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on veterinary medicinal products

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1. PROCEDURAL ISSUES AND CONSULTATION OF INTERESTED PARTIES

1.1. Overview

The legal environment for the authorisation, production, marketing, distribution and use of veterinary medicines is set out in Directive 2001/82/EC of the European Parliament and of the Council (Articles 95 of the Treaty establishing the European Community - TEC) and Regulation (EC) No 726/2004 of the European Parliament and of the Council (Articles 95 and 152 (4) (b) of the TEC). Following the entry into force of the Lisbon Treaty, amending the TEC, Articles 168 (4) (c) and Article 114 of the Treaty on the Functioning of the European Union (TFUE) give the legal basis for the legislation in the area of veterinary medicines.

Over the years, the regulatory standards and procedures set out in Directive 2001/82/EC have been adapted through legislative amendments in response to scientific advances in the pharmaceutical regulatory environment and the needs of the veterinary sector. However, stakeholders and Member States have expressed concerns that the legislation as it stands nowadays does not meet the needs of the Union regarding the availability of medicines and treatments for veterinary use and does not fully achieve the realisation of the internal market for veterinary medicinal products.

In response to the concerns raised by stakeholders the Commission agreed to conduct an assessment of the problems in the application of the veterinary medicinal products Directive, in its declaration under the co-decision procedure concerning the proposal for a regulation on residue limits of pharmaceutical products in foodstuffs[1]. The revision of the regulatory framework for veterinary medicinal products is included in the Commission Work Programme 2013[2].

1.2. Stakeholder consultation

A wide online public consultation took place from April to July 2010. A total of 172 responses were received. A summary report, showing a breakdown of the responses by type of respondent, was published online, as well as individual responses (unless they were submitted confidentially).

In addition, qualitative and quantitative data were collected on the impact of the legislation between February 2011 and April 2011 through in-depth consultation with the national competent authorities, the main industry trade association and the main veterinary association from six countries (Cyprus, Finland, Germany, Poland, Romania and the United Kingdom).

Various specific consultations were also carried out with key stakeholders in the veterinary sector and the industry, through questionnaires, meetings and workshops. The consultation exercise was complemented by a series of targeted meetings with smaller groups of experts on pharmacovigilance, antimicrobial resistance, and authorisations/data protection. Another meeting was organised specifically with small and medium-enterprises and micro-enterprises (SMEs) to discuss their specific views and needs.

Contact with Third Countries took place through participation in conferences and through meetings of the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) (a multinational programme between

[1] COM (2008) 912, 8/1/ 2009
[2] COM (2012) 629, 23/10/12.

the EU, Japan and the USA). The points discussed at the VICH meetings were taken on board for the development of the options listed in this impact assessment.

The impact assessment builds on the report 'An assessment of the impact of the revision of veterinary pharmaceutical legislation' carried out by the European Policy Evaluation Consortium (EPEC). One EPEC member, GHK Consulting, carried out the study assisted by Triveritas. This report was commissioned by the European Commission and the study was carried out from November 2009 to June 2011.

Information collected for the preparation of the impact assessment is in Annexes 3 and 9.

1.3. Inter-service Steering Group

A Commission Inter-Service Steering group (ISG) on the impact assessment of the revision of the legislation was set up in 2009. Initially the project was led by the Directorate-General Enterprise, but following organisational changes the area of pharmaceutical veterinary medicines was transferred to Directorate General Health and Consumers. The ISG included the following participants: Commission Directorates General Agriculture and Rural Development, Environment, Industry and Entrepreneurship, Maritime Affairs and Fisheries, Research and Innovation, Trade and the Secretariat General. The group met on 9 October 2009, 17 November 2009, 8 December 2009, 11 June 2010, 8 October 2010, 9 June 2011, 16 April 2012, 17 September 2012 and 25 October 2012.

1.4. Scrutiny by the Commission's Impact Assessment Board

The impact assessment was scrutinised by the Impact Assessment Board (IAB) on 18 December 2012. In its initial opinion, the Board requested the following improvements to the report:

- To better present the main problem, explain its drivers and support it with evidence;
- Improve the baseline scenario and better demonstrate the need to act;
- Improve the intervention logic and option design;
- Better assess and compare options;
- Improve monitoring and evaluation arrangements.

These points had been taken on board in the preparation of a new version of the report. In particular, this report concentrated on the problem of the lack of availability of medicines and its main drivers. The baseline scenarios regarding availability of medicines and the need to act were better explained, for example regarding the harmonisation of controls, retailing of medicines, novel therapies and antimicrobial resistance. The option design and intervention logic were modified to provide in depth analysis only for the more realistic options. The assessment of risk, and the cost and benefits of the policy options were better explored. The evaluation and monitoring arrangements were clarified.

The revised Impact Assessment was re-submitted to the IAB in July 2013 and some further changes were requested. The problem definition was strengthened and the analysis of the problem drivers streamlined by merging the description of market characteristics with the corresponding regulatory failures, i.e. merging multispecies market with legislation not suited to innovation, and pluri-national market with complex marketing authorisation requirements and procedures. A better explanation on the problems related to the current use of the Cascade was given under Section 2.3. The report was amended throughout, where relevant, to complement the views of industry with the views of national authorities and to better demonstrate the extent to which some of the regulatory requirements may be considered as

unnecessary (as it is for example the case for the submission of periodic safety update reports).

To better demonstrate the need for harmonisation at the EU level regarding internet retailing, new treatments and clinical trials, the report was amended through footnotes 28-31 and in Annex 6. The report was also amended in section 2.4, footnote 47 and Annex 6 to explain how the current rules prevent authorities from prohibiting or restricting the use of antimicrobials; to provide more details on the "disharmonised decisions" (and views) of Member States and to clarify if the concern that veterinary surgeons can be "pressurised" to prescribe unnecessary antimicrobials is only a hypothetical one (footnote 43). Specific and operational objectives were listed for antimicrobial resistance under section 3.2.

The options were better explained and their impact analysed, for example, regarding the more flexible use of the Cascade (option 2); the basis for reduction of data requirements for certain products and how the corresponding risks would be managed (option 4); the aspects of harmonisation for national control systems, new treatments and clinical trials (options 14, 25, 26); how a criteria to define safety risk of "legacy" medicines could be defined (option 11), and how the authorisation of certain classes of antimicrobials could be restricted (option 28). These points were addressed in sections 5 and 6, and Table 11. An indication of the total implementation costs for the EU budget and the EMA is provided in section 5. The need to address the issue of medicines for bees is explained in Annex 7.

The report was amended throughout, where relevant, to better explain how the standards of public and animal health would be maintained should the preferred options be implemented and also to indicate how the concerns of national authorities have been addressed. The views of all relevant stakeholder groups, including farmers and consumer organisations, are presented in the Annex 9. The report also links the assessment of the options' effectiveness to the corresponding policy objectives in table 3. The benchmark for the suggested monitoring indicators (linked to the specific objectives) is in page 45.

2. PROBLEM DEFINITION

2.1. Background

Veterinary medicines are regulated by Directive 2001/82/EC and Regulation (EC) 726/2004, from their manufacture to use, to ensure their quality, safety and efficacy and so safeguard animal and public health, whilst at the same time ensuring the functioning of the internal market for veterinary medicines[3].

The veterinary pharmaceutical sector is made of businesses involved in research and development of new veterinary medicines, manufacturers of veterinary medicinal medicines (including generics), importers, wholesalers and retailers. The veterinary pharmaceutical industry sales in Europe are estimated at 4.6 billion euros - 2005 prices (global sales represent over 13.4 billion euros in 2009). Around 14,600 people are directly employed by the veterinary medicines manufacturing industry in Europe.

[3] Directive 2001/82/EC covers the procedures and the data requirements (on quality, safety and efficacy) for the manufacture and authorisation of veterinary medicinal products, including clinical trials. It also covers their monitoring (pharmacovigilance), possession, distribution, dispensing and advertising. Requirements for inspections of manufacturers, wholesalers and retailers of veterinary medicines are also set out in this legislation.

The animal health market is divided into two sectors - farmed animals and companion animals - which are driven by different marketing rationales. The farmed livestock industry is a high volume market driven by economic, competition and food safety concerns, whereas the companion animal market represents a smaller market, but characterised by high value and high growth. It is also less prone to sudden market variations (such as those occurring from a sudden outbreak of disease) and linked to the changes to the purchasing power of pet owners[4]. More detailed information on the veterinary sector may be found in Annex 4; an overview of the regulatory framework for veterinary medicines is in Annex 5.

See Annex 2, Glossary, for an explanation on technical terms used throughout the impact assessment.

2.2. Problem identification

The private and public sectors have reported an overall lack of authorised veterinary medicines in the Union, for minor species[5] (in particular for bees – see Annex 7), for rare or emerging diseases and for the treatment and prevention of diseases in major species, as illustrated hereafter. There is a lack of certain veterinary medicines in all countries, but the availability of a number of medicines is a particular problem to some smaller Member States. This lack of authorised veterinary medicines poses significant problems for animals, their owners, farmers, veterinary surgeons, consumers and governments as the absence of treatments or the use of non-authorised treatments may result in[6]:

– Poorer animal health and welfare;
– Increased risk for public health due to the spread of untreated zoonosis, or through the exposure to residues of medicines;
– Negative economic consequences such as interruption of farming, compromised supply of foodstuffs (in case of disease outbreaks), economic and competitive disadvantage for EU farming, and trade implications when residues of unauthorised substances are detected[7],
– Legal implications for veterinary surgeons who prescribe medicines under the Cascade (e.g. where residues or unexpected animal losses occur).

See Annex 6 for further details of the problems with availability of veterinary medicines.

Examples of problems with veterinary medicines availability

Lack of veterinary medicines for minor species

FISH – There are no authorised medicines to treat any conditions in many of the food fish species farmed in the Union (sturgeons, perch, cod, char, turbot). There are on average 10 marketing authorisations per Member State (range from 0 to 29) for medicines for more established farmed species such as trout and salmon. This is very low compared to the number of marketing authorisations for medicines for dogs and chickens, for example (average 592 and 198 marketing authorisations per Member State respectively). There are no authorised vaccines against viral haemorrhagic septicaemia of salmonids (which can cause up to 80% mortality in fish), or medicines to conditions such as fish lice (*Argulus* sp), ichthyophthiriosis, fungal diseases (*Saprolegnia* sp), flatworms (mongenean infections), ulcerative dermatitis (*Uronema* sp).

The lack of veterinary medicines for use in aquaculture is highlighted in the Strategy for the future of the European aquaculture[8] as one of the major problems for the industry. In Europe, aquaculture accounts for almost

[4] Benchmarking the competitiveness of the global animal health industry report, 2011.
[5] Annex 2 Glossary.
[6] Report of the Task Force on the Availability of Veterinary Medicines, 2007.
[7] See the impact assessment for the proposal for regulation on animal health (http://ec.europa.eu/food/animal/docs/ah-law-impact-assesment_en.pdf) for illustrations of the scale of the impacts of recent animal disease outbreaks.
[8] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:52009DC0162:EN:NOT

20% of fish production, with a turnover of roughly EUR 2.9 billion and generating some 65 000 jobs. The sector is expanding to farming of "new" species such as sea bass, sea bream, cod, sole, scallops and octopus and the lack of authorised veterinary medicines is affecting business. Since only seven applications were received for new marketing authorisation or for extension of existing marketing authorisations to include fish in the period 2006-2009, it can be assumed that this situation will not improve in the near future if there are no changes. Fish farmers indicated that treatment of diseases in fish is done almost completely with medicines used under the Cascade, but the statutory withdrawal period of 500 ^{0}C/days reduces the availability of some treatments when this is required in proximity of the harvest.

TURKEYS - Currently there is no treatment against histomoniasis (blackhead), a disease caused by the protozoan *Histomonas meleagridis*. This disease has high morbidity and mortality in turkeys, with serious consequences to the European turkey farming industry, as most infected birds die (there are reports that some farmers had to cull entire flocks due to infection).

Lack of veterinary medicines for emerging diseases

SCHMALLENBERG VIRUS. This virus is responsible for abortion and foetal deformities in sheep, goat and cattle and was initially identified in 2011 in Germany and in The Netherlands. By October 2012 it had been reported in 14 countries. A vaccine was authorised in one Member State in May 2013 (2 years after the initial outbreak) but this vaccine only has a provisional marketing authorisation and therefore cannot be mutually recognised in other Member States - to be placed on the market in the other 28 countries of the Union a marketing authorisation needs to be sought in each of these countries, resulting in further delays on the control of the disease.

Lack of veterinary medicines for the treatment of diseases in major species

PARASITIC WORMS present a significant production threat to grazing animals; their control is thus vital for animal health but heavily depends on the effectiveness of medicines (anthelmintics)[9]. Resistance of worms to the anthelmintics currently authorised in sheep, cattle, goats, horses is increasing at an alarming rate, and in some regions of Europe multi-resistance to the three major anthelmintic classes has already been identified. There are few anthelmintic products in the pipeline: only one new class of anthelmintic for sheep has been developed since the 80s, and livestock producers are left with few options for effective treatment.

2.3. Underlying drivers

The reasons behind the lack of available authorised veterinary medicines are various and are discussed below in detail. In summary, the high cost of developing a regulatory dossier and applying for a marketing authorisation combined with the constraints existing in the legislation regarding the data requirements for multi-species deter the development of new, needed veterinary medicines. In addition, post marketing authorisation requirements (such as variations and renewals), to maintain a product on the market become decision-points for keeping or abandoning well-established but low volume sales medicines. This situation has more profound effects on medicines for less common indications and for less common animal species ("minor use-minor species"), with virtually no authorised medicines for "new" food-producing species, such as cod or ostriches. As a result, veterinary surgeons have to result to extensive use of the Cascade. When medicines are used under the Cascade in food producing animal species, specific (statutory) minimum withdrawal periods have to be observed; in some cases these withdrawal periods are impractical, for example for animals with a short life span, thereby limiting the possibilities for treatment.

2.3.1. A multi-species and stagnant market

The veterinary pharmaceutical sector is driven by commercial returns obtained through the sales of veterinary medicines on the resources spent (from product development to placing it

[9] http://www.merckmanuals.com/vet/pharmacology/anthelmintics/resistance_to_anthelmintics.html

on the market). But the market is split between food producing animals and companion animals and both sub-sectors are multi-species: this results in a fragmented market.

Over 50% of the pharmaceutical market is based on the agricultural sector which is cost-sensitive, and is under pressure from global competition. The market can rarely return high prices for sophisticated medicines (expensive treatments cannot be afforded for routine use in production animals as the emphasis is on flock or herd health rather than individual animals). For livestock farmers animal treatment must be cost effective. For example, meat production is a price-driven market with intensive international competition[10], thus livestock farmers aim to reduce the share of the costs of veterinary medicines of their total operating costs. For companion animals, the purchasing power of the consumer equally affects the market price of medicines.

The confined, fragmented markets both for companion and farming animals drive the pharmaceutical sector to concentrate on larger markets which permit a positive return on investments[11]. The 'top four' markets for veterinary medicines are dogs, cattle, pigs and cats species. This translates directly into the number of marketing authorisations in the EU - 70 % of all marketing authorisations are for those species, with dogs having more veterinary medicines authorised than any other species (as companion animals provide a better return to investments than farmed species).

In addition, there is a concern, expressed both by regulators and the pharmaceutical industry, that the current veterinary pharmaceutical legislation is not suited to innovation. There has been considerable consolidation of the veterinary medicines industry over the last twenty years, with fewer than two dozen international companies remaining in the sector, and with the development of a very strong generic industry. It is reported that there is a decline in the number of applications for new veterinary medicines whilst there is a growth in the number of generic applications. The development of a generic product is less expensive than that of a novel product and therefore the potential return to investment for generics is behind the development of a strong generic pharmaceutical industry.

Another reason behind this shift from innovation to the manufacture of generic products is that the current data protection provisions do not take into account the difficulty found by veterinary sector in recovering investments spent in the development of novel veterinary medicines. The data protection period currently lasts for 10 years (13 years for bees and fish) , with an extra year of data protection granted per new food-producing species added within 5 years of the initial authorisation. Since 1991 the costs for new product development (total costs from discovery to first sales, including application procedure) have risen by 229% for food-producing animals, 173% for companion animals and 108% for minor species. The cost of developing a regulatory dossier which would meet European requirements for a major species has been estimated at 15-50 million euros, while for an additional indication it has been estimated at 2-6 million euros.

[10] For example, the market price is 99 dollar cents per pound poultry (http://www.imf.org/external/np/res/commod/pdf/Commodity_Market_Monthly_February_2013.pdf).

[11] This price-driven, fragmented market results in an average operating profit margin of 17% for animal health. The margins for human pharmaceuticals (prescription), medical devices and consumer healthcare markets were estimated as respectively 29%, 22% and 20%. Mapping the Healthcare Landscape: Bring Pharmaceuticals into Focus, Datamonitor, 2009.

2.3.2. Costs to place a product on a pluri-national market

Prior to placing a veterinary medicine on the market, the applicant must obtain a marketing authorisation in all the countries where it intends to market it (Annex 5 describes the EU framework for authorisation of veterinary medicines). About 80% of the respondents to the public consultation were dissatisfied with the current regulatory environment.

The veterinary medicines legislation sets out the provisions concerning the scope and the procedures required for a marketing authorisation. Although the legislation has been amended[12, 13, 14, 15] to reduce administrative burdens, it still incurs in high costs to the industry regarding placing a veterinary medicine on the market. The total annual administrative burden imposed on business by the veterinary medicines legislation was estimated to be 537.9 million euros per year, which represents around 13% of the turnover of veterinary medicines sector - twice of that estimated for the human sector[16]. The table below summarises the costs incurred by the veterinary pharmaceutical industry.

Table 1: Break-down of overall administrative costs (resulting from staff time, overheads, equipment costs and outsourced costs (e.g. hiring an external expert to prepare a technical report) per activity per year

Activity	Administrative burden *[17]	% of the total administrative burden
Application for a marketing authorisation	91.1	17
Packaging and labelling	184.4	34
Applying for a variation to an existing marketing authorisation	133.5	25
Marketing authorisation renewals	69.5	13
Pharmacovigilance	59.4	11

* million euros per year

The highest burden concerns packaging and labelling. The requirements are that the text must be written in all the official languages of the country where the product is to be placed on the market. This translates ultimately into companies deciding not to apply for authorisation in some Member States because the costs associated with the country-specific product labelling and packaging in the relevant national language(s) represents a too high expense to justify the operation in those countries. For example, in some countries such as Malta and Finland there

[12] Directive 2004/28/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/82/EC on the Community code relating to veterinary medicinal products.
[13] Commission Directive 2009/9/EC of 10 February 2009 amending Directive 2001/82/EC of the European Parliament and of the Council on the Community code relating to medicinal products for veterinary use. OJ L 44, 14.2.2009, p. 10.
[14] Commission Regulation (EC) 1234/2008 of 24/11/2008 concerning the examination of variations to the terms of marketing authorisations for medical products for human use and veterinary medicinal products OJ L334, 24/11/2008, p.7.
[15] Directive 2004/28/EC of the European Parliament and of the Council of 31 March 2004 introduced provisions on generics and data protection, simplification of administrative procedures for supplying medicines for pets and the creation of the sunset clause (to avoid the administrative burdens associated with maintaining a marketing authorisation on the market). http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32004L0028:EN:HTML
[16] EU project on baseline and reduction of administrative costs, 2008; measurement of administrative burdens generated by EU legislation, 2009; http://ec.europa.eu/dgs/secretariat_general/admin_burden/index_en.htm.
[17] The figures were collected based on a standard cost model (SCM) developed by EPEC, which took into consideration staff cost per hour, staff time hours, number of actions per entity per annum, staff cost per action, equipment cost per action, equipment costs per entity per annum, total number of companies, operational and support costs per action and per annum and total number of actions per annum to calculate the total cost per annum for the industry. The data collected to develop the SCM were obtained through business surveys and analysis of data on marketing authorisations awarded through various marketing authorisation procedures. The results were reviewed and validated at an industry workshop attended by representatives of businesses that responded to the surveys. EPEC Report, Assessment of the impact of the revision of veterinary pharmaceutical legislation, p. 26, 96-99, 140-141.

are no veterinary medicines authorised for bees[18]. Some Member States such as Luxembourg and Austria have a large number of authorised medicines on their markets because they benefit from larger markets using the same language, such as France and Germany. But in general, the cost of small manufacturing runs for specific packaging and labelling outweighs the potential sales in smaller countries.

The cost of obtaining a marketing authorisation to place a product on the market is also high. Companies, often SMEs, decide to apply for a national authorisation to initially "test" their product on a market. To expand beyond those initial national borders, a re-assessment has to take place to obtain a marketing authorisation in other Member States even if the nationally marketed product has a record of safe use. This re-assessment is costly and burdensome both to the pharmaceutical companies and to the Member States and restrains companies from rolling-out their product across the EU.

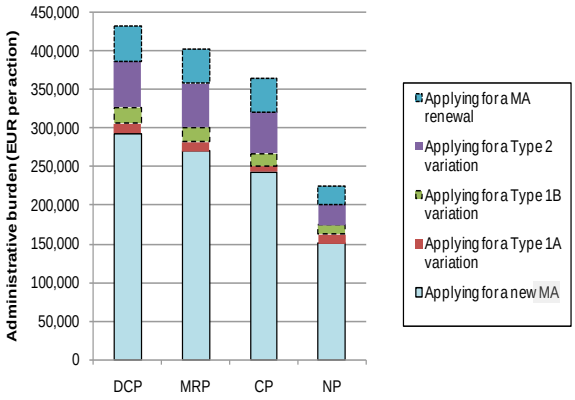
Even the "rolling out" of authorisations granted in the past through the national route for products that have been on the market for many years in different Member States is difficult. These "legacy" products have been authorised with significant differences on the summary of product characteristics regarding indications and withdrawal period, for example. Although most of these products have a record of safe use, and have been on the market in the EU for many years, a scientific reassessment still has to take place for the product to be marketed in a new Member State. However, this dossier re-assessment (or the evaluation for an application for a generic, where the reference product is one of these "legacy" veterinary medicines) often results in referrals to arbitration, when Member States have a disharmonised view from the initial assessment or regarding the information placed on the summary of product characteristics. These referrals are costly - the pharmaceutical industry estimated the cost of a referral (Article 34 referral) as 445,000 euros.

During the public consultation Member states and the industry indicated that some current requirements and procedures (for example regarding authorisation of antimicrobials) generate unpredictability and disagreements between Member States and are only resolved through referrals (in particular regarding the mutual recognised and decentralised procedures); the limited scope of the centralised procedure and the high administrative burdens. SMEs also indicated that the current legislation does not set out harmonised procedures and timelines for the regulation of clinical trials across the EU, and so different national regulations have been put in place at national level. This lack of harmonisation is burdensome and costly for the companies, in particular regarding the setting up of multi-centric trials. Another area identified by SMEs as burdensome and unnecessary is the current legal obligation for pharmaceutical companies to place a product on the market within three years of its approval (the Sunset clause)[19].

The figure below shows the administrative burden to the industry incurred in complying with the legislation in order to place and maintain a veterinary medicine on the market. The decentralised procedure is the most costly procedure to companies, on average, and the centralised procedure is the least costly of the three European procedures. The national procedure generates the lowest administrative burden of all procedures.

[18] Annex 7 presents a discussion on the issue of availability of medicines for bees.
[19] See Annex 8.

Figure 1 Average administrative burden (in euros) per product per action, by marketing authorisation procedure



DCP – decentralised procedure; MRP- mutual recognition procedure; CP-centralised procedure; NP-national procedure

2.3.3. Complex requirements for keeping medicines on the market There are disproportionate costs of "mandatory defensive research" for keeping a medicine on the market (that is, the expenditure necessary to maintain existing products in the market as a result of legal requirements by the regulatory authorities, through variations, renewals and pharmacovigilance)[20]. More than 80% of European businesses consulted consider that the EU regulatory requirements are too burdensome and a barrier to innovation – and the most negative aspect causing an impact on business is the re-direction of resources for development of new medicines into defensive research[21,22,23]. The average costs spent on defensive research in the EU was estimated at 35 % of the total global R&D budget (26% in Canada and 14-16% for Australia, Japan and USA). The industry claimed that the continuing demands for defensive research have intensified the balancing act between investment in new products and maintaining existing products on the market[24].

The requirements for variations are cited as a persistent high cost of defensive research. The veterinary pharmaceutical industry considers the procedures to introduce variations to the terms of marketing authorisations very cumbersome, and responsible for around 25% of the total administrative burden (133.5 million euros per year). Although in recent years attempts have been made to simplify arrangements for variations, and since 2009 variations legislation has been harmonised across all four marketing authorisation procedures, the number of variations to marketing authorisations is still high[25].

Another factor incriminated as a disproportionate cost to the industry is pharmacovigilance requirements. Pharmacovigilance aims to monitor the performance of veterinary medicines placed on the market. The legislation requires marketing authorisation holders to maintain databases of all suspected adverse events in animals

[20] Benchmarking the competitiveness of the global animal health industry report, p 2011, 61.
[21] EPEC Report, Assessment of the impact of the revision of veterinary pharmaceutical legislation, 2011, p. 25-26.
[22] Europe and Australia report the highest average expenditure on R&D (7.7%). Benchmarking the competitiveness of the global animal health strategy report 2011, p. 11.
[23] The biggest barriers to innovation identified were the packaging costs and preparation of the data dossier for a submission for a marketing authorisation and also the uncertainty in the sector resulting from unclear policies in the area, re-direction of resources to defensive R&D (that is, to maintain the product in the market) and insufficient data protection for novel medicines. It is reported that 87%of resources are redirected to defensive R&D in Europe, and 33-35% elsewhere in the world. Benchmarking the competitiveness of the global animal health strategy report 2011, p. 13,14.
[24] Benchmarking the competitiveness of the global animal health industry report, 2011, p. 14-15, 61.
[25] For further details see Annex 6.

and humans related to the use of their veterinary medicines. The marketing authorisation holders are also required to report adverse events to the competent authorities and prepare reports on the overall performance of the products (periodic safety update reports - PSUR). Following the initial placing on the market, PSURs must be submitted immediately upon request or at the following intervals: 6-monthly for the first 2 years; annually for the subsequent 2 years; thereafter, at 3-yearly intervals. This frequency of reporting is considered excessive by both the pharmaceutical industry and some regulators, in particular those from smaller countries[26]. The current pharmacovigilance requirements are based on those applied to the human sector and cost around 59.4 million euros per year[27] to the veterinary pharmaceutical industry.

It is important to note that although regulators agree that administrative costs are high, there is a need to maintain procedures in place to ensure public and animal health and safety to the environment.

2.3.4. Lack of clarity in the legislation

The legislation lacks clarity regarding provisions on the retailing of prescription and non-prescription veterinary medicines over the internet or through mail order[28]. As a consequence, some Member States introduced national controls on online sales of veterinary medicines (e.g.: United Kingdom, Germany, Ireland), and others have no controls or forbid it (Austria and Belgium). This fragmentation reduces the potential benefits that retailers of veterinary medicines (in particular SMEs and micro-enterprises) could have from operating on a larger, EU-wide market and developing new services for consumers. In addition, owners of companion animals and farmers cannot benefit from the growth of the market which could lead to competitiveness and lower-priced veterinary medicines. It is clear that online sales of veterinary medicines could benefit substantially these end-users as retail and wholesale prices of medicines differ up to 50% between Member States[29].

New technologies and therapies for animal treatment are emerging from developments in the human sector[30], but the provisions in the veterinary legislation are not sufficiently clear regarding these treatments. Therefore, some Member States have developed their own systems at national level to regulate products such as blood and stem cells; on the other hand, other Member States have no regulation on these areas and consider these treatments as clinical practice (e.g., Sweden). The current situation creates a fragmentation of the internal market and a problem of availability of such therapies in

[26] EPEC Report, Assessment of the impact of the revision of veterinary pharmaceutical legislation, 2011, p. 195-197
[27] For further details see Annex 6.
[28] In the public consultation 90% of the respondents considered that the veterinary medicines legislation should be supplemented with specific requirements on internet trade, mail order selling or parallel trade. The issue of internet retailing is not recent – there has been a court case regarding the internet retailing of human medicines: Judgment of the European Court of Justice from 11 December 2003 in Case C-322/01 (Deutscher Apothekerverband eV and 0800 DocMorris NV, Jacques Waterval).
[29] See Annex 6 for further details on differences in retail and wholesale prices between Member States.
[30] Blood, blood products – such as plasma and platelets - and stem cell products are already routinely used in veterinary medicine. Novel therapies, such as gene therapy - where a viral vector is used to deliver a therapeutic gene to treat a diseased tissue in the animal, as in the case of progressive retinal atrophy for example - are already experimentally attempted in veterinary medicine. Viral vectors for targeting the canine retina: a review. Petersen-Jones, SM. Veterinary Ophthalmology, 2012, 15: 29-34.

some countries, and overall a disharmonised approach to animal health and welfare in the Union[31].

Effective disease control requires a fast response, but the current legislation does not allow an effective, rapid response to a new or re-emerging animal health threat at a pan-European level. In this situation, veterinary medicines are authorised at national level in some Member States – those which have developed fast-track procedures to authorise medicines in exceptional circumstances. This creates an un-level playing field in the Union, which is particularly detrimental to farmers.

In addition, no harmonised legal framework exists at EU level regarding the way controls, including inspections of wholesale dealers and retailers, are organized and carried out by Member State competent authorities throughout the distribution chain of veterinary medicinal products. Consequently there is no uniformity throughout the Union on the application of such controls, and this generates an un-level playing field across the Union. For example, some Member States have not fully implemented or correctly transposed the requirements of the veterinary medicines legislation[32]. This represents a risk for animal safety and public health and causes distortion of competition in the Community, detrimental to the operation of the internal market[33].

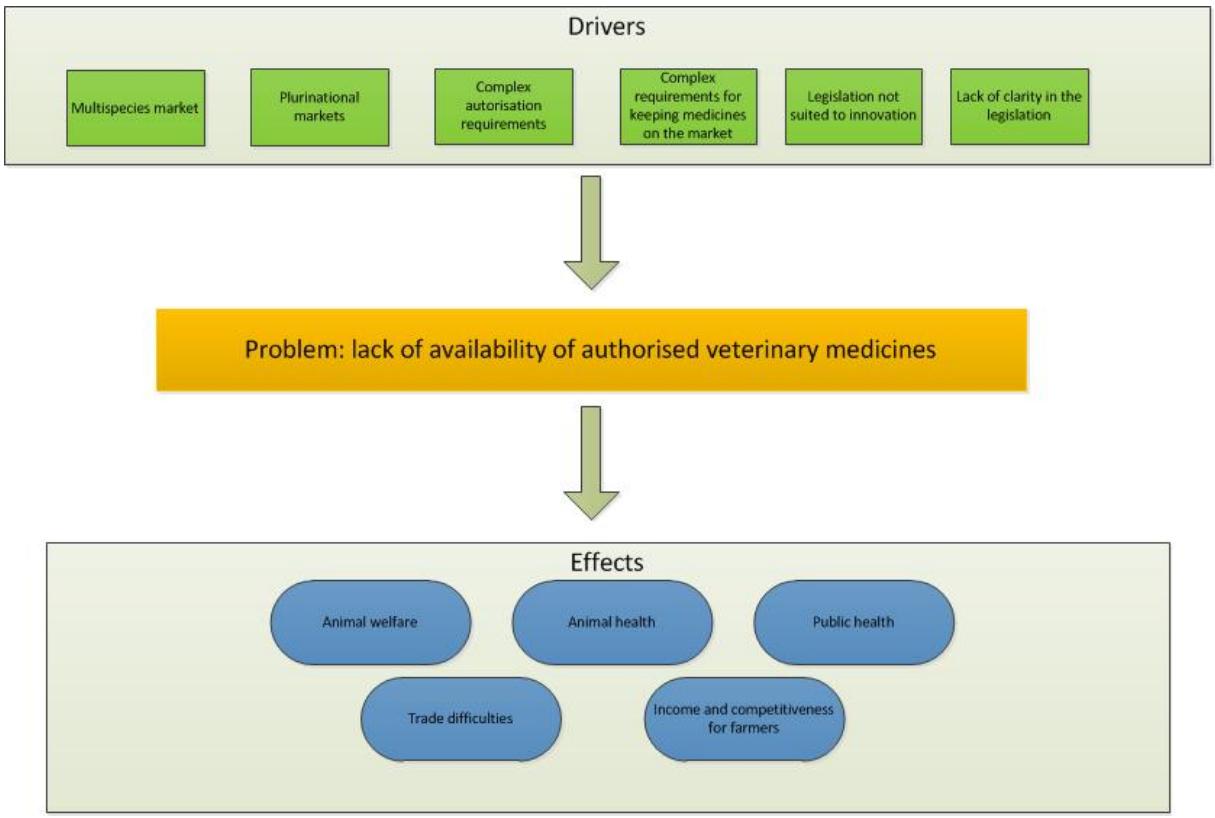
Annex 6 provides further information on the drivers behind the lack of availability of veterinary medicines.

Problem tree: Lack of availability of veterinary medicines

[31] Regulators indicated that the harmonisation in this area would remove a barrier to the free movement of goods. EPEC Report, Assessment of the impact of the revision of veterinary pharmaceutical legislation, 2011, p. 230

[32] Food and Veterinary Office's audit reports:
Malta(http://ec.europa.eu/food/fvo/rep_details_en.cfm?rep_id=2887)
Sweden(http://ec.europa.eu/food/fvo/rep_details_en.cfm?rep_id=2549);
Poland (http://ec.europa.eu/food/fvo/rep_details_en.cfm?rep_id=2504).

[33] The enforcement of the legislative framework for veterinary medicinal products is the responsibility of the national competent authorities, and there is presently little in the way of harmonisation between countries, or coordinated oversight of national in-market control systems (beyond the control of residues of veterinary medicines). Improved coordination of control systems is particularly important to improve trust between Member States.



2.4. Contribution to the fight against the development of resistance to antimicrobials

Antimicrobial resistance has increased in importance worldwide in recent years. It is reported to cause many deaths (25,000 patients die each year in the EU from infections caused by resistant bacteria) and great financial costs (extra health care costs and productivity losses were estimated as of at least 1.5 billion euros per year) in the human health care setting. According to the World Health Organisation, common, yet life-threatening infections caused by resistant bacteria are becoming difficult or even impossible to treat. The problem is aggravated by the scarcity of new antimicrobials being developed, which limits treatment options for patients with infections caused by multidrug-resistant organisms[34,35].

The Parliament and the Council have voiced their concerns regarding the problem of antimicrobial resistance. The Commission considers antimicrobial resistance a public health threat[36] and adopted an action plan to address the problem. This action plan list as key actions (regarding veterinary medicines):

– Action n° 2: Strengthen the regulatory framework on veterinary medicines and on medicated feed via the review package foreseen for 2013;

[34] ECDC/EMA Joint technical report The bacterial challenge, time to react, 2009, p 15.

[35] Scientific opinion on the public health risks of bacterial strains producing extended-spectrum beta lactmases and/or AmpC betalactamases in food and food producing animals. EFSA Journal, 2011, 9(8):2322.

[36] European Commission Communication of 15 November 2011 to the European Parliament and the Council - Action plan against the rising threats from antimicrobial resistance http://ec.europa.eu/dgs/health_consumer/docs/communication_amr_2011_748_en.pdf

– Action n° 7: Promote efforts to analyse the need for new antibiotics into veterinary medicine;
– Action n° 10: Strengthen surveillance systems on antimicrobial resistance and antimicrobial consumption in animal medicine.

Antimicrobial resistance in animals can be transmitted to humans through zoonotic diseases. The importance of animals and of food of animal origin in the emergence, spread and persistence of antimicrobial resistance in humans has not yet been completely established[37] but the inappropriate therapeutic use and the non-therapeutic use of antimicrobials in animals (such as use of antimicrobials to mask poor farm management or inadequate zootechnical practise) is considered to be one of the drivers for the development of resistance in the human sector[38].

Human medicines and veterinary medicines including antimicrobials are regularly used for non-approved indications and with non-approved dosages under the Cascade[39]. This ensures animal treatment but there is a concern that this practice, and in particular the use of last resort human antimicrobials, may contribute to the rise of antimicrobial resistance in humans. Another area of concern is the carry-over of antimicrobials in the production of medicated feed. This is out of the scope of this impact assessment but is addressed through the revision of the medicated feed legislation.

It is acknowledged that the current veterinary medicines legislation does not provide sufficient tools to ensure that risks to human health arising from the use of antimicrobials in animals are adequately managed, as the assessment process is based on data presented (product-specific). For example, there are no legal provisions to allow regulators to prohibit or place restrictions on the authorisation for animals of certain classes or groups of antimicrobials that are considered reserved for the treatment of human infections. As a consequence, these types of antimicrobials may be authorised in some Member States but not in others, or may be authorised and used under different conditions. This creates difficulties for the implementation of a holistic strategy to the control of antimicrobial resistance in the Union. The legislation also does not allow the prohibition or the restriction of the use of antimicrobials under the Cascade, and this also hampers the prudent use of antimicrobials in veterinary medicine. In addition, legislative and non-legislative national measures have been put in place at national level as an effort to tackle antimicrobial resistance, thus creating disharmonised decisions in the Member States which generate a constant stream of referrals for arbitration [40]. Furthermore, the different approaches regarding prescription, use and distribution of antimicrobials in the Member States hamper efforts to deal with the problem of antimicrobial resistance in a holistic manner in the EU. There is also a concern that the advertising of antimicrobials, under the disguise of informative material, enables or induce farmers and companion animal owners to pressurise veterinary surgeons to prescribe unnecessary antimicrobials or

[37] Joint opinion on antimicrobial resistance focused on zoonotic infections (ECDC, EFSA, EMA, SCENIHR), p. 34.
[38] European Commission Communication of 15 November 2011 to the European Parliament and the Council - Action plan against the rising threats from antimicrobial resistance http://ec.europa.eu/dgs/health_consumer/docs/communication_amr_2011_748_en.pdf
[39] In a joint survey of HMA-V and FVE in January 2012 veterinarians responded that they prescribe antimicrobials according to the to the Summary of Product Characteristics 'very regularly' (10%), 'regularly' (34%), 'occasionally' (43%) and 'seldom' (13%).
[40] Twelve referrals were submitted to the CVMP in 2011. EMA Annual report 2011, p. 51. An example of a referral due to divergent decisions of Member States re the authorisation of an antimicrobial may be seen here: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/veterinary/referrals/Baytril_10/vet_referral_000065.jsp&mid=WC0b01ac05805c5170

prescribe unsuitable (but convenient) antimicrobials, which leads to an overuse of these medicines[41].

For those reasons, although this is not directly related to the availability of veterinary medicines, the issue of antimicrobial resistance will be addressed as part of the revision of the veterinary legislation, in accordance with the actions of the Commission Action Plan against the rising threats of antimicrobial resistance.

Further discussion on the issue of antimicrobial resistance is included in Annex 6.

2.5. Principles of Conferral, Subsidiarity and Effectiveness (added value) tests

The primary purpose of the legislation is to ensure the quality, safety and efficacy of the veterinary medicines to safeguard public and animal health and safety to the environment. But this objective must be achieved without hindering the development of the industry and trade of veterinary medicinal products within the EU.

Legislation in the area of internal market (Art 114 TFEU), and regarding common safety concerns in public health matters and standards of quality and safety for medicinal products (Art 168(4) (c) TFEU) is a shared competence between Union and Member States. The current EU legislation on veterinary medicines, Directive 2001/82/EC and Regulation (EC) No 726/2004, based on Article 95, and Articles 95 and 152 (4)(b) of the TEC respectively, provide the legal environment on authorisation, production, marketing, distribution and use of veterinary medicines. The existing legislation on veterinary medicines brought some harmonisation to the procedures and rules required to place veterinary medicines on the EU market but there is evidence that the existing provisions do not completely deliver the ambition of a functioning internal market and do not match the current needs of the veterinary sector.

The Communication from the Commission Europe 2010 "A strategy for smart, sustainable and inclusive growth" identifies the incomplete functioning of the single market as a missing link and a bottle neck for growth in the Union:

"A stronger, deeper, extended single market is vital for growth and job creation…. Every day businesses and citizens are faced with the reality that bottlenecks to cross-border activity remain despite the legal existence of the single market. They realise that networks are not sufficiently inter-connected and that the enforcement of single market rules remains uneven. Often, businesses and citizens still need to deal with 27 different legal systems for one and the same transaction."

To fully achieve a strong internal market on the area of veterinary medicines, there is a need to simplify and streamline across the Union the regulatory system for the authorisation of veterinary medicines, removing inefficiencies and barriers to cross border trade. This would improve the availability of medicines thus benefiting the veterinary sector in general, from manufacturers to the end users (farmers and the general public).

[41] There is evidence in the US and Australia that direct-to-consumer advertising of human prescription drugs leads to overprescribing and the prescribing of new medicines over older, effective ones. No similar data exist in the EU for veterinary medicines, however, it can be assumed that the same mechanisms take place in the interaction between veterinarians and farmers and in the relationship between patients and doctor.

3. OBJECTIVES

3.1. General objective

In accordance with the Treaty, the objective of this proposal is to ensure a high level of public health protection, high standards of quality and safety of veterinary medicines and the optimal functioning of the internal market.

3.2. Specific and relevant operational objectives

Increasing the availability of veterinary medicines would contribute to achieving the overall goal of the proposal. Furthermore, using this opportunity to contribute to mitigating the risk of development of antimicrobial resistance would further reinforce the ambition of a high level of public health protection.

In practice, improving availability of veterinary medicines would require improving the regulatory environment to:

1) simplify it and reduce administrative burdens whilst maintaining safeguards to ensure public and animal health, safety to the environment and allowing more accessible use of medicines to fill therapeutic gaps via an improved Cascade;

2) foster the development of new medicines, including for minor use-minor species, while keeping those already on the market;

3) facilitate the circulation of veterinary medicines across the EU, through better authorisation procedures, and via new forms of retail such as internet.

This would translate in the following specific and operational objectives below:

Table 2 Framework on veterinary medicines - drivers and objectives

Lack of availability of veterinary medicines		
Drivers	**Specific objective**	**Operational objectives (OO)**
Multi-species market	A Expand market beyond the top four animal species	A.1. Improve the use of the Cascade
		A.2. Improve information on authorised veterinary medicines available in the Union
		A.3. Simplification of application requirements for veterinary medicines for limited markets
		E1. Strengthen data protection incentives
Pluri-national market	B. Simplify procedures for obtaining a marketing authorisation in multiple national markets	B.1. Review centralised, decentralised and mutual recognition procedures
		B.2. Revision of the situation with “legacy products”
Complex authorisation requirements	C. Review data requirements in marketing authorisation procedures	C.1. Revision of environmental requirements for generics
		C.2. Revision of provisions for authorisation of clinical trials
Complex requirements for keeping medicines on the market	D. Simplify post authorisation requirements	D.1. Simplification of pharmacovigilance
		D.2. Simplification of variation requirements
		D.3. Revise the Sunset clause
		D.4. Abolish renewals
		D.5. Simplify requirements for homeopathics
Legislation not suited to innovation	E. Review incentives for breakthrough medicines	E1. Strengthen data protection incentives

Lack of clarity in the legislation	F. Improve clarity: on rules on internet retailing of veterinary medicines	F.1. Specify rules for internet retailing of veterinary medicines
	on the authorisation of new treatments	F.2. Specify rules for new treatments
	on inspections	F.3. Harmonise national control systems
	on authorisation of medicines for emerging diseases	A.3. Simplification of application requirements for veterinary medicines for limited markets

The issue of antimicrobial resistance, recognised worldwide as an important public health threat, is not directly related to the availability of veterinary medicines. However, in response to concerns raised by the Parliament and the Council, the Commission adopted an action plan to tackle this problem in a holistic manner. This plan includes actions related to the authorisation and use of veterinary medicines and, therefore, it is proposed to address the issue of antimicrobial resistance in the context of the regulatory framework for veterinary medicines, focusing on the authorisation and use of antimicrobials in this area. The specific objective is an overall strengthening of the veterinary medicines' regulatory framework regarding the authorisation and use of antimicrobials which would contribute to lowering the risks to public and animal health. The operational objectives are the introduction of proportionate measures regarding the authorisation and use of antimicrobials and of measures to ensure an efficient surveillance system on the use of veterinary antimicrobials.

3.3. Consistency with other EU policies and horizontal objectives

The objectives listed are coherent with the EU and the Commission's strategic principles, in particular regarding decreasing administrative burden[42], simplifying the regulatory environment[43] and putting in place measures to complete the internal market[44] for veterinary medicinal products. This assessment is in addition conducted in parallel to that for the revision of the medicated feed and is consistent with the proposed revision of the EU system of official controls along the food chain, and the policies on animal health[45].

4. POLICY OPTIONS

4.1. Baseline scenario – "no EU action"

The baseline scenario for this impact assessment consists of no changes to the current regulatory framework ("no EU action"). Consultation with stakeholders indicated that, if there is no EU intervention, the problems described would continue to exist and the trend towards divergent national action is likely to continue. Duplication of efforts, the setting of different standards and the introduction of more administrative complexity to the regulatory system would remain.

[42] COM (2007) 23 final
[43] COM (2005) 535 final
[44] COM (2010) 608 final
[45] Animal and Plant Health Package: http://ec.europa.eu/dgs/health_consumer/pressroom/animal-plant-health_en.htm.

The problem with the availability of authorised medicines would continue or even worsen, presenting risks to animal health and welfare from existing and emerging diseases. The continued lack of availability of authorised veterinary medicines would lead to animal health and welfare consequences – and public health would also be at risk, as there is a link between animal diseases and public health. The lack of suitable authorised medicines, in particular to minor species, would force veterinary surgeons to resource more often to using medicines under the Cascade[46], increasing the potential public and animal health risks (as the use of medicines under the Cascade is not supported by specific safety and efficacy studies on their effects). No EU action also would mean that the public health threat of antimicrobial resistance would not be addressed through clear legal tools and would continue to be tackled by Member States without a holistic, consistent approach across the Union.

Further innovations are anticipated regarding the application of new technologies in veterinary medicine, such as gene therapy. At present these new types of treatment are not clearly defined within the legislation, causing confusion as to how they should be treated as part of the authorisation process[47]. If no EU action is taken, it is likely that this uncertainty will remain, with an uneven approach to animal treatment across the EU.

Due to different interpretations of the legislation, the rules on internet retailing of veterinary medicines vary widely in the Member States, leading to legal uncertainty. It also leads to an un-level playing field for businesses as internet retailers of veterinary medicines can be established in some but not all Member States; it also impacts on the pricing of veterinary medicines across the Union through interference with competition[48].

Control systems related to veterinary medicines are organised and carried out by Member States, and significant variations in the level and effectiveness of controls have been noted[49]. No EU action would mean that this disharmonised situation would remain.

If the option "no EU action" is adopted, situations like these described would continue to exist. On the other hand, action at EU level to draw up a harmonised and proportionate system to regulate the manufacture, distribution, possession, prescription, dispensing, administration and use of veterinary medicines would create a predictable legal environment, beneficial to innovation and to the availability of veterinary medicines. It would also prevent Member States from taking action which would result in a further fragmentation of the internal market.

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[46] See Annex 2 for an explanation on the use of the Cascade.

[47] For example, there is no specific legislation for novel treatments in Sweden, and the use of stem cells and blood within the veterinary field is considered as clinical practice. The Italian authorities are preparing guidelines on these therapies, whilst the UK authorities regulate blood banks for dogs and equine stem cell centres. These different approaches mean that animal care varies across the EU, interfering with trade between Member States and potentially with animal health across the Union.

[48] For example, internet retailing is not allowed or not regulated in some Member States (eg Austria and Belgium) but it is regulated or allowed in others (UK, Ireland, Germany).

[49] The enforcement of the legislation on veterinary medicines is the responsibility of the national competent authorities. Currently the European Commission has the competence to carry out inspections to audit control systems in Member States for residues of veterinary medicines, like other activities affecting food safety. Some Member States have not fully implemented or correctly transposed the requirements of the veterinary medicines legislation (eg: Malta, Sweden, Poland). Food and Veterinary Office's audit reports:
Malta (http://ec.europa.eu/food/fvo/rep_details_en.cfm?rep_id=2887);
Sweden (http://ec.europa.eu/food/fvo/rep_details_en.cfm?rep_id=2549);
Poland (http://ec.europa.eu/food/fvo/rep_details_en.cfm?rep_id=2504).

The "no new EU action" option has been taken as the baseline against which the policy options proposed below were measured to evaluate their potential impacts.

4.2. Policy options regarding lack of availability of veterinary medicines

The policy options considered most realistic are discussed below. For easy of reading, the options are grouped by specific objectives. Some of the options are alternative and some address more than one specific objective. “No new EU action” has always been taken into consideration as a possible option.

4.2.1. Policy options to expand the market beyond the top four animal species

The options discussed here concern the use of the Cascade, provision of information on the veterinary medicines authorised in the EU, the granting of MAs for limited markets, and innovation (operational objectives A1, A2, A3 and E1).

Specific objective	Operational objectives (OO)	Options
A. Expand market beyond the top four animal species	A.1. Improve the use of the Cascade	2 - Improve the Cascade
	A.2. Improve information on authorised medicines available in the Union	3 - Expand database to cover all veterinary medicines
	A.3. Simplification of application requirements for veterinary medicines for limited markets	4 – Reduced data requirements for MA for limited markets
	E1. Strengthen data protection incentives	5 - Reduced data requirements for medicines for bees

Option 1 - No new EU action
This option proposes no regulatory changes.

Option 2 - Improve the Cascade (OO A.1)
Currently veterinary surgeons must follow a ranking system to choose a medicine for use under the Cascade; the veterinary surgeons must also follow the withdrawal period set in legislation, if the animal under treatment is a food-producing species. This policy option proposes to abolish the ranking system to introduce more flexibility and so allow veterinary surgeons to choose the best available treatment to the animal under their care. The option also proposes to modify the way withdrawal periods are determined for use under the Cascade, so that a system based on multiplication factors is used taking into account any withdrawal period information available for the product.

Option 3 – Expand database to cover all veterinary medicines (OO A.2)
This option proposes to create a legislative requirement for the compulsory uploading of information on all marketing authorisations into a single, comprehensive EU database. This database would be linked to the already existing pharmacovigilance database (Eudravigilance).

Option 4 – Reduced data requirements for medicines for limited markets (OO A.3)
This policy option would introduce regulatory changes to allow applicants to submit applications with reduced data for certain products. The type of data that could be omitted would be decided on the scientific advice of the EMA, so that any safety risks are analysed and taken on board. This option aims to fill therapeutic gaps on the market for limited markets (minor uses and minor species), and to allow the authorisation of veterinary medicines in case of urgent need. This option also relates to specific objective F.

Option 5 – Reduced data requirements for medicines for bees (OO E.1)
This option proposes to reduce the quality and efficacy requirements for applications for bee medicines. In addition, this option proposes to allow veterinary surgeons, under their direct personal responsibility, to treat bees with medicines that are authorised in certain Third countries during the time period that no honey flow takes place. This would only be allowed if no authorised medicine exists in the EU for the disease and the use of the Cascade is not appropriate.

4.2.2. Policy options to simplify procedures for obtaining a marketing authorisation in multiple national markets

The options discussed here concern the authorisation procedures and the management of the problem with "legacy products" (operational objectives B1 and B2).

Specific objective	Operational objectives	Options
B. Simplify authorisation procedures	B.1. Review CP, DCP and MRP procedures	7 – Automatic recognition of a national MA
		8 – Single MA procedure for all products
		9 – Wider scope for the centralised procedure
		10 – Simpler packaging and labelling
	B.2. Revision of situation with "legacy products"	11 – Already nationally approved medicines allowed to freely circulate across the Union

Option 6 - No new EU action
This option proposes no regulatory changes.

Option 7 - Automatic recognition of a national marketing authorisation (OO B.1)
This option is to allow an application for a marketing authorisation to be assessed and issued by a Member State and made valid automatically throughout the Union. Pharmaceutical companies seeking to have a product authorised would be free to submit an application to any of the national competent authorities and, if approved, an authorisation would be granted entitling the product to be marketed anywhere within the EU.

Option 8 - Single marketing authorisation procedure for all products (OO B.1)
This option proposes that a single dossier is submitted to a committee composed by representatives from the Member States which then would assign an assessment team to evaluate its scientific contents. Once the assessment is concluded (and if positive), a single decision would be adopted by the Commission or an authorisation issued by all Member States. The pharmaceutical company then would be free to place the product on the market in all or on some Member States only, depending on its commercial strategy.

Option 9 – Wider scope for the centralised procedure (OO B1)
This option maintains the mandatory use of the centralised procedure for innovative medicines (as it is the case under the current legislation) and proposes to extend the scope of this procedure to make it available, upon choice by the applicant, to all types of veterinary medicines. To make the centralised procedure more accessible to SMEs, the option also proposes the introduction of a legal obligation to national authorities to introduce supportive measures (e.g., a help desk) to veterinary SMEs which intend to apply for a marketing authorisation through this procedure.

Option 10 – Simpler packaging and labelling (OO B.1)
This option is to simplify the packaging and labelling of a veterinary medicinal product, which is part of the marketing application dossier. The use of pictograms and abbreviations would be allowed as much as possible to reduce the amount of written text,

whilst still ensuring the safety of the product. Leaflets would still be required and the pharmaceutical companies would be allowed to provide information to veterinary surgeons and the public by other means (e.g. barcodes) too. The national authorities would no longer pre-approve the packaging and labelling layout of veterinary medicinal products. Under this option, the national authorities would be able to authorise the use of a non-official language on the packaging and labelling of the medicines placed on the market in their territory, if they so wish.

Option 11 – Already nationally approved veterinary medicines allowed to freely circulate across the Union (OO B.2)
This option proposes the "rolling out" to other countries of "legacy" veterinary medicines which already have national marketing authorisations in the EU. This would be carried out through a review, which would harmonise the summary of product characteristics of these products, allowing the widest scope possible (that is, taking on board all the indications and target species granted in all Member States). The decision on which products would require assessment prior to harmonisation would be carried out by a scientific committee, to ensure the safety of the product. The proposal also includes an option for pharmaceutical companies to join efforts to generate data if necessary, to be compiled in the form of a monograph (to cover gaps on data regarding environmental safety, for example).

4.2.3. Policy options to review data requirements in marketing authorisation procedures

The options discussed here concern provisions for the authorisation of veterinary medicines (operational objectives C1 and C2).

Specific objective	Operational objectives (OO)	Option
C. Review data requirements for marketing authorisation procedures	C.1. Revision of environmental requirements for generics	13 – Generics applications may refer to environmental data
	C.2. Revision of provisions for authorisation of clinical trials	14 – Harmonisation of clinical trials procedures across EU

Option 12 - No new EU action
This option proposes no regulatory changes.

Option 13 – Generic applications may refer to environmental data (OO C.1)
This option proposes to allow pharmaceutical companies applying for generic veterinary medicines to refer to environmental data as part of the safety dossier package, which already is no longer required for a generic application. Therefore a generic application would not require submission of data on environmental safety, as it is currently the case. Instead, pharmaceutical companies would have the possibility to take advantage of a system of data sharing between applicants, so that a report (monograph) could be generated to address environmental risk concerns.

Option 14 – Harmonisation of clinical trials procedures across the Union (OO C.2)
This option proposes to harmonise the timelines for the authorisation of clinical trials for veterinary medicines in the Union, which currently are not harmonised.

4.2.4. Policy options to simplify post authorisation requirements

The options discussed here concern, variations, the sunset clause, renewals and pharmacovigilance requirements (including for homeopathics) (operational objectives D1, D2, D3, D4 and D5).

Specific objective	Operational objectives (OO)	Options
D. Simplify post authorisation requirements	D.1. Simplification of pharmacovigilance	16 – Risk-based pharmacovigilance
	D.2. Simplification variation requirements	17 – Review procedures to change a marketing authorisation (variations)
	D.3. Revise sunset clause	18 – Delete the obligation to market a product within 3 years of approval
	D.4. Abolish renewals	19 – Delete requirements for renewals
	D.5. Simplify requirements for homeopathics	20 – Exempt homeopathic medicines from pharmacovigilance requirements

Option 15 - No new EU action
This option proposes no regulatory changes.

Option 16 – Risk-based pharmacovigilance (OO D.1)
This option proposes a risk-based approach to pharmacovigilance, where certain requirements (e.g. submission of repeated period safety update reports) that do not contribute effectively to public health, animal health or the protection of the environment are abolished. Pharmaceutical companies would have the responsibility to collect and introduce adverse event reports into an EU pharmacovigilance database and to analyse these data at product level through signal detection. This option would also introduce the concept of a Pharmacovigilance Master File dossier containing information on the pharmaceutical company's systems. Therefore, this option would remove the requirement for the description of the pharmacovigilance system to be placed on the dossier for each marketing authorisation application.

Option 17 – Review procedures to change a marketing authorisation (variations) (OO D.2)
This option proposes a risk-based approach to deal with variations to a marketing authorisation. Those variations which do not introduce changes that might substantially affect the product safety would not require scientific assessment. Other changes would still require prior authorisation by the competent authorities before implementation.

Option 18 – Delete the obligation to market a product within 3 years of approval (OO D.3)
The option proposes the removal of the Sunset clause (an existing obligation to market a medicine within three years of granting the marketing authorisation) from the legislation.

Option 19 – Delete the requirement for renewals (OO D.4)
This proposal is to abolish the general renewal requirements for veterinary medicines but maintain a renewal for specific marketing authorisations, granted to veterinary medicines submitted for assessment without a complete data dossier.

Option 20 – Exempt homeopathic veterinary medicines from pharmacovigilance requirements (OO D.5)
This option proposes to exempt veterinary homeopathic medicines from the requirements concerning pharmacovigilance.

4.2.5. Policy options for breakthrough medicines

The option discussed here concerns data protection (operational objectives E.1).

Specific objective	Operational objectives	Option
E. Review incentives for breakthrough medicines	E. 1 Strengthen data protection incentives	22 – Extend data protection period for new veterinary medicines

Option 21 - No new EU action
This option proposes no regulatory changes.

Option 22 - Extend the data protection period for new veterinary medicines: (OO E.1)
This option proposes an initial period of data protection of ten years with extensions to a new species receiving an added period protection of three years. The maximum period of data protection would be twenty years. The option would also create particular provisions for medicines for minor species, such as fish (products would receive an initial data protection period of fifteen years). A provision to particularly benefit the development of medicines for bees would be introduced: veterinary medicines initially authorised for bees would have an automatic initial period of data protection of twenty years, and any extension to a marketing authorisation to add bees as target species would have a data protection period of five years. To incentivise the development of novel antimicrobials specifically developed for use in veterinary medicine, these products could receive an initial data protection for fifteen years, and extensions to new species could receive five years data protection.

This option also supports the Specific objective A - *Expand the market beyond the top four animal species.*

4.2.6. Policy options to clarify rules on internet retail, on the authorisation of new treatments, on inspections and on authorisation of medicines for emerging diseases

These policy options address problems regarding lack of clarity on the legislation regarding internet retailing of veterinary medicines, new treatments and treatments in case of outbreaks (operational objectives F1, F2, F3 and A3).

Specific objective	Operational objectives	Options
F Improve clarity: on internet retailing of veterinary medicines	F.1. Specify rules for internet retailing of veterinary medicines	24 – Authorisation to sell veterinary medicines through the internet in all MS
on the authorisation of new treatments	F2 Specify rules for new treatments	25 – Establish a framework to authorise new treatments
on inspections	F3. Harmonise national control systems	26 – Establish a basis to harmonise the controls on the veterinary medicine distribution chain
on authorisation of veterinary medicines for emerging diseases	A3. Simplification of application requirements for veterinary medicines for small markets	4 – Reduced data requirements for veterinary medicines for limited markets

23 - No new EU action

This option proposes no regulatory changes.

Option 24 – Authorisation to sell veterinary medicines through the internet in all Member States (OO F1)
This option proposes the introduction of a requirement for the authorisation at national level of internet retailers wishing to sell prescription and non-prescription veterinary medicines in the Union. This authorisation would be valid across the EU.

Option 25 – Establish a framework to authorise new treatments (OO F.2)
This option proposes to set out in the legislation a framework for the authorisation of new treatments (e.g. stem cell treatments), indicating the data requirements and exemptions relevant to the area. In order to keep flexibility, important in this fast growing area, detailed scientific and technical requirements drawn out by the EMA would be placed in guidance.

Option 26 – Establish a basis to harmonise the controls on the veterinary medicine distribution chain (OO F3)
This option is to create a harmonised legal framework regarding the way controls on the distribution chain of veterinary medicine are organised and carried out by Member States' competent authorities.

Option 4 – Reduced data requirements for veterinary medicines for limited markets (OO A3)
This policy option would create the possibility to reduce some data requirements for certain types of veterinary medicines, to fill therapeutic gaps on the market for minor uses and minor species, or to allow the authorisation of veterinary medicines in case of urgent need. This would be done based on scientific advice from the EMA. This option also relates to specific objective A.

4.3. Additional policy options to strengthen the veterinary medicines legislation regarding the authorisation and use of veterinary antimicrobials in veterinary medicine

27 - No new EU action
This option does not imply any regulatory changes.

Option 28 - Introduction of legislative measures to allow restrictions to be placed on the authorisation and use of veterinary antimicrobials
This option is to introduce specific legislative requirements regarding the authorisation of antimicrobials and their use under the cascade. These requirements would refer to the submission and assessment of data for applications for veterinary medicines containing certain types or classes of antimicrobials, in connection with antimicrobial resistance. It would allow the competent authorities to decide, based on scientific advice drawn by the EMA, whether or not a) a class of antimicrobials of importance for human health may be authorised for use in animals and b) if it may be authorised, under which specific conditions. This option would provide that a decision could be taken even if a causal relationship between the potential use of veterinary antimicrobials and antimicrobial resistance in humans cannot be fully established at the time of assessment due to incomplete scientific knowledge in the area. As part of this proposal**,** authorities would be also able to prohibit or restrict the use of certain antimicrobials under the Cascade, based on scientific advice prepared by the EMA. Veterinary surgeons would be allowed to supply antimicrobials to animals under their care only.

Option 29 - Measures regarding advertising of veterinary medicines, including antimicrobials
The option is to clarify the current provisions on the advertising of veterinary medicines, including antimicrobials, aiming to ensure that marketing activities would not lead to the misuse of prescription medicines.

Option 30 - Measures regarding retailing of veterinary antimicrobials
The option proposes to allow veterinary surgeons to prescribe antimicrobials to the animals under his/her care but introduce a prohibition on the supply of these medicines.

Option 31 - Introduction of a legal basis for the compulsory collection of data on the use of antimicrobials
The proposal is to establish a harmonised and compulsory European system for collection of data on the sales and usage of antimicrobials in food-producing animals.

4.4. Options discarded at an early stage

The following options were discarded, as they were considered unfeasible, ineffective or would create unacceptable risks to animal or public health or to the environment:

- To completely abolish pharmacovigilance requirements;
- To replace the authorisation of low risk and generic veterinary medicines with a registration system;
- To make the centralised procedure compulsory to all veterinary medicines;
- To introduce exemptions to reduce legislative requirements regarding authorisation of veterinary medicines by pharmaceutical companies that are SMEs or micro-enterprises;
- To voluntarily harmonise the summary of product characteristics of the “legacy products;
- To standardise the distribution of veterinary medicines across the Union;
- To forbid generic applications for antimicrobials;
- To re-classify bees as non-food animals;
- To develop "soft law instruments" to achieve policy changes.

See Annex 10 for a detailed explanation on the discarded options.

5. ANALYSIS OF IMPACTS

The policy options to address the problems highlighted in the report are largely compatible from the perspective of an overall policy package (to simplify the regulatory environment, to reduce administrative burdens and to complete the internal market) but their simultaneous implementation may impact on costs and savings to stakeholders and regulators. The options were evaluated for their costs and benefits to the affected sectors based on the evidence obtained from the consultation exercises. For each option, consultees’ views are referred to if expressed during the public consultation (consultees’' views are presented in Annex 9).

Monetised costs and benefits were based on assumptions; sometimes they were not available or accurate due to lack of key data. This is indicated in each case. The baseline was "no new EU action".

See Annex 11 for a table showing a comparison of the costs and benefits of the policy options, and a table depicting their effectiveness, efficiency and coherence[50] with EU objectives.

5.1. Costs and benefits of options to expand the market beyond the top four animal species

5.1.1. Option 1 - No new EU action

As this option would not imply any change to the provisions already existing in the legislation, costs and benefits are expected to stay identical.

5.1.2. Option 2 - Improve the Cascade

It was clear from the consultation that the Cascade is important in veterinary medicine, and contributes to increase the availability of medicines in particular for limited markets (minor uses and minor species).
When medicines are used under the Cascade in food producing animal species, statutory minimum withdrawal periods must be observed. In some cases these withdrawal periods are impractical, for example for animals with a short life span, thereby limiting the possibilities for treatment. The option to improve the use of the Cascade is based on a CVMP's proposal. It would replace the current statutory withdrawal periods with a system based on safety factors which calculates the minimum withdrawal period that would still ensure food safety. In addition, the option proposes to abolish the current ranking system which determines the choice medicine for use under the Cascade, so that veterinary surgeons would have more freedom to choose the best medicine for the animal under their care.
Some national authorities and the pharmaceutical industry remarked that a liberal use of the Cascade, even for companion animals, might pose a risk to animal health and also lead to an increase in the inappropriate use of antimicrobials. However, the proposal allows more freedom to veterinary surgeons to choose the best available treatment for sick animals, by way of an exception, in the absence of suitably authorised veterinary medicines. This choice is carried out in accordance with a veterinary surgeons' professional judgment, and for animals under his/her care, thus ensuring animal and public health and environmental safety. Therefore the risks of misuse of the Cascade would not increase from the baseline. This policy option has no impact on administrative burdens to the industry.

5.1.3. Option 3 – Expand the database to cover all veterinary medicines

This option would introduce a requirement for the compulsory uploading of data on all marketing authorisations to an EU database. The major benefit of this option would be an improvement on the transparency within the authorisation system. The availability of an up-to-date database of authorised veterinary medicines, readily accessible across the Union, would help with the effective operation of the Cascade so that veterinary surgeons in one Member State may identify the needed veterinary medicines available from other Member States. Therefore, ultimately this policy option would benefit the protection of

[50] Effectiveness: the extent to which options achieve the objectives of the proposal; Efficiency: the extent to which objectives can be achieved for a given level of resources/at least cost; Coherence: the extent to which options are coherent with the overarching objectives of EU policy, and the extent to which they are likely to limit trade-offs across the economic, social, and environmental domain. Impact assessment guidelines.

animal and public health in general. A complete and up-to-date database of authorised veterinary medicines would also be a valuable tool for the pharmaceutical industry, to map the veterinary medicines on the market in the Union and therefore better target their R&D investments. The implementation of this option would lead to unquantified costs to the national authorities or pharmaceutical industry concerning the uploading of information on the marketing authorisations to the database. However, this may be balanced by a reduction in costs related to informing the EMA about the relevant national marketing authorisations falling in the scope of a referral, for example. The option would have a positive impact on the functioning of the internal market.

5.1.4. Option 4 – Reduced data requirements for veterinary medicines for limited markets

This proposal would reduce administrative burdens to the pharmaceutical industry regarding the preparation of a dossier for a marketing authorisation for medicines aiming to fill therapeutic gaps. This would be particularly beneficial to farmers, as medicines, in particular vaccines, could be quickly placed on the market in the event of emergency. The proposal would be beneficial to animal health and welfare and to public health.

5.1.5. Option 5 – Reduced data requirements for medicines for bees

This proposal is to allow regulators to wave some data requirements for the authorisation of medicines for bees, if the data are not considered essential to the safety of the product. The option could benefit the availability of medicines for this species by reducing the costs of product manufacture and the preparation of the application dossier. The proposal also envisages to allow the use in the EU of medicines for bees authorised in some Third Countries, with the treatment being carried out when no honey production takes place (to avoid the risk of residues in honey).

5.2. Costs and benefits of options to simplify authorisation procedures

5.2.1. Option 6 - No new EU action

As this option would not imply any change to the provisions already existing in the legislation, costs and benefits are expected to stay identical.

5.2.2. Option 7 - Automatic recognition of a national marketing authorisation

This option would reduce the administrative burdens to pharmaceutical companies (estimated savings of 67.9 million euros per year)[51]. These reduced costs would be

[51] The calculations on the administrative burdens took into account the cost of the centralised procedure as a baseline, and the replacing of the decentralised and mutual recognition procedures by what is in effect the national procedure (the application only needs to be submitted to one national authority). The estimate of the administrative burdens required a "shifting" of all applications currently going through the decentralised and the mutual recognition procedures to the national procedure (in one year). EPEC Assessment of the impact of the revision of veterinary pharmaceutical industry legislation report, 2011, p. 170-173.

particularly beneficial to SMEs/micro-enterprises as they could start business by placing a product on a national market and then progressively expand to reach other markets.

The success of this option would depend on Member States. The lack of peer review is a concern to some Member States, which fear a possible reduction in the quality of the current assessment standards. Although all Member States would be working to the same legislation and guidelines, differences in resources, expertise, policy context and geographical animal health status might affect the focus of the assessment of the data presented in the application dossier, rendering the opinion of a specific competent authority not acceptable to others. This could lead to a high number of referrals to the CVMP. Such situation may occur even despite the existence of a voluntary accreditation programme of the national authorities. This option would favour the free movement of veterinary medicines in the Union.

5.2.3. Option 8 - Single marketing authorisation procedure for all products

This option is estimated to have a positive impact on the simplification of the regulatory framework, and significantly reduce the administrative burdens imposed by the legislation. If this option is implemented it would cut an estimated 67.9 million euros each year to the pharmaceutical industry[52]. This option is supported by the pharmaceutical industry and other consultees[53].

Unlike the current European centralised procedures, this policy option does not include any element of peer review for the assessment of the application dossiers. This peer review process requires additional resources and is time consuming, but also provides quality assurance at the level of individual marketing authorisation assessment. As for option 7, many regulators expressed concerns regarding this lack of peer review, even if a proposed independent EU body is created to assess the quality assurance systems of the organisations that are responsible for carrying out scientific assessments. Member States remarked that this option would not be able to ensure the quality of the assessment process, which also would not be able to take on board geographical and policy differences in different countries. This might have a negative impact on animal and public health, and safety to the environment. However, it was recognised that this option would improve the functioning of the internal market.

5.2.4. Option 9 – Wider scope for the centralised procedure

This option combines the mandatory use of the centralised procedure for innovative medicines, as it is currently the case, and makes this procedure optional to all other types of veterinary medicines. In the public consultation more than 85% of the respondents favoured extending the scope of the centralised procedure. The SMEs/micro-enterprises consulted expressed their support for this proposal, as it introduces flexibility and choice into the system but indicated that they would still be inclined to use more the centralised

[52] The administrative burdens are estimated to be the same those in the option 7 (concerning costs related to the preparation of one dossier to be assessed only once), the only difference between the two options is that in option 7 a Member State is responsible for the assessment of the dossier and in option 8 the assessment is carried out by an EU body. EPEC Report on the assessment of the impact of the revision of pharmaceutical legislation, 2011, p. 170-174.

[53] More than 75% of the respondents consider it necessary that the number of authorisation procedures should be simplified by reducing it to only one. See Annex 9 for public consultation results.

procedure if the procedure is made more SME-friendly, by for example, the introduction of national helpdesks (see Annex 8 for a further discussion on SMEs/micro-enterprises).

It is possible that applications currently submitted through the decentralised and the mutual recognition procedures would shift to the centralised procedure, and overload the EMA. This concern was expressed by the regulators. It is difficult to estimate whether a significant shift would take place, as it would depend on the evaluation of veterinary pharmaceutical companies regarding what would the most appropriate marketing authorisation procedure for their products. This evaluation would be affected by many factors, for example the type of medicine, the way authorities would implement the marketing authorisation procedures and the fees linked to the procedure. To minimise a potentially excessive workload to the EMA and the CVMP from such shift, the handling of submissions for authorisation of well-established medicines such as generics (which require less expertise and assessment) could be fast-tracked. It is expected that the costs to the EMA of taking on new tasks (under this and other options) would be around 1-1,5 million euros per year, which could be covered by a new fee structure and efficiency measures, introduced by, for example, taking into account an increase in applications to the centralised procedure and an optimised use of systems already developed for human medicines.

This option would benefit human and animal health and the environment, as there would be a more consistent assessment across the Union of marketing authorisation applications. It would result in savings in administrative burdens of 5.6 million euros per year[54] to the pharmaceutical industry.

No additional resources would be required for the Commission for the management of marketing authorisations granted by centralised procedure as less resources would be required to manage variations of central marketing authorisations.

5.2.5. Option 10 - Simpler packaging and labelling

This policy option would reduce the costs of product authorisation to the pharmaceutical industry as the costs of language-specific packaging and labelling are high. There would be no significant impact on animal or human health or safety to the environment in terms of information provided on the safe and efficacious use of the product, as any risks associated with the reduction on the information provided in the packaging and labelling would be counterbalanced by placing the information on the product leaflet and by making the information available through other sources (e.g., through compendia, barcodes). The option also offers the possibility for Member States to allow the use of a non-official language on the packaging and labelling of the product if they so wish. The pre-approval of the packaging and labelling layout (but not the text) by the competent authorities would be abolished.

Having the packaging and labelling of a veterinary medicinal product prepared in fewer EU languages would reduce the administrative burden to the industry. It is difficult to quantify this potential benefit in terms of availability of medicines, but it is likely that

[54] The impact of this option on the administrative burdens was calculated taking on board the number of applications for new marketing authorisations, variations to existing authorisations and renewals that would switch from the mutual recognition, decentralised and national procedures to the centralised procedure. The industry was consulted and suggested that the best proxy indicator of demand for this switch would be the number of applications submitted through the mutual recognition and the decentralised procedures that involved at least ten countries. EPEC Report on the assessment of the impact of the revision of pharmaceutical legislation, 2011, p. 167-170.

some Member States considered to be small markets would be the most likely to benefit from this policy change. The relatively high number of products authorised in Belgium and Luxemburg shows the potential of this option. The risk that the package and labelling presented in a non-official language would not be understood by the end users, leading to a safety risk, would be mitigated by the authorities' assessment of the types of products that can be labelled with non-official languages (for example, restricting this to prescription only medicines as most veterinary surgeons can speak one of the major European languages) and the use of standardised abbreviations and symbols.

National authorities agreed with the industry that the reduction of the amount of text on outer packaging could be done without compromising the protection of animal and public health, but considered that no reductions should be made to the text within leaflets, which provide essential safety information.

5.2.6. Option 11 – Allow already nationally approved medicines to freely circulate across the Union

The estimated reduction in administrative burdens that this option would bring is 14.2 million euros per year as the administrative assessment would replace existing and relatively costly mechanisms for extending marketing authorisations to new national markets through mutual recognition[55]. The implementation of this option would also have a positive impact on the functioning of the internal market. Its effect on product availability is likely to be significant and positive, as the range of products available would increase: it is expected that pharmaceutical companies would be more inclined to place their products on smaller markets once the cost of obtaining a marketing authorisation is reduced.

Only medicines with a record of safe use would be extended across the EU, but in practice pharmacovigilance systems vary greatly between countries and may not be able to efficiently detect adverse reactions. Furthermore, a number of older products in some EU markets may have not been assessed for environmental safety in accordance with current standards[56]. Therefore, there is a risk that a purely administrative implementation of the option might have a negative impact on public and animal health, and the environment. To provide assurances regarding the safety of these medicines, it is possible to propose a system to harmonise the existing marketing authorisations to veterinary medicines through a risk-based review. This would allow the scientific assessment of those veterinary medicines that present, by their nature, a higher safety risk to the environment or to public or to animal health (for example, antimicrobials) whilst still allowing the granting of a harmonised marketing authorisation with the widest possible summary of product characteristics. Such review would lead to an increase in the administrative burden to the pharmaceutical industry, the EMA and the national authorities in the short term, but in the long term the administrative burdens would decrease due to the harmonisation of the authorisations. The collaboration between

[55] The impact on administrative burdens was roughly estimated by replacing the annual cost of an application for a new marketing authorisation submitted through mutual recognition with the cost of an administrative assessment (based on the cost of a simple variation). EPEC Report on the assessment of the impact of the revision of pharmaceutical legislation, 2011, p. 189-191.

[56] See Notice to applicants volume 6C Guidance on the assessment of environmental risks of veterinary medicinal products June 2009, p. 5. According to IFAH-Europe all originator products have gone through an environmental risk assessment (ERA) in at least one Member State either at a renewal or at first registration. ERAs have requested for renewals of existing products in several Member States. The level of assessment may have been different over time as guidelines and standards have changed.

pharmaceutical companies to generate data through a monograph to cover missing data (such as environmental risks, for example) identified during the review, could be established to decrease the costs of the review to the industry.

In the interest of the availability of medicines for bees, and considering the nature of these products, it is proposed that any medicines authorised for honey bees in any Member State be administratively recognised across the EU.

5.3. Costs and benefits of options to review data requirements for marketing authorisation procedures

5.3.1. Option 12 - No new EU action

As this option would not imply any change to the provisions already existing in the legislation, costs and benefits are expected to stay identical.

5.3.2. Option 13 – Generic applications may refer to environmental data

The current legislation requires that an environmental risk assessment (ERA) is provided for each new application, including applications for generics. This requirement applies, even if it is logical that the ERA for the generic will reach the same conclusions and outcome as for the originator product. For certain old veterinary medicines on the market, no ERA has been carried out in accordance with the current ERA requirements and this is a potential problem, in particular if these products are used as originator for a new generic application. The CVMP expressed an opinion that the current legal provisions requiring an ERA for each new application for generics is considered not suitable to address the matter, as it leads to the duplication of the generation of data and possibly inconsistencies in conclusions. This committee suggested that a flexible approach could be set up, using a risk-based approach.

The option presented here aims to remove this inconsistency in the legislation, so that ERA will be considered in the same way as any other safety data, and no new ERA data would need to be provided for each generics application. Instead, a system of data sharing between applicants would be implemented so that a report (monograph) could be generated on active ingredients to address environmental risk concerns.
The main beneficiaries of this option would be the manufacturers of generic medicines, for whom the cost of obtaining a marketing authorisation would decrease. This in turn might lead to an increase in the number of generics placed on the market, increasing competition and thus driving down the prices of veterinary medicines (and therefore increasing animal holders' access to medicines). It is expected that there would be no negative impact on the environment, as environmental data are already assessed as part of the safety dossier provided with the application for the reference product and companies would be able to join efforts to carry out supplementary or missing studies for particular ingredients, to cover any deficiencies detected. In addition, it is expected that the national competent authorities would elect to monitor these products more closely through pharmacovigilance. There is no significant impact on the functioning of the internal market.

5.3.3. *Option 14 – Harmonisation of clinical trial procedures across the Union*

This option aims to harmonise the procedures for authorisation of clinical trials for veterinary medicines. It is expected that it would bring a reduction of administrative burdens to the pharmaceutical industry and therefore it would potentially benefit the development of new medicines. This option would particularly benefit SMEs, which requested it.

5.4. Costs and benefits of options to simplify post authorisation procedures

5.4.1. *Option 15 - No new EU action*

As this option would not imply any change to the provisions already existing in the legislation, costs and benefits are expected to stay identical.

5.4.2. *Option 16 – Risk-based pharmacovigilance*

This option aims to introduce a risk-based approach for pharmacovigilance, by for example deleting the requirement of submission of periodic safety update reports (PSUR) for a product. At present the first PSUR is often due before the product has reached the market, having scarce value for the evaluation of the safety of the product. The administrative burden of PSURs is high, while only very rarely the PSURs lead to safety findings. It is considered that the establishment of an electronic reporting system and signal detection are more effective means to monitor suspected adverse events, including environmental incidents and withdrawal period violations, and could ensure that prompt action is taken when needed.
The national authorities agreed that the simplication of pharmacovigilance requirements, in particular regarding PSURs, would allow them to concentrate efforts on areas and products of higher risk, rather than using up resources on routine work. However, the authorities also indicated that a robust pharmacovigilance system is key to protection of human and animal health.

The implementation of this option would bring savings to the pharmaceutical industry worth 47.2 million euros per year, and allow it to focus their resources towards other areas[57]. SMEs/micro-enterprises were specifically consulted on the impact of the pharmacovigilance requirements to their business and indicated that they would welcome a simplification of the current requirements.

5.4.3. *Option 17 – Review of procedures to change a marketing authorisation (variations)*

The introduction of a risk-based approach to deal with changes to a marketing authorisation could reduce administrative burdens to the pharmaceutical industry by 10.9 million euros per year[58]. This option proposes that only changes to the marketing

[57] The calculation of the savings to the industry was based on the fact that this option would involve the abolition of the requirement for a marketing authorisation holder to submit periodic safety updates. EPEC Report on the assessment of the impact of the revision of pharmaceutical legislation, 2011, p. 195-197.
[58] The calculation on the savings to the industry were based on abolishing the requirements to submit Type IA variations, which no longer would be assessed by national authorities - the changes to the marketing authorisation would be implemented by the pharmaceutical company and simply notified to the national authorities. However, a more accurate estimate is not possible as this would depend on the types of

authorisation with an assumed effect on safety of the product would be assessed and approved by the competent authorities. Other changes would be dealt with as notifications. The option would reduce costs and resources to the competent authorities, as there would be fewer variations to be processed and scientifically assessed. No particular effect on the internal market is expected.

5.4.4. Option 18 – Delete the obligation to market a product within 3 years of approval (Sunset clause)

The removal of the Sunset clause from the legislation would benefit the whole pharmaceutical industry, but in particular SMEs/microenterprises which requested this during the consultation. The option would be beneficial to the availability of medicines. No particular effect is expected to occur regarding the functioning of the internal market.

5.4.5. Option 19 – Delete requirements for renewals

This proposal is to abolish the requirement for a renewal for marketing authorisations for veterinary medicines (innovators and generics) with exception of authorisations granted to products when some data have not been presented in the application dossier. This option would deliver significant reduction of annual savings to the pharmaceutical industry (at least 67.5 million euros per year)[59]. It would also reduce costs to competent authorities, which could then focus on the products which really require a renewal assessment. It is expected that the option would not have any significant effect on the operation of the internal market.

5.4.6. Option 20 Exempt homeopathic medicines from pharmacovigilance requirements

This option would deliver a simplification of the current requirements of the legislation regarding homeopathic medicines. However, homeopathic medicines are veterinary medicines and already subject to a simplified registration scheme. Abolishing the requirements to monitor the performance of such medicines might represent a risk to animal health.

5.5. Costs and benefits of options to review incentives for breakthrough medicines

5.5.1. Option 21 - No new EU action

This option implies no changes to the costs or benefits to any stakeholder.

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variations that could be included within the simplification exercise. EPEC Report on the assessment of the impact of the revision of pharmaceutical legislation, 2011, p. 208-209.

[59] Accurate figures for the savings resulting from the adoption of this policy option could not be calculated, as the proportion of the products that might require renewal is unknown. However, representatives of the industry considered that around 95% of the currently authorised products can be considered low risk and so it is possible that only 5 % would need to be renewed. EPEC Report on the assessment of the impact of the revision of pharmaceutical legislation, 2011, p. 199-200.

5.5.2. Option 22 – Extended data protection for new veterinary medicines

This option proposes to keep the initial period of data protection of ten years but extensions to a new species would receive an added period protection of three years, leading to a maximum of twenty years of protection. The option would also create particular provisions for minor species: veterinary medicines authorised for fish and other minor species. Extensions to an initial marketing authorisation to include new species would still be considered as part of the original marketing authorisation.

It is expected that the extension of the data protection period would increase the ability of pharmaceutical companies to recover product development and regulatory costs and make return on investments for novel medicines. The option would therefore benefit innovation and improve the availability of veterinary medicines, in particular for limited markets such as medicines for bees and fish.

This option would benefit primarily research-based pharmaceutical industry and would have some negative impact on generics manufacturers, as it would delay their access to data from originators and so their access to the market. On the other hand, the sustainability of the generic manufacturing industry depends on new medicines being placed on the market. It is clear that a balance is needed between providing incentives for innovation and at the same time allowing the generic industry to enter the market at a point where investments for innovators have been recovered.

The adequacy of the proposed 20 years maximum period of data protection for a product and its extensions is difficult to evaluate, as it depends on many factors such as the size of the investment, the profit margin of a product, the costs of keeping a product on the market, market competition and macro-economic conditions[60]. This issue was discussed in depth during the consultation with representatives of the pharmaceutical industry (both innovators and generics), competent authorities and end users but no specific information was provided. However, it is estimated that on average 37%, 29%, 12%, 8% and 13% of the marketing authorisations would contain one, two, three, four and five species[61]. Therefore, less than 20% of the marketing authorisations would achieve the full 20-years data protection. It can be concluded that for some veterinary medicines the proposed data protection system may be too long (because the cost of the development of the product could be recovered in less time) and for others too short.

5.6. Costs and benefits of options to improve clarity on internet retailing of veterinary medicines, authorisation of new treatments, inspections, authorisation of medicines for emerging diseases

5.6.1. Option 23 - No new EU action

This option does not imply any regulatory changes and therefore costs and benefits are expected to remain the same. Regarding internet retailing of veterinary medicines, if this option is chosen no harmonisation across EU for internet business will be achieved. Rulings of the European Court of Justice oblige Member States to allow internet retailing, and taking into account the different level of implementation of this ruling in

[60] The industry (IFAH-Europe) reported that a break-even point for the initial major product is ten years and the break-even for a major product with an additional minor product is about 15 years.

[61] Data of IFAH-Europe based on estimations of ten companies involving in total of 172 products.

the EU, it is expected that complaints will continue to be submitted to the authorities which will need time and resources to clarify the situation. It is expected that the trend for online shopping of veterinary medicines will continue, and the lack of authorised internet retailers may lead to a higher risk of purchase of substandard veterinary medicines.

5.6.2. Option 24 – Authorisation to sell veterinary medicines through the internet in all Member States

The option would create a harmonised framework for the internet retailing of veterinary medicines in the Union, which would be beneficial for the operation of the internal market for both non-prescription and prescription medicines. During the consultation, a significant proportion of respondents asked for the issue of internet retailing of veterinary medicines to be addressed during the revision of the veterinary medicines legislation. The option received strong support from SMEs.

The option would provide greater accessibility of products throughout the EU, create new business opportunities, increase competition and consequently potentially reduce the prices of veterinary medicines for end-users (both regarding food-producing and companion animals). Affordable prices, in turn, would lead to better treatment compliance and therefore benefit animal and human health.

The implementation of this option would ring-fence legitimate businesses in the Union, as end users would be able to recognise legal internet retailers (those with a logo) from the rogue ones and so be able to make an informed choice when deciding to purchase veterinary medicines in the internet. Member States would also be able to better enforce the legislation, and identify and pursue illegal internet traders.

A monetised quantification of costs and benefits of this option could not be made as the market for internet sales of veterinary medicines is fragmented and there is no detailed information on the number of retailers selling veterinary medicines across the EU. However, there are indications that there is a potential for business growth in this area: for example, since 2005, when on line pharmacies started to develop in a Member State (UK) the sales of veterinary medicines for non-food producing animals grew from 2-5% to 8.6% of the total sales of medicines. Regarding prescription medicines, only 1.4% of these medicines are sold on line (in the UK) although 78% of the overall market revenues are due to prescription only medicines[62]. Considering the difference in prices of medicines between Member States (up to 50%), this suggests that business could grow and potentially benefits end-users such as farmers[63], in particular if prescription medicines are retailed online - the majority of medicines authorised for food producing animals are prescription-only.

The implementation of this policy would lead to some costs to the national authorities which would need to put in place authorisation procedures to regulate the sector. The actual costs of implementing this policy could not be calculated, but the majority of the internet retailers are already authorised as an establishment to wholesale or retail veterinary medicines (veterinary practices, animal health adviser premises or pharmacies) and so it is expected that the costs would only be additional to the current ones. In

[62] MedicAnimal report on online sales of veterinary medicines, 2011.
[63] See Annex 6 for further details.

addition, internet retailing of veterinary medicines has already some form of regulation in at least five Member States (UK, Ireland, Hungary, Sweden, Germany) and therefore some systems and procedure are already in place.

Rulings of the European Court of Justice oblige Member States to allow on-line sales and therefore this policy option would be in line with these rulings. It is expected that the implementation of the option would have no impact on environmental safety.

5.6.3. Option 25 – Establish a framework to authorise new treatments

There are currently differences in approach between Member States on this area. Harmonisation would improve animal health across the Union and the overall operation of the internal market. In the short term, the implementation of this policy option would increase administrative costs to both the pharmaceutical industry and national authorities, which would need to introduce procedures and pay fees for the authorisation of the products. However, some Member States already have guidelines, requirements and procedures in place for this area, and therefore the industry already has costs associated with these products[64].

In the medium to longer term the implementation of this choice could provide regulatory predictability to industry and decrease administrative burden.

5.6.4. Option 26 – Establish a basis to harmonise the controls on the veterinary medicines distribution chain

Enforcement is primarily a role of the Member State's competent authorities, and this option seeks to create a legal tool to allow the Commission to evaluate controls systems applied by Member States on the distribution chain of veterinary medicines. The main benefits of the option would be the creation of a level playing field across the Union regarding the way Member States organise and carry out their control activities, and therefore provide assurances to the general public and competent authorities that harmonised standards are in place for veterinary medicines across the Union. The execution of these controls would remain the competence of Member States. It is expected that some Member States would need to invest in their inspections programmes to improve them and this would incur in costs. No significant impact is expected regarding availability of medicines or administrative burdens, and in principle harmonisation of control systems between countries would be beneficial to the operation of the internal market.

[64] As an example of the current costs to the industry of placing on the market novel treatments, the fees for operation of blood banks in the UK are £2,830 for a first inspection and £ 2,970 for a second inspection. The fees for the operation of a stem cell centre are £3,270. The fees for a variation are £ 305. There are three stem cell centres operating in the UK and one blood bank. Data from 2012.

5.7. Additional policy options to strengthen the veterinary medicines legislation regarding the authorisation and use of veterinary antimicrobials in veterinary medicine

5.7.1. Option 27- No new EU action

This option would maintain the status quo, and therefore there would be no additional costs or benefits. Under this option, the collection of data on the sales and usage of antimicrobials by Member States would continue to be carried out in a voluntary basis through the ESVAC project[65] and so there would be still different systems for the collection of data at national level.

5.7.2. Option 28 – Introduction of legislative measures to allow restrictions to be placed on the authorisation and use of veterinary antimicrobials

This option would introduce legislative requirements to ensure that the potential effects of the authorisation and use of veterinary antimicrobials on development of resistance in humans and animals are specifically assessed during an application for a marketing authorisation (some evaluation of risk of antimicrobial resistance is already included in the assessment process to grant a marketing authorisation to a veterinary antimicrobial). This option would in the medium to long term lead to a reduction in the numbers of referrals to the CVMP, and this would realise some savings to the pharmaceutical industry and the national competent authorities: a total of 42 (out of 66) cases referred for arbitration to the CVMP between 2001 and 2012 were related with concerns regarding veterinary antimicrobials, and the cost of dealing with a referral (regardless of its reason) was roughly estimated as 445,000 euros for the industry and 31,000 euros for a competent national authority. The implementation of this option would also bring clarity to the decision-making process on the authorisation of antimicrobials; this would contribute to a predictable regulatory environment which would be beneficial to the pharmaceutical industry. However, it is expected that the implementation of this option would result in some loss of income regarding the sales of some types of antimicrobials.

The introduction of measures to prohibit or restrict the authorisation and the use of some antimicrobials in veterinary medicines (for example, those reserved for human treatment), including under Cascade, could have a positive impact on the protection of human health. On the other hand, it would have a negative impact on the availability of medicines for both food-producing and companion animals and could have animal health and welfare implications. The magnitude of this impact would depend on the type and number of antimicrobials affected by the measures, and the time period and resources available for animal holders to implement management measures to reduce their dependence on those antimicrobials. Restrictions imposed on the use of the Cascade are likely to affect mainly minor species, for which there are less authorised medicines (including products used in preventative medicine such as vaccines). The implementation of this option might also lead to an increase of illegal usage of antimicrobials, and therefore the competent national authorities would need to focus resources on enforcement activities on this area. The costs to farmers, veterinary surgeons and national

[65] The latest ESVAC report compiled sales of antimicrobials in 19 countries. Sales of veterinary antimicrobial agents in nineteen EU/EEA countries in 2010 (EMA/88728/2012). http://www.ema.europa.eu/docs/en_GB/document_library/Report/2012/10/WC500133532.pdf.

authorities associated with possible restrictions on the use of the Cascade could not be calculated as there are only limited data on the use of the Cascade across the Union.

5.7.3. Option 29 - Measures regarding advertising of veterinary medicines, including antimicrobials

The option aims to clarify that direct-to- consumer advertising of antimicrobials (and also other prescription medicines) is forbidden, while advertising to veterinary surgeons is still allowed. The implementation of this option would be beneficial to public and animal health, as it would diminish the pressure that farmers and companion animal owners are reported to place on veterinary surgeons for the prescription of certain types of "convenient" antimicrobials (for example those which allow a short withdrawal period or are long acting) even if these antimicrobials are not appropriate. However, end-users sometimes benefit from the advertising and marketing materials which are made available to them, when these materials provide information on animal health issues. In this respect, this option could affect in particular farmers who could receive less information on veterinary medicines.

5.7.4. Option 30 - Measures regarding retailing of veterinary antimicrobials

The option proposes to restrict the retailing of veterinary antimicrobials by veterinary surgeons. Certain Member States already implement this option, based on the principle that the retailing of veterinary medicines is not consistent with the independent position of a veterinary surgeon. However, the impact of this policy on the reduction of antimicrobial resistance in humans is not yet clear as there appear to be no clear-cut relationship between this restriction and antimicrobial consumption in Member States. A report prepared for the Dutch[66] government on this issue concluded that a restriction could remove the income incentive for the veterinarian but would not sufficiently strengthen the veterinary surgeon' independence. On the other hand, a French report has been published recently and concluded that financial incentives for veterinarians may affect their prescription with regards to quality (type of medicine prescribed) and quantity (volume of antibiotics prescribed)[67].

The implementation of this option would have a significant, negative impact on veterinary practices, for which the income from selling medicines is often important. In some countries the implementation of this option would require a major change to the supply chain of veterinary medicines, with associated impact on costs to national authorities and retailers. It could also negatively affect access to medicines for farmers in rural areas, who rely on their veterinary surgeons for the purchase of medicines for their animals (although online sales could mitigate this effect). On the basis of current knowledge and evidence, it is not yet completely clear if this option would have a significant positive effect on public health regarding management of antimicrobial resistance. This option would have no significant impact on the single market

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[66] The sales of medicines generates 25% of the profits of veterinary surgeons in Denmark and generates between 30 and 75% of the turnover of veterinary practices in the Netherlands. Berenchot report, What would be the effects of decoupling the prescription and sale of veterinary medicines by veterinarians? 2010. http://www.fve.org/uploads/publications/docs/berenschot%20report_02_2010.pdf.

[67] Encadrement des pratiques commerciales pouvant influencer la prescription des antibiotiques vétérinaires. Rapport de Inspection générales des finances, Inspection générale des affaires sociales et Conseil général de l'agriculture, de l'alimentation et des espaces ruraux, Mai 2013.

5.7.5. Option 31 - Introduction of a legal basis for the compulsory collection of data on the use of antimicrobials

This option proposes to establish a harmonised and compulsory European system for collection of data on the sales and usage of antimicrobials in food-producing animals. It builds upon the current voluntary surveillance programme, ESVAC[68]. The costs of tasks related to this surveillance project vary from country to country and only partial data are available across the EU. For example, Sweden and Hungary estimated the costs for these activities at around 8,200 and 1,500 euros respectively, whereas the Czech Republic estimated that at least 200 000 euros per year are spend on activities related to antimicrobial resistance[69]. Despite these already existing costs, it is expected that the administrative costs to the national authorities would increase with the implementation of his policy, as their systems and procedures would need to be adapted to achieve harmonisation of data collection (type of data and collection systems) on antimicrobials across the EU. The implementation of this proposal would have a positive impact on animal and public health, as it is recognised that the analysis of reliable data on the use of antimicrobials in animals is an essential element for the identification and quantification of the risk of developing and spreading antimicrobial resistance between humans and animals. The option would have no significant impact on safety to the environment or on the functioning of the internal market.

6. COMPARISON OF THE POLICY OPTIONS

A comparison of the policy options against the objectives of the proposal and their impact on stakeholders, and in terms of efficiency, efficacy and coherence[70] with the EU policies, was carried out and is summarised in Annex 11. Based on this evaluation , the preferred options were compiled in a single package (2, 3, 4, 5, 9, 10, 11, 13, 14, 16, 17, 18, 19, 22, 24, 25, 26, 28, 29, 31), designed to improve the availability of veterinary medicines without sacrificing standards to public and animal health and safety to the environment. The measures proposed were developed taking on board the views of the regulatory authorities and scientific experts through consultations, workshops and bilateral meetings.

This package contains options which simplify the regulatory requirements for the authorisation of veterinary medicines and their maintenance on the market (addressing pre and post authorisation procedures). The preferred option for a revised authorisation procedure for veterinary medicines extends the scope of the centralised procedure (option 9), making it optional to all types of veterinary medicines, whilst still maintaining the possibility of national authorisations. This option does not bring the total harmonisation of the authorisation procedure, desired by the pharmaceutical industry, to the same extent that the option to create a single, obligatory route of authorisation for all veterinary

[68] Sales of veterinary antimicrobial agents in 19 EU/EEA countries in 2010 (EMA/88728/2012). http://www.ema.europa.eu/docs/en_GB/document_library/Report/2012/10/WC500133532.pdf.

[69] UK figures = 0.7 million pounds (February 2013). Source: Questionnaire from the European Commission to the CMDv on policy proposals for the revision of the veterinary medicines legislation.

[70] Effectiveness is the extent to which the options achieve the proposed objectives; efficacy is the extent to which the objectives can be achieved at the lowest cost; coherence is the extent the policy options are coherent with the objectives of the EU policies and the extent to which they are likely to limit trade-offs across the economic, social and environmental domains. Impact assessment guidelines.

medicines would. However, the preferred option introduces a level of flexibility to the authorisation system (which is beneficial to the SMEs/micro-enterprises in particular) whilst still allowing the pharmaceutical industry to a) seek an authorisation to place any type of veterinary medicine on the market throughout the Union via the centralised procedure if they so desire or b) seek national authorisations in selected countries if the markets for the product are restricted, due to national animal health status for example. In addition, the measures to simplify the requirements regarding packaging and labelling (option 10), variations procedures (option 17), and pharmacovigilance (option 16) should significantly reduce the administrative burdens to the industry and bring savings for the competent national authorities. The implementation of these measures should take on board the advice from scientific committees, whenever relevant, to ensure that simplification is not achieved at the cost of product safety. It is expected that overall these measures would free resources from the pharmaceutical industry for re-investment in new product development, therefore indirectly having a positive effect on the availability of novel medicines for companion and farmed animals. These measures are in line with the Commission's strategies in simplifying the regulatory environment and reducing administrative burdens in the Union.

The preferred package also introduces measures to extend the period of data protection for veterinary medicines to a maximum of 20 years (option 22), to better protect developments efforts leading to new products. These measures should stimulate innovation and consequently improve the availability of novel veterinary medicines, including antimicrobials and medicines for limited markets such as bees (option 5). Keeping the concept of global marketing authorisation would avoid an excessively long delay in the placing on the market of generics. This would benefit competition and consequently the pricing of veterinary medicines to end-users.

The removal of an inconsistency within the legislation to allow the protection period for safety data to cover environmental data (option 13) would potentially encourage applications for generics. This could improve market competitiveness and bring benefits to animal and public health. It is expected that there would be no negative impact on the environment, as environmental data are already assessed as part of the safety dossier provided with the application for the reference product. As part of the package of preferred options, it will also be possible for companies to join efforts to carry out studies to generate data (option 11), to cover any deficiencies regarding information on safety to the environment that may be detected. In addition, it is expected that the national competent authorities would elect to monitor these products more closely through pharmacovigilance.

The option to introduce a legislative framework to regulate the authorisation of new treatments (option 25) would bring harmonisation to the area and benefit to animal health across the Union. It would also benefit the operation of the internal market and business growth. The options to reduce data requirements for limited markets (option 4), improve the Cascade (option 2) and improve the database for products authorised in the Union (option 3) would benefit in particular animal health and welfare.

The “rolling out” of “legacy products” already authorised in the EU (option 11) would reduce administrative burdens to the pharmaceutical industry in the long term and improve the range of veterinary medicines available across the Union. This would possibly have an effect on the price of medicines in the Union through competition, therefore benefiting farmers and the general public through better animal health. In addition, the introduction of a legislative basis for the regulation of internet retailing

(option 24) would stimulate business growth, and so also provide greater accessibility of medicines to end-users across the Union. The circulation of legal veterinary medicines across borders would be improved, in particular considering the measures proposed to improve the use of the centralised procedure and to facilitate the labelling of veterinary medicinal products. An harmonised regulation of internet retailing across the EU would ring-fence legitimate businesses, allowing end-users to make an informed choice when deciding to buy veterinary medicines online, and facilitating enforcement by Member States against rogue traders. The option could potentially bring benefits to animal and public health.

An improved harmonisation of controls carried out by Member States would benefit consumers and provide further assurance on the quality and safety of veterinary medicines throughout the distribution chain (option 26), improving the trust between competent authorities. It would also help to ensure a level playing field in Member States, regarding enforcement of the legislation.

The package of preferred options also tackles the issue of antimicrobial resistance and introduces provisions to minimise risks to public health arising from the use of antimicrobials in veterinary medicine[71] (option 28). These proposals take on board as much as possible the need to promote the continued availability of effective antimicrobials for use in veterinary medicine but it is recognised that they may affect some sectors, such as the farming sector for example, which relies heavily on the use of antimicrobials as part of normal husbandry. It is difficult to evaluate with certainty how much the options proposed would effectively contribute to minimising the risks of developing antimicrobial resistance. However, it is clear that the prudent and responsible use of antimicrobials in veterinary medicine should be put in place to contribute to the management of antimicrobial resistance in humans[72]. The implementation of the options to harmonise the collection of data on antimicrobial use (option 31) and to incentivise the development of new antimicrobials specific for veterinary medicine should bring at medium and long term more clarity on this area and benefit public and animal health[73]. Clarification on the rules regarding advertising of veterinary medicines (option 29), including antimicrobials, would also support the responsible use of antimicrobials. The option to completely forbid veterinary surgeons from retailing antimicrobials (option 30) was discarded because of the economic impact that this measure would have on veterinarians in rural areas and of the accessibility of medicines to farmers in isolated regions, without solid evidence of benefits to public health.

The Union rules apply to all veterinary medicines, and any safety risks to the target animals, users, consumers and the environment are the same irrespective of the size of the business working on the sector. For this reason it is difficult to create exemptions to specifically benefit SMEs/micro-enterprises. However, most of the proposals selected simplify the regulatory environment and this is beneficial in particular to SMEs/microbusinesses, which often struggle to meet the demands of the current

[71]The OIE developed a list of critically important antimicrobials for veterinary medicine: http://web.oie.int/downld/Antimicrobials/OIE_list_antimicrobials.pdf.

[72] See Annex 6 for detailed information on the problem of antimicrobial resistance.

[73] Action point 7 in the Commission's action plan against the rising threat from antimicrobial resistance refers to the promotion of efforts to analyse the need for new antibiotics into veterinary medicine. To this effect, it recommends the evaluation of the need and possible introduction of incentives that trigger development in veterinary medicines to increase the likelihood that innovations reach the market within the review of the rules on veterinary medicines foreseen in 2013.

legislation on veterinary medicines. Furthermore, particular care was taken during the preparation of the impact assessment to take on board specific concerns raised by SMEs/micro-enterprises during the consultation. Thus the package of preferred options proposes the harmonisation of clinical trials across the Union, the removal of the sunset clause and the introduction of measures to assist these enterprises at national level (such as introduction of helpdesks). The first two measures would also benefit larger pharmaceutical companies but the latter may incur in costs to the national regulatory authorities.

Policy options 4, 5, 9, 10, 11, 14, 16, 17, 19 introduce cost reductions related to administrative burdens to the industry against the baseline. Options 11 and 25 would give rise to a cost increase to the industry in the short term but overall the selected options reduce administrative burdens to the industry. The impact assessment shows that the total estimated savings of all preferred options to the industry would amount to at least 145.4 million euros per year. The reduction, depending on the response of relevant authorities and pharmaceutical companies to the new rules, could be up to 6% of the total sales of veterinary pharmaceuticals. An overall impact on the benefits of the proposed package to industry (including SMEs/micro-enterprises), national competent authorities and end users could not be accurately quantified, but the package delivers a proportionate set of measures to simplify the rules concerning the authorisation, placing on the market, monitoring and use of veterinary medicines whilst introducing legislative tools to manage emerging threats to animal and public health. These changes create a clearer and more predicable regulatory environment for veterinary medicines, conducive to a reduction in the costs of placing a product on the market. This in turn would remove barriers to innovation, and may encourage the authorisation of more (new) products and authorisation in more markets further improving the availability of veterinary medicines in the Union and the functioning of the internal market and competition, with a positive effect on public and animal health. The simplification changes proposed are efficiency measures and do not lower the standards of the veterinary medicines placed on the market in the Union.

Table 3 Effectiveness and efficacy scoring of the preferred policy options

Options	Main trade-offs and synergies between the options	Efficiency	Effectiveness
Option 2	More flexibility on the use of Cascade benefits animal and public health.	++	++
Option 3	Introduces costs to the national competent authorities but improves the level of information on veterinary medicines authorised in the Union to stakeholders, including end users.	++	++
Option 4	Reduces data requirements for veterinary medicines for small markets and so improves the availability of medicines and animal and public health.	++	++
Option 5	Decreases administrative burdens to the industry, and so may improve the availability of medicines for bees.	++	++
Option 9	Introduces more flexibility to the system and improves the functioning of the internal market	++	++
Option 10	Decreases administrative burdens to the industry, and so may improve the availability of medicines in particular in smaller countries	++	++
Option 11	Introduces administrative burdens and costs to authorities in the short term but reduces them in the long term; introduces harmonisation on the placing of the market of veterinary	++	++

	medicines and improves animal and public health.		
Option 13	Removes repeated assessment of data and so reduces administrative burdens. May benefit product availability.	+	+/neutral
Option 14	Introduces more harmonisation to the procedure and may benefit innovation	++	++
Option 16	Introduces a risk-based system of pharmacovigilance; delivers cuts to administrative burdens.	++	++
Option 17	Delivers cuts to administrative burdens.	++	++
Option 18	Supports SMEs/microenterprises and business in general, decreases administrative burdens.	+++	+++
Option 19	Abolish renewals - thus less supervision by national competent authorities - but delivers cuts to administrative burdens.	++	+
Option 20	No new action, relevant to requirements to homeopathic medicines – option does not introduce any regulatory changes.	neutral	neutral
Option 22	Stimulates innovation but delays entry of generics onto the market	+	+
Option 24	Introduces administrative burdens and costs to internet retailers and authorities but introduces harmonisation on the sector; improves competition and pricing of veterinary medicines and so benefits animal and public health.	+	+++
Option 25	Introduces administrative burdens and costs to authorities in the short term but introduces harmonisation on the placing of the market of advanced therapies; improves animal health.	+	++
Option 26	Provides further assurance on the safety of veterinary medicines across the distribution chain, supporting changes that introduce risk-based procedures or reduce amount of data submitted for assessment; ensures a level playing field regarding enforcement across the Union.	+	neutral
Option 28	Introduces some administrative burdens to the industry and authorities but may improve public health; decreases the availability of antimicrobials to animals.	+	+
Option 29	May restrict information to farmers and other health professionals; improve public health.	+	+
Option 31	Introduces some costs to authorities; contributes to better public and animal health regarding antimicrobial resistance	neutral	+

None of the options proposed conflict with EU general policies. They link with specific policy objectives as follows:

- Specific policy objective Expand the market beyond the top four animal species: options 2, 3, 4, 5
- Specific policy objective Simplify authorisation procedures: options 9, 10, 11
- Specific policy objective Review data requirements for marketing authorisation procedures: options 13, 14
- Specific policy objective Simplify post authorisation requirements: options 16, 17, 18, 19

- Specific policy objective Review incentives for breakthrough medicines: option 22

- Specific policy objective Improve clarity: on internet retailing of veterinary medicines, on the authorisation of new treatments, on inspections, on authorisation of veterinary medicines for emerging diseases: options 24, 25, 26, 4

- Specific objective strengthening of the veterinary medicines' regulatory framework regarding the authorisation and use of antimicrobials: options 28, 29, 31

The choice of legal instrument

Analysis of the problems identified with the current legislation on veterinary medicines and the objectives of the proposal, in light of the Articles 14 and 168 (c) TFEU leads to the conclusion that the proposal should take the form of a Regulation. This is the appropriate legal instrument as it sets out clear and detailed rules which will become applicable in a uniform manner and at the same time across the Union. Diverging or incomplete transposition of the provisions of the Directive has led to different levels of public and animal health protection, as reflected in the numbers of referrals to the scientific committees, for example, and created obstacles to the functioning of the internal market. The choice of a Regulation still allows Member States to retain their competence for granting of marketing authorisations, enforcement, authorisation of clinical trials, pharmacovigilance monitoring, authorisation of wholesalers and retailers of veterinary medicines.

7. MONITORING AND EVALUATION

Monitoring and evaluation will be measured against the objectives set out in this impact assessment and the benchmark is the current situation. It is proposed to establish an EU database on marketing authorisation linked to pharmacovigilance and to have a legal basis for collecting data on the use of antimicrobials in all Member States. This will facilitate the collection and analysis of data necessary to evaluate the revision of the legislation. The core indicators and the data collection strategy are highlighted below.

Table 4 Future monitoring and evaluation

Problem	Indicators Objective: to expand market beyond the top four animal species	Data source
Lack of availability of authorised veterinary medicines	Number of new veterinary medicines authorised (for major and minor species, for small and larger markets)	Commission, EMA and the regulatory network
	Numbers of marketing authorisations by animal species	EMA
	Objective: to simplify procedures for obtaining a marketing authorisation in multiple national markets	

	Number of existing products authorised by national procedures "rolled out"	Member States
	Numbers of marketing authorisations by Member States	EMA
	Number of applications submitted by SMEs	EMA, Member States
	Number of complaints	EMA, Member States
	Number of referrals	EMA
	Time and costs of development of a medicine	Animal health industry
	Objective: review data requirements in marketing authorisation procedures	
	Numbers of clinical trials in the EU	EMA, Member States
	Objective: to simplify post authorisation requirements	
	Numbers of variations submitted	Commission, EMA, Member States
	Number of reported adverse events for food-producing animals and companion animals; number of executed pharmacovigilance inspections	EMA
	Percentage of budget spent on defensive R§D to maintain products on the market	Animal health industry
	Objective: to review incentives for breakthrough medicines	
	Ratio of number of marketing authorisations for generics and innovative products	EMA
	Number of extensions to new species	EMA
	Use of the Cascade	Member States
	Objective. Improve clarity: on rules on internet retailing of veterinary medicines, on the authorisation of	

	new treatments, on inspections, on authorisation of medicines for emerging diseases	
	Number of infringements to the veterinary medicines legislation regarding controls on the distribution chain of veterinary medicines	FVO reports
	Number of internet retailers authorised to sell veterinary medicines	Member States

The following is proposed regarding the monitoring of the changes introduced regarding the measures to deal with the problem of antimicrobial resistance:

	Objective: to strengthen the veterinary medicines' regulatory framework regarding the authorisation and use of antimicrobials	
Antimicrobial resistance	Number of specific antimicrobials authorised for veterinary medicines	Commission, EMA and the regulatory network
	Sales of antimicrobials used in veterinary medicines	EMA
	Number of referrals on veterinary antimicrobials	Commission

The legal instrument will contain a review clause concerning the evaluation of the Regulation and the submission of a report to the European Parliament and the Council. The Commission will consult national competent authorities, veterinarian' and farmers' associations, the pharmaceutical industry, SMEs/micro-enterprises, distributors and retailers of veterinary medicines to prepare the review, which should examine whether or not the policies implemented achieve their desired effect, and what are the actual costs and benefits to the sector affected. It is proposed that the review is carried out ten years after implementation, covering in particular the impact of the changes to the legislation on availability of medicines, animal health, public health, environment, internal market and innovation.

8. ANNEXES

Annex 1 Acronyms

ADI	Acceptable daily intake
AMR	Antimicrobial resistance
CMDv	Coordination Group for Mutual Recognition and Decentralised Procedures (veterinary)
CVMP	Committee for Medicinal Products for Veterinary Use
CoE	Council of Europe
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EGGVP	European Group for Generic Veterinary Products
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EMA	European Medicines Agency
IAB	Impact Assessment Board
MA	Marketing Authorisation
NCA	National Competent Authority
PSUR	Periodic Safety Update Report
SME	Small and Medium-sized Enterprise
SPC	Summary of Product Characteristics
TFEU	Treaty on the Functioning of the European Union
VICH	International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products

Annex 2 Glossary

Acceptable Daily Intake
The amount of a residue that is considered safe for a person to ingest daily for a life time (see also MRL).

Cascade
The Cascade is a provision in the veterinary medicines Directive that allows a veterinary surgeon to prescribe medicines in a way that would not otherwise be permitted. The principle of the Cascade is that, if there is no suitable veterinary medicine authorised in the Member State to treat a condition, the veterinary surgeon responsible for the animal may, in particular to avoid causing unacceptable suffering, treat the animal in accordance with the following sequence, in descending order of priority:

- A veterinary medicine authorised in the Member State for use in another animal species or for a different condition in the same species.
- If there is no such product, the next option is either –
  - a medicine authorised in the Member State for human use, or
  - a veterinary medicinal product not authorised in that Member State but authorised in another Member State for use in any animal species for the condition in question or for another condition.
- If there is no such product, the last option is a veterinary medicine prescribed by the veterinary surgeon and prepared extemporaneously by a person authorised to do so under national legislation.

Food producing animals may only be treated under the Cascade with medicines which contain pharmacologically active substances listed in the Table of Allowed Substances of Commission Regulation EU (European Union) No 37/2010, in the interest of food safety. A veterinary surgeon prescribing for, or administering a medicine to, food-producing animals under the Cascade is required to specify an appropriate withdrawal period to the animal produce. Unless the medicine indicates a withdrawal period for the species concerned, this should not be less than 7 days for eggs and milk, 8 days for meat from poultry and mammals and 500 degree days for meat from fish.

CMDv
The Coordination Group for Mutual Recognition and Decentralised Procedures (veterinary) (CMDv) is a group set up for the examination of technical questions and procedures relating to the marketing authorisation of a medicinal product in two or more Member States in accordance with the mutual recognition procedure or the decentralised procedure. This group aims to resolve any divergence that may arise between the Member States in these procedures. The group is composed of one representative per Member State, including Norway, Iceland and Liechtenstein. Observers from the European Commission and accession countries, where applicable, also participate in the meetings.The EMA provides the secretariat of the CMDv.

CVMP
The Committee for Medicinal Products for Veterinary Use (CVMP) is responsible for preparing the Agency's opinions on all scientific questions concerning veterinary medicines, and has a legal basis in Regulation (EC) No 726/2004. This Committee is responsible for conducting the initial assessment of centralised applications for veterinary medicines, and for post-authorisation activities, including the assessment of variations to existing marketing authorisations. The CVMP also arbitrates in cases where there is an unresolved disagreement between Member States concerning an application submitted

through the mutual recognition or decentralised procedure (referrals). Other CVMP's functions are the establishment of maximum residues limits, the provision of scientific advice to the pharmaceutical industry and the preparation of scientific and regulatory guidelines
The CVMP is composed of a chairperson, elected by serving CVMP members, one member and an alternate nominated by each Member State and one member and an alternate nominated by Iceland and by Norway. It may also have up to five co-opted members, chosen among experts nominated by Member States or the Agency and recruited, when necessary, to provide additional expertise in a particular scientific area.

Data protection
This is a period of time during which a veterinary medicine cannot be used as a reference for an application for a generic medicine. The current legislation states that an application for a generic product can be submitted after 8 years of authorisation of the originator product, but the generic product cannot be marketed until 10 years have passed from the initial authorisation of the originator (13 years for products indicated for the treatment of bees and fish).
Veterinary medicines for food production species may benefit from an extra 1 year protection for each extension to a food producing species, if the change is authorised within 5 years following the granting of the initial marketing authorisation. The total maximum protection period is 13 years, for a marketing authorisation for 4 or more food-producing species.
The data protection period should not be confused with patent protection. Patents protect the invention, not the data required for pre-market approval. Patents and data protection may run concurrently and so sometimes the data protection period will expire at the same time as the patent, but this is not always the case.

Generic veterinary medicinal product
A generic is a veterinary medicinal product which has the same active substance as a reference (originator) product and whose bioequivalence with the reference product has been demonstrated. If these conditions are met, a generic applicant for marketing authorisation is exempted from the requirement to prove safety and efficacy through pre-clinical tests and clinical trials, and the competent authority relies on the proof of safety and efficacy provided by the reference product to authorise the product. According to the current legislation, the applicant would need to provide an environmental risk assessment with the application for a generic product and, depending on the type of product, a user risk assessment. The name of the generic medicine and its packaging differs from those of the reference medicine.
There is a legislative basis in the veterinary legislation for hybrid applications for a generic product. Such applications are required when the applicant is not able to demonstrate bioequivalence to the reference product through bioavailability studies, or where bioequivalence can be demonstrated to the reference product, but the applicant desires to present the medicine as a different strength or a different route of administration to the reference product (for example, if the reference product is an oral medicine for cats and the applicant for the generic medicine wants to market the product as an injectable - in this case the applicant can refer to the reference product to cover some of the safety and efficacy data requirements, but needs to produce its own data to support the change in the route of administration). The authorisation of this type of generic product relies in part on the results of data from the reference medicine and in part on new data ("hybrid").

Global market concept

When a medicinal product has been granted an initial marketing authorisation, any additional changes (such as pharmaceutical forms, administration routes) are included in the initial marketing authorisation. All these changes are considered as part of the same global marketing authorisation. So the global marketing authorisation contains the initial authorisation and all variations and extensions thereof, as well as any additional strengths, pharmaceutical form, administration routes or presentations authorised through separate procedures and under a different name, granted to the marketing authorisation holder of the initial authorisation – these developments do not restart or prolong this period and have the same end-point of the data and market exclusivity periods, namely 8 and 10 years after the first marketing authorisation was granted, respectively.

Homeopathic veterinary medicinal product

A homeopathic veterinary medicinal product is defined in the Directive as "Any medicinal product prepared from substances called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in the Member States. A homeopathic medicinal product may contain a number of principles."

Companies wishing to place a homeopathic medicinal product on the market may apply for a marketing authorisation or may take advantage of the simplified registration procedure, which allows the product to be placed on the market with no stated therapeutic indications and where there is sufficient dilution to guarantee the safety of the remedy. Products authorised by national authorities on or before 31 December 1993 have automatic rights to be placed on the market. Homeopathic medicinal products intended for food producing species must comply with the provisions of the legislation on residues limits of pharmacologically actives substances in foodstuffs of animal origin.

Marketing authorisations

The legislation requires that before a medicine can be placed on the market it must be given a marketing authorisation.

There are four routes that applicants can take to obtain a marketing authorisation, and they all involved the assessment by competent authorities of the quality, safety and efficacy data submitted by the pharmaceutical company in accordance with the legislation:

- National procedure

Each EU Member State has its own procedures for the authorisation of medicines that fall outside the scope of the centralised procedure.

- Mutual recognition procedure

In the mutual recognition procedure, a medicine is first authorised in one EU Member State, in accordance with the national procedures of that country. Following this, the marketing authorisation holder can seek further marketing authorisations in other EU countries in a procedure whereby the countries concerned agree to recognise the validity of the original, national marketing authorisation following an assessment process.

- Decentralised procedure

Using the decentralised procedure, companies may apply for simultaneous authorisation in more than one EU country of products that have not yet been authorised in any EU country and that do not fall within the mandatory scope of the centralised procedure.

- Centralised procedure

In the EU a company may submit a single application to the EMA for a marketing authorisation that is valid simultaneously in all EU Member States, plus Iceland, Liechtenstein and Norway. This is called the centralised (or Community) authorisation procedure, and is mandatory for certain types of medicines and optional for others.

For medicines that do not fall within these categories, companies have the option of

submitting an application for a centralised marketing authorisation to the EMA if the product is of significant therapeutic, scientific or technical innovation, or if its authorisation would be in the interest of public or animal health.
Applications through the centralised procedure are submitted directly to the EMA, and the evaluation is carried out by the EMA's CVMP. Once the CVMP adopts an opinion on whether the medicine should be authorised or not, the opinion is transmitted to the European Commission, which has the ultimate authority for granting the marketing authorisation in the EU through a Commission Decision.

Maximum Residue Limits
The maximum residue limit (MRL) is the maximum concentration of residue accepted by the European Union (EU) in foodstuffs obtained from an animal that has received a veterinary medicine or that has been exposed to a biocidal product for use in animal husbandry.
MRLs are determined scientifically. The first step is to identify the No(A)EL (No Observed Adverse Effect Level) of the substance, which is the highest dose that does not cause adverse effects. Then the Acceptable Daily Intake (ADI) is determined. The ADI is estimated by dividing the No(A)EL level by an uncertainty level (100-1000 x) to a allow extrapolation between species and to take into account individual variations between individuals (a margin of safety). The MRL is set out by dividing the ADI between edible tissues and food stuffs such as milk, muscle, liver etc so that a limit level for residue is given to each tissue. The allocation of the ADI takes into account how much a particular food may be eaten every day (the so called "food basket").
The use of animal medicines in food producing species requires observance of the withdrawal period – the time period between the last treatment given to the animal and the time when the level of residues in the tissues (muscle, liver, kidney, skin/fat or products (milk, eggs, honey) is lower than or equal to the MRL. Until the withdrawal period has elapsed, the animal or its products must not be used for human consumption. The withdrawal period for veterinary medicines is listed in the summary of the product characteristics and on the product literature.

Minor use and minor species
There is no legal definition for major or minor species. The CVMP have defined major species based on animal population data and total consumption figures, using global numbers across the European Union:
Major food-producing species are cattle (dairy and meat animals), sheep (meat animals), pigs, chickens (including laying hens) and salmon. Major companion animal species are cats and dogs. All other species are considered to be minor species.
Minor use medicines are those for intended uses in major species for diseases that occur infrequently or in limited geographic areas and in only a small number of animals annually.

Product literature
This term refers to the label, the immediate packaging, the outer packaging and the package leaflet (if there is one) of a veterinary medicine. The immediate packaging is the container or any other form of packaging that is in direct contact with the VMP, e.g. vials, bottles, blister packs, etc. The outer packaging is the packaging into which the immediate packaging is placed, e.g. cartons, boxes, packets, etc. The package leaflet is the leaflet that accompanies the VMP.

Referral

A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. The medicine, or the class of medicines, is 'referred' to the EMA's Committee for Medicinal products for Veterinary Use (CVMP – see above), so that it can make a recommendation for a harmonised position across the European Union. The European Commission then issues a decision to all Member States reflecting the measures they need to take to implement the CVMP recommendation. The types of referrals are (based on Directive 2001/82):

- Article 33- Mutual-recognition and decentralised referral: initiated because of disagreement between Member States within the framework of the mutual-recognition or decentralised procedure.
- Article 34 - Divergent decision referral: initiated in order to obtain harmonisation within the EU of the conditions of authorisation for products already authorised by Member States.
- Article 35 - Community interest referral: initiated in cases involving the interests of the Community or concerns relating to the protection of human or animal health or the environment.
- Article 39 and 40 – Follow up referrals.
- Article 78 referrals - Pharmacovigilance urgent measures: initiated when, as a result of the evaluation of veterinary pharmacovigilance data, a Member State considers that a marketing authorisation should be suspended, withdrawn or varied to restrict the indications or availability, amend the posology, add a contraindication or add a new precautionary measure.

Summary of Product Characteristics
The summary of product characteristics (SPC) is a public document written and updated by pharmaceutical companies and based on the data submitted for product authorisation and approved by the competent authority. It is the basis for the preparation of the product literature.

Sunset clause
The Sunset clause is a legal obligation for all pharmaceutical companies to place a product on the market within three years of its granting.

Variations
Any changes to veterinary medicines authorisations, for example, change in the manufacturing process, change in the packaging or change in the address of the manufacturer.

Withdrawal period
See Maximum Residue Limits.

Annex 3 Information sources

Details of the consultation carried out for the preparation of this impact assessment

A wide public consultation took place from April to July 2010 to seek the views of the pharmaceutical industry representatives, including the generic medicines industry, Member States, animal health professional organisations, farmers, representatives of internet retailers of veterinary medicines, non-governmental institutions and individuals on the legal framework for veterinary medicines. The summary report on the results of this consultation as well as the individual responses was published on line (Annex 9). In addition, an evaluation of the European Medicines Agency concerning veterinary medicines was carried out in 2009 including. The final report was published January 2010.[74]

Between February 2011 and April 2011, qualitative and quantitative data were collected on the impact of the legislation. In-depth consultation with stakeholders (the national competent authorities, the main industry trade association and the main veterinary association) from six countries (Cyprus, Finland, Germany, Poland, Romania and the United Kingdom) took place – these countries were chosen in order to achieve a balance between small and large markets, and 'new' and 'old' Member States. A total of 13 organisations were consulted. Specific consultations were also carried out with three key stakeholders in the veterinary sector: the Federation of Veterinarians of Europe, Copa-Cogeca (representing farmers) and the European Medicines Agency.

A survey listing the policy options was submitted to all national competent authorities in the EU/EEA, IFAH-Europe and the FVE, and disseminated to national member organisations. A total of 31 responses were received (12 from industry representatives and individual companies, 14 from national competent authorities and five responses from end users groups (national veterinarian organisations, FVE and Copa-Cogeca). In addition, a questionnaire was sent to the (Coordination Group for Mutual Recognition and Decentralised Procedure (CMDv) to collect specific information on the costs to the Member States of work carried out on some specific policy areas, such as antimicrobial resistance, pharmacovigilance, authorisations.

An industry workshop was organised in March 2011. This workshop was attended by representatives of IFAH-Europe, the European Group for Generic products, and individuals from 12 animal health businesses, including a mixture of large and small companies, and manufacturers of novel and generic medicines.

On 23 September 2011 the Commission organised a stakeholder meeting to give stakeholders an opportunity to discuss the outcomes of the public consultation and to discuss key subjects. In addition, the Commission consulted the Animal Health Advisory Committee[75] on several occasions.

The consultation was complemented by a series of targeted meetings with smaller groups of experts on pharmacovigilance, antimicrobial resistance, and authorisations/data protection. Another meeting was organised specifically with SMEs and micro-enterprises to identify their specific views and needs.

[74] http://ec.europa.eu/health/files/pharmacos/news/emea_final_report_vfrev2.pdf

[75] http://ec.europa.eu/food/animal/diseases/strategy/animal_health_advisory_committee_en.htm

The review of the legislation on veterinary medicines was discussed at the meetings of the Standing Committee on Veterinary Medicinal Products of 29 May 2009, 8 September 2011, 27 September 2012, and the Veterinary Pharmaceutical Committee of 6 February 2011.

Competent authorities were also consulted as part of the preparation of the report by the European Policy Evaluation Consortium (EPEC) (February 2011 to April 2011). The purpose of this exercise was to collect quantitative and qualitative data, not only from the competent authorities but also from the veterinary medicines industry, farmers and veterinary surgeons, on the sector and on the possible impact of the proposed options.

The use of the 'Cascade' is considered by stakeholders an essential tool to treat or to prevent diseases if there is no authorised veterinary medicine on the market. Therefore, a questionnaire was sent to Member States to obtain specific information from competent authorities on the implementation of the rules and the use of the 'Cascade' (March 2011). A questionnaire was also sent to Member States' competent authorities aiming to collect information on their administrative burdens (September 2012).

List of consultations, communications, legislation, studies, workshops and other literature relevant to this impact assessment

Policy documents

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http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2006:0691:FIN:EN:PDF.

(2) COM (2007), 0023 final. Communication from the Commission to the Council, the European Parliament, the European Economic and Social committee and the committee of the regions – Action programme for Reducing Administrative Burdens in the European Union.

(3) COM (2008), 394 final. Communication from the Commission to the Council, the European Parliament, the European Economic and social Committee and the committee of the Regions “Think Small First” - A “Small Business Act” for Europe.

http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0394:FIN:en:PDF.

(4) Council (2008), Council conclusion of 10 June 2008 on antimicrobial resistance. http://www.eu2008.si/en/News_and_Documents/Council_Conclusions/June/0609_EPSCO-AMR.pdf.

(5) COM (2008), 912 final. Communication from the Commission to the European Parliament pursuant to the second subparagraph of Article 251(2) of the EC Treaty concerning the common position of the Council laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin, and repealing Regulation (EEC)No 21377/90. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0912:FIN:EN:HTML.

(6) COM (2007), 539 final and COM (2008), 545 final respectively. The Animal Health Strategy for the European Union 2007-2013 "Prevention is better than cure" and it's implementing Action Plan.

http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2007:0539:FIN:EN:PDF; and http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0545:FIN:EN:PDF.

(7) COM (2009), 162 final. Communication from the Commission to the European Parliament and the Council: Building a sustainable future for aquaculture, a new impetus for the strategy for the sustainable development of European aquaculture.

http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2009:0162:FIN:EN:PDF

(8) Council (2009), Council conclusions of 23 November 2009 on innovative incentives for effective antibiotics. http://register.consilium.europa.eu/pdf/en/09/st16/st16006.en09.pdf.

(9) Final report. Measurement data and analysis. Pharmaceuticals legislation priority Area. EU project on baseline and reduction of administrative costs. 5 March 2009.

(10) COM (2010), 714 final. Communication from the Commission to the European Parliament and the Council on Honeybee Health.
http://ec.europa.eu/food/animal/liveanimals/bees/docs/honeybee_health_communication_en.pdf.

(11) COM (2010) 245, final. Communication from the Commission to the Council, the European Parliament, the European Economic and Social Committee and the Committee of the Regions – a Digital Agenda for Europe.

http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2012:0009:FIN:EN:PDF

(12) COM (2011), Commission recommendation of 14 January 2011 establishing guidelines for the distinction between feed materials, feed additives, biocidal products and veterinary medicinal products (2011/25/EU).

(13) European Parliament (2011), European Parliament Resolution of 12 May 2011 on antibiotic resistance http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+TA+P7-TA-2011-0238+0+DOC+XML+V0//EN.

(14) European Parliament (2011), B7 0538/2011: European Parliament resolution of 27 October 2011 on the public health threat of antimicrobial resistance.
http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+TA+P7-TA-2011-0473+0+DOC+XML+V0//EN.

(15) COM (2011), European Commission Communication of 15 November 2011 to the European Parliament and the Council - Action plan against the rising threats from antimicrobial resistance http://ec.europa.eu/dgs/health_consumer/docs/communication_amr_2011_748_en.pdf.

(16) COM (2011), 777 final. Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions - Commission Work Programme 2012, Delivering European renewal
http://ec.europa.eu/atwork/programmes/docs/cwp2012_en.pdf.

(17) European Parliament (2011), European Parliament resolution of 15 November 2011 on honeybee health and the challenges of the beekeeping sector.

http://www.europarl.europa.eu/sides/getDoc.do?type=TA&reference=P7-TA-2011-0493&language=EN.

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http://www.consilium.europa.eu/uedocs/cms_data/docs/pressdata/en/agricult/122023.pdf

(19) Council (2012), Council conclusions on the impact of antimicrobial resistance in the human health sector and in the veterinary sector – a "One Health" perspective.
http://www.consilium.europa.eu/uedocs/cms_data/docs/pressdata/en/lsa/131126.pdf.

(20) COM (2012), 629 final. Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions, Commission Work Programme. http://ec.europa.eu/atwork/pdf/cwp2013_annex_en.pdf.

(21) European strategy for smart, sustainable and inclusive growth (Europe 2020). ftp://ftp.cordis.europa.eu/pub/etp/docs/europe2020_en.pdf.

(22) 2012 - Motion for a Parliamentary resolution on the microbial challenge – Rising threats from antimicrobials (2012)

Binding legislation

(1) Council (1990), Directive of 26 March 1990 laying down the conditions governing the preparation, placing on the market and use of medicated feedingstuffs in the community. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31990L0167:EN:HTML.

(2) COM (1991), Commission Directive of 23 July 1991 laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products. http://ec.europa.eu/health/files/eudralex/vol-5/dir_1991_412/dir_1991_412_en.pdf.

(3) Directive 2001/82/EC of the European Parliament and of the Council on the Community code relating to veterinary medicinal products came into force on 18 December 2001. http://faolex.fao.org/docs/pdf/eur36747.pdf.

(4) Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32004R0726:EN:NOT

(5) Commission Directive 2006/130/EC of 11 December 2006 implementing Directive 2001/82/EC of the European Parliament and of the Council as regards the establishment of criteria for exempting certain veterinary medicinal products for food-producing animals from the requirements of a veterinary prescription. http://ec.europa.eu/health/files/eudralex/vol-5/dir_2006_130/dir_2006_130_en.pdf.

(6) Commission Regulation (EC) No 1950/2006 of 13 December 2006 establishing, in accordance with Directive 2001/82/EC of the European Parliament and of the Council on the Community code relating to veterinary medicinal products, a list of substances essential for the treatment of equidae. http://ec.europa.eu/health/files/eudralex/vol-5/reg_2006_1950/reg_2006_1950_en.pdf.

(7) Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marking authorisations for medicinal products for human and veterinary medicinal products. http://ec.europa.eu/health/files/eudralex/vol-1/reg_2008_1234/reg_2008_1234_en.pdf.

(8) Commission Regulation (EC) No 470/2009 of the European Parliament and of the Council of 6 May 2009 laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin, repealing Council Regulation (EEC) No 2377/90 and amending Directive 2001/82/EC of the European Parliament and of the Council and Regulation (EC) No 726/2004 of the European Parliament and the Council. http://ec.europa.eu/health/files/eudralex/vol-5/reg_2009-470/reg_470_2009_en.pdf.

(9) Commission Regulation (EC) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin. http://ec.europa.eu/health/files/eudralex/vol-5/reg_2010_37/reg_2010_37_en.pdf.

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(3) Business Decisions Limited (2007), Benchmarking the competitiveness of the European animal health industry, a report by Business Decisions Limited for IFAH Europe.

(4) WHO (2007), Critically important antimicrobials for human medicine. Report of the second WHO expert meeting, Copenhagen, 29-31 May 2007.
http://www.who.int/foodborne_disease/resistance/antimicrobials_human.pdf;

2nd revision (2009): http://www.who.int/foodborne_disease/resistance/cia/en/.

(5) OIE List of antimicrobials of veterinary importance (2007): http://web.oie.int/downld/Antimicrobials/OIE_list_antimicrobials.pdf

(6) Agence Française de Sécurité Sanitaire des Aliments (2008), Conference of 30 September 2008 on Legislation on veterinary medicinal products: improvement opportunities.

(7) EGGVP (2008), Position paper of EGGVP on the review of legislation, December 2008.

(8) ECDC/EMA (2009), ECDC/EMA joint technical report – the bacterial challenge, time to react, 2009. http://www.ema.europa.eu/docs/en_GB/document_library/Report/2009/11/WC500008770.pdf

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Committee for Medicinal Products for Veterinary Use. http://www.efsa.europa.eu/it/efsajournal/doc/1372.pdf

(10) CVMP (2010), CVMP Strategy on antimicrobials 2011-2015. http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/01/WC500100649.pdf

(11) Summary of the responses to the public consultation (April-July 2010). http://ec.europa.eu/health/veterinary-use/pubcons_frame_index_en.htm.

(12) EMA (2011), Outcome of SME office survey on the implementation of the SME regulation – Commission Regulation (EC) no 2049/2005 – 19/12/2011.http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/12/WC500119946.pdf.

(13) SME Initiative (2011), Report on the SME Initiative 2006-2011. http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/12/WC500119970.pdf.

(14) EMA (2011), European Medicines Agency roundtable with small and medium-sized enterprise (SME) stakeholder organisations, 19/12/2011. http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/12/WC500119945.pdf.

(15) Transatlantic taskforce on antimicrobial resistance (2011), Report, 2011. http://ecdc.europa.eu/en/activities/diseaseprogrammes/TATFAR/Documents/210911_TATFAR_Report.pdf.

(16) Scientific Opinion on the public health risks of bacterial strains producing extended-spectrum β-lactamases and/or AmpC β-lactamases in food and food-producing animals. EFSA Journal, 2011, 9 (8): 2322. http://www.efsa.europa.eu/en/efsajournal/pub/2322.htm.

(17) Report of the response of Member States and EFTA countries to the questionnaire on the use of legal provisions of Directive 2001/82 as amended, which are intended to improve availability of veterinary medicines. 4 April 2011. http://www.hma.eu/fileadmin/dateien/Veterinary_medicines/00-HMA_Vet/02-HMA_Task_Force/02_Availability/2011_04_TF_Legislation_Report_of_MS_Responses.pdf.

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(19) EMA (2012), Sales of veterinary antimicrobial agents in 19 EU/EEA countries in 2010 (EMA/88728/2012).
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(20) Report from the Task Force on Zoonoses Data Collection including guidance for harmonized monitoring and reporting of antimicrobial resistance in commensal Escherichia coli and Enterococcus spp. from food animals http://www.efsa.europa.eu/en/efsajournal/pub/141r.htm

(21) IFAH-Europe Impact assessment data package report. http://www.ifaheurope.org/upl/4/default/doc/IA%20data%20pack.pdf.

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(1) Questionnaire on the activities of competent authorities related to the Directive 2001/82.

(2) GHK Consulting (2011), Study conducted by GHK Consulting on behalf of the Commission to assess the impact of the revision of Directive 2001/82- EPEC Report Assessment of the impact of the revision of veterinary pharmaceutical legislation, July 2011. http://ec.europa.eu/health/files/veterinary/11-07-2011_final_report_.pdf.

(3) Questionnaire directed to Member States regarding specifically the use of the prescribing cascade in veterinary medicine. 2011

(4) Questionnaire directed to the CMDV on specific points regarding the revision of the veterinary medicines legislation (internet, novel technologies, pharmacovigilance, antimicrobial resistance, borderline products). 2012

Discussions, workshops, conferences (major events from which feedback could be collected on issues related to the revision of the Directive):

Event	Participants
Targeted in depth-consultation	FVE, Copa-Cogeca, EMA
Industry workshop	Large and small pharmaceutical companies representatives
IFAH Europe/EMA Global Animal Health Conference on availability of medicines	EU and Third Countries pharmaceutical industry, regulators, veterinarians (8-9/3/11)
Stakeholders' consultation meeting	Pharmaceutical industry, Member States, EMA (23/9/11)
Veterinary Pharmaceutical Committee	Member States, EMA (6/2/ 2012)
Targeted Workshop_ Pharmacovigilance	pharmaceutical industry, Member States, veterinarians, EMA (29/5/12)
Targeted Workshop-Antimicrobial Resistance	pharmaceutical industry, Member States, veterinarians, academics, Copa-Cogeca, EMA (8/6/12)
Targeted Workshop-Authorisations/data protection	pharmaceutical industry, SMEs, Member States, EMA (22/6/12)
Targeted workshop - SMEs	SMEs, Member States, EMA, veterinarians
Workshop on bees	Member States, EMA, veterinarians, bee keeping organisations (14-15 December 2009)

List of legislation related to veterinary medicines

- Commission Directive of 23 July 1991 laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products.

- Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety.

- Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition.

- Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.

- Regulation (EC) No 882/2004 of the European Parliament and the Council of 29 April 2004 on official controls performed to ensure the verification of compliance with feed and food law, animal health and animal welfare rules.

- Commission Directive 2006/130/EC of 11 December 2006 implementing Directive 2001/82/EC of the European Parliament and of the Council as regards the establishment of criteria for exempting certain veterinary medicinal products for food-producing animals from the requirements of a veterinary prescription.

- Commission Regulation (EU) No 122/2013 of 12 February 2013 amending Regulation (EC) No 1950/2006 establishing, in accordance with Directive 2001/82/EC of the European Parliament and of the Council on the Community code relating to veterinary medicinal products, a list of substances essential for the treatment of equidae.

- Commission Regulation (EC) No 658/2007 of 14 June 2007 concerning financial penalties for infringement of certain obligations in connection with marketing authorisations granted under Regulation (EC) No 726/2004 of the European Parliament and of the Council.

- Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marking authorisations for medicinal products for human and veterinary medicinal products.

- Regulation (EC) No 470/2009 of the European Parliament and of the Council of 6 May 2009 laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin, repealing Council Regulation (EEC) No 2377/90 and amending Directive 2001/82/EC of the European Parliament and of the Council and Regulation (EC) No 726/2004 of the European Parliament and the Council.

- Commission Regulation (EC) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin.

- Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 of the protection of animals used for scientific purposes.

- At the time of writing the Commission is working on a new EU Animal Health Law, which aims to create a regulatory framework for animal health in the EU. There are interrelated areas of policy between this legislation and the veterinary medicines Directive, in particular regarding animal disease and animal welfare, which were taken on board when preparing this impact assessment.

Annex 4 Background information on the veterinary sector

(a) The farming sector

Two fifths (an estimated 40.1 %) of the total land area of the EU-27 is farmed (2007). This proportion rises to two thirds (an estimated 66.3 %) of the land area of the United Kingdom, but is less than one tenth of the total in Sweden and Finland. Arable land (which includes cereals and other arable land) accounts for a little less than one quarter (24.2 %) of the total land area of the EU-27, with permanent grassland (which is composed of pasture, meadow and rough grazing) accounting for 13.2 %. During the ten years through until 2007, the make-up of land use in the EU-27 did not change substantially.

There were 7.3 million commercial agricultural holdings in the EU-27 in 2007, with a further 6.4 million small holdings (those below a threshold of one European size unit (ESU)). Almost half (48 %) of the small holdings in the EU-27, mainly classified as subsistence holdings, were found in Romania. A little over one third of the EU-27's commercial agricultural holdings greater than one ESU is located in Poland (15.4 %) and Italy (18.9 %), while Spain (12.9 %), Romania (11.9 %) and Greece (9.7 %) also contribute with about a third of the total commercial holdings as recorded in 2007.

Among most Member States and across the EU-27 as a whole, there has been a steady decline in the number of agricultural holdings during the period between 2003 and 2007. In this four-year period, the number of agricultural holdings in the EU-27 declined by 1.3 million (or 8.8 %), of which almost half were commercial holdings. There were particularly fast structural changes in Estonia, where the number of holdings declined by more than one third (-36.7 %), as well as in Bulgaria (-25.9 %), Portugal (-23.4 %) and Hungary (-19.0 %).

In 2007, the total farm labour force in the EU-27 was the equivalent of 11.7 million full-time workers, of which 9.0 million worked on commercial holdings. Agriculture remains a family-oriented activity in the majority of Member States; almost four fifths (78 %) of the total agricultural labour force were farm holders or members of their family. The main exceptions were Slovakia (44 %) and the Czech Republic (27 %), where there is a different ownership structure compared with the majority of Member States. Just over one third (34 %) of the regular agricultural labour force in the EU-27 was female, although in the Baltic Member States this share was closer to half, reaching 50 % in Latvia. There were relatively few (6.1 %) agricultural holders in the EU-27 under the age of 35 years, but a relatively large proportion (34.1 %) were aged 65 years or over.

Besides agricultural activity, other gainful activities were also conducted in the EU farms. These activities, carried out on the holding itself (camp sites, accommodation for tourists, etc.) or that use its resources (machinery, etc.) or products (such as processing farm products, renewable energy production), have an economic impact on and are carried out by the holder, his/her family members, or one or more partners on a group holding. Gainful activities were conducted in about one in every ten (9.9 %) of the EU's agricultural holdings in 2007, this proportion being slightly higher (13.5 %) among commercial holdings.

In 2007, the total livestock population in the EU-27 amounted to 136 million livestock units (LSUs), of which cattle represented 47.7 %, followed by pigs (27.6 %), poultry

(13.8 %) and sheep (7.6 %). In 2007, cattle were particularly dominant in Luxembourg (85.0 %) and Ireland (81.0 %), and a majority of the livestock population (in LSUs) were composed of cattle in 13 of the Member States. In one MS (Denmark), pigs represented 70.6 % of the total livestock population although pigs were the largest category of livestock in four other Member States (Cyprus, Hungary, Spain and Malta).

There is some evidence that the number of livestock in Europe is decreasing, with a more noticeable declined in cattle although there is some stabilisation of the swine population.

Table 5 Cattle and swine population in the EU (in thousands)

	2005		2008		2009	
	Cattle	Swine	Cattle	Swine	Cattle	Swine
EU (15 Member States)	76,210	122,235	75,536	122,994	75,207	122,897
Germany	12,919	26,989	12,988	26,719	12,897	26,841
France	18,930	15,123	19,366	14,796	19,199	14,552
United Kingdom	10,545	4,726	9,910	4,550	9,901	4,601

The principal meat produce in the EU 27 is pig meat (21.3 million tonnes produced) and beef/veal production (7.7 Million tonnes). In comparison, sheep meat production is small (0.7 million tonnes).

A quarter (24.7 %) of the EU-27's pig meat production is from Germany, the next highest contributions coming from Spain (15.5 %) and France (9.4 %), while 7.6 % is produced by Poland and 7.4 % by Denmark. A little under one fifth (19.0 %) of the beef/ veal produced in the EU-27 originated from France in 2009. Ireland reported a relatively high share of the EU-27's production of cattle meat.

Dairy production has a diverse structure across the Member States, in terms of farm and dairy herd sizes, as well as milk yields. The total collection of cows' milk in the EU-27 in 2009 amounted to 133.5 million tonnes. Germany recorded the highest share (21.1 %) of EU-27 milk collected in 2009 and also accounted for the highest proportions of EU-27 butter (25.2 %) and cheese (22.8 %) production.

Aquaculture is the farming of aquatic organisms including fish, molluscs, crustaceans and aquatic plants. Farming implies some form of intervention in the rearing process to enhance production, such as regular stocking, feeding and protection from predators. Farming also implies individual or corporate ownership of, or rights resulting from contractual arrangements to, the stock being cultivated. The level of aquaculture production in the EU-27 remained relatively stable between 1.2 million tonnes and 1.4 million tonnes during the period 1998 to 2007. The five largest aquaculture producers among the EU Member States were Spain, France, Italy, the United Kingdom and Greece, which together accounted for around three quarters of total aquaculture production in 2007. Aquaculture production was extremely large in Norway – higher than the combined output of the three largest Member States. The development of aquaculture production between 1998 and 2007 followed different patterns across the EU Member States. Production in the Netherlands more than halved and there were also large percentage reductions in aquaculture output in Germany and Denmark, whereas, among the larger producers, aquaculture output rose by 90 % in Greece.

Source: Eurostat yearbook 2011

http://epp.eurostat.ec.europa.eu/cache/ITY_OFFPUB/CH_08_2011/EN/CH_08_2011-EN.PDF

(b) The companion animal sector

Around 70 million European households own at least 1 pet. The pet population is distributed as follows (2010):

Table 6 Pet population in the EU

Species	**Population**	**Largest populations in:**
Cats	64 448 500	France (11 M); Germany (8.2 M)
Dogs	60 226 400	UK (8 M); France (7.6 M)
Birds	39 215 000	Italy (13 M); France (6 M)
Small mammals	24 614 000	Germany (5.3 M); Spain (3.8 M)
Aquaria	8 272 000	Germany (2 M); UK and Italy (1.5 M)

There is evidence that the dog and cat population in the EU is increasing, at least in some Member States:

Table 7 Population of cats and dogs (millions) in some Member States[76]

Member State	Dogs		Cats	
	2009	2010	2009	2010
Germany	5,300	5,400	7,900	8,200
France	7,800	7,570	10,700	11,480
United Kingdom	7,300	8,024	7,200	10,490

There are approximately 200.000 veterinarians in Europe, and an estimated 60.000 pet specialist stores.

The estimated annual value of pet related services, including those offered by breeders, groomers, dog trainers, and veterinarians and related to sales of pet accessories, insurances, medication, vaccination is around 10.5 billion euros.

There are no definitive statistics on the equine sector, but it is estimated that there are around 6 million horses in Europe, and that the total impact of equine activities are around 100 billion euros a year. This takes into account the direct economic impact of all horse industry activities (breeding, industrial companies and services linked to horses, education, research etc) and also the indirect and induced impact of horse activities such as organisation of events and betting (30 billion euros/year).

It is estimated that the equine sector in Europe represents around 400 000 full time jobs equivalent. There are some economic clusters of horse businesses in EU regions, such as those in Basse-Normandie in France, Kecskemét, Hungary and Newmarket in the UK,

[76] Vetoquinol Annual Financial report 2010

where around a third of the jobs are related to the horseracing industry. The yearling sales alone in Deauville in August 2010 have generated 26 million euros.

Sources:

- The European Pet Food Industry Facts and Figures Report, 2010

http://www.fediaf.org/facts-figures/

- The European Horse Network

http://www.europeanhorsenetwork.eu/index.php?page=horse-industry-in-europe

- The Federation of Veterinarians of Europe

http://www.fve.org/about_fve/index.php

- Eurostat

(c) The veterinary pharmaceutical sector

The veterinary pharmaceutical sector is formed by businesses acting in the areas of Research and Development, manufacture of veterinary medicines (originators and generics), importation of medicines, wholesaling and retailing. The veterinary pharmaceutical industry responsible for developing and placing on the market veterinary medicinal products is largely composed by stand alone, self-funding subsidiaries of larger human companies and independent specialist companies. It creates around 50,000 direct jobs in Europe. The consensus is that there are strong growth opportunities for development of veterinary medicines for food producing species outside Europe (USA, China, India, Russia and Brazil), as the growth is driven by the world's demands for milk, meat and eggs. The prospects for the companion animal sector are linked with the general economic performance of a country, and it is expected that emerging markets will also offer opportunities for growth in this sector[77]. Therefore, it is likely that corporate strategic decisions will be strongly influenced by market forces and regulatory approaches existing outside the EU.

A rough estimate from the industry and analysis of Member States' databases suggests there are around 108 manufacturers of veterinary medicines in Europe. Data collected for the assessment of the impact of the revision of veterinary pharmaceutical legislation suggest that the animal health industry in Europe consists of a small number of companies that hold marketing authorisations in multiple national markets, and a larger number of companies that only hold marketing authorisations on one national market. The former group includes high-profile large multinational pharmaceutical companies, which typically hold large numbers of marketing authorisations. Companies that are present on one national market make up the majority of the animal health sector in terms of the number of companies, but the minority in terms of its share of total EU-wide marketing authorisations. These companies in average each hold six marketing authorisations. Of the 463 companies that held a marketing authorisation as at of May 2010, 101 companies (22% of the total) held a single marketing authorisation on a single national market.

In 2009, the global sales of veterinary medicines were estimated at approximately 13.4 billion euros. The sales in the European market were estimated at around 4.6 billion euros (at 2005 prices). Between 2005 and 2008 the size of the European market increased by 23 % compared to an increase of 18 % globally but dropped back to its 2007 levels in

[77] Benchmarking the Competitiveness of the Global Animal Health Industry report, 2011, p. 31.

2009. The animal pharmaceutical industry is estimated to be around 2.4 % of the size of the human pharmaceutical industry. The total sector sales for veterinary medicines in 2008 were estimated to be 4.3 billion euros.

In 2004 generic products had a share of 45% of the total global sales of animal health products. Generic animal health products are very prevalent in Latin American, African and Asian countries with a market share of two thirds or more. In North America and the EU the share is approximately one third. It is expected that generics will become a more dominant factor in the future. This is confirmed by the EU data on MRP/DCP procedures showing that most procedures concern generic products.

Eurostat data indicate that in 2007 a total of 606,500 people were employed in the pharmaceutical manufacturing industry in Europe. As the animal pharmaceutical industry is estimated to be 2.4% of the human pharmaceutical industry, this suggests that around 14,600 people are directly employed by the veterinary medicinal products manufacturing industry in Europe.

Sources:

- EPEC Assessment of the impact of the revision of veterinary pharmaceutical legislation report, 2011
- IFAH-Europe Impact assessment data package report, 2010
- Research and Markets, Generics in the Animal Health Industry.

Annex 5 Overview of the institutional landscape and of the regulatory framework for veterinary medicines

Overview of the marketing authorisation procedures

The legislation requires that before a veterinary medicine may be placed on the market it must have been granted a marketing authorisation. There are four routes that applicants can take to obtain a marketing authorisation, and they require assessment by competent authorities of the quality, safety and efficacy data submitted by the pharmaceutical company in accordance with the legislation:

Centralised procedure

In the EU a company may submit a single application to the EMA for a marketing authorisation valid simultaneously in all EU Member States, plus Iceland, Liechtenstein and Norway. This centralised (or Community) authorisation procedure is mandatory for certain types of medicines and optional for others.
The centralised procedure is compulsory for veterinary medicines that are for use as growth or yield enhancers and medicines derived from biotechnology processes,. For medicines that do not fall within these categories, companies have the option of submitting an application for a centralised marketing authorisation to the EMA if the product is of significant therapeutic, scientific or technical innovation, or if its authorisation would be in the interest of public or animal health at community level. Applications through the centralised procedure are submitted directly to the EMA, and the evaluation is carried out by the EMA's CVMP, a board of Member States' experts chosen by their qualifications and expertise regarding evaluation of veterinary medicines. Once the CVMP adopts an opinion on whether the medicine should be authorised or not, the opinion is transmitted to the European Commission, which has the ultimate authority for granting the marketing authorisation in the EU through a Commission Decision.
A detailed description of the centralised procedure can be found in the guidance Notice to Applicants, Veterinary Medicinal Products, Volume 6A, Procedures for Marketing Authorisations, chapter 4 – Centralised procedure:
http://ec.europa.eu/health/files/eudralex/vol-6/a/vol6a_chap4_2006_05_en.pdf

Mutual recognition procedure

In the mutual recognition procedure, a medicine is initially authorised in one EU Member State in accordance with the national procedures of that country. Following this, the marketing authorisation holder can seek further marketing authorisations in other EU countries in a procedure whereby the countries concerned agree to recognise (following assessment of an application dossier) the validity of the original, national marketing authorisation.
A detailed description of the mutual procedure can be found in the guidance Notice to Applicants, Veterinary Medicinal Products, Volume 6A, Procedures for Marketing Authorisations, chapter 2 – Mutual Recognition and Decentralised procedures: http://ec.europa.eu/health/files/eudralex/vol-6/a/vol6a_chap2_2005-11_en.pdf.

Decentralised procedure

Using the decentralised procedure, companies may apply for simultaneous authorisation in more than one EU country of products that have not yet been authorised in any EU country and that do not fall within the mandatory scope of the centralised procedure.
A detailed description of the decentralised procedure can be found in the guidance Notice to Applicants, Veterinary Medicinal Products, Volume 6A, Procedures for Marketing Authorisations, chapter 2 – Mutual Recognition and Decentralised procedures: http://ec.europa.eu/health/files/eudralex/vol-6/a/vol6a_chap2_2005-11_en.pdf.

National procedure

Each EU Member State has its own procedures and timelines for the authorisation of medicines through a national procedure. Currently a marketing authorisation issued in one Member State through the national procedure is valid only in that Member State. To place the product on the market in other Member States the marketing authorisation holder has to submit an application to the desired countries through the mutual recognition procedure with a dossier for assessment. Each national competent authority will assess the dossier and approve the contents of the summary of product characteristics and product literature.

Description of the steps involved in each procedure:

Centralised procedure

Day 1 Start of the procedure

Day 70 Rapporteur's assessment report sent to the Co-rapporteur, CVMP members and EMA Secretariat.

Day 85 Co-rapporteur's critique of the Rapporteur's assessment report sent to Rapporteur, CVMP members and EMA Secretariat. The Rapporteur's assessment report and the Co-Rapporteur's critique are sent to the applicant by the EMA Secretariat

Day 100 Rapporteur, Co-rapporteur, other CVMP members and EMA receive comments from Members of the CVMP. Between Day 70 and Day 100, a quality check on the English version of the Product Information is carried out.

Day 115 Receipt of draft list of questions (including overall conclusions and overview of the scientific data) from Rapporteur and Co-Rapporteur by CVMP members and EMA.

Day 120 CVMP adopts the list of questions as well as the overall conclusions and review of the scientific data to be sent to the applicant by the EMA. Clock stop. At the latest by Day 120, adoption by CVMP of request for GMP inspection, if necessary (the inspection procedure starts).

Day 121 Submission of the responses, including revised summary of product characteristics, labelling and package leaflet text in English and restart of the clock. After receipt of the responses, the project manager will prepare a revised timetable in consultation with Rapporteur and Co-Rapporteur for the evaluation of the responses. In general the following standard timetable will apply:

Day 160 Joint response assessment report from Rapporteur and Co-Rapporteur received by CVMP members and EMA. EMA sends joint response assessment report to the applicant, making it clear that it only sets out their preliminary conclusions and that it is sent for information only and does not yet represent the position of the CVMP. Where applicable, inspection to be carried out.

Day 170 Deadline for comments from CVMP Members to be sent to Rapporteur and Co-Rapporteur, EMA and other CVMP members.

Day 180 CVMP discussion of the draft opinion (summary of product characteristics, labelling and package leaflet) and decision taken on the need for an oral explanation by the applicant. If oral explanation is needed, the clock is stopped to allow the applicant to prepare the oral explanation. Submission of final inspection report to EMA, Rapporteur and Co-Rapporteur by the inspections team (at the latest by day 180).

Day 181 Restart of the clock and oral explanation (if needed). The project manager sends updated summary of product characteristics and product literature in English to the applicant.

By 210 Adoption of CVMP Opinion + CVMP assessment report.

Day 211 Transmission to applicant of CVMP Opinion + CVMP assessment report

Day 215 at the latest Applicant provides the EMA with summary of product characteristics, Annex II, labelling, package leaflet and Annex A in all EU languages and Norwegian.
Day 232 Applicant provides the EMA with summary of product characteristics, Annex II, labelling, package leaflet and Annex A in all EU languages, taking account of comments received from Member States by Day 229.
By Day 237 EMA Transmission of Opinion and Annexes in all EU languages to the applicant, Commission and Members of the Standing Committee, Norway and Iceland.

Mutual recognition procedure
Before day -14 Applicant discusses the application with the Reference member state (RMS)
The RMS updates the assessment report and inform the Concerned Member States (CMS) of proposed start date
Submission of the dossier to the CMS (and RMS if necessary)
Circulation of the assessment report to CMS
-14 Days Automatic validation of the application
Day 0 Start of the procedure
Day 54 CMS send comments to RMS and applicant (via RMS)
Day 57 RMS circulates the List of Questions (LOQ) to the applicant and CMS
Day 65 Applicant sends response to LOQ to RMS, who forwards this to CMS
Day 70 RMS circulates assessment of response to LOQ to applicant and CMS
Day 77/78 CMD(v) meeting -RMS informs applicant of outcome of discussions after the meeting
Day 82 Applicant sends new drafts of SPC, product literature and labelling (with translation) to RMS, who forwards them to CMS
Day 85 If necessary, final drafts of SPC, product literature and labelling are prepared
Day 88 CMS send final comment to RMS
Day 89 RMS circulates final assessment report, SPC, product literature and labelling to CMS and applicant
Day 90 If consensus is reached, the RMS will close the procedure; if consensus not reached, a referral is initiated to CMD(v).
Start of national phase
Day 95 Applicant sends translations to all CMS
Day 120 Granting of national marketing authorisation in RMS and CMSs if no
referral to the Co-ordination group. The national agencies adopt the decision and issue the marketing authorisation subject to submission of acceptable translations/mock-ups.
Day 180 Granting of national marketing authorisation in RMS and CMSs if positive
conclusion by the Co-ordination group and no referral to the CVMP. National agencies adopt the decision and issue the marketing authorisation subject to submission of acceptable translations/mock-ups.

Decentralise procedure
At least 3 months before the DCP, the applicant discusses the application with RMS. The RMS then inform CMS of proposed start date.
-14 Days Submission of the dossier to the RMS and CMS and validation of the application (may be extended to 30 days for generics when the reference product is not authorised in the RMS)
Assessment step I
Day 0 RMS starts the procedure
Day 70 RMS circulates drafts of LOQ, SPC, product literature and labelling with the preliminary assessment report to CMS

Day 100 CMS send comments to RMS
Day 105 RMS forwards LOQ to the applicant and CMS
Clock-off period – the applicant has 3 (6) months to submit a response
Day 106 Valid submission of response.
RMS re-starts the clock
Assessment step II
Day 120 (0) RMS forwards to applicant and CMS Draft AR, and drafts of SPC, product literature and labelling
Start of Assessment step II
If consensus reached, the RMS can close the procedure
Day 145 (25) CMS send comments to RMS and applicant (via RMS)
Day 150 (30) RMS circulates LOQ to applicant and CMS
If consensus reached, the RMS can close the procedure
Day 170 (50) Applicant sends response to LOQ to RMS
RMS immediately forwards this to CMS
Day 190 (70) RMS circulates assessment of response to LOQ to applicant and CMS
Day 197/198 (77/78) CMD(v) meeting
The RMS informs applicant of outcome of discussions after the meeting
Day 202 (82) the applicant sends new drafts of SPC, PL and labelling to RMS.
Translations may be included. The RMS forwards this to CMS.
Day 205 (85) If necessary, final drafts of SPC, product literature and labelling
Day 208 (88) CMS send final comment to RMS
Day 209 (89) RMS circulates final AR, SPC, product literature and labelling to CMS and applicant
Day 210 (90) If consensus reached, the RMS will close the procedure
If consensus not reached, a referral to CMD(v) is triggered.
National phase
Day 125/155/215/275 Applicant sends translations to all CMS
Day 150/180/240 Granting of national marketing authorisation in RMS and CMSs if no referral to the Co-ordination group. National agencies will adopt the decision and will issue the marketing authorisation subject to submission of acceptable translations/mock-ups.
Day 300 Granting of national marketing authorisation in RMS and CMSs if positive conclusion by the CMD (v) and no referral to the CVMP. National Agencies adopt the decision and issue the marketing authorisation subject to submission of acceptable translations/ mock-ups.

Analysis of the number of marketing authorisations per type of process[78]

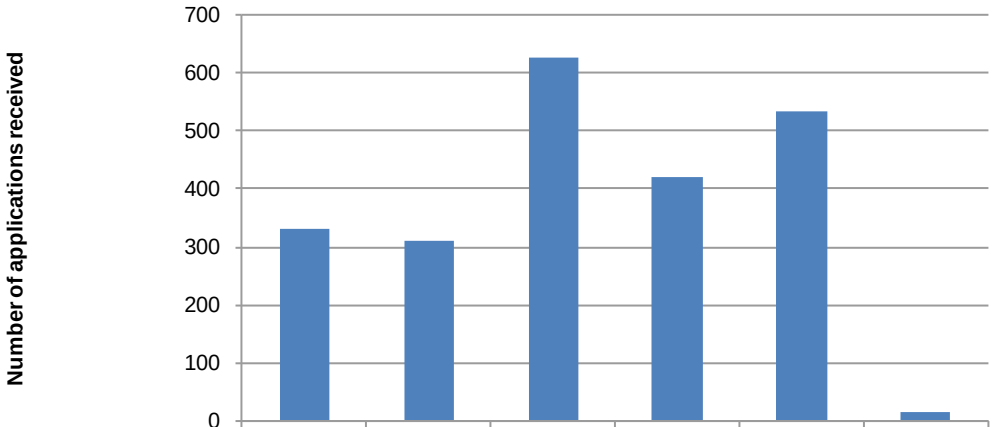
Information on the numbers of applications for marketing authorisations received by the competent authorities through the four authorisation procedures are analysed below.
Applications for the centralised procedure were received by the EMA whilst national competent authorities received applications for either the MRP or DCP. The HMA provided information on those types of applications. There is no comprehensive information across the EU for applications received by the national competent authorities through the national procedure. The UK was the only competent authority that provided these data, which is therefore used here as an example.

[78] Source: EPEC Report, Assessment of the impact of the revision of veterinary pharmaceutical legislation, 2011.

Applications processed through the Mutual Recognition procedure

The Heads of Medicines Agency (HMA) provided data on marketing authorisation applications received through the Mutual Recognition Procedure. These data covered applications for new marketing authorisations, line extensions[79], variations, and renewals received between 2006 and 2009. A total of 2,235 applications were received in this period, of which 330 (15 %) concerned new marketing authorisations or line extensions.

Figure 2 Number of applications received through the MRP, by type of application (2006-2009)

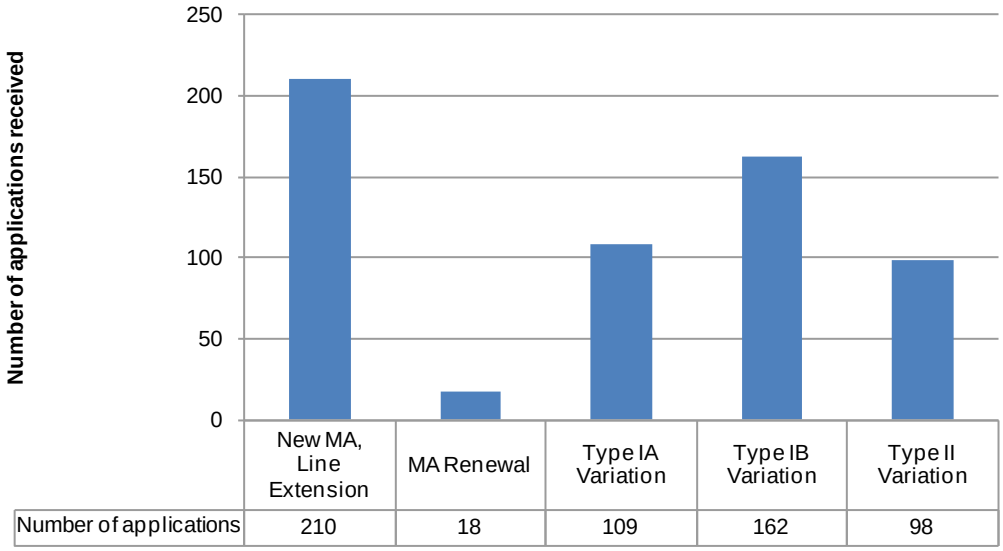


Applications processed through the Decentralised procedure

The HMA provided data on marketing authorisation applications received through the decentralised procedure. These data covered applications for new marketing authorisations, line extensions, variations, and renewals received between 2006 and 2009. A total of 597 applications were submitted, of which 210 applications concerned new MAs or line extensions.

Figure 3 The number of applications received by the competent authorities through the DCP, by type of application (2006-2009)

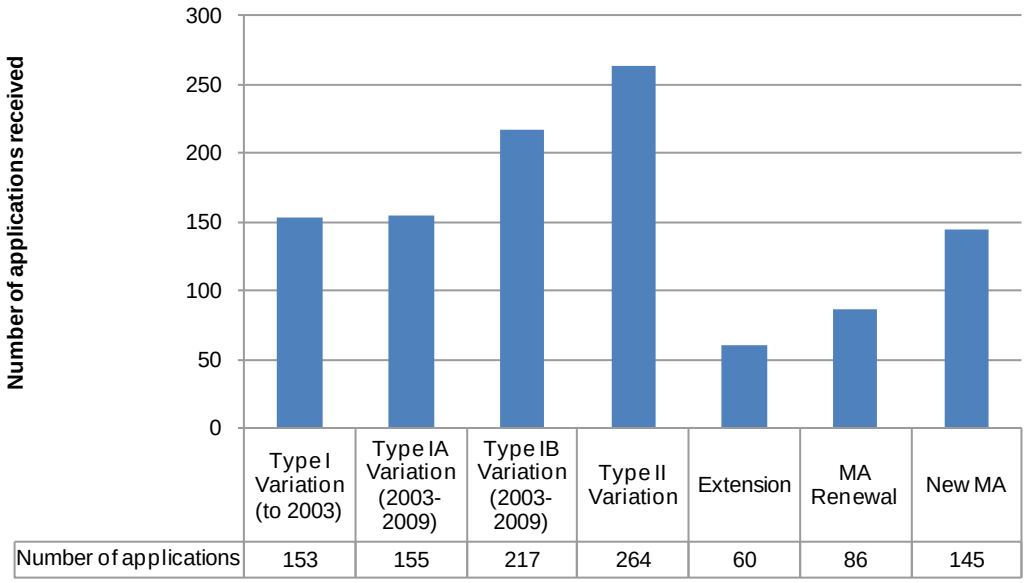
[79] The scope of line extensions covers changes to active ingredients, pharmaceutical form or route of administration, and also addition of a new food-producing species to the market authorisation.



Applications processed through the Centralised Procedure

The figure below shows the total number of applications received by the EMA through the Centralised Procedure between 1997 and 2009. There were 145 applications for new marketing authorisations. The most common form of Centralised procedure application was for a Type II variation to an existing marketing authorisation (214).

Figure 4 Number of applications received through the Centralised Procedure, by type of application (1997-2009)



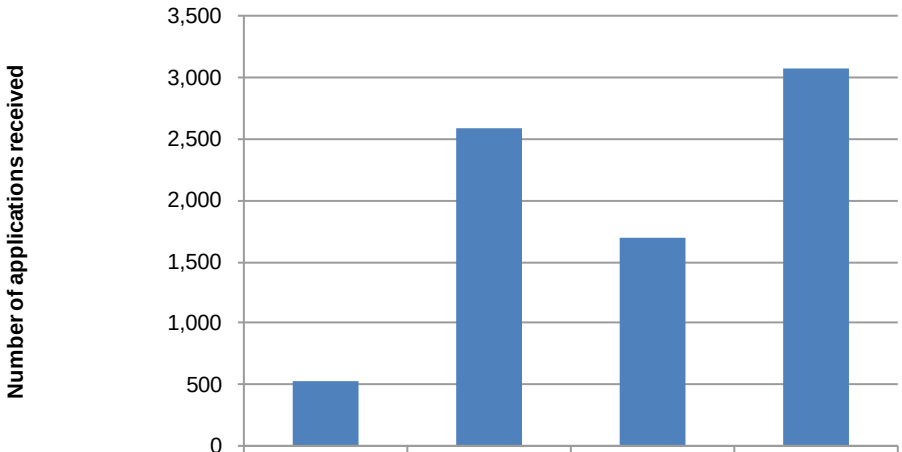
Applications processed through the National Procedure

Data on MA applications received through the national procedure were requested from the competent authorities in the Member States during the consultation but only UK data became available. The data provided by the UK authorities cover the period 2000 to

2009, and shows applications received for: new marketing authorisations, renewals, and certain types of variations.

The figure below shows the total number of applications received by the competent authority in the UK between 2000 and 2009. A total of 7,895 applications were received, of which 7% were applications for new marketing authorisations and 33 % applications for renewals. The majority (61%) of applications received were for variations.

Figure 5 Number of applications received, by type of application (2000-2009)



Authorisation of antimicrobials for use in veterinary medicine

There are no particular restrictions in the current veterinary medicines legislation regarding the authorisation or use under the Cascade of antimicrobials in animals. However, there is a requirement for submission of data on potential emergence of resistant bacteria as part of the application dossier. Decisions on the authorisation of veterinary antimicrobials are product-related, made on a case-by-case basis and based on the data presented in the dossier.

Clinical trials

Applications for marketing authorisations for veterinary medicines require data from clinical trials to demonstrate their safety and efficacy under normal conditions of use. The data requirements for clinical trials are set out in Directive 2001/82/EC but EU Member States have their own procedures and timelines to authorise clinical trials, as these are not set in legislation.

Product literature (packaging and labelling)

The Directive 2001/82 sets out that mock-ups of immediate and outer packaging of the veterinary medicines must be submitted for approval by the competent authorities as part of the application process. The product literature of veterinary medicinal product must be in the official language or languages of the country where the product is to be placed on the market.

Placing veterinary medicines on the market in the event of an emergency

The current legislative provisions in the Directive 2001/82 allow the placing of a veterinary medicine on the market without a marketing authorisation if the health

situation in the country so demands and the medicine has already been authorised in one Member State. It also regulates, in the event of a serious epizootic disease, the provisional use of an immunological veterinary medicine without a marketing authorisation, after informing the Commission. Member States have their own national procedures and timelines to streamline the authorisation of veterinary medicines when there is an urgent need.

Placing on the market of homeopathics

Homeopathic veterinary medicinal medicines may be placed on the market if they hold a marketing authorisation or have been registered in accordance with a simplified procedure for homeopathics. Homeopathic medicinal products intended for food producing species need to comply with the provisions of the legislation on residues limits in foodstuffs of animal origin in order to be placed on the market. For homeopathic immunologicals, the same rules for regular immunologicals apply.

Maintenance of marketing authorisations

Pharmacovigilance

Directive 2001/82/EC sets out the arrangements for pharmacovigilance for veterinary medicines. Marketing authorisation holders must report serious suspected adverse events within 15 days to the competent authorities and prepare periodic safety update reports on the overall performance of the product at set intervals for all veterinary medicines. Marketing authorisation holders must submit the details of their pharmacovigilance systems as part of every application for a marketing authorisation. Any changes to this system require a variation. There is a requirement for the inspection of marketing authorisation holders by the competent authorities for compliance with the legislation regarding pharmacovigilance.

Renewals

Directive 2001/82/EC sets out the requirements for ensuring the continued quality and safety of a veterinary medicine once marketed. Under the current legislation, marketing authorisations are valid for five years and then may be renewed on the basis of a re-evaluation of the risk-benefit balance. Once renewed, marketing authorisations are valid for an unlimited period unless there are justified grounds relating to pharmacovigilance to proceed with one additional five-year renewal.

Variations

The legislation requires that any amendments to a marketing authorisation require the submission of a variation. Variations are categorised according to their complexity, ranging from Type 1A variations (the least complex), through Type 1B variations, to Type 2 variations (the most complex). Some variations concerning purely administrative changes (such as changes to the address of the marketing authorisation holder, for example) may be implemented before the competent authorities are notified, but other equally simple changes will still require assessment by the competent authorities.

Provisions regarding data protection and authorisation of generic veterinary medicines

The legislation sets out the provisions regarding data protection for new veterinary medicines and the requirements for the authorisation of generics. A generic medicine may only be placed on the market 10 years (13 years, if the product is for bees or fish) after the initial authorisation of the originator medicine. Veterinary medicines for food producing species benefit from an extra 1 year protection for each extension to a food producing species, if the extension is authorised within 5 years following the granting of the initial marketing authorisation ("window of opportunity"). There is a requirement for

environmental safety data to be submitted with a generic application, but other safety data are not required.
The legislation sets out that any extensions to a veterinary medicine are "rolled back" into the initial marketing authorisation (the global marketing concept), and therefore developments of the product do not restart or prolong the data protection period of the marketing authorisation.

Other provisions

The wholesale dealing and retailing of veterinary medicinal products activities are regulated under Directive 2001/82/EC, as well as the advertising of veterinary medicines. The legislation also sets out the requirements for inspections of manufacturing sites for Good Manufacturing Practice, and of sites of marketing authorisation holders regarding compliance with pharmacovigilance obligations.

Annex 6 Further information related to the problems identified with the veterinary medicines legislation and on antimicrobial resistance

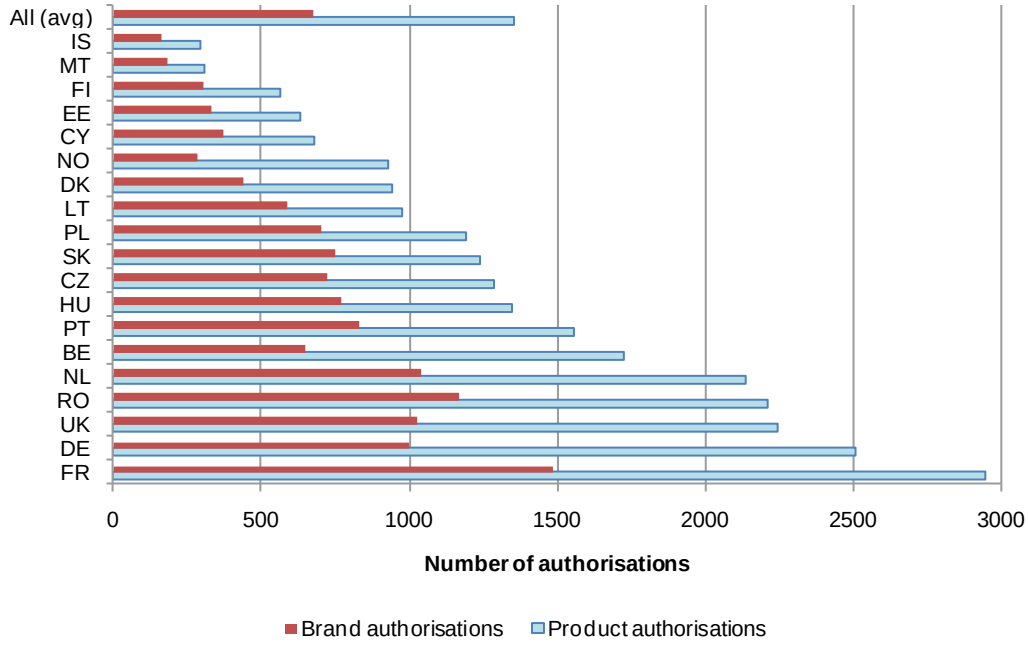
Some facts and figures concerning the availability of medicines in the Union are presented below:

Authorisation issues

- Smaller countries tend to have fewer authorised medicines

There is considerable variation between countries in terms of the number of authorised products – from 296 products in Iceland to 2,944 products in France. Smaller countries tend to have fewer authorised veterinary medicinal products.

Figure 6 Number of authorised products and authorised 'brands[80]' on national markets, as at May 2010



- High proportion of products authorised in small countries are not placed on the market

Commercial decisions regarding return on investiments drive actual product availability, even where a marketing authorisation holder has spent resources obtaining a marketing authorisation. This is particularly true of the centralised procedure, where companies are granted a pan-european authorisation but may decide not to market the product in non-profitable markets. From the point of view of the farming sector, some EU farmers are at

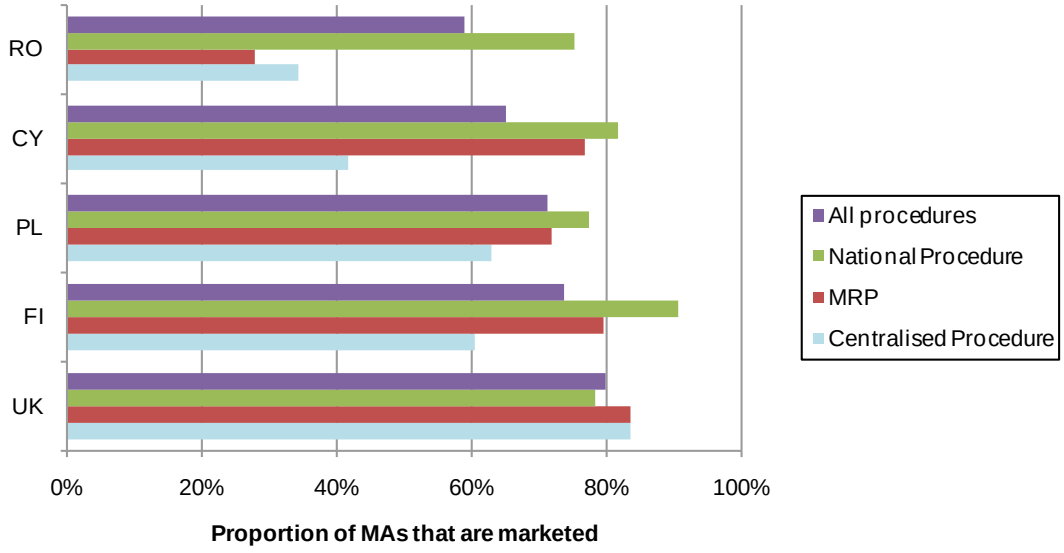
[80] Brand' is used to identify an individual product name. For example, in the UK there are 8 distinct authorisations for the product 'Advantage', differentiated by the species (cats or dogs), the animal size (small or large), and the dosage. For the purposes of analysis of product brands, these 8 authorisations are reduced to a single record for the brand 'Advantage'. In addition, the impact of the differences in national recording protocols on product authorisation data is significant. For example, in Finland the product 'Advocate' is recorded as 2 authorisations (differentiated by species), whereas in Belgium the same product is recorded as 30 authorisations (differentiated by species, animal size, dosage etc).

a competitive disadvantage within the EU (and indeed with the world) regarding optimal opportunities for animal treatment and consequently productivity.

Data from the consultation showed that products authorised through the national procedure were most likely to be marketed (on average 80 % of marketing authorisations were marketed). In contrast, on average 56 % of products authorised through the Centralised Procedure were marketed, though in Romania the proportion was as low as 34 %. [81]

The use of a national route to place a veterinary medicine on the market is widely used. Data obtained through the consultation[82] indicate that the majority of the pharmaceutical companies operating in the veterinary pharmaceutical sector hold marketing authorisations (brands) only in a single national market (67 %)[83]. Most of the veterinary medicines available in the Member States historically have been authorised through the national procedure. This creates a barrier to the single market as a veterinary medicine must have a marketing authorisation in the Member State before it can be placed on the market in that Member State, and the current Mutual recognition procedure leads to the re-assessment of products that already have a marketing authorisation in at least one Member State.

Figure 7 Proportion of a sample of marketing authorisations which are marketed in selected countries, as at January 2011



[81] The authorised product databases provided by competent authorities did not indicate which products are actually marketed. Instead, the availability of authorised products was investigated by collecting data from a sample of marketing authorisation holders for 5 of the 6 case study countries[81].

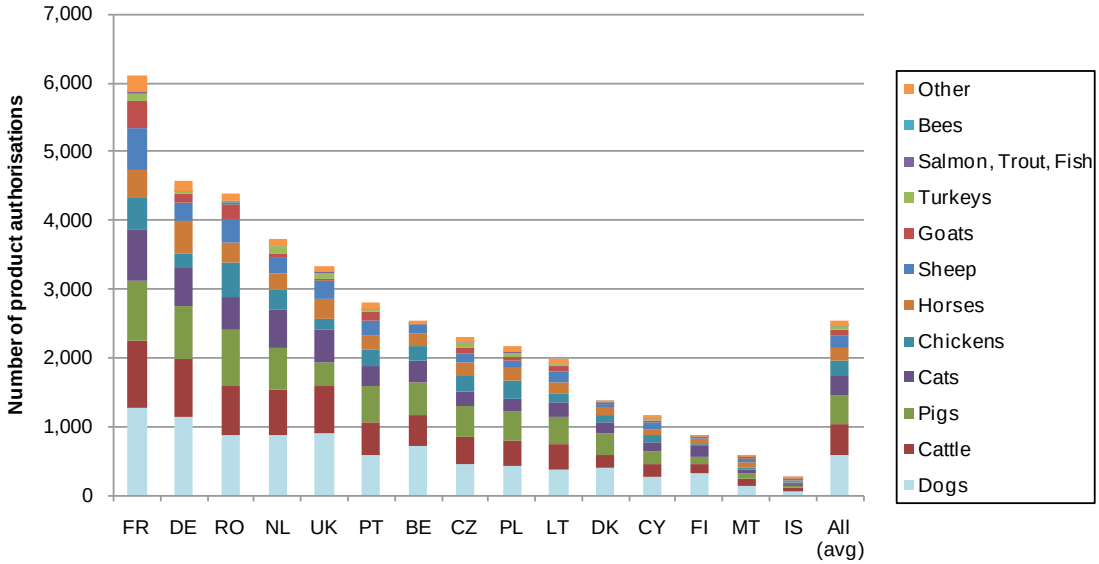
[82] It should be noted that the data collected is not complete, due to the lack of a centralised EU wide source of information on product authorisations and errors and omission in the Member States' databases. EPEC Report Assessment of the impact of the revision of veterinary pharmaceutical legislation, 2011, p. 90.

[83] The data refer more correctly to the number of authorised "brands" (the individual product name) rather than the number of marketing authorisations as the methodology to record products in databases may vary in the Member States. For example, as indicated previously in Finland the product Advocate is recorded as 2 authorisations (differentiated by species) but the same product is recorded as 30 authorisations in Belgium (differentiated by species, animal size, dosage etc). For the purpose of the study the various authorisations were recorded as one brand. EPEC Report Assessment of the impact of the revision of veterinary pharmaceutical legislation, 2011, p. 20, 23.

- There are few authorised veterinary medicines for minor species[84]

The analysis of marketing authorisations for eleven 'case study' species[85] demonstrated that there are considerable variations in the number of products authorised for use per species. More products are authorised for use in dogs than any other species. The 'top 4' species in terms of the number of authorisations (dogs, cattle, pigs and cats) on average accounted for 70 % of all authorisations.

Figure 8 Number of products authorised for use per species, as at May 2010. Note that products can have multiple target species.



- There are few authorised products for therapeutic categories

Using the Anatomical Therapeutic Chemical (ATC) (vet) classification system[86], it was possible to examine the therapeutic categories of veterinary medicinal products authorised in Europe. The ATCvet classification system categorises products according to their therapeutic use, starting with 15 categories labelled QA to QV (the ATCvet classification systems does not enable the analysis of the distribution of medicines for particular conditions (e.g. diseases), only broad therapeutic categories).

Certain therapeutic categories appear to be relatively unimportant within animal health, whilst others – e.g. QB (blood products) – are considered to be emerging areas where developments may take place in the future.

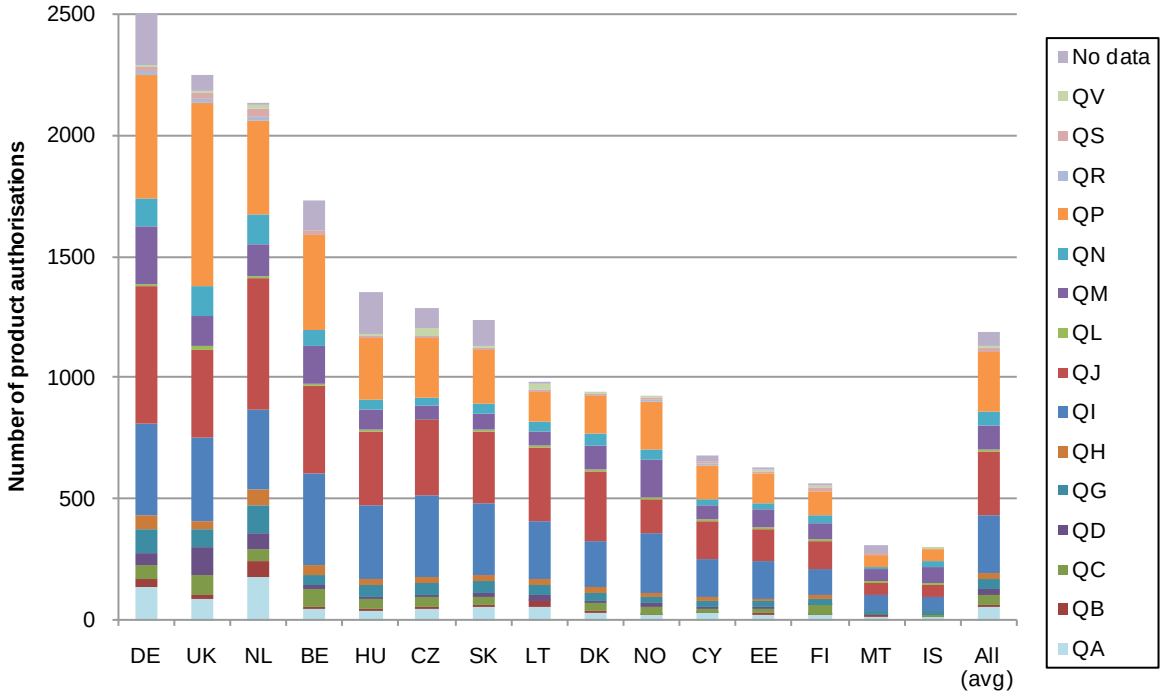
Antiparasitics (ATCvet categories QP), anti-infectives (QJ)) and immunologicals (QI) accounted for the largest numbers of authorised products, on average making up 63% of the total number of medicines. In smaller markets in particular there were very few authorised products (typically under 5) within many therapeutic categories.

[84] There is presently no EU definition of a minor species, though a paper produced by the EMA has defined 'major species' as cattle, sheep (for meat), pigs, chickens, salmon, dogs and cats. EMA (2009) Guidane for companies requesting classification as MUMS/limited markets.

[85] Consisting of the two types of companion animal (dogs and cats) together with the principal food-producing species, as well as bees and fish species. All other animals were grouped together into an 'other category' (e.g. rabbits, ducks, geese and other companion animals).

[86] WHO Collaborating Centre for Drug Statistics Methodology (2010) Guidelines for ATCvet classification 2010

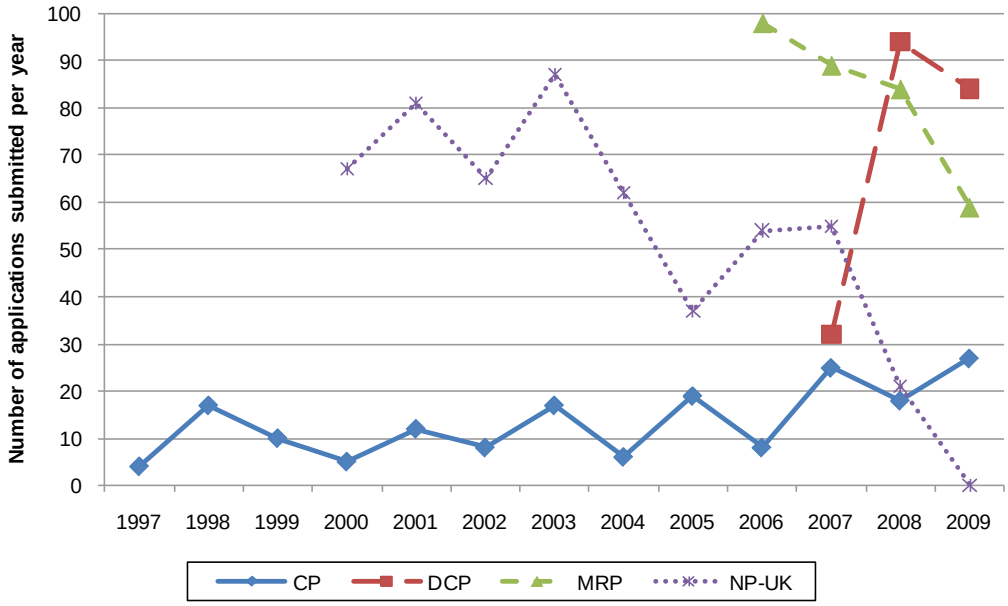
Figure 9 Therapeutic categories (ATCvet system) for all authorised products on national markets, as at May 2010.



- The number of applications for new authorisations submitted each year is low, and few applications concern minor species

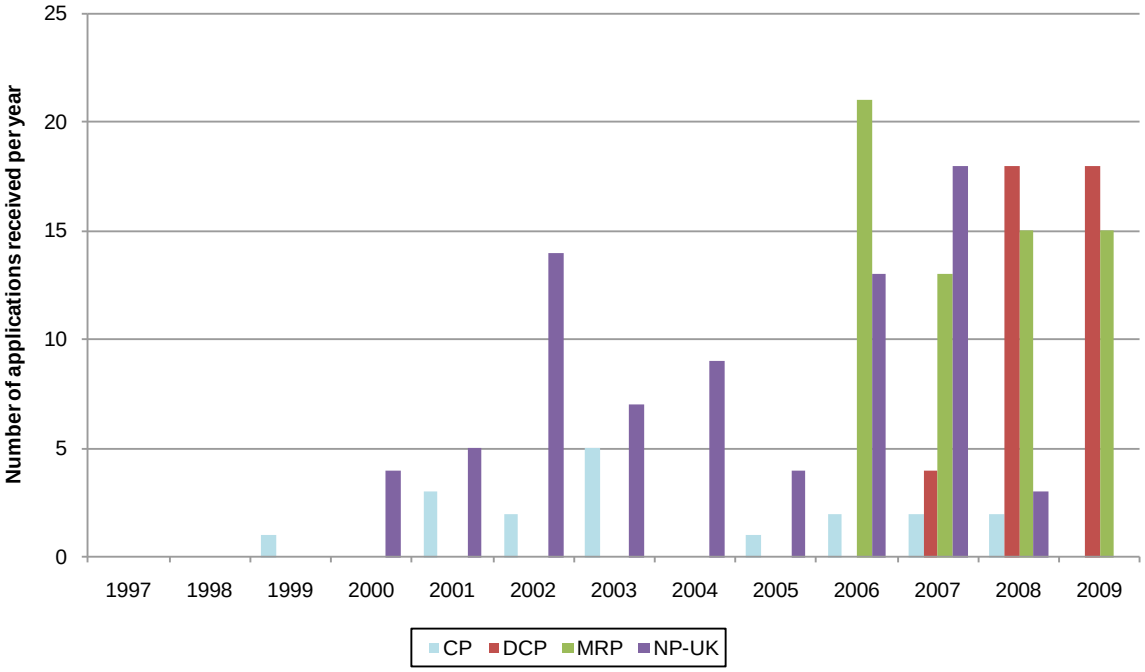
The graph below shows that the EMA typically receives around 20 applications for a new marketing authorisation/line extension (that is, innovative products) through the centralised procedure each year. Data as regards applications through the mutual recognition and decentralised procedures are limited, but do show that both routes are used more frequently by businesses than the centralised procedure. In the UK (the only Member State that that provided data regarding applications received through the national procedure) applications received through the national procedure have declined in number in recent years.

Figure 10 Number of applications for new marketing authorisations/line extensions received by the authorities through the centralised (1997-2009), mutual recognition (2006-2009), decentralised (2007-2009) and national (UK only, 2000-2009) procedures each year:



The number of applications for new marketing authorisations/line extensions is low. Of all the applications concerning minor species plotted in the figure below, 62 % involved horses and just 4 applications (2 %) involved bees.

Figure 11 Number of applications for new marketings/ line extensions involving horses, goats, turkeys, bees, or salmon, trout or other fish received by the authorities through the centralised (1997-2009), mutual recognition (2006-2009), decentralised (2007-2009) and national (UK only, 2000-2009) procedures each year



The lack of innovation for products for food-producing species is also, to a certain extent, reflected in the number of applications to establish Maximum Residue Limits (MRLs). For example, whilst an increase of 50% in the number of applications for the extension of MRL to new species was reported in 2011 in comparison to 2010, the number of applications for MRL for new molecule remained low (3 applications in 2010; 1 application in 2011)[87]. Changes to the legislation were made to permit the extrapolation of MRLs to minor species, but this has not yet generated the expected benefits for minor species.

- Defined medicine availability problems in various species

Several lists of needed veterinary medicines have been produced along the years. The European Technology Platform on Global Animal Health[88], a technology platform led by the pharmaceutical industry, has prepared an action plan which includes a gap analysis of available products required to deliver new and improved tools for the control of major diseases. The Federation of European Veterinarians identified the following as most needed in the Union[89]

Species	Conditions
Turkeys	Histomoniasis
Rabbits	Scabies enterocolitis
Fish	Kidney disease, anaesthetics
Bees	American fowlbrood, nosemosis
Dairy sheep and goats	Coccidiosis, nematode and trematode infections
Dairy goats	Mastitis
Pigs	Anaesthetics

A discussion on the reasons behind the problem with the availability of medicines is presented here.

[87] EMA Annual report 2011, p. 47.
[88] http://www.etpgah.eu/action-plan.html

[89] Report of the Task Force on Availability of Veterinary Medicines, 2007

Complexity of the authorisation system

The current system for authorisation of veterinary medicines offers four different routes of application: the centralised (CP), the decentralised (DCP), the mutual recognition (MRP) and the national procedures. This framework has become very complex and introduced a high level of bureaucracy both for industry and regulators. A further problem is the existence of various legal bases for applications. This complex structure seems to lead to ever new aspects and possibilities in using the legislation posing increasing regulatory demands and disharmonisation. Furthermore, the mutual recognition and decentralised procedures often leads repeated evaluations of dossiers and discussions over the acceptable level of documentation provided by the applicants and the interpretation of data. This has often led to costly referrals to CMDv and CVMP to arbitrate over disagreements.

Case study – the cost of a referral

A generic company applied for a marketing authorisation in various countries through the decentralised procedure. One of the Member States calls a referral on the basis of divergent opinion during the procedure. The referral is accepted and the pioneer company is requested to harmonise the SPC across all the Member States:

Costs to the marketing authorisation holder of the originator product

Activity	Costs*
Compilation and publication of the dossiers	6,000
Resources for internal and external experts	15,000
Translations	20,000
Preparation of variations to amend SPC and product literature	9,000
Regulatory national fees for variations	
Write off of label inventory, packaging	120,000
Cost of new labels, label development	120,000
Total	308,000
Man days = 137 *	137,000
Overall cost	445,000
Overall timeline	18-24 months

* man cost estimated as 1,000 Euros per day

Costs for the two Member States leading on the assessment work for the referral was estimated by the UK: 375 hours (appr 31,500 Euros). The costs to the EMA and CVMP members and their experts considering the assessment reports produced by the leading Member States have not been estimated.

* Euros

There have been 66 referrals from 2001-2013. More than half of the cases concern antimicrobials (42 / 66). Nearly half of the cases are Art. 33 referrals (30/66) (concerning mutual recognition/decentralised procedures).

This complexity in the regulatory environment makes it difficult for smaller companies to make applications for marketing authorisations and to maintain products on the market once an authorisation has been issued. The pharmaceutical industry also indicated that the changes over time of the regulatory framework increased product development time[90]

[90] The pharmaceutical industry reported that in the EU major new veterinary medicines take around 8 to 12 years to be developed and authorised, at a cost of around 80-300 million dollars. These figures take into account project failures,

and this is of crucial importance to them, as minimising time-to-market is an important factor in successful innovation.

Administrative burdens

Stakeholders have reported that the costs and the time needed for new product development in Europe has significantly increased over recent decades. The administrative burdens vary with the marketing authorisation procedures[91]:

Table 8 Administrative burden associated with the current marketing authorisation procedures

Marketing authorisation procedure	Total cost per product year *
Centralised	243,729
Decentralised	291,568
Mutual recognition	269,799
National procedure	151,408

*Euros

The centralised procedure is the least costly of the three European procedures. The decentralised procedure is the most costly option to the companies, and the national procedure generates the lowest administrative burden. The majority of the marketing authorisation holders (62%) only hold marketing authorisations in a single national market, and just 4 % marketing authorisation holders hold marketing authorisations within 18 national markets (for which data were available for the consultation).

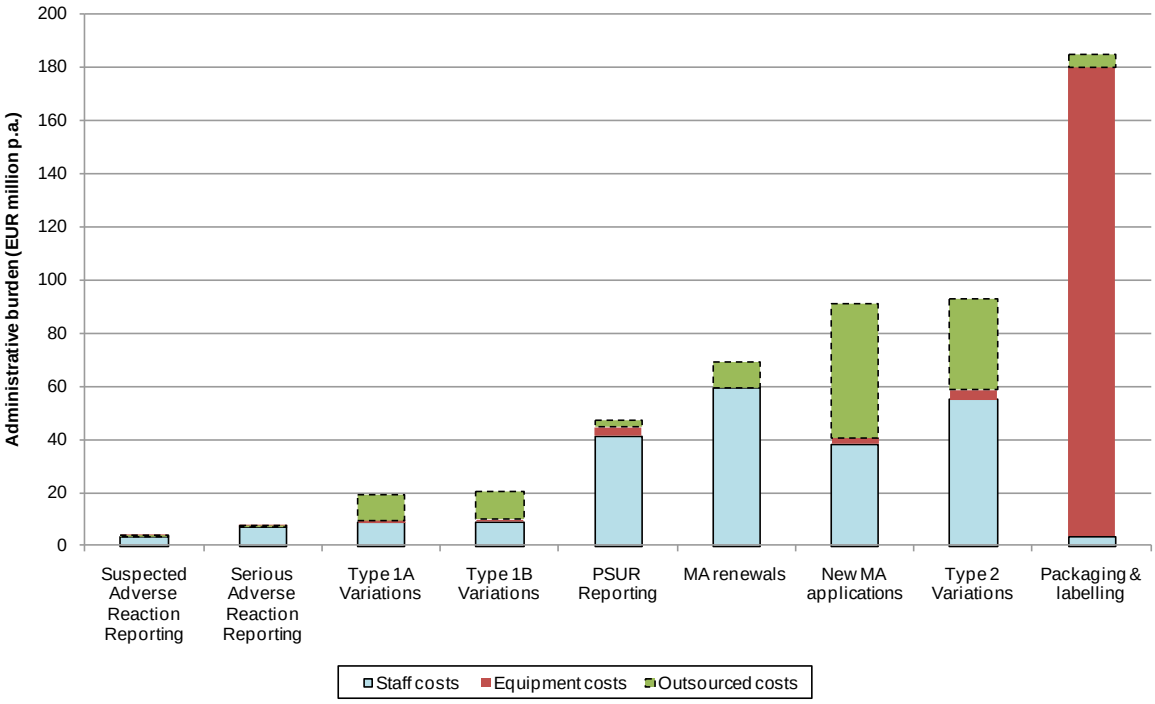
A break down of the costs of administrative burdens to the industry is shown in the figure below[92].

capital costs and the time needed to complete the development cycle. Figures are given in US dollars, the functional currency of the global animal health industry. It is estimated that around 10-15 years of sales are required for a company to recover this investment. IFAH-Europa Impact Assessment Data Package report, 2010, p. 21; . Benchmarking the competitiveness of the global animal health strategy report 2011, p. 12.

[91] EPEC Report assessment of the impact of the revision of the veterinary medicines legislation, 2011, p. 140.

[92] In most cases, staff costs comprise the majority of the administrative burden incurred by businesses. Equipment costs are typically low, except in the case of packaging and labelling costs. Outsourced costs are relatively large where external expertise is used significantly (e.g. as part of the compilation of a dossier for an application for a new MA). EPEC Report assessment of the impact of the revision of the veterinary medicines legislation, 2011, p 27.

Figure 12 Administrative burdens imposed on business



These costs are equivalent to a high proportion of the industry turnover: and it is estimated to amount to 537.9 million per year across the Union. Considering that the total sales of veterinary medicines industry in Europe were estimated as 4.3 billion (2008), the administrative burden associated with meeting legislative requirements is equivalent to 13 % of the annual turnover of the sector:

Table 9 Estimated value of the annual administrative burdens imposed by the legislative framework for veterinary medicinal products

Information Obligation		**Administrative burden (million euros p.a.)**	**% of total administrative burden**
Applying for a new MA	**Sub-total**	**91.1**	**17%**
Applying for a variation to an existing MA	Type 1A	19.7	4%
	Type 1B	20.6	4%
	Type 2	93.1	17%
	Sub-total	**133.5**	**25%**
Renewing a MA	**Sub-total**	**69.5**	**13%**
Pharmacovigilance reporting	Suspected Adverse Reactions	4.3	1%
	Serious Adverse	8.0	1%

	Reactions		
	PSURs[93]	47.2	9%
	Sub-total	**59.4**	**11%**
Packaging & labelling	**Sub-total**	**184.4**	**34%**
Grand total		**537.9**	**100%**

Source: GHK calculations based surveys & engagement with industry and regulators

Use of the Cascade

The European Commission consulted Member States on the use of the Cascade by means of a questionnaire (March to June 2011). Twenty replies were received. More than half of the respondents indicated that they have a procedure for importation of medicines for use under the Cascade. Most respondents could not provide any precise data on the extent of the usage of the Cascade. Four respondents indicated that 1-5% of total use of medicines for food producing species and 2-40% for companion animals.is under the Cascade Three respondents provided data suggesting that all veterinary surgeons make use of the Cascade. The use of the Cascade is reported to be particularly frequent in pet animals (dogs, cats, horses) and minor species.

Packaging and labelling

The legislation sets out that the mock ups of immediate and outer packaging of veterinary medicines should be submitted as part of the application process for approval. The legislation also requires that the product literature of the veterinary medicinal product should be in the language of the country where the product is placed on the market. The cost of complying with the legislative requirements for packaging and labelling is cited as the single largest administrative burden for the industry.

Case study:

Costs to the industry of the packaging activities required for a product consisting of blister packs of tablets, contained in a carton with a leaflet (multilingual pack, with texts in 13 different languages for 17 countries)[94]:

Activities	**13 individual presentations (pallet load of 1920 packs) costs***
Artwork: creation/preparation	23,000
Costs of the printed materials (blister, folding box, package leaflet) and costs of packaging operations (for example, labelling, boxing per packaging line and line clearance)	Blister: 106,640 Folding box: 84,000 Package leaflet: 18,800 Total: 209,440
Warehousing	0.0032 per pack
Total	253,775
Write offs (expired or soon to	21,335

[93] Period Safety Update Reports (PSURs)

[94] IFAH-Europe Impact Assessment Data Package Report, 2010, p. 77-78.

be expired material)	
Batch release by QA/QC	13 batches **

*Euros
** Cost not specified

The pharmaceutical industry indicated that the manufacture of small batches of veterinary medicines to supply small markets is expensive and the cost of labelling such medicines with the national languages is too high to justify the operation. The adoption of multi-lingual packaging could overcome this problem by making a larger batch of product available in several markets, but the current legal requirements for extensive written information to be present on the product literature hinder the use of multi-lingual labels.
For this reason not all products that are authorised via the centralised procedure (that is, have a pan-European marketing authorisation and therefore could be put on the market in all Member States) are actually available in smaller markets in the EU. As discussed above, in Romania, for example, only 34 % of centrally authorised medicines are on the market[95]. Some small markets such as Luxembourg and Austria do have a large number of centrally authorised medicines in their markets, but this could be because they benefit from larger markets with the same language, such as France and Germany[96].

There is a provision in the Directive 2001/82 (Art 61 (1)) which allows Member States' authorities to exempt labels and package leaflets for small containers from the obligation to have the text in the official language of the Member State where the product is authorised. This provision is used in particular for immunological products, for example for single dose vaccine vials, but it is considered by the pharmaceutical industry and some Member States as insufficient to alleviate the administrative burden on packaging and labelling in general.

Data protection
The legislation is based on the granting of 10 years data protection for the first application for a medicine. Any extension by a food producing species would add a further year to this period up to a maximum of 13 years. Below are provided the estimated costs for development of a veterinary medicine and extending it to a new animal species.

Table 10 Estimated average development costs for generic medicines (source: EGGVP):

	Food producing animal	Companion animal
Standard generic application	€0.4-0.95 M	€0.15-035 M
Hybrid generic	€0.6-1.25 M	€0.35-0.05 M
Well-established use	€0.5-1.25 M	€0.35-0.75 M

[95] EPEC report, Assessment of the impact of the revision of veterinary pharmaceutical legislation, 2011, p. 20.
[96] IFAH-Europe Impact Assessment Data Package Report, 2010, p. 45.

Table 11. Average of direct costs of product development based on figures of nine pharmaceutical companies (source: IFAH-Europe)

New medicine	Extension to another species	Extension to new species with new formulation
€6.3 M-€ 9.6 M	€1.9 M-€ 3.5 M	€2.6 M-€ 4.8 M

Table 12 Estimated costs by a contract research organisation for costs of product development (source: IFAH-Europe)

	New medicine	Extension to another species	Extension to new species with new formulation
Companion animal (non-antibiotic)	€4.3 M	€1.1 M	€1.4 M
Companion animal (antibiotic)	€4.4 M	€1.2 M	€1.5 M
Food-producing animal (non antibiotic)	€5.4 M	€1.6 M	€2.0 M
Food-producing animal	€5.5 M	€ 1.7 M	€2.1 M

Variations to an existing marketing authorisation

The legislation sets out that any amendment to the formal documentation and/or underlying data submitted in support of a marketing authorisation requires the submission by the marketing authorisation holder of a variation application to the relevant competent authorities. The number of competent authorities to whom variation applications have to be submitted depends on the procedure followed, and ranges from one (the EMA in the case of the centralised procedure), up to all EU/EEA countries in the (unlikely) event that a veterinary medicine was authorised through individual national procedures.

Variations are categorised according to their complexity, ranging from Type 1A variations[97] (the least complex), through Type 1B variations, to Type 2 variations (the most complex). In recent years attempts have been made to simplify arrangements for variations, and since 2009 variations legislation has been harmonised across all four marketing authorisation procedures[98].

[97] Type IA variations are minor changes to the marketing authorisation that have only a minimal impact or no impact on the quality, safety or efficacy of the product).

[98] Approaches towards variations submitted through the CP, MRP and DCP were harmonised in 2008 with Commission Regulation (EC) No.1234/2008, and in 2009 variations submitted through the National Procedure were included within this framework through Directive 2009/53/EC, the deadline for the transposition of which was 20 January 2011.

Table 13 Number of variations for different marketing authorisation procedures in the period 2006-2009

	Type IA	Type IB	Type II
Centralised procedure	104	112	164
Mutual recognition procedure	628	420	534
Decentralised procedure	109	162	98

However, the costs to the industry are still high as a large number of variations concerns the most complex variations type II (27% for mutual recognition procedure, 34% for decentralised procedure and 43% for centralised procedure). For example, the estimated cost of applying for a Type 1A variation (e.g., a change to the address of the marketing authorisation holder) through the centralised procedure is 8,354 euros. As it is likely that multiple applications for Type 1A variations would be submitted over the life time of a marketing authorisation, the administrative burden per product is high. The amendments of the variation legislation did not decrease the number of variations per application.

Table 14 Ratio of variations per valid marketing authorisation procedure for centralised procedure in period 1997-2011

	Number of variations	Number of valid marketing authorisations	Variations ratio		Number of variations	Number of valid marketing authorisations	Variations ratio
1997	4	5	0.8	2006	56	65	0.9
1998	8	10	0.8	2007	103	76	1,4
1999	19	17	1,1	2008	102	88	1,2
2000	39	27	1,5	2009	119	100	1,2
2001	50	29	1,7	2010	162	114	1,4
2002	39	35	1,1	2011	287	128	2,2
2003	64	40	1,6				
2004	65	51	1,3				
2005	69	52	1,3				

It is estimated that variations can account for 50% of the workload of regulatory staff, and represent a large portion of the overall post marketing administrative burdens to the industry.

Marketing authorisation renewals

Marketing authorisation holders are required to apply for a renewal five years after the initial granting of an authorisation. No further renewals are required, unless the competent authorities determine that a renewal is needed based on pharmacovigilance data. The industry argues that the requirements for a mandatory renewal provide regulators with a formal opportunity to seek new, additional test data, even if the products have been on the market for many years with a good pharmacovigilance record (in order to comply with new guidelines for example). According to the pharmaceutical industry, this forces the industry to direct a significant proportion of the research and development budget (around 35 %[99]) into "defensive research", instead of concentrating their efforts on the development of new medicines. The industry claims that, in contrast, companies outside the EU spend much less resources[100] in this area. As a consequence of the transfer of resources from the innovative research into defensive research, there is a negative impact on the availability of new veterinary medicines in the EU, and a reduction of the attractiveness of the EU markets for product development. Post-marketing costs such as those described above have been cited by SMEs as particularly challenging to that sector of the industry[101].

Pharmacovigilance

Pharmacovigilance aims to monitor the performance of veterinary medicines placed on the market and involves the collection of data on suspected adverse events and their reporting to the competent authorities. It is a key area for animal and public health safety. The legislation requires that marketing authorisation holders maintain databases of all suspected adverse events in animals and humans related to their veterinary medicines. The marketing authorisation holders are also required to report serious suspected adverse events within 15 days to the competent authorities and prepare reports on the overall performance of the product at set intervals (periodic safety update reports, PSUR). The current system requires a PSUR every 6 months for the first year of a product's life, then every year for the next 2 years, and then every 3 years thereafter. Taking into account that a small company may have up to 100 product authorisations and a large company 1000 (the largest animal health company may have 5000 authorisations), the estimated total work days per year dedicated to dealing with this task is large. The pharmaceutical industry estimated that the average number of PSURs is 50 per year, representing around 500 workdays (involving many staff across the company) per PSUR.[102] The inspection of manufacturers for compliance with the legislation regarding pharmacovigilance also adds to the overall cost: The pharmaceutical industry estimated that tasks related to inspections take 30 days work per year.

[99] Benchmarking the Competitiveness of the Global Animal Health Industry Report, 2012, p. 61.
[100] Companies in Canada spend overall 26 % of their local budget on defensive research and only around 14-16 % in Australia, Japan and USA. But the reasons for maintaining or increasing expenditure in defensive research are the same worldwide: deterioration in the regulatory environment (for 79% of companies in Europe), acquisition of companies with products on the market and regulator product reviews. Benchmarking the Competitiveness of the Global Animal Health Industry Report, 2012, p. 14.
[101] Report Outcome of SME office survey on the implementation of the SME Regulation Commission Regulation (EC) 2049/2005.
[102] IFAH-Europe Impact Assessment Data Package Report, 2010, p 40-43.

In addition to these post authorisation activities, applicants also need to submit, at application stage, details of their pharmacovigilance systems together with each new application.

The pharmaceutical industry estimated that on average 4.3 full time staff per company work on pharmacovigilance per year (pharmacovigilance managers, dealing with inspections, case handling, report writing, gathering information on Third Country reports)[103]. The current system is based on that applied in the human sector, and the industry argues that the investment needed to maintain this system is not justifiable in terms of animal health.

Table 16. Pharmacovigilance data for centrally authorised products.

Year	Submitted reports on adverse reactions	Submitted Periodic Safety Update Reports	Initiation of pharmacovigilance referral (Art 78 of Directive 2001/82/EC)
2004	187	45	
2005	354	42	
2006	738	52	1
2007	1424	81	
2008	1943	95	
2009	3129	112	
2010	4474	118	1
2011	4888	132	1

Homeopathic medicines

Homeopathic veterinary medicinal products fall within the scope of the legislation on veterinary medicines[104]. Stakeholders working in the area of homeopathic medicines raised a concern regarding the regulatory burdens existing in this sector and indicated that they are disproportionate in relation to the risks involved.

Internet retailing of veterinary medicines

Internet retailing of veterinary medicines is a sector that is growing[105]. Internet pharmacies have estimated that from 2005 to 2011, the sales of non-prescription medicines through the internet in the UK (a Member State that allows sales of prescription and non-prescriptions medicines on line), have increased to take from 2.5% to 8.6% of the total sales of medicines, and now [106]around 48% of non-prescription medicines (such as spot on external anti-parasitic medicines for pets) are bought through the internet in the UK. On the other hand, although prescription-only medicines represent 78% of the market in revenue in that country, only 1.4 % of these medicines are bought online. In comparison with Third Countries, data from the consultation indicated

[103] IFAH-Europe Impact Assessment Data Package Report, 2010, p. 40-43.

[104] Please refer to Glossary for a brief description of the current legal requirements for placing a homeopathic product on the market.

[105] For example, there are 69 businesses selling veterinary medicines in the UK (turnover between £130.000 and £230 million). Germany has over 100 human online pharmacies that also sell veterinary medicines. White paper Medicanimal, State of Play of the online sales of veterinary medicines, December 2011.

[106] White paper Medicanimal, State of Play of the online sales of veterinary medicines, December 2011.

that the market penetration of a leading online veterinary pharmacy in the US, for example, grew from 3.1% in 2004 to 6.3% in 2010, and around 38% of their sales are prescription medicines (2011)[107]. The whole sale price differences between Member States and the price level of online medicines compared to recommended retail prices in Member States indicate the scope for reducing the costs of animal health for end users by internet retailing.

Table 17A Available information from consultation with Member States on internet retailing of veterinary medicines in the Union:

Situation in the Union	**Comments**
Countries where internet retailing of veterinary medicines is not allowed or not regulated: Austria, Belgium, Czech Republic, France	
Countries which allow or regulate internet retailing of veterinary medicines:	
Hungary	Allowed for wholesalers and distributors having licence to sell veterinary medicines in their stores and maintain a web-shop.
Ireland	Licences are granted under national legislation to holders of a Merchant Licence (Retailers) to sell certain categories of animal remedies within the State via a specified website (only products classified as Licensed Merchant medicines or Companion Animal Medicines). The cost of an internet Licence is €76 and is of unlimited duration, subject to compliance with the Animal Remedies Regulations. Compliance is monitored via an inspection programme. The cost to the NCA is not known.
Sweden	Only allowed through pharmacies with authorisation. The authorisation for a pharmacy is 20 000 SEK and thereafter 11 500 SEK every year.

[107] White paper Medicanimal, State of Play of the online sales of veterinary medicines, December 2011.

UK	Allowed. There is no specific legislation on internet retailing of veterinary medicines in the UK. The retail supply of veterinary medicines through internet channels is covered by the relevant general national legislation on retail supply. The VMD introduced a voluntary scheme in May 2012 which facilitates self-regulation by UK-based internet retailers supplying veterinary medicines. Following accreditation, on-site inspections of accredited internet retailers' premises (if they have not been inspected already) are carried out, to check on-going compliance with the legislation. There is no cost to the industry as the scheme is voluntary but the internet retailers must be approved as a wholesale dealers or as retailers of veterinary medicinal products (and as such would have already been approved and inspected by the VMD and paid the appropriate fees).The fees for various inspection types can be found in Schedule 7 of the Veterinary Medicines Regulations 2011. http://www.vmd.defra.gov.uk/public/vmr.aspx The cost to the NCA of administering the system is not known.
Germany	Prescription and non-prescription medicines for pets allowed.

Table 17B. Price difference between online retail price of some veterinary medicines in relation to recommended retail price in Germany and France (source MedicAnimal).

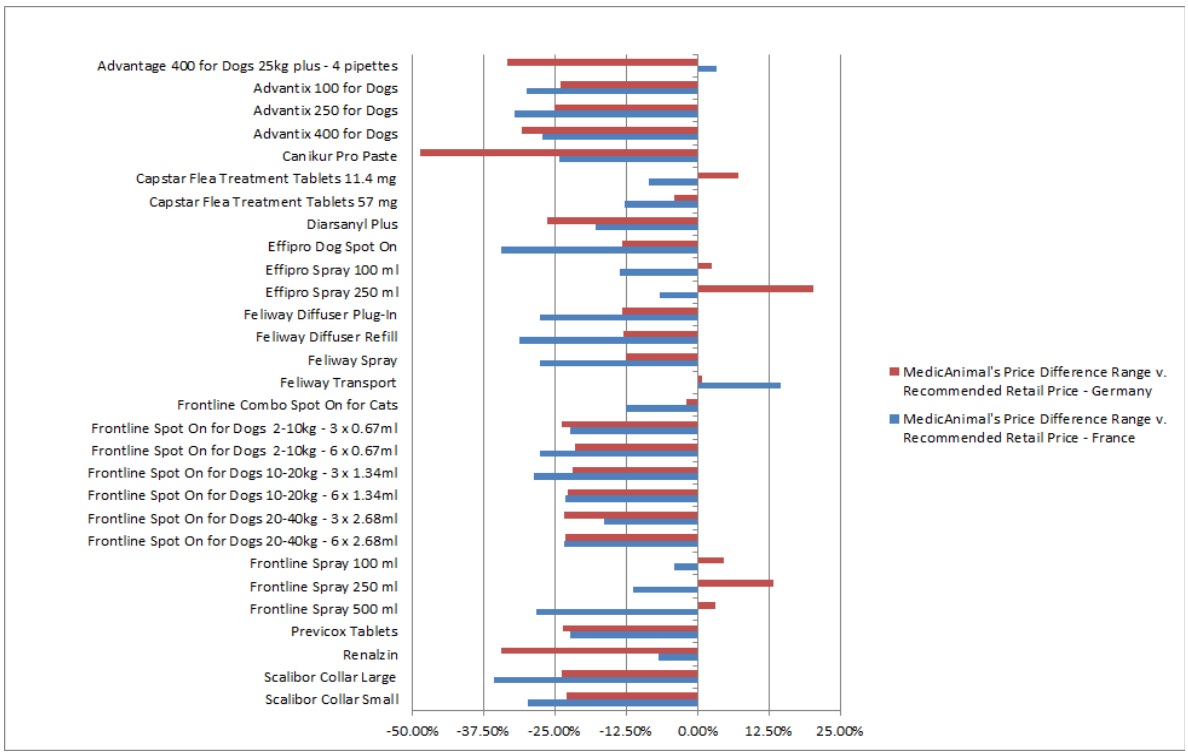
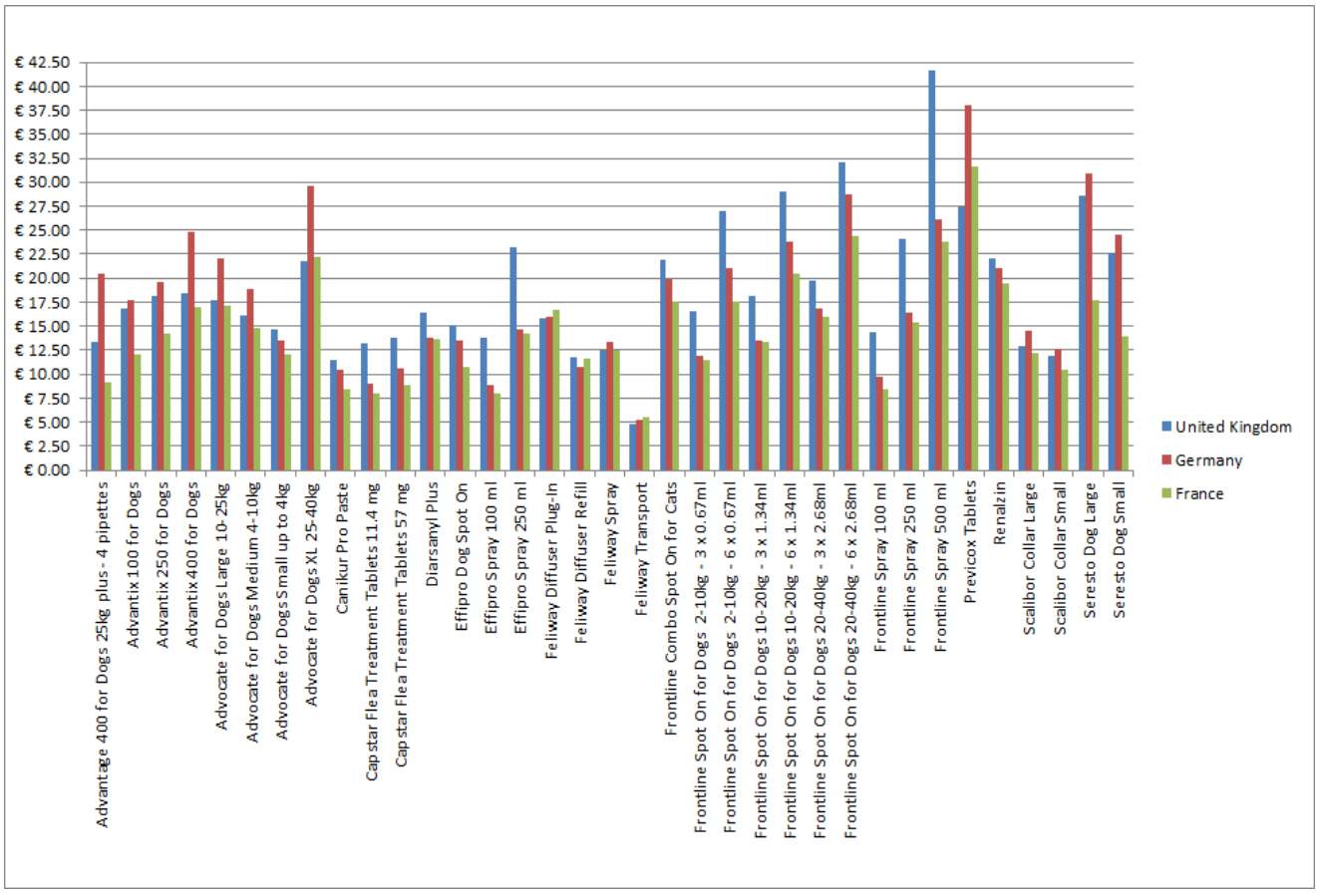


Table 17C Wholesale price comparison between United Kingdom, Germany and France (source MedicAnimal)



Antimicrobial resistance

Background information

Organisms resistant to antimicrobials are found in humans, animals and the environment and may be transferred from animals to humans and between species of bacteria. Antimicrobial resistance is resistance of a microorganism to an antimicrobial medicine to which it was previously sensitive. According to World Health Organisation common, yet life-threatening infections by resistant bacteria are becoming difficult or even impossible to treat[108] and it is a serious, growing, and global threat to health[109]. Replacement treatments are more costly, more toxic, need much longer durations of treatment, and may require treatment in intensive care. In the EU 25000 patients die each year from infections caused by resistant bacteria and causes great financial costs (extra health care costs and productivity losses were estimated as of at least 1.5 billion euros per year) [110,111,112]. The problem of antimicrobial resistance is aggravated by the scarcity of new antimicrobials being brought to the market by pharmaceutical industry. The lack of a new supply of new effective antibiotics limits treatment options for patients with infections caused by multidrug-resistant organisms.

The Food and Agriculture Organisation concluded that antimicrobial resistance has profound impacts on animal health and production. It means that essential veterinary medicines may no longer be available for the treatment of animal diseases, the failure of disease control programmes, increased severity and longevity of diseases, increased mortality, reduced productivity, and increased risk of disease spread in animal populations[113].

The causes of antimicrobial resistance are various and complex. Antimicrobial resistance in humans is often caused by inappropriate use, poor infection prevention and control practices, and through the constant exposure of bacteria to antimicrobials in healthcare settings. These important drivers of antimicrobial resistance are outside the scope of the revision of the legislation on veterinary medicines.

Animals and humans are often susceptible to the same microorganisms causing infections, and in the EU the same classes of antimicrobials are being used in human medicine and veterinary medicine to treat these infections. Therefore the use of antimicrobials in animals will generate resistance to the same classes of antimicrobials as being used in human. Indications exist that antimicrobial resistance in animals is transmitted to humans through zoonotic bacteria, by direct contact or through the food chain. The importance of animals and of food of animal origin to the emergence, spread

[108] http://www.who.int/patientsafety/implementation/amr/en/index.html
[109] www.fvm.dk/.../DWSDownload.aspx?...resistance%2F**AMR**...**Margar**.
[110] A subset of drug-resistant bacteria is responsible for about 25,000 human deaths annually in 29 countries in the EU and 12,000 deaths in the US. In the EU, Iceland and Norway, the costs of these infections reach at least 1.5 billion euros every year. Approximately 4 million patients are estimated to acquire a health-care associated infection in the EU every year. In the veterinary sector, common bacteria causing diarrhoea or respiratory infections in several species have become more resistant to commonly used veterinary antimicrobials, causing increased suffering and mortality in animals, and consequently production losses and extra costs as well as occupational hazards to animal keepers. Communication from the Commission to the European Parliament and Council – Action plan against the rising threats from antimicrobials resistance. 2011, p. 2. Transatlantic taskforce on antimicrobial resistance, 2011, p. 3.
[111] ECDC/EMA Joint technical report The bacterial challenge, time to react, 2009. p 15.
[112] Scientific opinion on the public health risks of bacterial strains producing extended-spectrum beta lactmases and/or AmpC betalactamases in food and food producing animals. EFSA Journal, 2011, 9(8):2322.
[113] http://www.fao.org/ag/againfo/programmes/en/empres/news_270412.html.

and persistence of antimicrobial resistance in humans has not yet been completely established[114].

The risk of antimicrobial resistance grows in proportion to the amount and frequency of antimicrobial use. In veterinary medicine, animals are treated either individually or in groups against infections (so-called mass or herd treatment). Recently published data[115] form 19 EU/EEA countries shows that the major proportion of veterinary antimicrobials sold is for herd treatment. This may be required because animals have likely become infected or individual treatment is not possible in practice (for example for certain diseases on poultry farms), or for preventive use (in the absence of a disease or clinical signs). However, some livestock farmers, operating in a heavily price-driven market with intensive international competition, consider the use of medicines as a cost-effective management tool[116]. The inappropriate use of herd treatment (such as use of antimicrobials to mask poor farm management or inadequate zootechnical practices) provides favourable conditions for microorganisms to emerge and spread and accelerates the growth of resistance. It is argued that the low price of antibiotics, related to competition by generic companies, increase the use of antimicrobials[117]. It should be highlighted that the use of antimicrobials in the EU requires a prescription by a veterinary surgeon, and so the decision whether or not herd or preventive treatment is necessary is primarily the responsibility of a veterinary surgeon.

Farmers and companion animal holders are reported to put pressure on veterinary surgeons to prescribe antimicrobials (for example to treat animals preventive with antimicrobials instead of taking measures to prevent infection) or to prescribe certain types of antimicrobials (for example those which can deliver a higher profit to farmers by having a shorter withdrawal period or are long acting respectively). There is evidence in the US and Australia that direct-to-consumer advertising of human prescription drugs leads to overprescribing and the prescribing of new medicines over older, effective ones[118]. No similar data exist in the EU for veterinary medicines, however, it can be assumed that the same mechanisms take place in the interaction between veterinarian-farmer and in the relationship between patients and doctor.

The incorrect use of antimicrobials is also an area of risk for the development of antimicrobial resistance. Veterinary medicinal products including antimicrobials are regularly used for non-approved indications and with non-approved dosages under the Cascade[119]. This ensures the availability of medicines but this practice, and in particular

[114] The problem of zoonotic bacteria transmitting antimicrobial resistance is complex, as besides the use of antimicrobials there are also other factors linked to bacterial populations, such as the characteristics of the bacteria under consideration, including their virulence and their capacity to spread. Joint opinion on antimicrobial resistance focused on zoonotic infections (ECDC, EFSA, EMA, SCENIHR), p. 34.

[115] ESVAC 2012 report,
http://www.ema.europa.eu/docs/en_GB/document_library/Report/2012/10/WC500133532.pdf

[116] The average cost of veterinary medicines is 1.8-4.4% of the total operating costs, Berenschot Report 2010, What would be the effects of decoupling the prescription and sale of veterinary medicines by veterinarians?; http://www.cbg-meb.nl/CBG/en/veterinary-medicines/actueel/20100309-Berenschot-report-on-antibiotics-use/default.htm

[117] U.S. Jensen et al., 2010. Journal of Antimicrobial Chemotherapy, April 2010.

[118] Influence of patients' requests for direct-to-consumer advertised antidepressants a randomized controlled trial. Kravitz L.R. et al, *JAMA.* 2005;293(16):1995-2002; Influence of direct to consumer pharmaceutical advertising and patients' requests on prescribing decisions: two site cross sectional survey. Mintzes, B. et al. *BMJ 2002; 324: 278*

[119] In a joint survey of HMA-V and FVE in January 2012 veterinarians responded that they prescribe antimicrobials according to the to the Summary of Product Characteristics 'very regularly' (10%), 'regularly' (34%), 'occasionally' (43%) and 'seldom' (13%).

the use of antimicrobials important in human medicine, may contribute to the problem of antimicrobial resistance as there are no scientific data supporting the optimal dosage of medicines used under the Cascade.

Another area of concern is the carry-over of antimicrobials in the production medicated feed, but this is out of the scope of this revision[120]. The Commission has already tackled the use of antibiotics in sub-therapeutic doses as growth promoters[121] in the EU by introducing a ban on this practice from 1 January 2006[122]. However, antimicrobials used at low doses in animal feeds are used in certain parts of the world to improve animal's growth performance. In the USA it is being discussed whether the use of antibiotics as growth promoters should be continued[123,124].

It is possible to reduce the need for antimicrobials in animal husbandry, for example through improved disease prevention, good hygiene and management practices which would reduce the production costs in the long term. This important measure to reduce antimicrobial resistance is outside the scope of the revision of the legislation on veterinary medicines, but several organisations are already promoting the prudent use of antimicrobials. For example, the European Platform for the Responsible Use of Animal Medicines (EPRUMA) has issued guidelines promoting best practices and responsible use of antimicrobials in food producing species. Also, other guidelines have been prepared or are under preparation at national level, at European level by the Commission, by veterinary practitioners and by the World Organisation for Animal Health on how to maximise therapeutic efficacy of antimicrobials and minimise selection of resistant micro-organisms.

Regardless of the efforts carried out to improve the effectiveness of antimicrobials in human and veterinary medicine through guidance, it is recognised that the current veterinary medicines legislation does not provide sufficient tools both to ensure an adequate supply of effective antimicrobials in the interests of animal health and at the same time provide tools for the management of any risks to human health arising from the use of antimicrobials in animals [125]. In addition, whilst national measures, legislative and non-legislative, are put in place at national level as an effort to tackle antimicrobial

[120] The production of medicated feed is regulated by Council Directive 90/167/EEC of 26 March 1990 laying down the conditions governing the preparation, placing on the market and use of medicated feedingstuffs in the Community. The revision of the medicated feed legislation is included in the Commission Working Programme 2013.

[121] Antibiotics used at low doses in animal feeds are considered to improve animals' growth performance.

[122] http Regulation (EC) No 1831/2003 of the European Parliament and of the Council on 22 September 2003 on additives for use in animal nutrition. ://irmm.jrc.ec.europa.eu/SiteCollectionDocuments/EC-1831-2003.pdf

[123] http://www.gao.gov/Products/GAO-11-801

[124] In the USA a US federal court ruled that the FDA should start proceedings to withdraw the approval of certain uses of antibiotics used in food production. The FDA is introducing a voluntary initiative to change how medically important antimicrobials are labeled and used in food-producing animals, and is stopping the use of certain antibiotics to enhance growth or improve feed conversion efficiency in animals. http://www.fda.gov/downloads/animalveterinary/guidancecomplianceenforcement/guidanceforindustry/ucm216936.pdf.

[125] The current legislation does not provide a legal tool to restrict the use of the cascade, the current legislation is based on an assessment of each application of a veterinary medicinal product and does not specify that for the assessment of risk of antimicrobial resistance the similarities with other products have to be considered (a new product may lead to a decrease or increase of the overall risk of use of a class of veterinary antimicrobials) and the risks from contact with treated animals should be included.

resistance, this created the opportunity for disharmonised decisions and views in the EU on this issue. This is shown by the fact that most cases referred for arbitration (so called referrals) to the veterinary scientific committee of the EMA concern antimicrobials[126]. The development of new veterinary antimicrobials is reported to have been stalled because of the uncertainty of future regulatory requirements for antimicrobials. There is an overall view amongst stakeholders that that this area needs to be improved.

The role of the veterinary surgeon in selling antimicrobials is also not harmonised in the Member States. In six Member States prescribers of antimicrobials are not allowed to sell them, to eliminate economic incentives for prescriptions. It is clear that in other countries veterinarians obtain income from the sale of medicines and therefore have an economic incentive to prescribe them, but this incentive can be counterbalanced by personal ethics, peer pressure and the threat of disciplinary action by veterinary professional boards.

Table 18 Relationship between a restriction on selling antimicrobials by veterinarians and the use of antimicrobials in a Member State

Member States with a restriction on sales of antimicrobials by veterinary surgeons	
Country	**Mg/PCU[i]**
Denmark	47
Finland	25
Italy	Unknown
Norway	11
Portugal	166
Spain	241
Sweden	15

Member States without a restriction on sales of antimicrobials by veterinary surgeons	
Country	**Mg / PCU**
Austria	63
Belgium	180
Bulgaria	Unknown
Czech Republic	94
France	132
Germany	Unknown
Greece	Unknown
Hungary	268

[1] ESVAC report 2010: Sales, in tones of active ingredient, of veterinary antimicrobial agents marketed mainly for food-producing animals[1] (including horses), population correction unit (PCU) and sales in mg/PCU, by country, for 2010.

It is agreed that it is important to establish a strategy for the containment of antimicrobial resistance in the veterinary sector, based on the surveillance of antimicrobial resistance prevalence and trends and antimicrobial use. Data collection on the usage of antimicrobials in veterinary medicines has already been initiated through the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC)[127]. This is a voluntary system and therefore not all Member States participate. The type of data collected differs in the Member States. The information collected by ESVAC and other bodies such as the European Surveillance on Antimicrobial Consumption (ESAC), the European Centre for Disease Prevention and Control (ECDC)[128] and the European Food Safety Authority (EFSA)[129] is so far still insufficient to allow a clear identification and quantification of the risk of developing and spreading antibiotic resistance in the food chain. For this it is necessary that data should be collected in all Member States in a similar quality and format.

[126] Since 2000, 66 referrals took place of which 42 concerned antimicrobials.
[127] http://www.ema.europa.eu/ema/index.jsp?curl=pages/home/Home_Page.jsp&mid=
[128] http://www.ecdc.europa.eu/en/Pages/home.aspx
[129] http://www.efsa.europa.eu/

It needs to be highlighted that antimicrobial resistance is affected by world trade in food commodities and travel by humans. The supply of food commodities is a global undertaking, with food being imported into the EU from numerous third countries and so potentially being a source of resistant bacteria. Also, travellers bring resistant bacteria with them from foreign countries[130,131]. Addressing these factors requires cooperation at regional and global levels and cannot be dealt with through the revision of the veterinary medicines legislation.

The issue of antimicrobial resistance is of great importance in the EU. Recently (June 2012) the Council adopted its conclusions on the impact of antimicrobial resistance in the human health sector and in the veterinary sector – a "One Health" perspective under the Danish Presidency[132]. In December 2012, the European Parliament adopted the own initiative "Report on the Microbial Challenge- rising threats from Antimicrobial Resistance"[133]. Both demonstrate the Council's and the EP's continued political commitment to combating antimicrobial resistance.

Contribution of antimicrobial use in animal sector to the presence of resistant bacteria in humans

The problem of zoonotic bacteria transmitting antimicrobial resistance is complex. In addition to the use of antimicrobials there are also other factors linked to bacterial populations, such as the characteristics of the bacteria under consideration, including their virulence and their capacity to spread. The current knowledge does not permit a clear conclusion as to which extent food animal production contributes to the spread of resistance in humans. The report Joint opinion on antimicrobial resistance focused on zoonotic infections [134] states that there is some evidence available on possible links between the use of quinolones in animals and emerging/increase of resistance in Salmonella from humans, and a temporal association between the emergence of quinolone resistance in the bacterium Campylobacter and its increase in isolates both from animals and humans following the introduction of quinolones in animal production has also been shown in several studies. The report provides an analysis on the link between the use of antimicrobials in animals and the development of resistance in humans for four important combinations of group of bacteria and class of antimicrobials.

Quinolone resistance in Salmonella

Several studies have shown that the use of fluoroquinolones (FQs) in food producing animals has resulted in the emergence of FQ-resistant isolates. Such strains have spread from food animals to humans. In order to quantify to which extent a link between the use of antimicrobials in animals and emerging/increase of quinolone resistance in Salmonella from human exists, a quantitative risk assessment is needed. Elements provided in this report in terms of prevalence of bacteria and prevalence of resistance may help to focus on specific usages of medicines in different animal species, and highlight areas where

[130] Joint opinion on antimicrobial resistance focused on zoonotic infections, EFSA Journal 2009, 7 (11):1372, p. 7.
[131] Joint opinion on antimicrobial resistance focused on zoonotic infections, EFSA Journal 2009, 7 (11):1372, p. 7.
[132] http://www.consilium.europa.eu/uedocs/cms_data/docs/pressdata/en/lsa/131126.pdf.
[133] http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+REPORT+A7-2012-0373+0+DOC+XML+V0//EN.
[134] Joint opinion on antimicrobial resistance focused on zoonotic infections (The joint opinion on antimicrobial resistance (AMR) focused on zoonotic infections (ECDC/EFSA/EMA/SCENIHR (2009)) http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/11/WC500015452.pdf).

further work is necessary to inform the debate on the link, if any, between the use of antimicrobials in animals and the emerging/increase of AMR in humans.

Quinolone resistance in Campylobacter

A temporal association between the emergence of quinolone resistance and its increase in isolates both from animals and humans following the introduction of this class of antimicrobial in animal production has been shown by several studies.

Cephalosporin resistance in Salmonella

Studies in cattle and swine have established a link between cephalosporin administration, including treatment frequency, and resistance selection in E. coli. In vivo transfer to, as well as the presence of, many of these ESBL genes in Salmonella has been demonstrated in several studies.

Macrolide resistance in Campylobacter

In a Canadian study which examined the resistance patterns of porcine Campylobacter, over 70% of isolates were resistant to macrolides. Risk analysis revealed a clear association between the (oral) administration of macrolides and the presence of resistance in faecal isolates. There is controversy regarding the public health aspects of macrolide resistance in Campylobacter, with estimates based on a recent risk analysis not exceeding 1 out of 49,000 impaired human treatments in cases of infection with macrolide-resistant C. coli of porcine origin. The risk for suboptimal treatment of human cases due to macrolide- resistant C. jejuni infections from broiler and bovine sources was even lower.

Recently additional interesting information was released. An article was published demonstrating the relation between the use of an antimicrobial of the class of cephalosporins and the development of resistance in humans (" Ceftiofur Resistance in Salmonella enterica Serovar Heidelberg from Chicken Meat and Humans, Canada," Dutil et al. 2012, http://wwwnc.cdc.gov/eid/article/16/1/09-0729_article.htm):"These events provide evidence that ceftiofur use in chickens results in extended-spectrum cephalosporin resistance in bacteria from chicken and humans." Leverstein-van Hall MA et al. concluded that their findings are suggestive for transmission of ESBL genes, plasmids and *E.coli* isolates from poultry to humans, most likely through the food chain (Dutch patients, retail chicken meat and poultry share the same ESBL genes, plasmids and strains; *Clin Microbiol Infect* 2011 Jun; 17:873).

In 2011 the Panel on Biological Hazards (BIOHAZ) delivered an opinion on the public health risks of bacterial strains producing extended-spectrum beta (β)-lactamases (ESBL) and/or AmpC β-lactamases (AmpC) in food and food-producing animals (see: http://www.efsa.europa.eu/en/efsajournal/pub/2322.htm). It was concluded that there are no data on the comparative efficiency of individual control options presented in this document in reducing public health risks caused by ESBL and/or AmpC-producing bacteria related to food-producing animals. Prioritisation is considered complex, and the effectiveness of measures discussed based on the best available evidence and expert opinion. As such it is considered that a highly effective control option to reduce selection of ESBL/AmpC-producing bacteria at an EU level, would be to stop all uses of cephalosporins/systemically active 3^{rd}/4^{th} generation cephalosporins, or to restrict their use (use only allowed under specific circumstances). Measures intended to minimize off label use should focus on increased compliance with existing legislation. As co-resistance is an important issue, it is also of high priority to decrease the total antimicrobial use in animal production in the EU. Also of importance (more so after the ESBL/AmpC-producing microorganisms have emerged) are the measures to control

dissemination, for example by implementing increased farm biosecurity and controls on animal trade (of ESBL/AmpC-carriers), and by improving hygiene throughout the food chain, and implementing other general post-harvest controls for food-borne pathogens. Because most evidence is available for high prevalence of ESBL/AmpC-producing bacteria in the poultry production pyramid, and their consequent involvement in public health, it is of high priority to reduce selection pressure imposed by the use of antimicrobials, to prevent vertical transmission from the top of the poultry production pyramid, and to prevent local recirculation within subsequent flocks.

Commission's commitments in the Action plan against the rising threats from antimicrobial resistance regard veterinary medicines:

Action n° 2: Strengthen the regulatory framework on veterinary medicines and on medicated feed via the review package foreseen for 2013, in particular:
– To ensure appropriate warnings and guidance on the labels of veterinary antimicrobials.
– To consider restrictions on the regular or the off-label use of certain new or critically important antimicrobials for humans in the veterinary sector.
– To consider amending the rules for the advertisement of veterinary antimicrobials.
– To revisit the authorisation requirements in order to sufficiently address the risks and benefits of antimicrobial medicines.

Action n° 7: Promote efforts to analyse the need for new antibiotics into veterinary medicine
– Establishing request for scientific advice to clarify in particular whether the development of new veterinary antimicrobials would reduce AMR.
– Evaluation of the need and possible introduction of incentives that trigger development in veterinary medicines to increase the likelihood that innovations reach the market within the review of the rules on veterinary medicines foreseen in 2013.

Action n° 10: Strengthen surveillance systems on AMR and antimicrobial consumption in animal medicine
– Inclusion of a legal basis for the monitoring of AMR in animal pathogens in its forthcoming proposal for a new Animal Health Law.
– Promotion and extension of the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) with the collaboration of EMA to obtain harmonised data on the usage per animal species and production categories as well as for different indications from all Member States.
– Review of the monitoring of AMR in zoonotic bacteria and/or indicators.
– With the support of the relevant EU agencies, establish harmonisation between human and veterinary surveillance to allow comparison of data.

Table 19 Detailed Standard Cost Model Results used to the calculation of administrative burden to the industry of complying with the legislation on veterinary medicines

(a) Details of the SCM for the legislative framework for veterinary medicinal products

Activity	MA proc-edure/ details	Staff cost per hour	Staff time hrs	No. actions per entity p.a.	Staff costs per action	Staff costs per entity p.a.	Equip costs per action	Equip costs per entity p.a.	O/S costs per action	O/S costs per entity p.a.	Total no. of entities	Total no. of actions p.a.	Total cost p.a.
Applying for a new MA	CP	121	1,123	0.4	135,607	53,064	4,500	1,761	103,622	40,548	23	9	2,193,564
	DCP	121	1,160	0.9	140,093	124,659	5,662	5,038	148,591	132,221	59	53	15,453,153
	MRP	121	902	1.0	108,974	107,028	5,662	5,561	156,799	153,999	84	83	22,393,368
	NP	100	627	0.6	62,644	35,519	4,805	2,724	84,138	47,705	594	337	51,024,658
	Sub-total												**91,064,743**
Applying for a Type 1A Variation	CP	121	38	1.0	4,604	4,433	100	96	3,650	3,514	23	22	184,992
	DCP	121	47	0.4	5,629	2,080	200	74	6,333	2,340	59	22	265,130
	MRP	121	45	1.5	5,397	8,070	200	299	5,479	8,193	84	126	1,391,180
	NP	100	35	2.5	5,270	13,971	500	1,263	5,893	14,889	594	1,500	17,883,462
	Sub-total												**19,724,765**
Applying for a Type 1B Variation	CP	121	64	1.0	7,675	7,771	100	101	7,890	7,988	23	23	364,780
	DCP	121	79	0.5	9,599	5,271	500	275	10,854	5,961	59	32	678,886
	MRP	121	72	1.0	8,745	8,745	500	500	10,500	10,500	84	84	1,658,556
	NP	100	55	2.5	5,529	13,971	500	1,263	5,893	14,889	594	1,500	17,883,462
	Sub-total												**20,585,684**
Applying for a Type 2	CP	121	185	0.9	22,371	19,752	150	132	31,095	27,455	23	20	1,088,814
	DCP	121	238	0.3	28,692	9,532	1,175	390	30,385	10,094	59	20	1,180,941

Activity	MA proc-edure/ details	Staff cost per hour	Staff time hrs	No. actions per entity p.a.	Staff costs per action	Staff costs per entity p.a.	Equip costs per action	Equip costs per entity p.a.	O/S costs per action	O/S costs per entity p.a.	Total no. of entities	Total no. of actions p.a.	Total cost p.a.
Variation	MRP	121	230	1.3	27,771	35,308	1,175	1,494	27,833	35,388	84	107	6,063,995
	NP	100	164	5.3	16,378	86,204	1,175	6,185	9,588	50,467	594	3,125	84,808,648
	Sub-total												**93,142,399**
Applying for a MA renewal	CP	121	302	0.3	36,447	10,483	n/a	n/a	7,500	2,157	23	7	290,727
	DCP	121	244	0.1	29,411	1,795	n/a	n/a	16,000	976	59	4	163,481
	MRP	121	262	0.7	31,602	23,250	n/a	n/a	12,833	9,442	84	62	2,746,100
	NP	100	194	5.0	19,404	96,355	n/a	n/a	3,100	15,394	594	2,948	66,341,291
	Sub-total												**69,541,598**
Pharmacovigilance reporting	Adverse	100	5	13.6	474	6,458	7	95	40	545	594	8,082	4,213,901
	Serious adverse	100	8	15.1	818	12,340	7	106	53	804	594	8,953	7,866,284
	PSUR	100	39	17.6	3,903	68,501	335	5,880	201	3,522	594	10,420	46,248,391
	Sub-total												**58,328,576**
Packing & labelling	-	100	n/a	732,578	0.01	6,889	0.40	296,157	0.01	7,482	594	434,907,365	184,350,250
	Sub-total												**184,350,250**
GRAND TOTAL													**537,852,751**

Notes: All costs are in EUR; n/a means not available; Equip means equipment costs; O/S means outsourced costs

Source: GHK analysis

Annex 7 Availability of veterinary medicines for bees

Background information on the sector

It is estimated that there are around 700 000 beekeepers in the EU; around 97% of these are amateur beekeepers (that is, have less than 150 hives). Almost half of the hives in the EU are concentrated in Spain (17.8 %), Greece (10.9%), France (9.7%) and Italy (8.2%). Honey production in Europe is estimated at around 200 000 tons, and about 60% of the consumed amount of honey is produced in the EU. Other commercial activities are also associated with beekeeping - production of wax, royal jelly and propolis. Apiculture generates an annual value of 1 billion euros, and also contributes to the total amount of at least 22 billion euros related to pollination of crops and plants.

Honeybees are susceptible to a wide range of pests and diseases which, together with other environmental and agricultural practices and factors, have been incriminated in the decline in the number of bee colonies and/or higher than normal losses, especially due to increased winter mortality in the EU and certain parts of the world. The syndrome "colony collapse disorder (CCD)" results in a very high rate of honeybee colony losses and has not been observed in the EU but has been reported in the United States, where it is estimated that less than 2 million colonies remain. This has great economic impact: for 725.000 acres of almond crops in California alone, 1.4 million of bees are needed for pollination. The European situation is significantly different both in the manifestation of the losses and the type and magnitude of negative impacts. So far scientific studies and data from competent authorities have not been able to establish either the extent or the exact cause(s) for these losses. Nevertheless most stakeholders agree that effective pest control in bee colonies is a cornerstone for the sustainability of the apiculture sector.

The main parasites and diseases of bees are the mite *Varroa destructor*, the *Nosema* family of fungi, foulbrood bacteria (European and African Foulbrood) and a number of viruses. European legislation has been put in place to prevent American foulbrood outbreaks due the trade of bees (Directive 92/62/EEC as last amended) and on the import of bees and bee products as regards other, exotic diseases in bees (Regulation(EC) No 206/2010, and Regulation (EU) No 142/2011 adapting earlier similar rules existing since the mid-2000's).

A major concern regarding the control of bee pests and diseases is the limited availability of medicines for existing conditions, for example Varroa mite infestations. The number of active ingredients in authorised veterinary medicines for bees in the EU/EEA is limited[135] and resistance of *Varroa* to standard treatments such as pyrethroids is of great concern. Nosema infection is also growing in significance but there is no authorised medicine for this condition.

Information from Discontools identified the registration procedure ("difficult and not harmonised registration in the EU") as a challenge for the authorisation of medicines

135 List of products for bees authorised in the Member States as per October 2011: http://www.hma.eu/uploads/media/136_Questionnaire_-_Bee_products_in_EU_24.10.11_EMA-CMDv-36668-2009.pdf.

for the control of Varroa in bees, and pointed out that the due to the relatively small market, an investment into the beekeeping business represents a high financial risk. The establishment of Maximum Residue Limits (MRLs) for honey is a particularly challenging step in the development of products for bees. It is estimated that development of a new pharmaceutical (new compound) for the treatment of varroa would take 10-15 years and cost 30-50 million euros. [136]

The cost of preparing a dossier in line with the quality, safety and efficacy requirements set out in the legislation is not recovered through the sales of the medicine and the pharmaceutical industry and beekeeping organisations have expressed their concern that the current requirements are excessive considering the nature of the target species. This was discussed at various meetings and in particular at the Workshop on medicines for bees organised by EMA (December 2009 - http://ec.europa.eu/food/animal/liveanimals/bees/docs/EMA_conclusions.pdf).

Stakeholders suggested some measures to incentivise the authorisation of medicines for bees in Europe: reduction of the data needed for the authorisation, extended data protection, and automatic mutual recognition of authorisations (that is, once a medicine is authorised in one Member State it would automatically be authorised in all Member States).

The classification of honeybees as food producing animals was another area discussed during the consultation. Honeybees fall within the definition of food producing animals ("animals bred, raised, kept, slaughtered or harvested for the purpose of providing food") in Regulation 470/2009 of the European Parliament and of the Council on the establishment of residues limits of pharmacologically active substances of animal origin. This means that veterinary medicines developed for bees need to comply with the extensive legislative requirements regarding maximum residues in foodstuff of animal origin. However, the evaluation of residues of veterinary medicines in honey is complicated by the fact that, due to the bee physiology as an insect, there is no time-dependent depletion or elimination of the substance in honey: in contrast to the situation in other food producing species, where a medicine is metabolised in the animal through a period of time, medicines are applied or given to bees but if residues are in the honey they remain there without significant degradation. Therefore, in practical terms, only substances that do not require a MRL (that is, which will have a zero day withdrawal period) may be authorised for bees. Stakeholders proposed to consider bees as non-food producing animal or as a specific category of food producing animals (following the example of pet and food producing horses) because of their specific metabolism as insect and also because only the collected product made by the animal is eaten (honey) and the animal itself is not consumed. However, it is not possible to exempt honey from the scope of regulations on residues of veterinary medicines in animal produce, for food safety reasons.

[136] Discontools is a joint initiative of the industry and stakeholders such as the research community, regulators and users, and encouraged by the European Commission , aiming to provide a mechanism for focusing and prioritising research to deliver new and improved vaccines, pharmaceuticals and diagnostic tests. http://www.discontools.eu/Diseases/Detail/87.

It is acknowledged that the problems related to the decline in honeybee population is complex and multi-factorial, and effective measures to improve bee health need to concern the development of novel medicines but also cover farming activities, prudent use of pesticides in agriculture, habitat and bee species conservation amongst others[137], [138], [139].

The small size of the market for bee medicines is the main drive for the lack of available medicines, as ultimately product development is a decision made by companies based on commercial returns. There is anecdotal evidence that beekeepers prefer to use "home-made" preparations instead of authorised medicines to treat their colonies, due to costs. This activity not only is illegal but also does not help the authorisation of veterinary medicines for bees. More effective enforcement by the national competent authorities is encouraged to correct this situation. In addition, more intensive information campaigns by authorities and beekeepers' associations on 'good husbandry' and good practice is needed, together with training of beekeepers, for better and proper management of diseases.

[137] COM (2010) 714, final;

[138] European Parliament resolution of 15 November 2011 on honeybee health and the challenges of the beekeeping sector

[139] Council conclusions on the Communication from the Commission to the European Parliament and the Council on Honeybee Health http://www.consilium.europa.eu/uedocs/cms_data/docs/pressdata/en/agricult/122023.pdf

Annex 8 SMEs and micro-enterprises

Background on the SME/micro-enterprises sector- veterinary medicines

The European Medicines Agency has established the SME Office following the European Commission's adoption of Commission Regulation (EC) No 2049/2005. The office promotes innovation and the development of new medicinal products for human and veterinary use by SMEs. Data on the SME/micro-enterprises environment regarding pharmaceutical medicines is relatively scant, but information from the EMA's report on the SME initiative 2006-2011 and the survey on implementation of the SME/micro-enterprises regulation revealed that around 679 companies registered with the EMA as SMEs in that period. Of these, approximately 6 % are veterinary companies, 7% are companies developing products for both human and veterinary use and 14 % are regulatory consultants.

SMEs involved in the pharmaceutical industry have been profiled as development stage companies (research/discovery stage), academic spin offs and (bio) pharmaceutical enterprises developing therapeutic or vaccines and generics manufacturers. Regarding funding, no specific profiling of SMEs/micro-enterprises involved in the veterinary sector is available, but in the human sector, stakeholders are individual private investors (investors founders and employees/directors - 48%), corporate ownership (venture capital companies - 42%), public bodies (regional development funds - 96%) and foundations (4%). It is likely that a similar profile is applicable to the veterinary sector.

Regarding the participation of SMEs/micro-enterprises in the pharmaceutical sector, since 2005 there have been 71 centralised applications for marketing authorisations submitted by SMEs to the EMA. Of these, 12 were for veterinary medicines. The centralised route is attractive to large multinational companies, but SMEs are reluctant to use this route due to the high regulatory fees and overall costs associated with the procedure: industry data show that the total administrative cost for a centralised application is estimated as 119 000 euros, which is equivalent to 119 administrative workload-days. This is often too expensive to SMEs.

SMEs in the agricultural sector and health professionals would benefit in general of the proposed options by an increased availability of veterinary medicines and reduced administrative burden.

Consultation with SMEs and micro-enterprises representatives

Consultation with SME/micro-enterprises took place throughout the following process:

- Public consultation which ended on July 2010.
- Targeted experts' meeting on Authorisations/Data protection (22/6/2012).
- Targeted experts' meeting with SMEs (4/10/12).

The attendees consulted indicated support to the revision of the Directive 2001/82 and highlighted the following particular points of concern regarding the current legislation:

Sunset clause

The Sunset clause is a legal obligation for all pharmaceutical companies to place a product on the market within three years of its granting. Companies also need to avoid not marketing an authorised medicine for a period of three consecutive years - otherwise they would lose the marketing authorisation for the product. SMEs have indicated that this provision is challenging to the sector, as smaller companies often find difficulties in distributing their product.

Clinical trials

There are already requirements in the veterinary medicines legislation for clinical trials to be carried out as part of an application for a marketing authorisation. Member States have, however, created different national procedures and requirements to implement these provisions as there are no harmonised timelines or procedures for granting an authorisation for the trial to be carried out. SMEs indicated that this lack of harmonisation across the EU is particularly burdensome to them, in particular in connection with multicentric trials for rare diseases, and requested that this issue be addressed through the revision of the legislation on veterinary medicines.

Support for SNEs at national level

SMEs indicated that there is a lack of local, practical support at national level (such as a local help desk in the language of the country). They also indicated that financial support, in the form of incentive such as those that already exists for centralised procedures (90% fee reduction for scientific advice and inspections and deferral of the fee for marketing authorisations) would be greatly beneficial to the sector.

Internet retailing

SMEs indicated that the lack of harmonisation regarding internet retailing of veterinary medicines interferes with the development of business in the Union.

References

(1) Outcome of SME office survey on the implementation of the SME regulation – Commission Regulation (EC) no 2049/2005 – 19/12/2011

(http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/12/WC500119946.pdf)

(2) Report on the SME Initiative 2006-2011

(http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/12/WC500119970.pdf)

(3) European Medicines agency roundtable with small and medium-sized enterprise (SME) stakeholder organisations, 19/12/2011

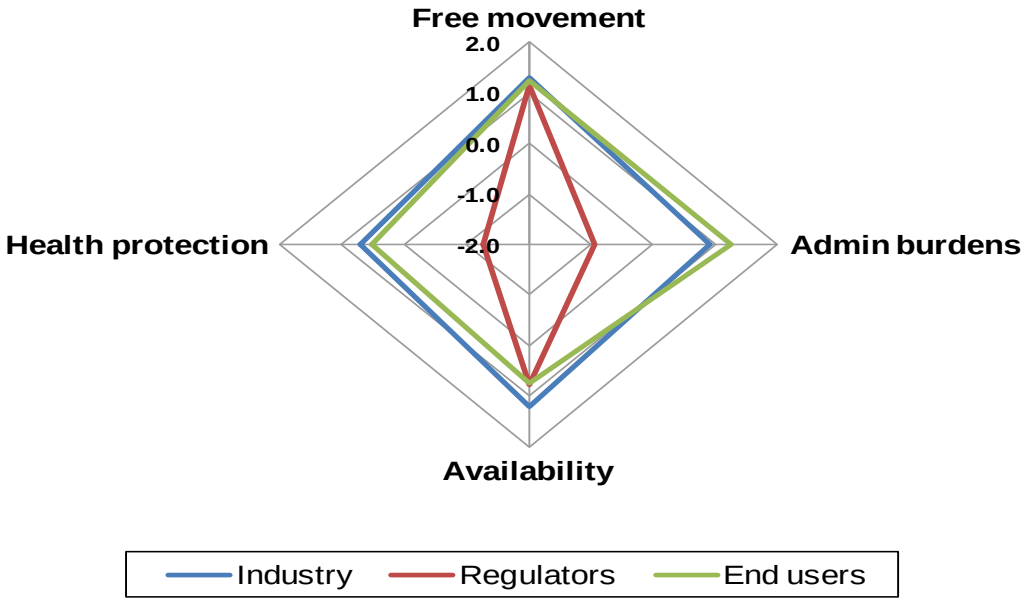
(http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/12/WC500119945.pdf

Annex 9 Consultation results and stakeholders ‘ views

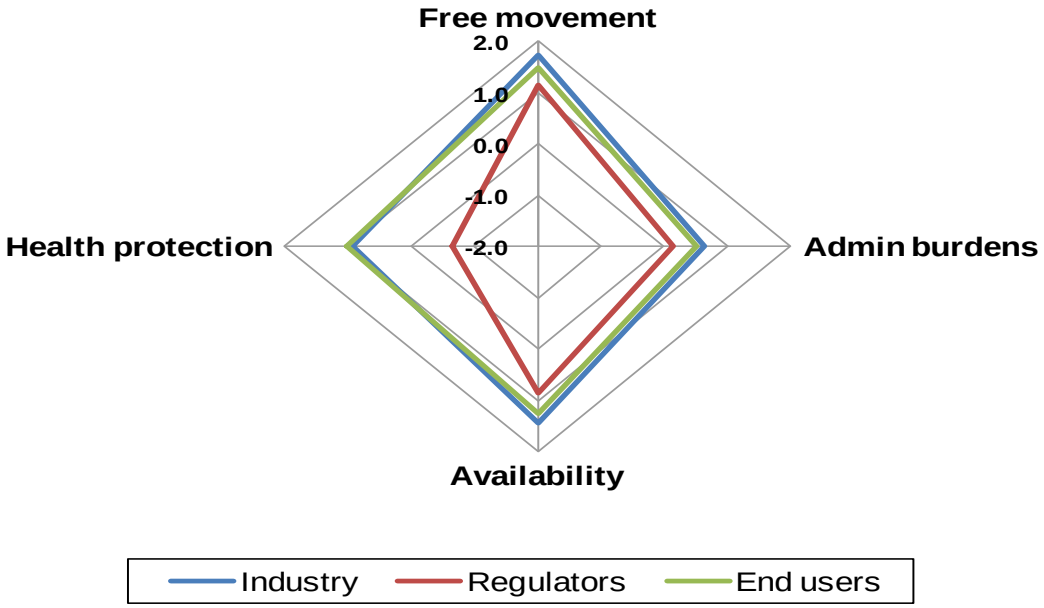
A Summary of stakeholders' views on proposals for the amending of the framework on veterinary medicines

Source: EPEC report on the assessment of the impact of the revision oh pharmaceutical legislation. The average score awarded by stakeholders to the options was based on a scale where -2 means ‘significant negative impact’ and +2 means ‘significant positive impact’ (base = 12 responses (industry); 14 responses (regulators); 5 responses (end users).

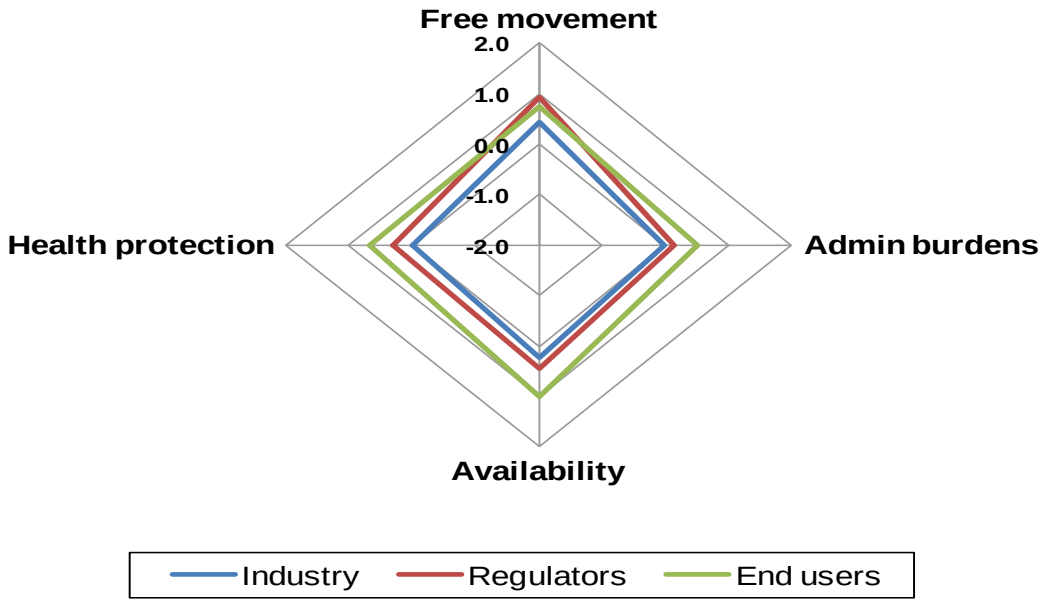
Policy option A2- Automatic recognition of a marketing authorisation granted by a Member State



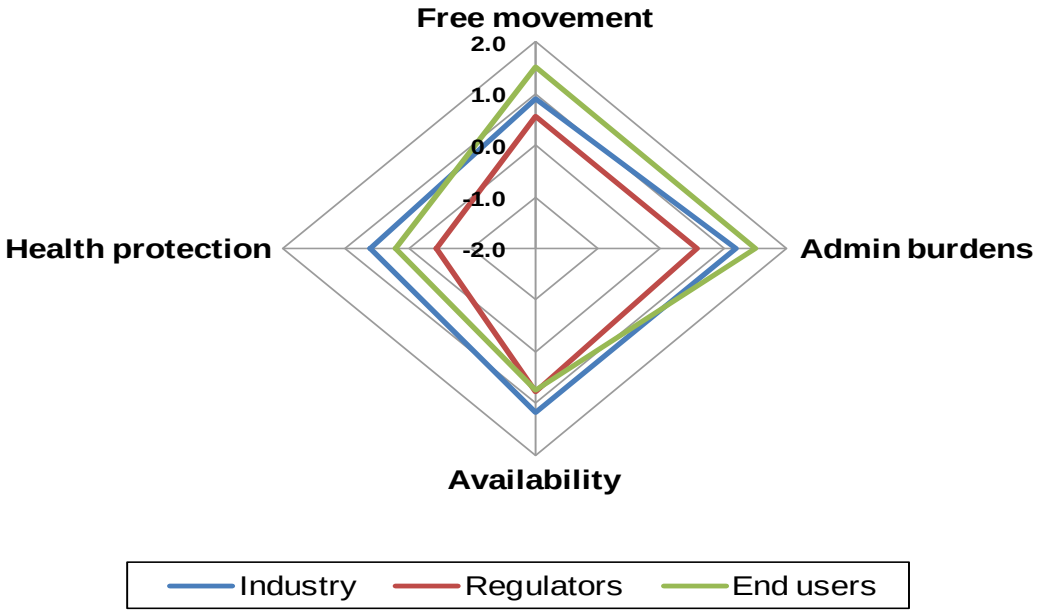
Policy option A3 - Introduction of a single marketing authorisation procedure for all products



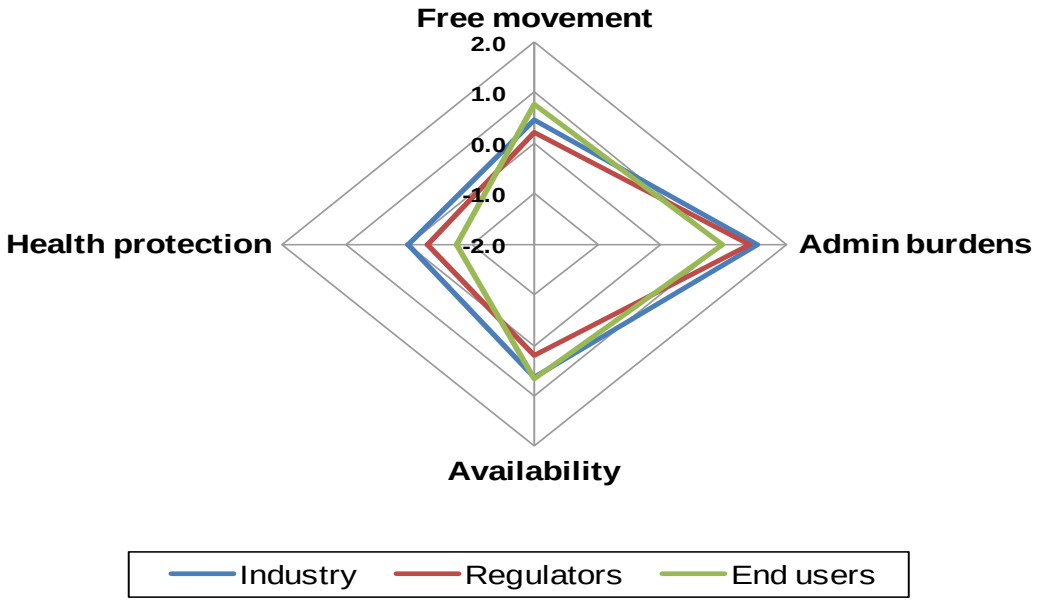
Policy option A4 – Extension of the scope of the centralised procedure



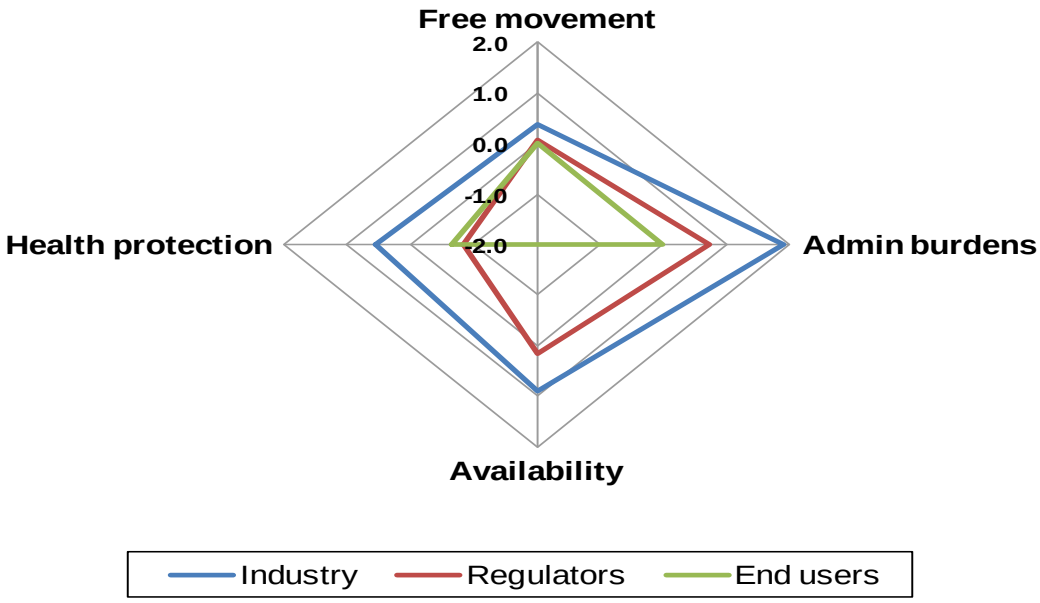
Policy option A5 - Simplification of the requirements for packaging and labelling



Policy option A6 Simplification of pharmacovigilance system

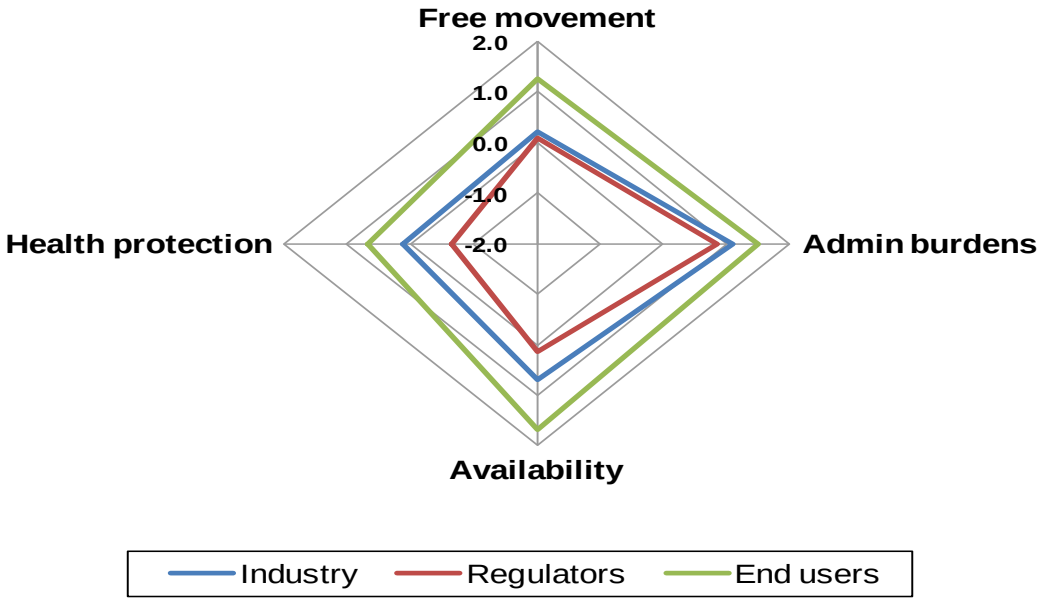


Policy option A7 Simplification of requirements for variations to marketing authorisations



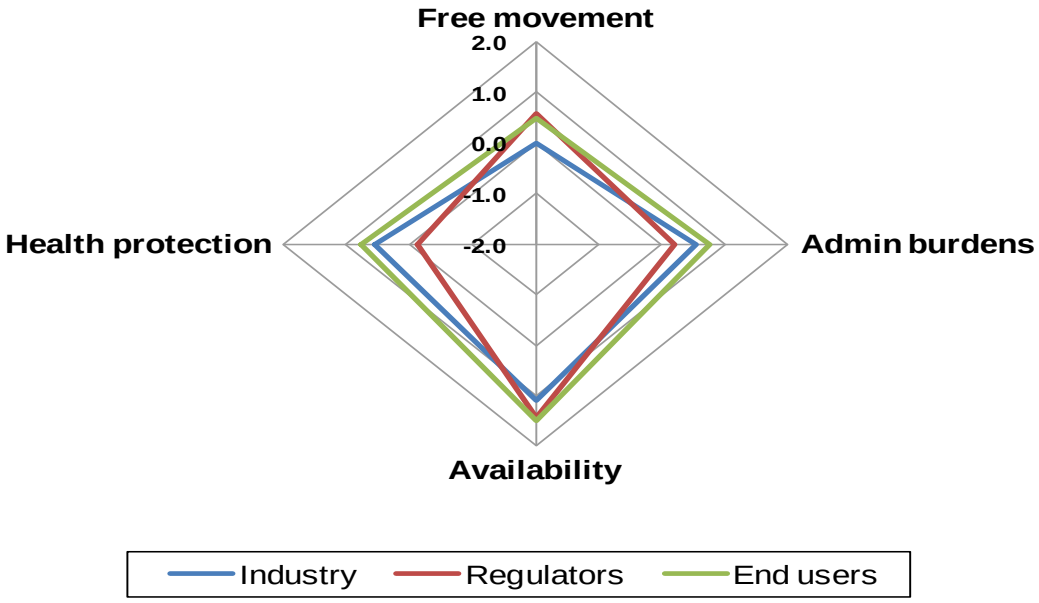
Base = 12 responses (industry); 14 responses (regulators); 5 responses (end users)

Policy option A8 Restriction of marketing authorisation renewals to specific cases

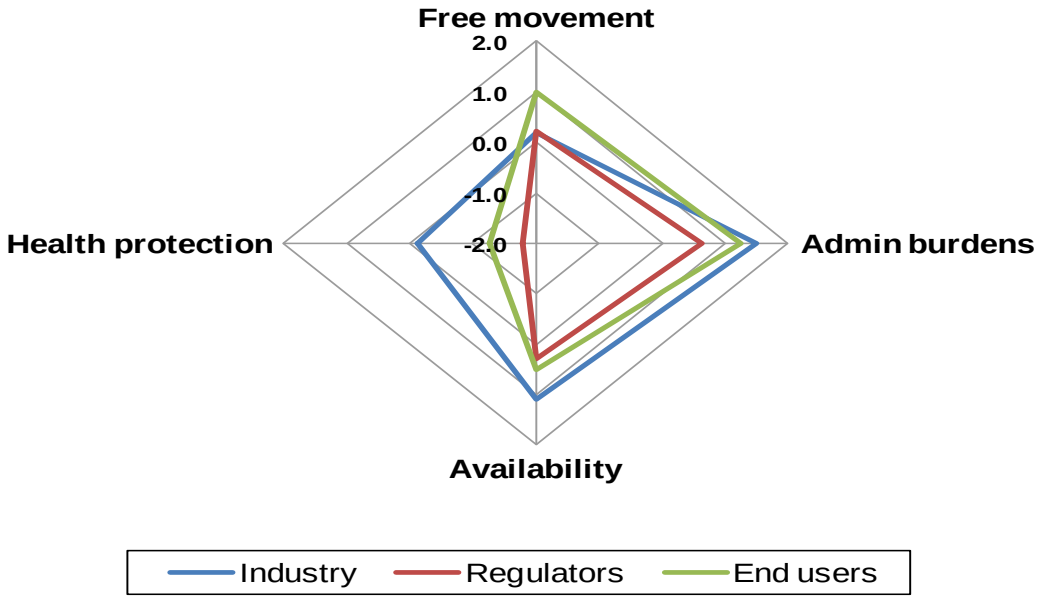


Policy option A9 Harmonisation of requirements for granting a marketing authorisation in exceptional circumstances

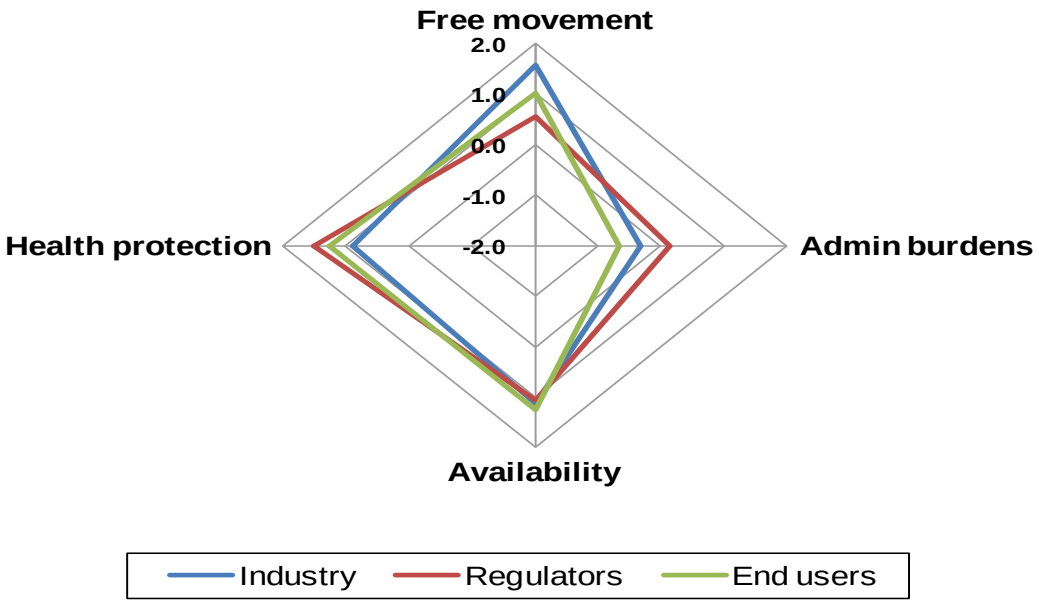
Survey respondents' scoring of the policy option 'under certain circumstances products are granted authorisations without the submission of full dossiers'



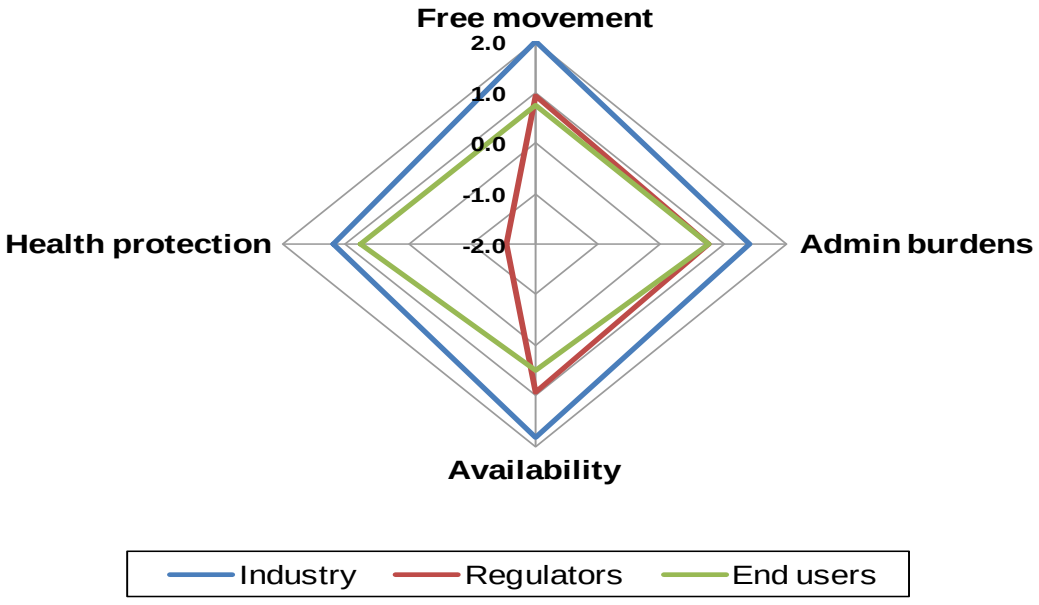
Survey respondents' scoring of the policy option 'data requirements for product authorisations are reduced'



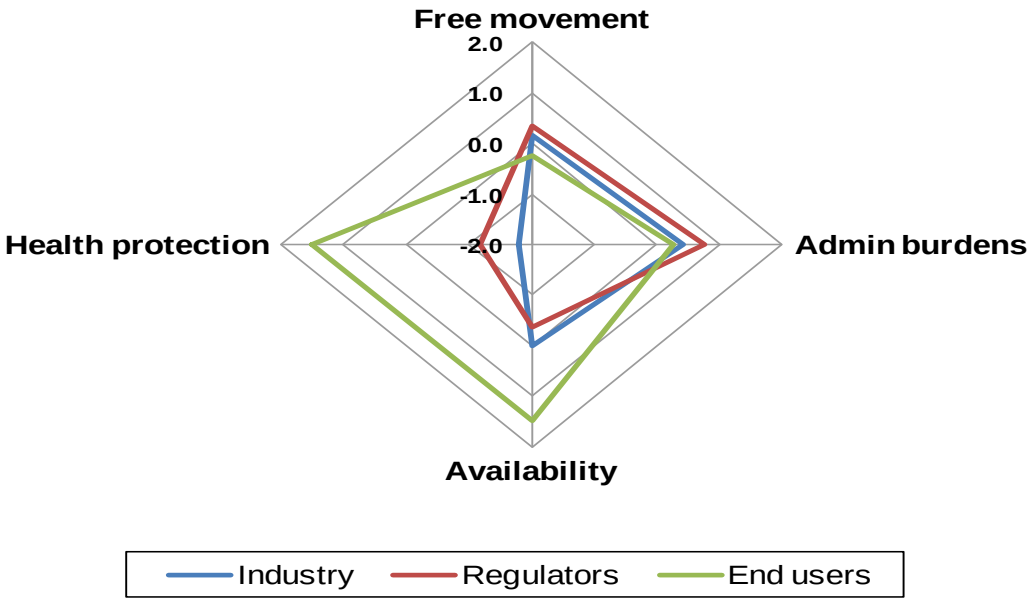
Policy option A10 Introduction of legislative measures regarding advanced veterinary therapies



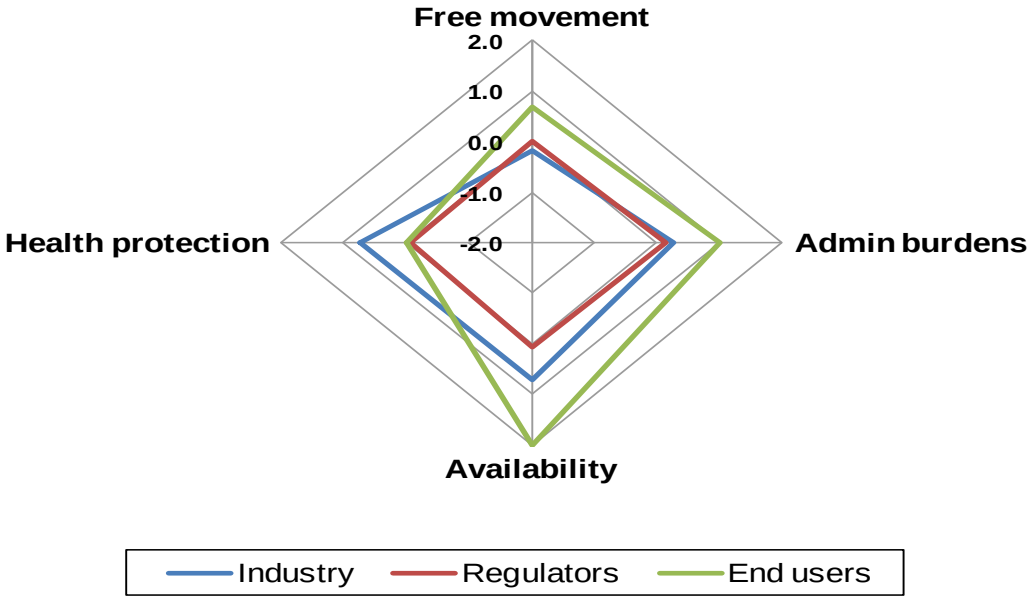
Policy option A11 Enabling existing nationally authorised veterinary medicines to freely circulate across the Union



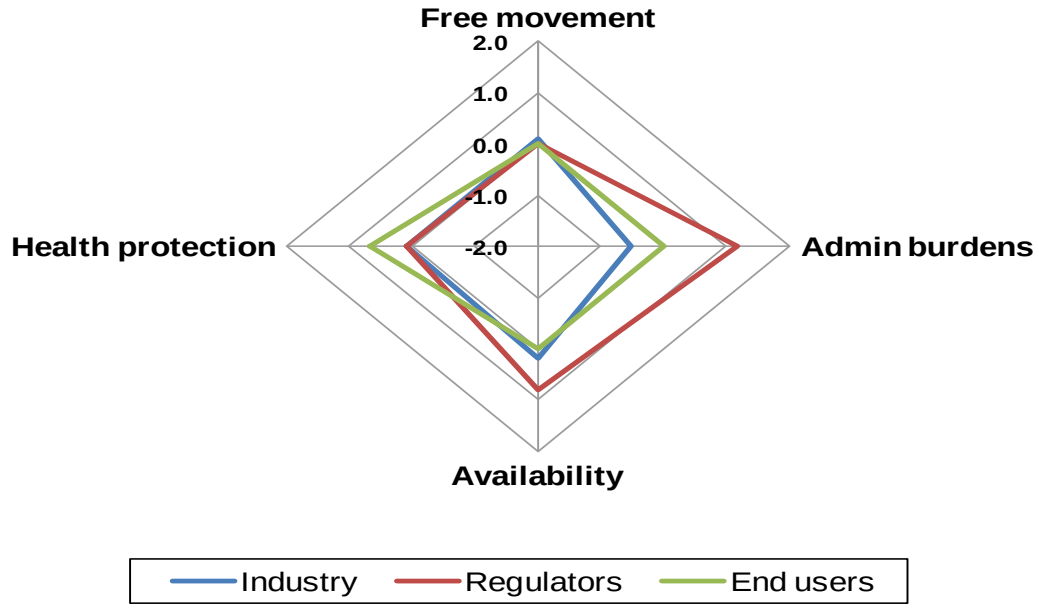
Policy option A13 Exclusion of homeopathic veterinary medicines from the scope of the legislation



Policy option B2 Extension of the data protection period for new veterinary medicines



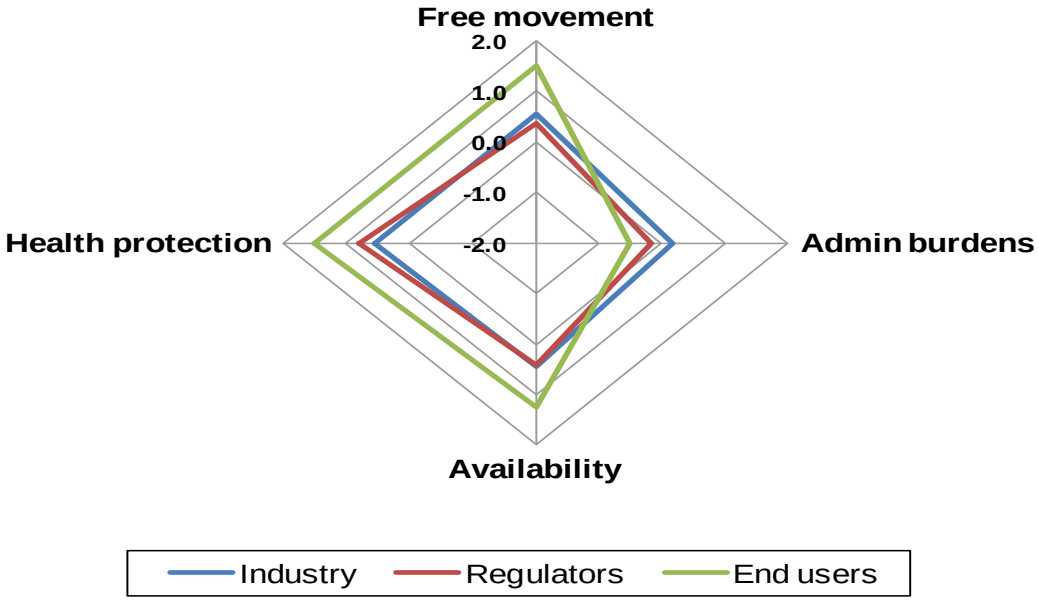
Policy option B3 Revision of data protection for environmental data



Policy option C2 Introduction of legislative measures regarding internet sales of veterinary medicines

Policy option C3 Enhance the transparency regarding veterinary medicines authorised in the Union

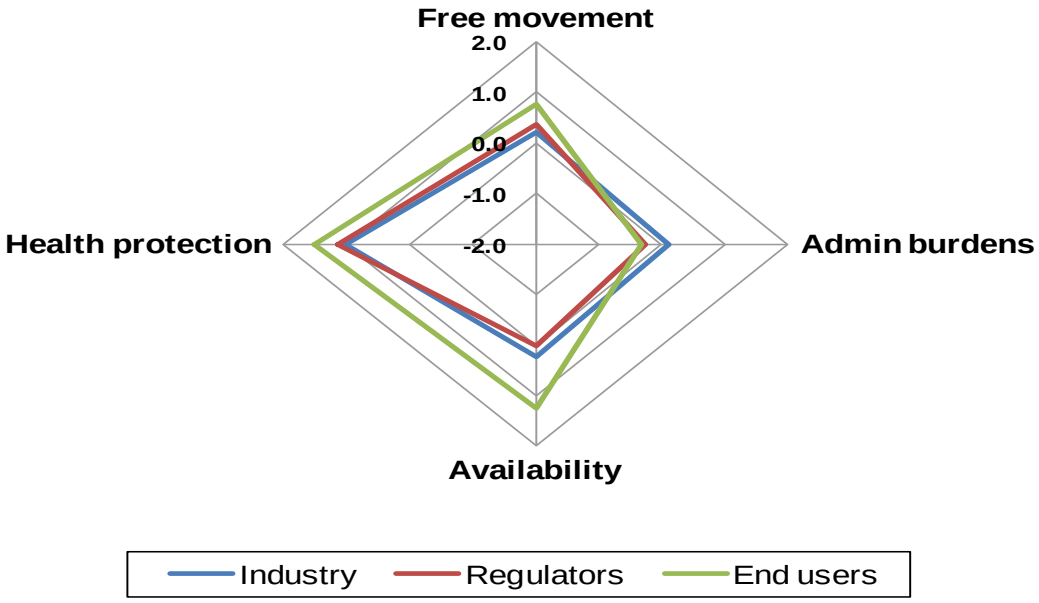
Survey respondents' scoring of the policy option 'enforcing a European database of authorised products'



Base = 12 responses (industry); 14 responses (regulators); 5 responses (end users)

Policy option C4 Introduction of a legal basis for the harmonisation of the national control systems

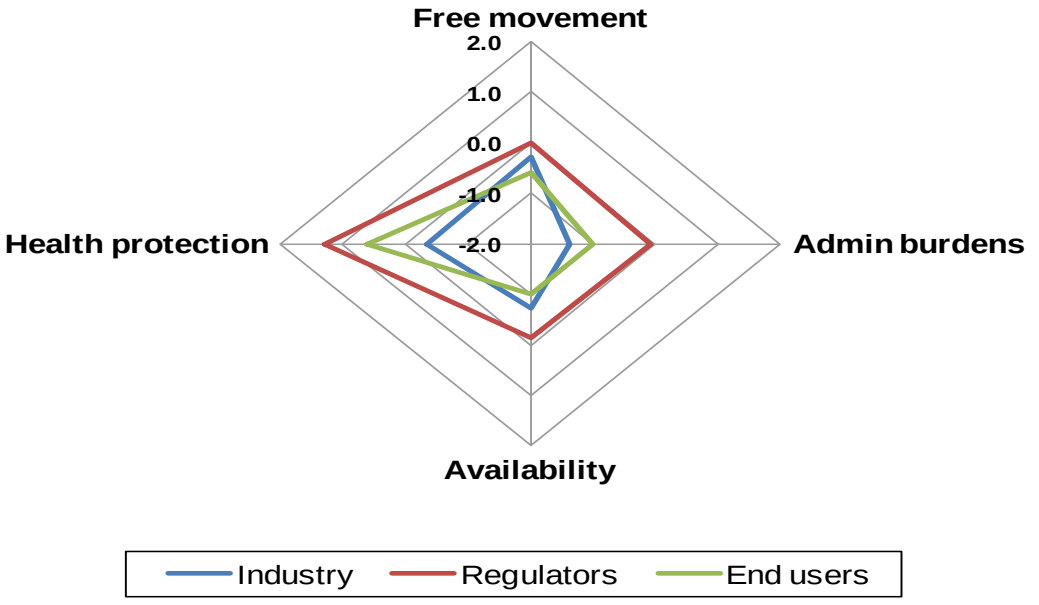
Survey respondents' scoring of the policy option 'national control systems are required to meet agreed European standards, and the Commission has the powers to check such systems'



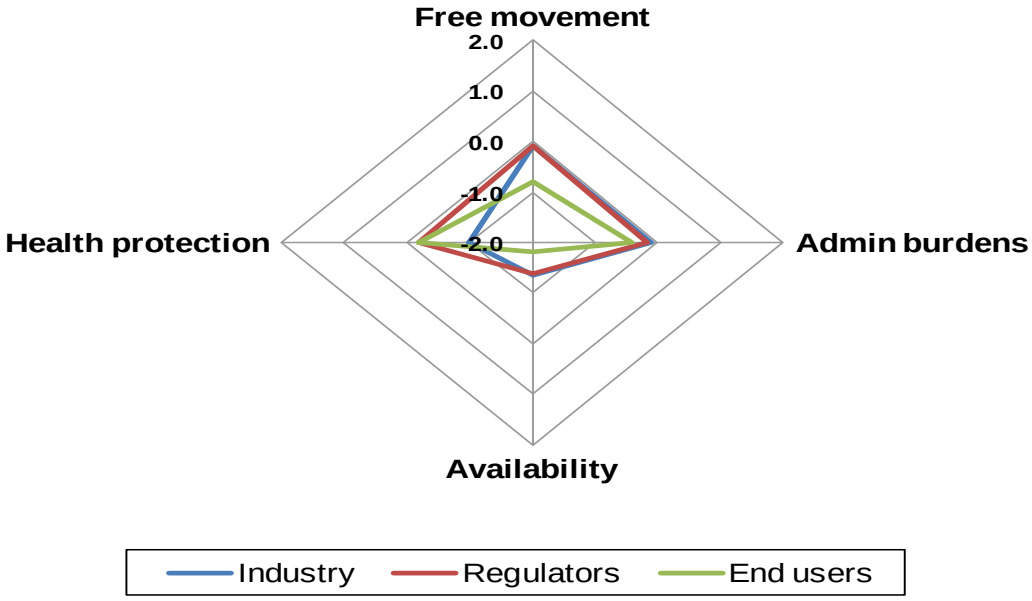
Base = 12 responses (industry); 14 responses (regulators); 5 responses (end users)

Policy option D2 Introduction of legislative measures to allow restrictions to be placed on the authorisation and use of veterinary antimicrobials

Survey respondents' scoring of the policy option 'potential impacts on antimicrobial resistance are addressed as part of the MA process'

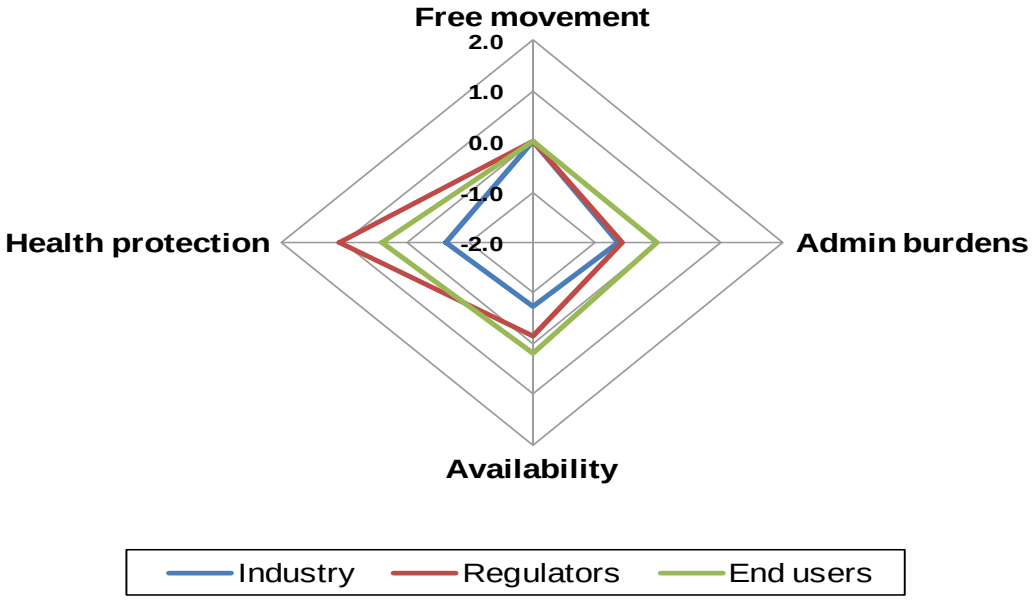


Survey respondents' scoring of the policy option 'critical antimicrobials for human use are prohibited for use in the veterinary sector'

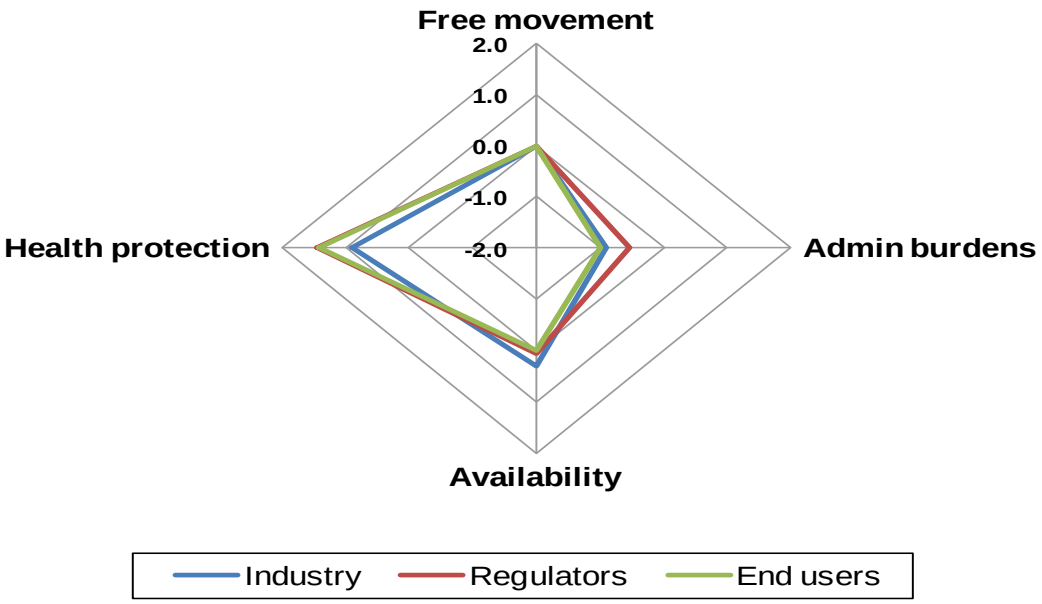


Policy option D3 Clarification on the provisions regarding advertising and retailing of veterinary antimicrobials

Survey respondents' scoring of the policy option 'controls on the advertising and marketing of antimicrobials to veterinarians'



Policy option D5 Introduction of a legal basis for the compulsory collection of data on the use of antimicrobials



B Report on the European Commission's Public Online Consultation:

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.

- **INTRODUCTION**

The European Commission is preparing a legal proposal on the review of the legal framework for veterinary medicinal products.

On 13 April 2010 a public consultation was launched on the key issues of the forthcoming legal proposal. The consultation document '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' was published on the Commission website and was available through the 'Commission's IPM tool (Interactive Policy Making) from 13 April until 15 July 2010. The consultation document is presented in Annex 1.

Annex 2 contains a full list of the names of all responding organisations or citizens. The individual responses of those respondents who did not make a specific request for confidentiality will be published on the Pharmaceuticals website.

- **BREAKDOWN OF RESPONSES**

We received 172 responses to the web-based consultation via the Interactive Policy Making Tool. We received four additional responses to the consultation by letter or email outside the Interactive Policy Making Tool. The comments in these additional responses are included in this report. However, they have not been integrated in the

tables setting out a quantitative analysis of the results. Table 2.1 gives a breakdown of the responses by type of respondent.

2.1 Category of participants			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (172)**
Citizen	26	15,12%	15,12%
Non-business organisation	28	16,28%	16,28%
Business organisation / enterprise	89	51,74%	51,74%
A public authority	29	16,86%	16,86%
In case of business organisation or enterprise, type of stakeholder			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (172)**
Farmer	7	7,87%	4,07%
Veterinarian	40	44,94%	23,26%
Manufacturer	4	4,49%	2,33%
Wholesaler	1	1,12%	0,58%
Pharmaceutical industry	35	39,33%	20,35%
Importer	0	0,00%	0,00%
Researcher	1	1,12%	0,58%
Other	4	4,49%	2,33%

- **RESPONSES TO KEY ISSUES**

The statistics of the public consultation are included in this report. The percentages are calculated on both the total number of replies to the consultation and total replies to the specific question.

- **KEY ISSUES:**
    - **Data exclusivity**

Stakeholders' views differ as to the appropriateness of the level of data protection provided by the current legal framework (see table 4.1.1). Overall, the responses can be divided into two categories. One large group (70 respondents; about 41%) considers that the level of data protection is satisfactory without substantiating their position any further. This group is made up mostly of veterinarians and farmers. Another group considers that the level of data protection is unsatisfactory (47 respondents; 27%) or very unsatisfactory (8 respondents; about 5%). This category is made up entirely of pharmaceutical companies.

4.1.1 Please indicate your satisfaction with the level of data protection provided by the current legal framework			
	Number of replies to the question	**% of total replies to the consultation**	**% of replies to the question (138)**

		(172)	
No opinion	12	6.98%	8.70%
Very unsatisfactory	8	4.65%	5.80%
Unsatisfactory	47	27.33%	34.06%
Satisfactory	70	40.70%	50.72%
Very satisfactory	1	0.58%	0.72%
N/A	-	19.77%	-

4.1.2 Do you have quantitative or qualitative data showing the impact of the current data exclusivity period on innovation (yes, no)? If so please provide estimate of impact?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (130)
Yes	27	15.70%	20.77%
No	103	59.88%	79.23%
N/A	-	24.42%	-

Limited data was provided on the effective data protection period for the first application of a new veterinary medicinal product.

4.1.3 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?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (172)
Yes	13	7.56%	7.56%
No	159	92.44%	92.44%

Only six respondents disagree with the statement that generic companies are conducive to a competitive market (see table 4.1.4). Most respondents (124; 72%) agreed with this statement.

4.1.4 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?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (138)
No opinion	8	4.65%	5.80%
Strongly disagree	6	3.49%	4.35%
Agree	116	67.44%	84.06%
Strongly agree	8	4.65%	5.80%

N/A	-	19.77%	-

A total of fifty respondents considered the current data exclusivity period to be unsatisfactory or very unsatisfactory; nineteen respondents indicated that the current situation was satisfactory or very satisfactory (see table 4.1.5). Almost all pharmaceutical companies developing new products consider the current data exclusivity period to be unsatisfactory.

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

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (136)
No opinion	67	38.95%	49.26%
Very unsatisfactory	23	13.37%	16.91%
Unsatisfactory	27	15.70%	19.85%
Satisfactory	15	8.72%	11.03%
Very satisfactory	4	2.33%	2.94%
N/A	-	20.93%	-

Most respondents (101; 69%) agree that the general data protection period of 10 years should be increased (table 4.1.6). The vast majority (109; 63%) consider that the current additional data exclusivity period of one year for each extension of the original authorisation is inappropriate (see table 4.1.7) and would be in favour of major product developments having their own period of data protection (120; 71%) (see table 4.1.8).

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

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (135)
No opinion	12	6.98%	8.89%
Strongly disagree	22	12.79%	16.30%
Agree	69	40.12%	51.11%
Strongly agree	32	18.60%	23.70%
N/A	-	21.51%	-

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

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (135)
No opinion	10	5.81%	7.41%
Very unsatisfactory	27	15.70%	20.00%
Unsatisfactory	82	47.67%	60.74%

Satisfactory	14	8.14%	10.37%
Very satisfactory	2A	1.16%	1.48%
N/A	-	21.51%	-

4.1.8 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)?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (135)
Favour not at all	4	2.33%	2.96%
Favour not	5	2.91%	3.70%
Favour somewhat	70	40.70%	51.85%
Favour clearly	17	9.88%	12.59%
Favour very much	35	20.35%	25.93%
Do not know	4	2.33%	2.96%
N/A	-	21.51%	-

Most respondents (63%) would be in favour of amending the condition whereby it is only in a five-year period following the granting of the initial marketing authorisation that an extension of the period of data exclusivity can be obtained (see table 4.1.9).

4.1.9 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?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (135)
Favour not at all	4	2.33%	2.96%
Favour not	14	8.14%	10.37%
Favour somewhat	70	40.70%	51.85%
Favour clearly	8	4.65%	5.93%
Favour very much	30	17.44%	22.22%
Do not know	9	5.23%	6.67%
N/A	-	21.51%	-

Many respondents refer to the negative effects which the global marketing authorisation concept has on innovations. This concept does not take into account the investment and innovation involved into further developing a product.

Most respondents consider that data protection rules place a particularly heavy burden on SMEs (see table 4.1.10). Further analysis shows that the majority of industry respondents do not consider that there is a specific burden on SMEs (Yes 3%, No 53%, Do not know 27%, N/A 17%). Veterinarians, however, hold the opposite opinion (Yes 75%, No 2%, Do not know 11%, N/A 12%).

4.1.10 Do you consider that in data protection rules there are particular burdens in relation to the features of SMEs?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (132)**
Yes	70	40.70%	53.03%
No	34	19.77%	25.76%
Do not know	28	16.28%	21.21%
N/A	-	23.26%	-

Most respondents (65%) would like to introduce specific intellectual property incentives for small markets (see table 4.1.11). Only a very small majority (5%) would not be in favour.

4.1.11 Should specific intellectual property incentives be developed for small markets?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (130)**
Yes	111	64.53%	85.38%
No	8	4.65%	6.15%
Do not know	11	6.40%	8.46%
N/A	-	24.42%	-

The respondents considered that the current exclusivity period of 13 years for fish and bees is insufficient (54%) and should be extended (56%) (see table 4.1.12).

4.1.12 Do you consider the current data protection period of 13 years for fish and bees appropriate?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (134)**
Yes	17	9.88%	12.69%
No	93	54.07%	69.40%
Do not know	24	13.95%	17.91%
N/A	-	22.09%	-

The public were asked to indicate which species should receive the same approach as bees and fish. Almost all those who provided comments considered that the same exclusivity period should apply for all minor species and minor uses.

4.1.13 Should the data period of 13 years for bees and fish be extended to other species?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (134)**
No opinion	11	6.40%	8.21%
Very unsatisfactory	8	4.65%	5.97%

Unsatisfactory	5	2.91%	3.73%
Satisfactory	97	56.40%	72.39%
Very satisfactory	13	7.56%	9.70%
N/A	-	22.09%	-

Most respondents considered that generics increase the availability of medicines (see table 4.1.14).

4.1.14 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)?

	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (136)**
No opinion	8	4.65%	5.88%
Strongly disagree	34	19.77%	25.00%
Agree	35	20.35%	25.74%
Strongly agree	59	34.30%	43.38%
N/A	-	20.93%	-

About half of the respondents (48%) consider that generic veterinary products based on old reference products could pose a risk for public or animal health (see table 4.1.15).

4.1.15 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?

	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (140)**
Yes	84	48.84%	60.00%
No	50	29.07%	35.71%
Do not know	6	3.49%	4.29%
N/A	-	18.60%	-

Most respondents (100; 58%) felt that an generic should be allowed to use environmental data (see table 4.1.16). Industry respondents pointed out that environmental safety data requirements could be adapted if a level playing field was guaranteed for all marketing authorisation holders.

4.1.16 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?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (128)**
Yes	100	58.14%	78.13%
No	14	8.14%	10.94%
Do not know	14	8.14%	10.94%
N/A	-	25.58%	-

No clear position emerged on the establishment of a monograph system for environmental risks: 34% of the respondents had no opinion, 18% were not in favour, 10% somewhat in favour and 18% clearly or very much in favour.

4.1.17 Would you favour a monograph system for environmental risks?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (138)**
Favour not at all	25	14.53%	18.12%
Favour not	6	3.49%	4.35%
Favour somewhat	18	10.47%	13.04%
Favour clearly	14	8.14%	10.14%
Favour very much	17	9.88%	12.32%
Do not know	58	33.72%	42.03%
N/A	-	19.77%	-

- **Authorisation procedure**

About 74% of the respondents are dissatisfied or very dissatisfied with the current authorisation procedure and only a minority (23; 13%) appears to be satisfied. This last group of respondents consists mostly of authorities (11), veterinarians (4) and two business respondents active in homeopathics.

4.2.1 How do you rank your satisfaction with the current authorisation procedures?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (136)**
No opinion	4	2,33%	2,94%
Very dissatisfied	4	2,33%	2,94%
Dissatisfied	105	61,05%	77,21%
Satisfied	23	13,37%	16,91%
Very satisfied	0	0,00%	0,00%
N/A	-	20,93%	-

A majority of respondents (100; 58%) considered that there is no need for several authorisation procedures in the EU (see table 4.2.2). However, a substantial minority (35; 20%) believed that there is a need for several procedures. This minority consisted

of authorities (12), veterinarians (10) and almost all respondents active in aquaculture (3). Similar results were obtained on the question whether it is necessary that the number of authorisation procedures should be simplified by reducing it to one as 62% of the respondents agreed to this position (see table 4.2.3).

4.2.2 Do you consider that there is a need for several authorisation procedures in the EU?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (138)
Yes	35	20,35%	25,36%
No	100	58,14%	72,46%
Don't know	3	1,74%	2,17%
N/A	-	19,77%	-

4.2.3 Do you consider it necessary that the number of authorisation procedures should be simplified by reducing it to only one?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (139)
No opinion	4	2,33%	2,88%
Strongly disagree	27	15,70%	19,42%
Agree	76	44,19%	54,68%
Strongly agree	32	18,60%	23,02%
N/A	-	19,19%	-

A majority of the respondents (71; 41%) consider that there are parts in the authorisation procedures in particular burdensome for SMEs. The respondents that did not agree with this statement (29;17%) consisted mostly of industry (19) and authorities (5).

4.2.4 Do you consider that there are parts in the authorisation procedures in particular burdensome for SMEs?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (124)
Yes	71	41,28%	57,26%
No	29	16,86%	23,39%
Do not know	24	13,95%	19,35%
N/A	-	27,91%	-

About 59% of the respondents expressed to be satisfied or very satisfied with the current centralised procedure and about 12% of respondents appear to be dissatisfied or very dissatisfied (table 4.2.5). This last group of respondents consists of industry (8), veterinarians (5), authorities (3) and food producers (3).

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

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (133)
No opinion	8	4,65%	6,02%
Very dissatisfied	3	1,74%	2,26%
Dissatisfied	20	11,63%	15,04%
Satisfied	96	55,81%	72,18%
Very satisfied	6	3,49%	4,51%
N/A	-	22,67%	-

There appears to be strong support among respondents (120; 72%) to extend the scope of the centralised procedure (see table 4.2.6).

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

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (136)
Favour not at all	4	2,33%	2,94%
Favour not	8	4,65%	5,88%
Favour somewhat	15	8,72%	11,03%
Favour clearly	93	54,07%	68,38%
Favour very much	12	6,98%	8,82%
Do not know	4	2,33%	2,94%
N/A	-	20,93%	-

About 64% of the respondents are dissatisfied or very dissatisfied with the current mutual recognition and decentralised procedure (see table 4.2.7). A minority (18; 10 %) appeared to be satisfied. This last group of respondents consisted mostly of authorities (11).

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

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (135)
No opinion	7	4,07%	5,19%
Very dissatisfied	5	2,91%	3,70%
Dissatisfied	105	61,05%	77,78%
Satisfied	18	10,47%	13,33%
Very satisfied	0	0,00%	0,00%
N/A	-	21,51%	-

The reputation for efficiency and scientific expertise of the competent authority appear the most important criteria for selecting it as reference member state, followed closely by previous favourable experience and reputation for communication (see table 4.2.8). The geographical location seems to be of less importance.

4.2.8 What are your criteria for selecting the reference Member State in the decentralised procedure?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (172)**
Previous favourable experience	34	19,77%	19,77%
Reputation for efficiency	42	24,42%	24,42%
Reputation for scientific expertise	38	22,09%	22,09%
Reputation for communication	28	16,28%	16,28%
Geographical location	24	13,95%	13,95%
Other	12	6,98%	6,98%

There appears to be a strong support (68% of respondents) for a conditional authorisation system (see table 4.2.9).

4.2.9 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?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (131)**
No opinion	9	5,23%	6,87%
Strongly disagree	4	2,33%	3,05%
Agree	113	65,70%	86,26%
Strongly agree	5	2,91%	3,82%
N/A	-	23,84%	-

Most respondents to the public consultation (51%) did not favour to include indirect risks in the risk-benefit assessment of veterinary medicines (table 4.2.10). However, a majority (58%) favoured to include in the legal framework a basis for restricting a marketing application in cases where authorisation of a specific medicine would pose an indirect risk to animal or human health (see table 4.2.11).

4.2.10 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?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (132)**
Favour not at all	26	15,12%	19,70%
Favour not	62	36,05%	46,97%
Favour somewhat	13	7,56%	9,85%
Favour clearly	15	8,72%	11,36%
Favour very much	12	6,98%	9,09%
Do not know	4	2,33%	3,03%
N/A	-	23,26%	-

4.2.11 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?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (139)**
Favour not at all	23	13,37%	16,55%
Favour not	9	5,23%	6,47%
Favour somewhat	69	40,12%	49,64%
Favour clearly	18	10,47%	12,95%
Favour very much	13	7,56%	9,35%
Do not know	7	4,07%	5,04%
N/A	-	19,19%	-

A majority (51%) of respondents favoured not to include in the legal framework a specific legal basis to restrict the use of antimicrobials which are critical for human medicines (table 4.2.12).

4.2.12 Would you favour that the legal framework provides a specific legal basis to restrict the use of antimicrobials which are critical for human medicine?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (138)**
Favour not at all	80	46,51%	57,97%
Favour not	7	4,07%	5,07%
Favour somewhat	22	12,79%	15,94%
Favour clearly	13	7,56%	9,42%
Favour very much	13	7,56%	9,42%
Do not know	3	1,74%	2,17%
N/A	-	19,77%	-

- **Packaging and labelling**

Regarding packaging and labelling requirements for veterinary medicines the stakeholders were asked six questions. It can be extracted from their answers, firstly, that the majority of the stakeholders believe that it is clearly essential or very much essential to have packaging and labelling requirements at EU level (see table 4.3.1).

4.3.1 Do you consider EU - packaging and labelling requirements essential in terms of providing appropriate information to the users of veterinary medicines?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (142)**
Not essential at all	1	(0.6%)	(0.7%)
Not essential	5	(2.9%)	(3.5%)
Somewhat essential	11	(6.4%)	(7.7%)
Clearly essential	104	(60.5%)	(73.2%)
Very much essential	20	(11.6%)	(14.1%)
Don't know	1	(0.6%)	(0.7%)
N/A	30	(17.4%)	-

When they were asked if they would be in favour of reducing the requirement and the information needed in the packages and labels (see tables 4.3.2 and 4.3.3) most of the participants were positive about the idea.

Concerning the possibility of having fewer or non packaging and labelling requirements at all (see table 4.3.2) half of the stakeholders, mostly consisting of veterinarians, are somewhat in favour. The authorities answered mostly negatively to this question. Respondents of industry were clearly or very much in favour.

4.3.2 Would you be in favour of fewer packaging and labelling requirements, or none at all, in the EU legal framework?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (140)
Favour not at all	14	(8.1%)	(10%)
Favour not	17	(9.9%)	(12.1%)
Favour somewhat	71	(41.3%)	(50.7%)
Favour clearly	9	(5.2%)	(6.4%)
Favour very much	29	(16.9%)	(20.7%)
Do not know	0	(0%)	(0%)
N/A	32	(18.6%)	-

With regard to the possibility of reducing the information on the label, most of the participants would be somewhat in favour of the measure (see table 4.3.3). They are basically veterinarians and the authorities. Stakeholders from the industry are mainly the ones clearly or very much in favour of this idea.

4.3.3 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?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (138)
Favour not at all	5	(2.9%)	(3.6%)
Favour not	8	(4.7%)	(5.8%)
Favour somewhat	74	(43%)	(53.6%)
Favour clearly	9	(5.2%)	(6.5%)
Favour very much	42	(24.4%)	(30.4%)
Do not know	0	(0%)	(0%)
N/A	34	(19.8%)	-

On the issue about allowing Member States to decide which language is be used for labelling and packaging (see table 4.3.4), the majority are positive.

4.3.4 Would you favour Member States being allowed to decide which language is to be used for labelling and packaging?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (139)
Favour not at all	2	(1.2%)	(1.4%)
Favour not	5	(2.9%)	(3.6%)
Favour somewhat	67	(39%)	(48.2%)
Favour clearly	43	(25%)	(30.9%)
Favour very much	21	(12.2%)	(15.1%)
Do not know	1	(0.6%)	(0.7%)
N/A	33	(19.2%)	-

Regarding the possibility of having specific requirements for small packs (see table 4.3.5) most the stakeholders agree or strongly agree with it.

4.3.5 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?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (137)**
No opinion	2	(1.2%)	(1.5%)
Strongly disagree	1	(0.6%)	(0.7%)
Agree	92	(53.5%)	(67.2%)
Strongly agree	42	(24.4%)	(30.7%)
N/A	35	(20.3%)	-

About half of the respondents (79 out of the 172 participants in the public consultation) gave concrete proposals to amend the legal framework. Two main groups of proposals could be established.

- **Pharmacovigilance and monitoring**

The majority of respondents agree or strongly agree that the needs and expectations concerning the safety level of veterinary pharmacovigilance should be different from those concerning human medical products (see table 4.4.1). Most of those respondents are veterinarians and representatives from the industry.

4.4.1 Do you consider that the needs and expectations concerning the safety level of veterinary pharmacovigilance could be different for human pharmacovigilance?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (140)**
No opinion	3	(1.7%)	(2.1%)
Strongly disagree	20	(11.6%)	(14.3%)
Agree	83	(48.3%)	(59.3%)
Strongly agree	34	(19.8%)	(24.3%)
N/A	32	(18.6%)	-

As table 4.4.2 shows, the majority of respondents are positive about introducing a master file for pharmacovigilance or any other way of reducing the regulatory burden on authorisation holders. At sectorial level, the authorities and industry are very much in favour of such measures, whereas most veterinarians are merely 'somewhat in favour'.

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

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (139)
Favour not at all	2	(1.2%)	(1.4%)
Favour not	2	(1.2%)	(1.4%)
Favour somewhat	69	(40.1%)	(49.6%)
Favour clearly	18	(10.5%)	(12.9%)
Favour very much	46	(26.7%)	(33.1%)
Do not know	2	(1.2%)	(1.4%)
N/A	33	(19.2%)	-

On the question whether the participants in the consultation think that there are particular problems in the legislation for pharmacovigilance for SMEs (see table 4.4.3), it can be seen from the data that most of the respondents do not have a position on this particular issue.

Among those who have an opinion, the majority think that there are problems.

4.4.3 Do you think that there are particular problems in the legislation for pharmacovigilance for SMEs?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (130)**
Yes	42	(24.4%)	(32.3%)
No	11	(6.4%)	(8.5%)
Do not know	77	(44.8%)	(59.2%)
N/A	42	(24.4%)	-

Finally, as regards the possibility of establishing a harmonised system for data collection on the sales and use of medicines in the EU, the majority of respondents are just somewhat in favour of the measure (see table 4.4.4). They are mainly veterinarians and representatives from the industry. Those who are clearly or very much in favour are the authorities and non-business organisations.

4.4.4 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?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (139)**
Favour not at all	4	(2.3%)	(2.9%)
Favour not	2	(1.2%)	(1.4%)
Favour somewhat	83	(48.3%)	(59.7%)
Favour clearly	27	(15.7%)	(19.4%)
Favour very much	18	(10.5%)	(12.9%)
Do not know	5	(2.9%)	(3.6%)
N/A	33	(19.2%)	-

o The Distribution Channel

A majority of the respondents (66%) agree or strongly agree (see table 4.5.1) that there is a need to standardise and harmonise the conditions for operators in the EU distribution channel. When the participants were asked if they would be in favour of standardisation by amending the European legal framework, the same results were obtained: a majority replied positively (see table 4.5.2).

4.5.1 Do you consider that there is a need to standardise and harmonise the conditions for operators in the EU distribution channel			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (142)**
No opinion	7	(4.1%)	(4.9%)
Strongly disagree	31	(18%)	(21.8%)
Agree	83	(48.3%)	(58.5%)
Strongly agree	21	(12.2%)	(14.8%)

N/A	30	(17.4%)	-

4.5.2 If so, would you favour standardisation by amending the European legal framework?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (138)**
Favour not at all	28	(16.3%)	(20.3%)
Favour not	5	(2.9%)	(3.6%)
Favour somewhat	15	(8.7%)	(10.9%)
Favour clearly	70	(40.7%)	(50.7%)
Favour very much	16	(9.3%)	(11.6%)
Do not know	4	(2.3%)	(2.9%)
N/A	34	(19.8%)	-

Most of the participants are very much in favour or clearly in favour of the prescription of medicines being standardised in the EU (see table 4.5.3), especially veterinarians, authorities and non-business organisations. Industry representatives are mainly not at all in favour.

4.5.3 Would you be in favour of the prescription of medicines being standardised in the EU			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (142)**
Favour not at all	27	(15.7%)	(19%)
Favour not	5	(2.9%)	(3.5%)
Favour somewhat	9	(5.2%)	(6.3%)
Favour clearly	23	(13.4%)	(16.2%)
Favour very much	76	(44.2%)	(53.5%)
Do not know	2	(1.2%)	(1.4%)
N/A	30	(17.4%)	-

Most respondents (60%) consider that cross-border activities of the sector are hampered by the current rules (see table 4.5.4).

4.5.4 Do you consider that cross-border activities, for example involving veterinarians active in two Member States, are hampered by the current rules?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (142)**
Yes	103	(59.9%)	(72.5%)
No	24	(14%)	(16.9%)
Do not know	15	(8.7%)	(10.6%)
N/A	30	(17.4%)	-

As far as counterfeit veterinary medicines are concerned, a majority agrees that they have penetrated the veterinary supply chain (see table 4.5.5). However, it needs to be emphasised that a number of participants strongly disagree with the above statement, especially stakeholders from the industry.

4.5.5 Do you agree that counterfeit medicines have penetrated the veterinary supply chain?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (139)**
No opinion	31	(18%)	(22.3%)
Strongly disagree	25	(14.5%)	(18%)
Agree	80	(46.5%)	(57.6%)
Strongly agree	3	(1.7%)	(2.2%)
N/A	33	(19.2%)	-

A lot of the respondents consider that there are risks to public health from the penetration of counterfeit medicines into the veterinary supply chain (see table 4.5.6).

4.5.6 If so, do you consider that there are risks to public health from the penetration of counterfeit medicines into the veterinary supply chain?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (132)**
No opinion	6	(3.5%)	(4.5%)
Strongly disagree	4	(2.3%)	(3%)
Agree	102	(59.3%)	(77.3%)
Strongly agree	20	(11.6%)	(15.2%)
N/A	40	(23.3%)	-

When the participants in the consultation were asked about whether they consider counterfeiting of veterinary medicinal products to be a problem for animal health and/or public health in the EU, a large proportion (40%) said they did not have an opinion (table 4.5.7).

4.5.7 Do you consider counterfeiting of veterinary medicinal products to be a problem for animal health and/or public health in the EU?			
	Number of replies to the question	**% of total replies to the consultation (172)**	**% of replies to the question (143)**
No opinion	68	(39.5%)	(47.6%)
Strongly disagree	22	(12.8%)	(15.4%)
Agree	36	(20.9%)	(25.2%)
Strongly agree	17	(9.9%)	(11.9%)
N/A	29	(16.9%)	-

Notwithstanding the clear positions on counterfeit medicines, the great majority of respondents (9578%) indicated that they had neither quantitative nor qualitative data on counterfeit veterinary medicinal products (see table 4.5.8). It can be concluded that there is a consensus among stakeholders (129 out of 131 respondents to this question) that legislative measures are necessary to tackle counterfeit veterinary medicinal products (table 4.5.9).

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

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (140)
Yes	6	(3.5%)	(4.3%)
No	134	(77.9%)	(95.7%)
N/A	32	(18.6%)	-

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

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (145)
Yes	129	(75%)	(89%)
No	2	(1.2%)	(1.4%)
Do not know	14	(8.1%)	(9.7%)
N/A	27	(15.7%)	-

The majority (76%) of participants in the consultation agree or strongly agree that issues such as internet trade, mail order selling or parallel import should be addressed in the revision of the legal framework for veterinary medicines (table 4.5.10). In this connection, as we can see from table 4.5.11, most of the participants consider that the legal framework should be supplemented with specific requirements on these aspects.

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

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (143)
No opinion	2	(1.2%)	(1.4%)
Strongly disagree	9	(5.2%)	(6.3%)
Agree	53	(30.8%)	(37.1%)
Strongly agree	79	(45.9%)	(55.2%)
N/A	29	(16.9%)	-

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

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (142)
Yes	129	(75%)	(90.8%)

No	9	(5.2%)	(6.3%)
Do not know	4	(2.3%)	(2.8%)
N/A	30	(17.4%)	-

- **The use of drugs not in accordance with the summary of product characteristics (off-label use)**

About 86% of respondents considered the description in the public consultation accurate (see table 4.6.1). A minority (34 replies; 19%) considered that off-label use of medicines was too common in the EU; the majority (99 replies; 58%) did not agree with this statement (table 4.6.2). This last group consisted mostly of veterinarians and respondents from the pharmaceutical industry.

4.6.1 Is the above an accurate description of the situation?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (151)
Yes	148	86.05%	98.01%
No	3	1.74%	1.99%
N/A	-	12.21%	-

4.6.2 Do you consider that off-label use of medicines is too common in the EU?

	Number of replies to the question	% of total replies to the consultation (172)	% of replies to the question (152)
No opinion	19	11.05%	12.50%
Strongly disagree	99	57.56%	65.13%
Agree	28	16.28%	18.42%
Strongly agree	6	3.49%	3.95%
N/A	-	11.63%	-

Respondents clarified that limited data existed on off-label use (only 14 out of 147 respondents reported that they had such data) (see table 4.6.3). Some qualitative data were provided on rabbits, horses, poultry and aquaculture for certain Member States. One authority provided data on the extent veterinarians had to rely on veterinary medicines imported from other Member States for use under the cascade. It appeared that the vast majority of applications for importation were for pets. One pharmaceutical company stated that 25-30% of suspected adverse reactions reported involved off-label use.

4.6.3 Do you have quantitative or qualitative data on off-label use?

	Number of replies	% of total replies to the questionnaire (172)	% of replies to the question (147)
Yes	14	8.14%	9.52%
No	133	77.33%	90.48%
N/A	-	14.53%	-

Most of the respondents (115 replies; 67%) considered off-label use a potential hazard (see table 4.6.4). However, a substantial minority (32 replies; 19%) did not agree with this statement; these were mainly producers (10 replies), veterinarians (6 replies) or from industry (5 replies).

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

	Number of replies	% of total replies to the questionnaire (172)	% of replies to the question (151)
Yes	115	66.86%	76.16%
No	32	18.60%	21.19%
Do not know	4	2.33%	2.65%
N/A	-	12.21%	-

A minority (47 replies; 27%) considered it appropriate to exclude certain medicines from off-label use (see table 4.6.5). These were mainly authorities (17 replies), producers (10 replies), veterinarians (10 replies) and industry (5 replies). Most of the respondents (104 replies, 69%) did not agree with the statement to exclude certain medicines from off-label use.

4.6.5 Would you consider it appropriate to exclude certain medicines from off-label use?

	Number of replies	% of total replies to the questionnaire (172)	% of replies to the question (151)
No opinion	12	6.98%	7.95%
Strongly disagree	92	53.49%	60.93%
Agree	39	22.67%	25.83%
Strongly agree	8	4.65%	5.30%
N/A	-	12.21%	-

Many respondents (86 replies) took the opportunity to put forward proposals for amending the legal framework concerning off-label use.

o Harmonisation of already authorised veterinary products

Regarding this key issue, the vast majority of the respondents agree with the description of the situation done by the Commission (see table 4.7.1).

4.7.1 Do you agree with the description of the issue?

	Number of replies	% of total replies to the questionnaire (172)	% of replies to the question (141)
Yes	139	(80.8%)	(98.6%)
No	2	(1.2%)	(1.4%)
N/A	31	(18%)	-

However, when they were asked if they consider necessary to update and to harmonise the already authorised medicines, the majority (52%) disagreed (see table 4.7.2), mainly consisting of participants from the industry and veterinaries. The authorities, even if they are divided in their opinions, most of them are the ones who agree or strongly agree with the idea of updating and harmonising the already authorised veterinary medicines. Respondents from non business organisations are equally divided between agree and disagree.

4.7.2 Do you consider it necessary to update and to harmonise already authorised medicines?			
	Number of replies	**% of total replies to the questionnaire (172)**	**% of replies to the question (142)**
No opinion	5	(2.9%)	(3.5%)
Strongly disagree	90	(52.3%)	(63.4%)
Agree	36	(20.9%)	(25.4%)
Strongly agree	11	(6.4%)	(7.7%)
N/A	30	(17.4%)	-

A majority of respondents agreed to a risk-based harmonisation (to update and to harmonise already authorised medicines differently according to the public health risks involved) (table 4.7.3).

4.7.3 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)?			
	Number of replies	**% of total replies to the questionnaire (172)**	**% of replies to the question (142)**
Yes	131	(76.2%)	(92.3%)
No	11	(6.4%)	(7.7%)
N/A	30	(17.4%)	-

The majority of the respondents (57%) preferred a compulsory approach to update and to harmonise already authorised medicines (see table 4.7.4), consisting mainly of veterinarians, authorities and non business organisations.

4.7.4 If a procedure were established to update and to harmonise already authorised medicines, would you prefer a compulsory approach?			
	Number of replies	**% of total replies to the questionnaire (172)**	**% of replies to the question (143)**
No opinion	10	(5.8%)	(7%)
Strongly disagree	34	(19.8%)	(23.8%)
Agree	92	(53.5%)	(64.3%)
Strongly agree	7	(4.1%)	(4.9%)
N/A	29	(16.9%)	-

- **New needs and new challenges**

The aim of this last chapter of the public consultation is to see if the participants perceived that there is a real need to change the legal framework to better respond to new veterinary needs, new circumstances and new technologies.

In reply to this, as we can see in table 4.8.1, most of the respondents (81%) agree that this issue needs to be addressed in the review of the veterinary medicinal legislation.

4.8.1 Should this issue of new needs and new challenges be addressed in the review?			
	Number of replies	**% of total replies to the questionnaire (172)**	**% of replies to the question (146)**
No opinion	6	(3.5%)	(4.1%)
Strongly disagree	0	(0%)	(0%)
Agree	123	(71.5%)	(84.2%)
Strongly agree	17	(9.9%)	(11.6%)
N/A	26	(15.1%)	-

Regarding the development and production of medicines through new technologies, when the stakeholders were asked if they agree that there are difficulties to assess them, more agree (44%) than disagree (1%). It is important to note that about 40% of the respondents do not have a fixed opinion on the subject.

4.8.2 Do you agree that there are difficulties in the assessment of medicines developed or produced by new technologies?			
	Number of replies	**% of total replies to the questionnaire (172)**	**% of replies to the question (146)**
No opinion	69	(40.1%)	(47.3%)
Strongly disagree	2	(1.2%)	(1.4%)
Agree	65	(37.8%)	(44.5%)
Strongly agree	10	(5.8%)	(6.8%)
N/A	26	(15.1%)	-

Not many participants in the public consultation, just about 20%, had specific proposals how to authorise veterinary medicinal products urgently in the event of an emergency. Several participants provided concrete proposals in relation to new needs and challenges.

Responding organisations and individuals in alphabetical order

Dr Hans-Jürgen Abmayr	Enterprise
ADS ACUIVAL — Agrupacion de Defensa Sanitaria Acuicultura de la Comunitat Valenciana	Non-business organisation
ADSG — Galician Association of Trout Farmas	Non-business organisation

AEMPS — Agencia Espanola de Medicamentos y Productos Sanitarios Directora	Public authority
Agence Nationale du Médicament Vétérinaire, Agence Nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail, Ministère de la Santé et des Sports, Ministère de l'Alimentation, de l'Agriculture et de la Pêche, France	Public authority
AVEC — Association of European Poultry Processors; EPB — European Poultry Breeders; AEH — Association of European Hatcheries	Enterprise
Chiara Agnoli	Enterprise
Dr Peter Aigner	Enterprise
AHDA — Animal Health Distributors Association	Non-business organisation
Alpharma Animal Health	Enterprise
Andermatt Biovet	Enterprise
Animal and Plant Health Association	Enterprise
ANMVI — Italian National Association of Veterinarians	Non-business organisation
Ann Williams	Enterprise
Associazione Piscicoltori Italiani	Non-business organisation
Brendan Barnes	Citizen
Franz Barth	Enterprise
Burkard Barthel	Enterprise
Bayer Animal Health	Enterprise
Bayerische Staatsministerium für Umwelt und Gesundheit	Public authority
Kirstin Becker	Enterprise
Dr Christian Blaschke	Citizen
Borion	Enterprise
Jean Bouchet	Enterprise
British Trout Association	Non-business organisation
Boehringer Ingelheim Animal Health	Enterprise
Bundesverband für Tiergesundheit	Enterprise
Bundestierärztekammer	Non-business organisation
Bundesverband Praktizierender Tierärzte	Non-business organsisation
Camilla Cammelli	Enterprise
CEVA Santé Animale	Enterprise
Coophavet	Enterprise
CVMP — Committee for Medicinal Products for Veterinary Use	Public authority
European Directorate for the Quality of Medicines & HealthCare (EDQM), Council of Europe	Non-business organisation
Danish Medicines Agency	Public authority
Dr Elke Deus	Citizen
Department of Agriculture, Fisheries and Food, Ireland	Public authority
Barbara Dihlmann	Enterprise
Dociu	Enterprise
ECEAE — European Coalition to End Animal Experiments	Non-business organisation
ECVH — European Coalition on Veterinary Homeopathy	Non-business organisation
Elanco Animal Health	Enterprise
EGGVP — European Group for Generic Veterinary Products	Enterprise
Dr Susanne Elsner	Enterprise
Dr Reinhold Erbing	Citizen
Eurovet Animal Health	Enterprise
Andrea Fabris	Citizen
FAMHP — Federal Agency for Medicines and Health Products, Belgium	Public authority
FEADSA — Federacion Espanola de Agrupaciones de Defensa Sanitaria de Acuicultura	Non-business organisation

FEAP — Federation of European Aquaculture Producers	Business organisation
Federal Ministry of Food, Agriculture and Consumer Protection; Federal Ministry of Health, Germany	Public authority
FEEDM — Féderation Européenne des Emballeurs et Distributeurs de Miel Grosse	Non-business organisation
FFA — Fédération Française d'Aquaculture	Enterprise
FIDIN — Fabrikanten en Importeurs van Diergeneesmiddelen in Nederland	Enterprise
FNOVI — Federiazione Nazionale degli Ordini dei veterinari Italiani	Public authority
Gianluca Fortino	Enterprise
Mirella Fossaluzza	Enterprise
FVE — Federation of Veterinarians of Europe, Belgium	Non-business organisation
FVE — Federation of Veterinarians of Europe, Germany	Non-business organisation
Dr Stefan Gabrie	Citizen
Dr Volker Gerlitzki	Citizen
German Federal Environment Agency	Public authority
Michaela Gambs	Citizen
Bettina Graefenstedt	Enterprise
Dr Frank Hildenbrand	Enterprise
IMB — Irish Medicines Board	Public authority
Icelandic Medicines Agency	Public authority
Ittica Tranquilli	Enterprise
Regierungspräsidium Tübingen	Public authority
Roberto Giavenni	Enterprise
IFAH-Europe — International Federation of Animal Health	Enterprise
Christophe Hugnet	Citizen
Janssen Animal Health	Enterprise
Dr Peter Kellner	Enterprise
Dr Silke Knoll	Enterprise
Dr Thomas Knacker	Enterprise
Dr Heidi Kübler	Non-business organisation
Dott. Vet. Beate Kuhl	Citizen
Laboratorios Ovejero	Enterprise
Dr Stephan Lübke	Citizen
Holger Maschke	Citizen
Matthias Link	Citizen
MedicAnimal	Enterprise
Medical Prducts Agency, Sweden	Public authority
Merial, Belgium	Enterprise
Merial, France	Enterprise
Marian Mestdagh	Enterprise
Ministerium für Umwelt und Naturschutz, Landwirtschaft und Verbraucherschutz des Landes Nordrhein-Westfalen	Public authority
Ministerium für Ländlichen Raum, Ernährung und Verbraucherschutz, Allgemeine Veterinärangelegenheiten, Germany	Public authority
Ministero della Slute Direzione Generale Sanita Animale e Farmaco Veterinario	Public authority
Ministry of Agriculture, Environment and Consumer Protection, Germany	Public authority
Ministry of Agriculture and Forestry, Finland	Public authority
Ministry of Agriculture, Nature and Food Quality, Department of Food, Animal Health and Welfare and Consumer Policy, The Netherlands	Public authority

Ministry of Environment, Health and Consumer Protection, Department for Consumer Protection, State of Brandenburg	Public authority
Ulrich Möhnle	Enterprise
National Office of Animal Health, UK	Enterprise
National Organisation for Medicines, Greece	Public authority
Niedersächsisches Landesamt für Verbracherschutz und Lebensmittelsicherheit	Public authority
Dr Jo-Ann Lawrence	Enterprise
Dr Ines Ott	Enterprise
Novartis Animal Health	Enterprise
PAN Germany –Pesticide Action Network Germany	Non-business organisation
PEI — Paul Ehrlich Institut	Public Authority
PETA — People for the Ethical Treatment of Animals	Non-business sorganization
Georg Petry	Enterprise
sPfizer Animal Health, UK	Enterprise
PGEU — Pharmaceutical Group of the European Union	Non-business organisation
sPfizer, Italy	Enterprise
Stephan Plank	Citizen
Paky Prenota	Citizen
Annegret Rehrmann	Non-business organisation
Dr Ulrike Quante	Enterprise
Dr Gerd Ricker	Citizen
Richter Pharma	Enterprise
Dr Ulli Rösel	Enterprise
Royal College of Veterinary Surgeons	Public authority
Pier Antonia Salvador	Enterprise
Sebastian Scala	Enterprise
Christoph Schäuble	Citizen
Dr Waltraude Scheffel	Public authority
Julia Scholl	Citizen
Dr Bernd Schulze	Enterprise
Scottish Salmon Producers' Organisation	Enterprise
SIMV	Enterprise
Slovenia	Public Authority
Dr Petra Sindern Seevering	Enterprise
SME Ireland	Enterprise
SNVEL –Syndicat National des Vétérinaires d'Exercice Libéral	Business organisation
SNVECO	Business organisation
Société Nationale des Groupements Techniques Vétérinaires, France	Non-business organisation
Dr Mary-Anne Sommer	Enterprise
Dr Martina Spangenberg	Enterprise
Are Thoresen	Enterprise
Tierärztliche Gemeinschaftspraxis WEK Lohe	Enterprise
TVM	Enterprise
Veterinary Council of Ireland	Public authority
VIRBAC SA	Enterprise
VMD — Veterinary Medicines Directorate	Public authority
Rupert Weber	Enterprise
Kai Boris Wiese	Enterprise
Dr Ulrike Zeyen-Blumrich	Citizen

http://ec.europa.eu/health/veterinary-use/pubcons_frame_index_en.htm

C Summary responses of the target consultations:

C1 Pharmacovigilance

EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products — quality, safety and efficacy

Subject: Summary report of expert meeting on pharmacovigilance in the context of the review of the veterinary medicinal products legislation

On 29 May 2012, an expert meeting took place on pharmacovigilance. The meeting was held under Chatham House rules and objective of this meeting was to gather experts' inputs for the revision of the legislation on veterinary medicines. Participants were invited based on their expertise and received a discussion paper on pharmacovigilance shortly before the meeting.

Ten experts participated in the meeting. The discussion focused mostly on the advantages and disadvantages of the current pharmacovigilance system and possible amendments: the scope of pharmacovigilance, the different categories of adverse reactions in pharmacovigilance, the type of reporting and means of providing information, signal detection, the organisation and implementation of inspections, the scope, development and maintenance of pharmacovigilance database(s) and access to them, the sharing of information between parties, the responsibilities and tasks of actors, regulatory tools for action, and transitional provisions.

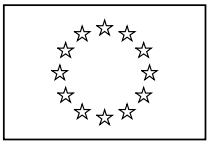
The participants agreed to have a risk-based approach for pharmacovigilance in the future and to develop a veterinary pharmacovigilance better adapted to the characteristics of the veterinary sector. However, views differed as to how these principles should take shape in practice, in particular in relation to the tasks and responsibilities of the different actors. Another key question discussed was the level of events or accuracy that the new veterinary pharmacovigilance system has to detect.

The group agreed that environmental and residue violation events should be better covered by other systems, but no EU-wide alternatives appear to exist.

Both the duplication of tasks by actors in the system and the repetition of providing and collecting similar information repeatedly surfaced in the discussion. Also frequently mentioned were the differences in the way European pharmacovigilance requirements are implemented by Member States. In general the participants favoured a harmonised, proportionate pharmacovigilance system in the future. The development of an EU pharmacovigilance database was supported by the participants; it was pointed out that actors should be able to continue using their own databases for signal detection. Surveillance should be based in principle on the active substance,

and the establishment of a masterfile should be made possible. There was no agreement on the access of actors to the new EU database and how the quality of the input should be ensured.

Clearly different views were expressed on several items in the discussion paper, for example the organisation and implementation of inspections and the need to report on events in third countries.



EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products — quality, safety and efficacy

Subject: **Subject: Summary report of expert meeting on authorisation procedures and data protection in the context of the review of the veterinary medicinal products legislation**

On 22 June 2012, an expert meeting took place on authorisation procedures and data protection. The meeting was held under Chatham House rules. The aim was to gather experts' inputs for the revision of the legislation on veterinary medicines. Participants were invited on the basis of their expertise and received a discussion paper shortly before the meeting.

The discussion focused mainly on the advantages and disadvantages of the current marketing authorisation and data protection system and how it could be amended: the type and scope of marketing authorisation procedures; ways of increasing the availability of medicines by introducing specific procedures for marketing authorisation and targeted data protection measures; the harmonisation of existing products; the tasks of the scientific committee and the Member States' coordination group; the definition of biological medicine; marketing authorisation procedures for generic medicines; the concept of global marketing authorisation; and the level of data protection required to ensure sufficient innovation in the animal health industry.

The participants were unable to agree whether in the future one or several marketing authorisation procedures would be appropriate. Most participants were in favour of letting companies choose whether to use the centralised, national or decentralised procedure.

The group agreed on the need to harmonise existing products. However, views differed as to how this should be carried out in practice, particularly in relation to the tasks and responsibilities of the various players.

Generally speaking, the group were in favour of updating the system for generics, particularly with respect to the reference products that may be used. For environmental risk assessment, the same rules would apply as for other safety data requirements.

The participants were in favour of developing a data protection system that would provide better support for innovation in the animal health industry. Opinions differed on the appropriate duration of data protection and whether it should be linked to the global marketing authorisation concept.

EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products — quality, safety and efficacy

Subject: Summary report of expert meeting on antimicrobial resistance in the context of the review of the legislation on veterinary medicinal products

An expert meeting on antimicrobial resistance took place on 8 June. The aim of the meeting, held under the Chatham House rules, was to get input from experts for the revision of the legislation on veterinary medicines. Before the meeting, the experts received a discussion paper.

Twenty experts attended the meeting. They discussed whether or not the current evidence-based evaluation of an application for a marketing authorisation for an antimicrobial product was still appropriate, or whether it would be better to take a precautionary approach. They agreed that any policy measure should be science-base, however, it was acknowledged the fact that data on use of antimicrobials as a risk to public health due to antimicrobial resistance is limited. It was emphasised that a precautionary approach would impact negatively on innovation.

They also discussed the effect any changes to the legislative requirements on the authorisation of antimicrobials could have on the availability of medicines. It was argued that regulatory unpredictability may discourage companies from investing in the development of new antimicrobials. Some experts were in favour of developing a regulatory framework, with more detailed guidance from the European Medicines Agency, claiming that it would be a good idea to define some terms in the legislation, such as ‘antimicrobial’, ‘antibacterial’, ‘metaphylaxis’ and ‘prophylaxis’.

The issue of ‘conditional authorisations’ was discussed. Although some experts were in favour of them, others were concerned that they could lead to uncertainty and even interfere with the availability of products. 'Conditional authorisations' would work if it is possible to respond appropriately to the conditions imposed.

The experts discussed imposing restrictions on the authorisation of antimicrobials that are last resort medicines for the treatment of infections in humans in case there is a possible link between use of the compound in animals and resistance in humans. There was support for this proposal, provided the restrictions were not product-specific and provided that the need for these antibiotics to protect animal health is recognised and taken into account. They also discussed whether or not to include a list of restricted categories of antimicrobials in the legislation. Many of them expressed concern that this would not allow flexibility to change the list in the light of scientific progress. Others stressed the fact that experience showed that such lists are being changed frequently and therefore creating a high degree of uncertainty. They discussed the sale of antimicrobials by veterinarians. Some experts thought that veterinarians should be allowed to sell antimicrobials to treat the animals under their care.

All the experts agreed that the legislation should clarify that all antimicrobials should be classified as prescription only-medicines, including those for pets.

They said that it would be a good idea to make the collection of data on sales of antimicrobials per species compulsory.

EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products – quality, safety and efficacy

Subject: Summary report of experts' meeting with SMEs to discuss the review of the veterinary medicinal product legislation

On 4th October 2012 a targeted expert meeting took place with SMEs. The meeting was held under the Chatham House rules and aimed to gather experts' input for the revision of the legislation on veterinary medicines. Participants were invited based on their expertise and received a discussion paper on points for discussion before the meeting.

There have been fifteen participants. The following topics were discussed: (i) authorisation procedures, (ii) packaging and labelling requirements, (iii) rules on advertising, (iv) pharmacovigilance, (v) "sunset clause", (vi) renewals, (vii) referrals, (viii) variations, (ix) data protection and (x) clinical trials.

The group agreed that the current authorization procedures do incur large administrative costs to SMEs and microenterprises, in particular regarding variations and renewals. The issue of lack of medicines for bees was discussed as an example of problems for minor species. It was suggested that mutual recognition should be obligatory and automatic for medicines for minor species. The centralized procedure was discussed and attendees indicated that this is potentially attractive procedure but the fees are expensive for SMEs, and also the application procedure is difficult for them, which in general do not have a dedicated regulatory department. Participants indicated that the national procedure is important for SMEs, which once obtain approval in one Member State then roll the product authorisation to other countries through mutual recognition. The relevance of the decentralized procedure was discussed, as it would potentially be ideal when a company wishes to obtain an authorization in various countries at the same time, but attendees explained that the decentralized procedure is very difficult: MS often have different interpretation of the guidelines and therefore their requirements are disharmonized. SMEs considered that a helpdesk in the MS to offer support and free advice to SMEs would be very welcome.

Attendees discussed the possibility of allowing SMEs to obtain a conditional marketing authorization for minor species, with an incomplete efficacy package, with commitments to provide the remaining data at a later date. This type of authorization already exists in some countries but the annual renewal is an administrative burden to the company.

Attendees explained that the procedures and requirements to approve a clinical trial differ considerably between MS, and this hampers the authorization process for SMEs. Some harmonization on this area would be welcome.

The classification of bees as food producing species was also raised. It was argued that this current classification is not appropriate as the bees' husbandry methods differ from those for cattle or sheep, for example, as well as their metabolism. For these reasons, it was argued that the technical requirements in Annex I are excessive for bee medicines. However, it was agreed that whilst some data requirements could be reduced for bees, such as quality requirements regarding GMP compliance, for example, the safety of honey as a produce for human consumption is important.

There was a discussion about the requirements for packaging and labeling of veterinary medicines. Attendees proposed to remove from the legislation the need for approval of mock ups.

During the short discussion about advertising, experts commented that MS have different opinions about what can be advertised, in particular regarding what is allowed to appear in the internet (and searched through online searching engines). It was agreed that the rules of advertising could be clarified.

The experts agreed that the requirements as to the pharmacovigilance should be simplified. Periodic reports were found too costly – even if no adverse reaction occurred, the report must be prepared, which generates workload. The experts share also the same view on renewals - unnecessary workload, if no adverse reactions occur.

According to the experts, the sunset clause should be deleted.

It was highlighted that if, for instance, a company has a marketing authorization for two types of vaccines – one for outbreak and the other one for prevention, usually the second one is being marketed.

SMEs representative were also in favor of having longer data protection periods, as they argue that it takes longer for the SME to develop new products and extending the data protection would be beneficial and rewarding.

The experts would also support simplifying the variations procedures.

Annex 10 Discarded options

- Option to completely abolish pharmacovigilance requirements: This option was discarded because it would introduce risks to animal and public health and to the environment, as pharmacovigilance data are essential for the monitoring of authorised veterinary medicines safety. Even though it is estimated that the implementation of this option could generate savings to the pharmaceutical industry of around 59.4 million euros per year, neither the industry nor regulators nor end-users supported this proposal.

- Option to replace the authorisation of low risk and generic veterinary medicines with a registration system: Currently all veterinary medicines must comply with the quality, safety and efficacy requirements set out in the legislation – the legislation does not distinguish between low and high risk medicines regarding the scientific data required. This option considered creating a registration system for generics and lower risk medicines (e.g. teat dips), which would not be subjected to scientific assessment. But it was argued that it is wrong to assume that known active substances are safe, and that the option ignored the risks posed by variable quality and manufacturing standards of veterinary medicines. The option received some support from end-users who considered that the proposal would increase the supply and the level of competition for certain medicines, and improve the internal market. It would also lead to a significant reduction of the administrative burdens to the industry, associated with obtaining a marketing authorisation (it was estimated that the savings to the industry would be 181.9 million euros per year).[140] On the other hand, the industry objected to this option on the basis that it would distort the market by favouring generics and make recently authorised medicines uncompetitive. For these reasons the option was discarded.

- Option to make the centralised procedure compulsory to all veterinary medicines: This option would make the centralised procedure compulsory for all new applications, and would abolish the national, mutual recognition and decentralised procedures. The EMA would be responsible for the assessment of the applications and their post authorisation maintenance. Member States would be responsible for maintaining the existing national marketing authorisations. This option would have a positive impact on the free movements of veterinary medicines in the EU. However, it was discarded on the basis that it would increase the administrative burden to the industry (by an estimated 170.8 million euros per year) without in fact leading to an increase on the availability of medicines (just because a product is authorised does not mean it is actually placed on the market). In addition, SMEs objected to this option, and regulators and the industry argued that the EMA would not be able to process the volume of applications that it would receive with the current capacity and procedures.

[140]Based on the industry estimation, it was calculated that only 5% of the current veterinary medicines would require a full scientific assessment per year. The administrative burdens associated with the registration exercise was assumed to cost the equivalent of applying for a type 1A variation (simple administrative procedure), which would also be applicable to subsequent product maintenance requirements. EPEC Report on the assessment of the impact of the revision of pharmaceutical legislation, 2011, p. 178-182.

- Option to introduce exemptions to reduce legislative requirements regarding authorisation of veterinary medicines by pharmaceutical companies that are SMEs or micro-enterprises: This option was considered in light of the Commission's policy to support SMEs and micro-enterprises[141]. However, it was discarded because it runs against the fundamental principles of the legislation on veterinary medicines, which is to safeguard public and animal health and environmental safety. It is not possible to relax veterinary medicines standards for a particular business sector.

- Option to voluntarily harmonise the summary of product characteristics of the "legacy products": This option proposed a programme of voluntarily harmonisation of the summary of product characteristics (regarding the indications, target species, warnings and withdrawal periods) and product literature for all veterinary medicines already nationally authorised in the Union. This could involve scientific assessment of all products, and a decision would be reached based on a benefit:risk evaluation. This option was discarded because it would impose a significant burden on the national competent authorities and on the pharmaceutical companies and could lead to the withdrawal from the market of many "unprofitable" products. In addition, a pilot scheme has been already tested by the CMDv and considered by both competent authorities and pharmaceutical industry laborious and time-consuming.

- Option to standardise the distribution of veterinary medicines across the Union: There was support by stakeholders regarding the need to standardise and harmonise the EU distribution of veterinary medicines. However, it was considered that the classification of a veterinary medicine as prescription or over the counter, and its distribution, is within the Member States' competence and therefore EU action would represent a breach of the subsidiarity principle.

- Option to forbid generic applications for antimicrobials: It was argued that the relatively low price of antimicrobials is an incentive for their excessive use. However, the adoption of this proposal would be not compatible with the EU objectives of enhancing the internal market and improving the availability of medicines.

- Option to re-classify bees as non-food producing animals: Stakeholders proposed this option as a measure to improve the availability of medicines for bees, as the data requirements for non-food producing animals are less stringent than those for food-producing animals. Therefore, the classification of bees as non-food producing animals could theoretically facilitate the authorisation of medicines for bees. This option was discarded for food safety reasons, as there would be no procedures in place to ensure that honey from treated hives would be free from residues or would not enter the human food chain (a system based on the identification of individual treated from untreated hives, similar to horse passports, cannot be introduced for the bees).

- To develop "soft law instruments" to achieve policy changes: This option would rely exclusively on guidance to introduce changes to the regulatory

[141] Minimising regulatory burdens for SMEs – adapting EU regulation to the needs of micro-enterprises.

framework. This general option was discarded as its non-binding nature would not be sufficient to tackle the differences in the interpretation and implementation of the legislation. They would be ineffective to achieve the objectives of the revision of the legislation on veterinary medicines. In addition, informal guidelines do not provide legal certainty and are considered inappropriate to ensure the free movement of veterinary medicines within the internal market. The industry and regulators did not support this option.

Annex 11 Comparison tables of policy options

Table 13 Comparison of costs and benefits of policy options:

Specific objective A Expand market beyond the top four species			
Options	**Stakeholders**		
	Industry	End-users	National competent authorities, European Commission, EMA
Option 1 No new EU action	No additional costs or benefits	No additional costs or benefits	No additional costs or benefits
Option 2 Improve the Cascade	Benefits: none Costs: no changes	Benefits: more flexibility and so improved availability of medicines Costs: no changes	Benefits: better management of therapeutic gaps Costs: no changes
Option 3 Expand database to cover all veterinary medicines	Benefits: better information exchange within the authorisation system. Costs: none	Benefits: more transparency and information Costs: no changes	Benefits: better information exchange within the authorisation system. Costs: administrative costs to the competent authorities
Option 4 Reduced data requirement for	Benefits: reduction of	Benefits: increase on the availability of medicines for	Benefits: closing of some therapeutic gaps

MAs for medicines for limited markets	administrative burdens Costs: no changes	limited markets; more harmonised levels of animal and public health and environmental protection levels. Costs: no changes	Benefits: closing of some therapeutic gaps Costs: no changes
Option 5 Reduced data requirements for medicines for bees	Benefits: reduction of administrative burdens and indirectly will provide incentive for innovation Costs: no changes	Benefits: improved availability of new medicines for bees Costs: no changes	Benefits: Benefits: closing of some therapeutic gaps Costs: No changes
Specific objective B Simplify procedures for obtaining a marketing authorisation in multiple national markets			
Option 6 No new EU action	No additional costs or benefits	No additional costs or benefits	No additional costs or benefits
Option 7 Automatic recognition of a national marketing	Benefits: reduction of administrative	Benefits: better functioning of the internal market; possible increase in the availability of	Benefits: increase in income from fees for assessment for some national competent authorities; less resource intensive to certain national competent authorities

authorisation	burdens (estimated as savings of 67.9 million euros per year; increase in innovation Costs: possibly increase in referrals	veterinary medicines (innovators and generics); more harmonised animal and public health, and environmental protection levels. Costs: no changes	Costs: costs related to work on referrals
Option 8 Single marketing authorisation procedure for all products	Benefits: estimated reduction in administrative burdens of 67.9 million euros each year; increase in innovation Costs: loss of flexibility for SMEs	Benefits: better functioning of the internal market; may increase the availability of veterinary medicines (both innovators and generics) for companion animals and farmed animals and in some smaller Member States; more harmonised animal and public health and environmental protection levels. Costs: concerns that the lack of peer review and Member States' input might be detrimental to animal and public health, and the	Benefits: less resource intensive to certain competent authorities Costs: possibly more referrals

		environment	
Option 9 Wider scope for the centralised procedure	Benefits: estimated reduction in administrative burdens of 5.6 million euros/year; increase in innovation; maintains flexibility and opportunity of choice, important for SMEs Costs: none	Benefits: possibly increase in the availability of medicines for companion and farmed animals: more harmonised animal and public health and environmental protection levels; improved internal market. Costs: no changes	Benefits: more harmonised assessment of applications; less resource intensive to some national competent authorities, improved internal market Costs: increased pressure on the EMA's resources (fast tracking or exclusion of some types of veterinary medicines applications could alleviate this); administrative costs to the Commission (regarding issuing marketing authorisations)
Option 10 Simpler packaging and labelling	Benefits: reduction of administrative costs; increase in innovation Costs: possible costs associated	Benefits: increase in the availability of medicines in particular in smaller Member States Costs: possibly less intelligible product labels and packaging	Benefits: some efficiency measures to national competent authorities from checking product literature Costs: potential need for increase in in-market inspections, therefore additional costs to the national competent authorities

	with product recalls from the market		
Option 11 Allow already approved veterinary medicines to freely circulate across the Union	Benefits: reduction of administrative burdens estimated as around 14.2 million euros per year; indirectly increase in innovation Costs: increase in the administrative burdens in the short term to harmonise the SPCs for some products following assessment by the competent authorities	Benefits: improved functioning of the internal market; increase in availability and price competitiveness (therefore reduction in price of veterinary medicines; increase of product availability in smaller countries). Costs: none	Benefits: efficiency measures to national competent authorities in medium and long term Costs: some administrative costs to the Commission, EMA and national competent authorities in the short term regarding the work needed to harmonise the SPCs of some products
Specific objective C Review data requirements for marketing authorisation procedures			

Option 12 No new EU action	No additional costs or benefits	No additional costs or benefits	No additional costs or benefits
Option 13 Generic applications may refer to environmental data	Benefits: decrease to generics manufacturers to the costs of obtaining a marketing authorisation Costs: none	Benefits: possibly increase on the availability of generics placed on the market and so possibly reduction on price of medicines; potential public and animal health benefits Costs: none	Benefits: less resource intensive to national competent authorities as no new assessment required for data already assessed as part of innovators ' data package and new data assessed within a monograph system Costs: possibly more national competent authorities' resources for pharmacovigilance monitoring
Option 14 Harmonisation of clinical trials procedures across the Union	Benefits: Reduction of administrative burdens and indirectly stimulate innovation; particularly beneficial to SMEs Costs: None	Benefits: improve the functioning of the internal market; increase the availability of medicines; growth of the SME sector Costs: none	Benefits: some efficiency measures re assessment of clinical trials data Costs: increase in resources to some national competent authorities

Specific objective D Simplify post authorisation requirements			
Option 15 No new EU action	No additional costs or benefits	No additional costs or benefits	No additional costs or benefits
Option 16 Risk-based pharmacovigilance	Benefits: reduction of administrative burdens of around 47.2 million euros per year; indirectly – increase in innovation Costs: none	Benefits: redirection of resources by industry might lead to increased availability of medicines; improve internal market Costs: no changes	Benefits: efficiency savings for national competent authorities from assessing period safety updates; Costs: no changes
Option 17 Review procedures to change a marketing authorisation (variations)	Benefits: reduce administrative burdens to the pharmaceutical industry by 10.9 million euros per year; indirectly – increase in innovation	Benefits: potentially increase on the availability of veterinary medicines to companion and farmed animals Costs: no changes	Benefits: efficiency savings due more targeted evaluation of variations; reduction of administrative costs to the Commission Costs: potential costs associates with increase in number of referrals if safety risks identified

	Costs: potential costs associates with referrals if safety risks are raised		
Option 18 Delete the obligation to market a product within 3 years of approval	Benefits: reduction of administrative burdens to the industry, especially SMEs Costs: no changes	Benefits: possibly more available products Costs: no changes	Benefits: some reduction in costs of dealing with administration of sunset clause Costs: no changes
Option 19 Delete the requirements for renewals	Benefits: reduction of administrative burdens of at least 67.5 million euros per year: indirectly – increase in innovation Costs: no changes	Benefits: possible increase on the availability of veterinary medicines to companion and farmed animals if resources redirected to new product development Costs: no changes	Benefits: efficiency savings due more targeted evaluation of renewals Costs: no changes

Option 20 Exempt homeopathic medicines from pharmacovigilance requirements	Benefits: reduction of administrative burdens Costs: no changes	Benefits: possibly lower price of homeopathics medicines Costs: potentially negative animal health effects	Benefits: none Costs: possibly potentially negative animal health effects
Specific objective E Review incentives for breakthrough medicines			
Option 21 No new EU action	No additional costs or benefits	No additional costs or benefits	No additional costs or benefits
Option 22 Extend data protection period for new veterinary medicines	Benefits: better return to investments for R&D companies; increase in innovation; novel veterinary medicines on the market ensure sustainability of generic companies in the long term	Benefits: incentives to innovation may improve the availability of new veterinary medicines; development of antimicrobials specifically developed for use in veterinary medicine could benefit public and animal health Costs: in the short/medium term, less generic medicines placed on the market and so high price of novel veterinary medicines	Benefits: more innovative products to fill therapeutic gaps Costs: no changes

	Costs: loss of income to generics industry in the short/medium term due to delay for application for generics		
Specific objective F Improve clarity: on rules on internet retailing, on the authorisation of new treatments, on inspections, on authorisation of medicines for emerging diseases			
Option 23 No new EU action	No additional costs or benefits	No additional costs or benefits	No additional costs or benefits
Option 24 Authorisation to sell veterinary medicines through the internet in all MS	Benefits: clearer, harmonised and predictable legal environment; benefits SMEs/micro-enterprises Costs: some increase of the	Benefits: greater accessibility of products throughout the EU; improved internal market; increase the competition and reduce the prices of veterinary medicines; public and animal health benefits Costs: no changes	Benefits: clear legal environment implement ECJ-ruling and so less risks of legal disputes Costs: some increase in costs to the national competent authorities regarding administration of the authorisation procedure and enforcement of the legislation

	administrative burdens		
Option 25 Establish a framework to authorise new treatments	Benefits: clearer, harmonised and predictable legal environment; benefits to internal market Costs: some increase administrative burdens regarding data production and fees to obtain an authorisation	Benefits: assurance regarding the quality and safety of advanced therapy products; improved animal health, improved internal market Costs: no changes	Benefits: harmonisation of decisions; improved animal health, Costs: increase in costs related to the introduction of procedures for assessment and authorisation of advanced therapy products;
Option 26 Establish a basis to harmonise the controls on the veterinary medicine distribution chain	Benefits: clearer, predictable and harmonised regulatory environment Costs: no changes	Benefits: more harmonised public and animal health protection, protection to the environment across the Union	Benefits: harmonised systems across the Union leading to a level playing field; less costs related to infractions Costs: some Member states may need to invest in their inspections programmes
Option 4 Reduced data requirement for	Benefits: reduction of	Benefits: increase on the availability of medicines for	Benefits: closing of some therapeutic gaps

medicines for limited markets	administrative burdens Costs: no changes	limited markets; more harmonised levels of animal and public health and environmental protection levels. Costs: no changes	Benefits: closing of some therapeutic gaps Costs: no changes

Comparison of costs and benefits of policy options regarding measures to strengthen the veterinary medicines legislation regarding the authorisation and use of veterinary antimicrobials

	Stakeholders		
Options	Industry	End-users	National competent authorities, European Commission, EMA
Option 27 No new EU action	No additional costs or benefits	No additional costs or benefits	No additional costs or benefits
Option 28 Introduction of legislative measures to allow restrictions to be placed on the authorisation and use of veterinary antimicrobials	Benefits: savings to the pharmaceutical industry due to reduction in number of referrals to arbitration; more clarity and predictable regulatory environment regarding authorisation of antimicrobials	Benefits: possible positive impact on the protection of human health regarding antimicrobial resistance; Costs: negative impact on the availability of medicines for both	Benefits: savings to the national authorities, the EMA and the Commission due to reduction in numbers of referrals to arbitration Costs: potential more resources needed by national competent authorities for enforcement

	Costs: loss of income regarding the sales of some types of antimicrobials	farmed and companion animals	activities to combat illegal use of antimicrobials; administrative costs to the Commission and the competent authorities in preparing guidance
Option 29 Measures regarding advertising of veterinary medicines, including antimicrobials	Benefits: clearer legal environment Costs: no changes	Benefits: less pressure on veterinary surgeons for prescription of antimicrobials; Costs: possibly less information transmitted by advertising to non-prescribers regarding animal health issues	Benefits: clearer legal environment Costs: potential more resources needed by national competent authorities for enforcement of advertising restrictions
Option 30 Measures regarding retailing of veterinary antimicrobials	Benefits: no changes Costs: no changes	Benefits: possible reduction on the sales of antimicrobials Costs: less income to veterinary surgeons from the sales of antimicrobials; reduced accessibility of veterinary medicines in remote rural areas if not non-veterinarian retail exists	Benefits: no changes Costs: administrative costs to the competent authorities regarding enforcement

Option 31 Introduction of a legal basis for the compulsory collection of data on the use of antimicrobials	Benefits: transparency on the sales and usage of antimicrobials in the veterinary sector Costs: no changes	Benefits: more science-based measures regarding the management of antimicrobial resistance leading to a positive impact on public and animal health Costs: no changes	Benefits: more robust evidence to permit implementation of risk management measures regarding antimicrobial resistance Costs: some costs to the competent authorities regarding adaptation of systems and procedures for collection and analysis of data

Table 14 Comparison of the options regarding effectiveness, efficiency and coherence[142] with EU objectives.

Options 1, 6, 12, 15, 21, 23, 27 are baseline (no new EU action) - neutral

Options	Effectiveness	Efficiency	Coherence with EU objectives
Option 2 Improve the Cascade	++	++	++

[142] Effectiveness is the extent to which the options achieve the proposed objectives; efficacy is the extent to which the objectives can be achieved at the lowest cost; coherence is the extent the policy options are coherent with the objectives of the EU policies and the extent to which they are likely to limit trade-offs across the economic, social and environmental domain. Impact assessment guidelines

Option 3 Expand database to cover all veterinary medicines	++	++	+++
Option 4 Reduced data requirement for medicines for limited markets	++	++	+++
Option 5 Reduced data requirements for medicines for bees	++	++	+++
Option 7 Automatic recognition of a national marketing authorisation	+++	++	+++
Option 8 Single marketing authorisation procedure for all products	+++	++	+++
Option 9 Wider scope of the centralised procedure	+++	++	+++
Option 10 Simpler packaging and labelling	++	++	+++
Option 11 Already nationally approved veterinary medicines allowed to freely circulate across the Union	++	+	+++
Option 13 Generic applications may refer to environmental data	+/neutral	+	+
Option 14 Harmonisation of clinical trials procedures across the Union	++	++	+++
Option 16 Risk-based pharmacovigilance	++	++	+++
Option 17 Review procedures to change a marketing authorisation (variations)	++	++	+++
Option 18 Delete obligation to market a product within 3 years of approval	+++	+++	+++
Option 19 Delete the requirement for renewals	++	++	+++

Option 20 Exempt homeopathic veterinary medicines from pharmacovigilance requirements	+	+	+
Option 22 Extend the data protection period for new veterinary medicines:	++	++	++
Option 24 Authorisation to sell veterinary medicines through the internet in all MS	++	++	++
Option 25 Establish a framework to authorise new treatments	++	+	+
Option 26 Establish a basis to harmonise the controls on the veterinary medicines distribution chain	neutral	+	+++
Option 28 Introduction of legislative measures to allow restrictions to be placed on the authorisation and use of veterinary antimicrobials	+	+	+++
Option 29 Measures regarding advertising of veterinary medicines, including antimicrobials	+	+	+++
Option 30 Measures regarding retailing of veterinary antimicrobials	- - -	-	++
Option 31 Introduction of a legal basis for the compulsory collection of data on the use of antimicrobials	neutral	+	+++

Annex 12 Table providing an overview of problems, specific objectives, operational objectives and preferred policy options regarding the problem of lack availability of veterinary medicines

Options for no new EU actions: 1, 6, 12, 15, 21, 23, 27

Problem	Specific objective	Operational objective	Options
Lack of availability of authorised veterinary medicines	A Expand market beyond the top four animal species	A.1. Improve the use of the Cascade A.2. Improve information on authorised medicines available in the Union A.3. Simplification of application requirements for veterinary medicines for limited markets E1. Strengthen data protection incentives	2 Improve the Cascade 3 Expand database to cover all veterinary medicines 4 Reduced data requirements for medicines for limited markets 5 Reduced data requirements for medicines for bees
	B. Simplify procedures for obtaining a marketing authorisation in multiple national markets	B.1. Review CP, DCP and MRP procedures B.2. Revision of situation with “legacy products”	7 – Automatic recognition of national MA 8 – Single MA procedure for all products 9 – Wider scope for centralised procedure 10 – Simpler packaging and labelling 11 – Allow already nationally approved

			medicines to freely circulate across the Union
	C. Review data requirements in marketing authorisation procedures	C.1. Revision of environmental data requirements for generics C.2. Revision of provisions on authorisation of clinical trials	13 – Generic applications may refer to environmental data 14 – Harmonisation of authorisation for clinical trials procedures across EU
	D. Simplify post authorisation requirements	D.1. Simplification of pharmacovigilance D.2. Simplification of variation requirements D.3. Revise Sunset clause D.4. Abolish renewals D.5. Simplify requirements for homeopathics	16 – Risk based pharmacovigilance 17 – Review procedures to change a marketing authorisation (variations) 18 – Delete the obligation to market a product within 3 years of approval 19 – Delete the requirement for renewals
	E. Review incentives for breakthrough medicines	E1. Strengthen data protection incentives	22 – Extend data protection period for new veterinary medicines
	Improve clarity: On rules on internet retailing of veterinary	F.1. Specify rules for internet retailing of veterinary medicines F.2. Specify rules for new treatments F.3. Harmonise national control systems	24 – Authorisation to sell veterinary medicines through the internet in all MS 25 – Establish a framework to authorise new treatments

	medicines on the authorisation of new treatments on inspections on authorisation of medicines for emerging diseases	A.3. Simplification of application requirements for veterinary medicines for limited markets	26 – Establish a basis to harmonise the controls on the veterinary medicine distribution chain 4 – Reduced data requirements for medicines for limited markets