17 June 2021
EMA/CVMP/692904/2018
Committee for Medicinal Products for Veterinary Use

Overview of comments received on ' Guideline on the summary of product characteristics (SPC) for veterinary medicinal products containing antimicrobial substances ' (EMA/CVMP/383441/2005-Rev.1)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1.	AnimalhealthEurope
2.	British Veterinary Association (BVA)
3.	Finnish Food Authority

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1. General comments – overview

Stakeholder no.	General comment	Outcome
1.	AnimalhealthEurope welcomes the opportunity to comment on this draft guideline. With this draft revised GL a SPC-update will be generally required in context of a renewal. The wording for a broad indication, which can be found quite often on old, national SPCs, will no longer be acceptable. Indications will need to be clearly linked to relevant target pathogens. As a result, indications will be restricted and target species may be lost. This may lead to a serious limitation in the availability of products for certain indications and target species. It is difficult to see how the SPC-updates could be done in a consistent manner throughout the EU countries, particularly for national products. The national assessment could be rather different, in some cases supportive clinical data may be requested whilst in others not. And what about products which are not subjected to license renewal anymore? In theory, they can keep their broad indications. Ideally, a harmonised approach towards the update of SPCs for antimicrobial products should be taken. The update of antimicrobial susceptibility data already occurs upon requests by competent authorities both at Central and National level. Although we agree in principle, we would like to point out that, particularly for National licenses, the request to include National-based data is leading to substantial deviations in the SPC of a VMP nationally registered in several MSs. This practice might result not only in unharmonised SPCs across the EU, but can also complicate	Thank you for your comments. According to the NVR, renewals are no longer foreseen. The scope of the guideline has been revised: The guideline applies to new marketing authorisation applications, referrals, re-examinations (Articles 24 and 27), and variation applications that require a reconsideration of the overall benefit risk balance. The provisions of Regulation (EC) 2019/6 enable a harmonisation of the SPCs for nationally authorised products (Section 4). The concern is acknowledged. It is important that the information in the SPC should be kept up to date with current scientific knowledge, in line with the responsibilities of the MAH (Article 58.4), in particular to enable on-going responsible use of antimicrobials. Antimicrobial susceptibility data should be updated preferably based on findings from relevant European surveillance and other information that becomes available.

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	labelling logistics since SPCs need to be frequently redrafted and reprinted accordingly. Moreover, the increasing quantity of such requests is adding considerably to the workload of MAHs, and this might be a problem particularly for SMEs. Section 4.9 states that 'ranges in doses should be avoided unless there is clear guidance for the user as to when to administer the product at the upper or lower limit of the range'. We would like to point out, that for many already registered national products such a request may trigger new expensive studies most likely making the VMP defence economically unsustainable and forcing MAHs to withdraw effective VMPs from the market. We agree with the principle of having appropriate pack size(s) for products intended for group treatment. However, as it is also stated in section 6.5 and Annex II, the mean sized group of animals might be highly variable across MSs. If strictly applied, this requirement will lead to a multiplication of pack sizes for the same VMP bearing additional costs and logistic constraints to distribution operations, which will eventually impact availability.	The recommendation on dose ranges is primarily aimed at new applications. New studies are usually not requested in other procedures unless an associated 'serious risk' has been identified. It is fully acknowledged that establishing the appropriate pack size is challenging. A reasonable balance has to be established between the need for different pack sizes to allow correct dosing without a significant amount of leftovers, and the practical and economic difficulties that could be connected to the supply of many different packages. Depending on the type of the VMP (administered or not by the owner/farmer, intended for group or individual treatment or for both, number of target species, number and type of indications, doses and durations of treatment), the pack sizes should always be justified in connection to an application for a marketing authorisation or a relevant variation as being adequate pack size(s) to ensure the minimum amount necessary for the appropriate treatment of a single animal or a group of the intended target animal(s).
2.	Who we are: The British Veterinary Association (BVA) is the national representative body for the veterinary profession in the United	Thank you for your comment, your concern on 'excess of information' is acknowledged. In line with that observation,

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	Kingdom. With over 17,000 members, our primary aim is to represent, support and champion the interests of the United Kingdom's veterinary profession. We, therefore, take a keen interest in all issues affecting the profession, including animal health and welfare, public health, regulatory issues and employment matters. Introduction We welcome the opportunity to respond to this consultation on the second revision of the guideline on the Summary of Product Characteristics (SPC) for antimicrobial products. The UK veterinary profession is concerned by the implications of the development of antimicrobial resistance. Each use of antimicrobials increases the risk of selection for resistant bacteria and other micro-organisms, so we must ensure the use of antimicrobials is responsible across human and animal health. Presentation of information BVA welcomes the emphasis placed on changing prescribing behaviour, which is found within the revised guidelines. We would ask that additional consideration is given to how the proposals will impact on behaviour. We are concerned that the proposals may provide an excess of information for vets, which would be counterproductive. To encourage a behaviour, it is important for an intervention to be Easy, Attractive, Social and Timely (EAST).[1] These principles for applying behavioural insights are based on the work of the Behavioural Insights Team and a large body of evidence on what influences behaviour.[2]	only few standard sentences are proposed in the draft guideline, which are deemed indispensable with particular regard to the responsible use of antimicrobials.

[1] Behavioural Insights Team, EAST Four simple ways to apply behavioural, 2014 https://www.behaviouralinsights.co.uk/publications/east-four-simple-ways-to-apply-behavioural-insights
[2] Behavioural Insights Team, About US, https://www.behaviouralinsights.co.uk/about-us/

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	It is absolutely correct to provide vets with the material necessary to make informed decisions in the interest of animal health, animal welfare and wider public health: including the maintenance of antimicrobials. However, the level of detail in an SPC should be relevant to the end user. In particular, we note that the proposals for the PDynamic section will present a large amount of data. This information will be of use to veterinary surgeons but be impractical in a clinical setting where decision making can be time limited. Furthermore, inclusion of "relevant pharmacokinetic parameters such as Vd, Cmax, Tmax, elimination half-life, clearance, bioavailability and area under the concentration curve (AUC)" may also be inappropriate. Such data will be important for specialists who advise primary care practitioners and should be made available, however the SPC is the wrong place for this. BVA agrees with the emphasis placed on behaviour change within the document. To further this ambition within the scope of this consultation we would suggest a very clear indication of: the class of antibiotic the particular active(s) belong to. whether the product is a time dependent or a concentration antimicrobial	It is of note that information on pharmacodynamics (PD) and pharmacokinetic (PK) is included only in the SPCs, while information of these sections does not appear in the package leaflets, the source of information more likely to be used by primary care veterinarians. Including the information in the SPC allows easy access for specialists. Details on PD and PK are included in SPCs of all VMPs but are in particular considered relevant for antibiotics. It allows the prescriber to relate actual susceptibility data (that may have changed over time) to the kinetic profile of the antibiotic in order to decide whether the recommended treatment dose is sufficient to achieve an optimal antibacterial effect and minimise the potential for selection of resistance in a given situation. The class of antibiotic the particular active(s) belong(s) to, is indicated in section 4.1: ATCvet Code (Anatomical Therapeutic Chemical Veterinary Code) by stating the therapeutic group (VOLUME 6C Summary of the Product Characteristics SPC – Pharmaceuticals, QRD Template Version 9XX/2021). It is already recommended in the draft guideline, to mention the time dependent or concentration dependent effect of the antimicrobial substance (section 4.2).
3	Finnish Food Authority thanks for the opportunity to provide comments on the draft Guideline on the summary of product characteristics (SPC) for veterinary medicinal products containing	Thank you for your comments.

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	antimicrobial substances. Updating the SPC guideline is seen very important as it gives the backbone for the product information. One more general comment: It is not clear when this revised guideline will come into effect. These comments are made assuming that there will be another revision before January 2022.	The guideline will come into effect January 2022 to be in line with the date of application of Regulation (EC) 2019/6.

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
66 - 74	3	**Comment**: The guideline should be applied to all procedures. Out-of-date-SPCs of the old products are causing confusion among the veterinarians when they compare newly authorised products where the SPC is based on an old reference product with those already on the market. From user point of view, it is important that SPCs are updated also when the reference product in a mutual recognition/decentralised procedure is old and out-of-date. Failing to do so could lead to misunderstandings and make it more difficult for the practitioners to use veterinary medicinal products prudently.	Not accepted. The concern is acknowledged. Article 18 requires that the SPC of a generic VMP shall be essentially similar to that of the reference VMP (with exceptions relating to patent law). The update of out-of-date SPCs of newly authorised VMPs (generic or hybrid) and reference products is subject to referral procedures, if serious risks for safety or efficacy are identified.
122 - 124	3	**Comment**: It is proposed to clarify that only relevant species should be mentioned. **Proposed change**: … and rodents) should be stated for relevant species.	Accepted.
173	1	**Comment:** it should be focused on one categorization scheme only, i.e. AMEG **Proposed change:** these categories (**AMEG**) should	Accepted.
185 - 186	3	**Comment**: The phrase is too weak when considering the scale of AMR threat and should be strengthened. **Proposed change** :	Not accepted. The proposal directly reflects Art 107.1 and is considered good veterinary practice. It is therefore not strengthened.

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		The <product name/active substance> shall not be applied routinely nor used to compensate for poor hygiene, inadequate animal husbandry or lack of care or to compensate for poor farm management.	
227	3	**Comment**: Delete unnecessary words in a long sentence. **Proposed change**: The information ~~submitted in this section~~ should allow…	Accepted.
306 - 307	1	**Comment:** EMA/CVMP/627/2001-Rev.1 provides a clearer definition of 'Co-resistance' (Codex). Where possible we suggest to consistently refer to already established definitions. **Proposed change:** please substitute the current text with the Codex definition reported in EMA/CVMP/627/2001-Rev.1: 'The ability of a microorganism to multiply or persist in the presence of different classes of antimicrobials due to possession of various resistance mechanisms'.	Not accepted. The definitions were aligned with those used in the EMA and EFSA Joint Scientific Opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety (RONAFA) and the draft guideline on the assessment of the risk to public health from antimicrobial resistance due to the use of an antimicrobial veterinary medicinal product in food-producing animals (EMA/CVMP/AWP/706442/2013).
316 - 320	1	**Comment:** as above **Proposed change:** please substitute the current text with the Codex definition reported in EMA/CVMP/627/2001-Rev.1: 'The ability of a microorganism to multiply or persist in the presence of other members of a particular class of antimicrobial agents or across different classes due to a shared resistance mechanism'.	Not accepted. See previous comment.