investigate and to quantify. No specific statistics exist on the level of counterfeit veterinary products on the European market. Therefore it is unknown whether counterfeiting provides a real risk for animal or public health. What is known is that counterfeiting of medicines occurs worldwide and the problem is not confined to human medicines as also instances of counterfeited veterinary medicinal products are recorded in Europe, China and the U.S.A.

Parallel trading could encourage trade and help strengthen competition. However, the current legal situation for parallel trade may affect the whole EU authorisation system as it provides a way, in addition to the relevant authorisation procedures, of placing a product on the market that is less expensive for companies. Some interested parties question whether the parallel trade system provides sufficient guarantees on the quality, efficacy and safety of the medicine than the planned authorisation procedures and they point out that parallel trade can result in a less effective pharmacovigilance system.
4.5.3 Options to address this issue

The legal framework could help to standardise the requirements for operators in the distribution chain. For example, harmonisation to the full extent of the prescription status could improve the functioning of the EU system of food control and at the same time contribute to the realisation of a common market in veterinary medicines. Also cross-border activities of veterinarian practitioners could be facilitated compared to the current system laid down in Article 70 of the Directive 2001/82/EC. Regulators, companies and consumers should have confidence in the effective functioning of the veterinary supply chain in Europe. The comprehensive approach for veterinary medicines of the EU, including a risk-based inspection system, should also better tie in with the European rules for foodstuffs and feed.

Do you consider that there is a need to standardise and harmonise the conditions for operators in the EU distribution channel?

Strongly disagree

If so, would you favour standardisation by amending the European legal framework?

Favour not at all

Would you be in favour of the prescription of medicines being standardised in the EU?

Favour not at all

Do you consider that cross-border activities, for example involving veterinarians active in two Member States, are hampered by the current rules?

Yes

Do you agree that counterfeit medicines have penetrated the veterinary supply chain?

Strongly disagree

If so, do you consider that there are risks to public health from the penetration of counterfeit medicines into the veterinary supply chain?

Agree

Should the issues of internet trade, mail order selling or parallel import be addressed in the revision of the legal framework for veterinary medicines?

Agree

Do you consider that the legal framework should be supplemented with specific requirements on internet trade, mail order selling or parallel import?

Yes

If so, do you have any proposals?

The cases where parallel trade is used to circumvent the prescribed authorisation procedures for veterinary medicinal products need to be analysed in depth. By means of harmonisation and simplification of the authorisation procedure according to the 1-1-1 concept there would no longer be a need for parallel trade in the future.

Do you consider counterfeiting of veterinary medicinal products to be a problem for animal health and/or public health EU?

Strongly disagree
If so, what do you consider to be the most important stages where counterfeit veterinary medicinal products enter the production and distribution chain of veterinary medicinal products or human medicines?

We do not believe that currently counterfeit of veterinary medicinal products is a problem to our industry in Europe, but where it exists, the entry points would be internet trade, mail order and possibly further down the distribution chain.

Do you have qualitative or quantitative data on counterfeit veterinary medicinal products?

No

If yes, please provide data

........................

Do you think that legislative measures are necessary to tackle counterfeit veterinary medicinal products?

Yes

4.6 Key issue N° 6: The use of drugs not in accordance with the summary of the product characteristics (off-label use)

4.6.1 The issue

According to Articles 10 and 11 of Directive 2001/82/EC Member States shall ensure that, where there is no authorised veterinary medicinal product in a Member State for a condition affecting an animal species, measures exist that would allow a veterinarian, by way of exception, and where it is necessary in order to avoid unacceptable suffering of the animal, to use medicines off-label within strict limits (this procedure is called "cascade"). These limits include the restriction that the medicine must be administered by the veterinarian or given under his/her personal responsibility and that the veterinarian specifies an appropriate withdrawal period. The veterinarian shall also keep adequate records of the off-label use. For food-producing species, the legal framework specifies the minimum period necessary between the last administration of veterinary medicinal product to animals and the production of foodstuffs from such animals for off-label use ("a minimum withdrawal period")\(^2\). This withdrawal period is standard for all types of foodstuffs. Off-label use - which is an exception to the principle that authorised veterinary medicines have to be used to treat animals for a specific disease - seems to be applied very frequently in Europe. Moreover, the conditions for the application of Articles 10 and 11 in the Member States also appear to differ in the EU. The question is whether the current off-label use could be simplified and whether it should be adapted in order to lower the risks for human and animal health.

The current legal framework does not contain a basis to restrict the off-label use of antimicrobials which are critical in human medicine or where their use would constitute an indirect risk to public health.

4.6.2 Consequences

There are not enough authorised medicinal products available to treat diseases occurring in animals, particularly in the case of minor species. Due to this deficiency, the off-label use of products is a frequent occurrence. The extent to which and the manner in which the "cascade" has been implemented across the EU also differs and has therefore led to disharmony on EU market for the use of veterinary medicines.

As stated earlier Directive 2001/82/EC allows a veterinarian to use a product that is authorised in another Member State where there is none available in the veterinarians Member State. However, this has led, in some cases, to a situation where products for which an authorisation in a Member State has not been accepted, are being used there legally by the "cascade".

The current legal framework does not provide for the possibility of excluding certain antimicrobials for off-label use which are critical in human medicines. Therefore it is the responsibility of the veterinarian to ensure that off-label use is applied in an appropriate way, also taking into consideration the potential risks it may create for public and animal health.
For some food species, stakeholders consider the specified minimum withdrawal periods to be too long in relation to the (economical) life expectancy of the treated animals. Moreover, for pharmacologically active substances for which the scientific committee concluded that it is not necessary to establish a maximum residue limit in order to protect human health (see Article 14 of Regulation (EC) No 470/2009), the minimum withdrawal periods also apply where the cascade is used.

4.6.3 Options to address this issue
The legal framework could be amended in order to have a clarified and simplified legal framework for the treatment of animals in the absence of authorised medicinal products.

For off-label use a withdrawal period could be introduced that is more closely geared to the type of foodstuff, animal species and medicinal product.

Is the above an accurate description of the situation?
Yes

What is your appraisal of the situation?
In respect to the Cascade we support the development of rules allowing a flexible but science based approach to setting standard Withdraw Periods (WP) and that those should be established at the EU level. We also support the implementation of a fully harmonised Cascade across all Member States. But the Cascade was intended only for exceptional use. A consequent implementation of a single market would reduce the need for recourse to the Cascade.

Do you consider that off-label use of medicines is too common in the EU?
No opinion Strongly disagree Agree X Strongly agree

Please substantiate your reply
The cascade, correctly used, is a useful tool to overcome availability issues. Instead of more restrictive conditions for the off-label usage it is necessary to create a regulatory environment that encourages the development and marketing of a full range of needed medicines appropriately authorised for veterinary uses. Therefore major improvements are necessary previously described.

Do you have quantitative or qualitative data on off-label use?
No

If so, please provide.

Are you aware of different national procedures or interpretations of the legal framework?

Do you consider the off-label use a potential hazard for animal and/or public health?
Yes

Would you consider it appropriate to exclude certain medicines from off-label use?
Strongly disagree
Please give reasons for your answer.
The continued discussion and strong recourse to the cascade is a sign for an overregulated segment. The excessive data requirements especially with regard to the demonstration of efficacy leads to the situation that only bigger indications can be developed by industry. Therefore - in the actual system – off-label use (cascade, not misuse!) is important to overcome availability issues and to treat animals suffering on diseases. Instead of more restrictive conditions for the off-label usage it is necessary to create a regulatory environment that encourages veterinary industry to develop and distribute a full range of needed medicines appropriately authorised for veterinary uses.

Would you favour more or less restrictive conditions for off-label use in order to increase the availability of veterinary medicinal products?
Favour not at all

Do you have concrete proposals (to amend the legal framework) concerning off-label use?

4.7 Key issue N° 7: Harmonisation of already authorised veterinary products

4.7.1 The issue
Once a marketing authorisation has been granted, new requirements may be implemented by means of amendments to the legal framework. Therefore, over time, marketing authorisations for the same product may differ from one Member State to another. Also, the competent authorities of the Member States may have adopted divergent decisions for the same product under the same rules. Directive 2001/82/EC provides a mechanism, the so-called referral procedure, to promote the harmonisation of veterinary medicinal products that are authorised in the Community. This referral culminates in a scientific opinion from the Committee for Medicinal Products for Veterinary Use (CVMP) which the Commission will use as a basis to draft a single decision. Member States are required to either grant, maintain, suspend, or withdraw the marketing authorisation, or vary the terms of authorisation as necessary to comply with the Commission decision. Stakeholders have indicated that the referral procedure has not lead to sufficient harmonisation of the veterinary medicinal products market in the Community.

4.7.2 Consequences
Marketing authorisations may exist with different conditions in the EU for the same veterinary product. This may lead to a public health concern and/or an animal health concern; it may complicate the functioning of authorisation procedures and may impose an additional administrative burden on enterprises. Since referral procedures demand of the CVMP a substantial part of its available capacity, this will impact on the Committee's other essential activities.

Harmonization presents a risk in terms of availability, as the data relating to old products may not be sufficient according to current standards. In most cases it is not economically feasible for pharmaceutical companies to conduct additional studies to update the dossier and, as a result, products disappear. Over the short term harmonisation means an increase in additional administrative burden. This should be weighed against the reduced additional burden for marketing authorisation holders in the future.

4.7.3 Options to address this issue
A voluntary or compulsory procedure could be developed to harmonise veterinary medicinal products that are already authorised in the Community. It is noted that old products have been assessed and authorised in the past, and there is experience of the use of these veterinary medicinal products and periodic safety reports were submitted. It has to be discussed whether "old products" should be assessed on the current data requirements. Another option could be to have free circulation of the already authorised products in the EU if there is no evidence of any negative effects of these medicines.

Do you agree with the description of the issue?
Yes
Do you consider it necessary to update and to harmonise already authorised medicines?
Strongly disagree

Please explain your position, and try to specify it in particular with type of data should be requested for this update of already authorised medicines.

The current pharmacovigilance system allows a close monitoring of adverse events. Hereby old products demonstrate their safety in the field and there is predominantly no need to update already authorised medicines. If there is no evidence of adverse effects of these medicines any procedure should be voluntary. Over the short term the harmonisation of the Summaries of Product Characteristics means a considerable additional administrative burden. To overcome this burden Marketing Authorisation Holders would only have an incentive to harmonise the SPC if Member States accept a comparatively broad approach. This would also be appreciated to get a level playing field, because generic companies can legally try to get approval via the “European reference product mutual procedure” for the broadest SPC approved in one Member State. However, authorities deny this procedure for the originator company of this product and require expensive tests and studies for a variation.

If a procedure were established to update and to harmonise already authorised medicines, would you consider it appropriate to apply the procedure differently according to the public health risks involved or to other criteria (e.g. to prioritize the harmonisation of products with high public health concern)?
Yes

Please substantiate your position.

Only concrete safety findings justify a compulsory procedure.

If a procedure were established to update and to harmonise already authorised medicines, would you prefer a compulsory approach?
Strongly disagree

4.8 Key issue N° 8: New needs and new challenges

4.8.1 The issue

There are many serious animal diseases on the borders of the EU. A rise in the level of international trade and travel has increased the threat from previously unknown diseases in Europe. Climate change may further enhance the probability of accidental introduction of diseases in the EU. There is also the possibility that vectors of diseases will move into new habitats and spread beyond their existing areas. Therefore new animal health challenges have emerged and will continue to emerge. Last decades the emergence of for example Bovine Spongiform Encephalopathy (BSE), Foot and Mouth disease (FMD) and Classical Swine Fever has reminded us of the economic and social impacts animal diseases can have. Effective disease control requires a fast and effective response to a disease outbreak and alternative approaches which can supplement existing methods are needed. The current legal framework already provides some tools to respond to new needs and challenges. Pursuant to Article 7 of Directive 2001/82/EC a Member State may authorise the marketing or administration to animals of veterinary medicinal products which have been authorised by another Member State. Article 8 of Directive 2001/82/EC provides the possibility, in the event of serious epizootic diseases, to allow the use of immunological veterinary medicinal products without a marketing authorisation in the absence of a suitable medicinal product. Whilst authorisation at EU level against transboundary diseases is the preferred option, experience has shown that in the event of disease emergencies Member States have made use of the legal provisions to allow use of products at national level. Authorisation of products at EU-level has been much slower, which has often led to the veterinary medicines being authorised too late to be of widespread use.

New technologies, therapies and medicines for animals are emerging. They offer new opportunities for treating or preventing animal diseases. Some of these new developments may be complex and have a new
technical specificity, and therefore lie at the border of being a veterinary medicinal products or another type of product (e.g. medical devices). The current veterinary legal framework does not have specific provisions for advanced therapies as is the case in human medicines.

The issue is whether the legal framework can respond appropriately to new needs and new challenges.

4.8.2 Consequences
If the legal framework is not properly designed to respond effectively to new veterinary needs and challenges, this would pose significant problems in term of ensuring a fast and effective response to outbreaks of new diseases. In order to exploit the results of research, and to support its development, the regulatory requirements and environment should evolve in parallel with advances in technology.

4.8.3 Options to address this issue
The legal framework and environment could be better designed to respond effectively to new veterinary needs, new circumstances and new technologies. However, it is unclear whether there is a real need to change the legal framework.

Can you specify the new veterinary needs and challenges to which the legal framework may have difficulties in responding effectively?

There is a need for new veterinary medicines for companion animals due to the fact that those are getting much older and are kept much longer in companionship with their “families”. This is the case for non infectious disease remedies, such as for cancer, congestive heart failure or renal diseases. Steadily raising and excessive data requirements on efficacy and safety demonstration almost prohibit developments in this area. In consequence the vets do not have any other option than to use products from the human side "off-label". The existing legislation which is intended to protect the animal and owner results in the opposite. The human products used will not contain any information regarding a proper treatment of the animal or potential safety measures for the owner. Legislation which provides for a better balance of this risk management aspect appears necessary.

There is also a need for specific provisions for advanced therapies using GMO. In order to get the authorisation it is of critical importance for the innovative industry to have reliable and harmonised licensing requirements

Furthermore it would be helpful to have a clear demarcation between veterinary medicinal products and biocides.

Do you agree that there are difficulties in the assessment of medicines developed or produced by new technologies?
Agree

Should this issue of new needs and new challenges be addressed in the review?
Agree

Do you have proposals how the need to authorise veterinary medicinal products urgently in the event of an emergency can be better balanced against the need for an appropriate benefit-risk assessment of the use of these products (for which companies have to provide extensive data)?

It should be possible to issue a conditional licence with the condition that the MAH supplies the normal set of data post-authorisation. It should provide an opportunity in emergency cases to prevent major damages to animal health if no treatment alternatives are available.

Do you have concrete proposals (to amend the legal framework) in relation to new needs and challenges?
No.
5. General information on submitting parties

Please give name, telephone number, e-mail address, Member State / country

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Please indicate to what category you belong as submitting party:
Business organisation / enterprise

We thank you for your kind co-operation.


2. See SANCO pharmaceuticals website


At the EU-US summit of 3 November 2009 was agreed to establish an EU-US transatlantic taskforce on urgent antimicrobial resistance issues focused on appropriate therapeutic use of antimicrobial drugs in the medicinal and veterinary communities, prevention of both healthcare- and community-associated drug-resistant infections, and strategies for improving the pipeline of new antimicrobial drugs, which could be better addressed by intensified cooperation between us

Joint opinion on antimicrobial resistance (AMR) focused on zoonotic infections (ECDC, EFSA, EMEA, SCENIHR) 2009

Analysis of the baseline survey on the prevalence of methicillin resistant Staphylococcus aureus (MRSA) in holdings with breeding pigs, in the EU, 2008. (EFSA) 2009
Staff working paper of the services of the Commission on antimicrobial resistance (18 November 2009)
Assessment of the Public Health significance of methicillin resistant Staphylococcus aureus (MRSA) in animals and foods (EFSA) 2009
Reflection paper on MRSA in food producing and companion animals in the EU (EMEA) 2009
Revised reflection paper on the use of 3rd and 4th generation cephalosporins in food-producing animals in the EU (EMEA) 2009
The opinion of the EFSA BIOHAZ Panel on food-borne antimicrobial resistance as a biological hazard (EFSA) 2008
Public Statement on the use of (fluoro)quinolones in food-producing animals in the EU: Development of resistance and impact on human and animal health (EMEA) 2007
11. Article 13 of Directive 2001/82/EC specifies that the applicant for marketing authorisation shall not be required to provide the results of safety and residue tests or of the pre-clinical and clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product which is or has been authorised under Article 5 for not less than eight years in a Member State of the Community.
12. See Article 12 (3) (j) of Directive 2001/82/EC for this information requirement.
13. For further details it is recommended to consult Notice to Applicants Veterinary Medicinal Products Volume 6c, Guidance on the Assessment of environmental risks of veterinary medicinal products.
14. Patent protection gives the innovator an exclusive right to the commercial exploitation of the invention for a certain period of time. In Europe, patent protection may be obtained for up to 20 years.
15. A monographs provide a harmonised approach to the scientific assessment of medicinal product in the EU, and the Member States shall take them into account when they examine an application relating to a product for which a Community monograph has been established.
16. Information that would not fit on the immediate label and outer carton could be put in the leaflet; pictograms could clarify text instructions and provide a way to reduce or to replace text in multilingual labels.
18. Parallel import is the practice of importing into and then the marketing in one Member State from another and it allows distributors to capitalise on price differences between Member States. It is accepted by the European Court of Justice as a way to market pharmaceutical products in EU. A parallel-import marketing authorisation is needed to be able to market a parallel-imported product (this does not apply to products with a Community Marketing Authorisation).
19. According to the World Health Organisation, a counterfeit medicine is "a medicine, which is deliberately ad fraudulently mislabelled with respect to identity and/or source". Counterfeiting includes medicines with wrong ingredients, incorrect quantities of active ingredients, and/or products with fake packaging. It can apply to both branded and generic products.
23. See Article 11(2) of Directive 2001/82/EC