9 December 2021
EMA/CVMP/EWP/524331/2021
Committee for Veterinary Medicinal Products (CVMP)

Overview of comments received on 'Draft guideline on the summary of product characteristics for antiparasitic veterinary medicinal products - Revision 1' (EMA/CVMP/EWP/170208/2005-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	Domes Pharma
2	Sustainable Control of Parasites in Sheep (SCOPS) & Control of Worms Sustainably (COWS)
3	AnimalhealthEurope
4	EGGVP – European Group for Generic Veterinary Products
5	FVE – Federation of Veterinarians of Europe

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1. General comments – overview

Stakeholder no.	General comment	Outcome (if applicable)
2	The guidance on good practice and resistance mitigation included in this version of the document is more practical and reflective of the current epidemiological situation relating to livestock parasites than that included in the previous draft.	Thank you for the comments.
3	AnimalhealthEurope welcomes the opportunity to comment on this draft guideline. Whilst there may be pressure to minimise use of parasticides in companion animals, until there is an effective alternative (i.e. test and treat protocols that don't leave pet owners at risk of parasite-related / -borne diseases or that miss many infections/infestation, leaving affected pets untreated) it may place prescribing vets in an untenable position if they have SPCs that discourage regular/routine/long-term use, yet the vet still needs to make sure that they don't leave their patients or their clients at risk. Where do public-health risks sit against concerns around resistance (which is not really documented in companion animals – presumably due to the very different selection pressures compared to large animals where closed herds are grazed together)? It is understood why authorities want to bring companion animals into the spotlight here, but to industry it doesn't work just to fold them in with large animals / equine – where the situation and selection pressures for resistance are massively different.	Thank you for the comments. The guideline has been elaborated with the intention to distinguish, where necessary, between the requirements for different categories of domestic animals, e.g. companion and farmed animals. When it comes to companion animals, the aim of the guideline is not to discourage repeated or regular use where this is needed, but to promote tailored use considering each individual situation, i.e. to avoid unnecessary use following too general or even promotional statements. Accordingly, in our view, the texts to be included in the product information do not contain negative advice against repeated use. The veterinarian would not be limited in his/her prescription right, but is advised to tailor the treatment schedule based on his/her professional judgement, i.e. on the epidemiological situation of each individual animal, on appropriate diagnostics where feasible, on the product

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		characteristics and on the possible alternatives with a narrower spectrum. It is acknowledged that the reported resistance prevalence and the pattern of exposure to antiparasitics are not comparable between companion animals and large, grazing animals kept in groups. However, there are reports of resistance in companion animals, which may not reflect the actual extent of the issue, and there is an overall need to avoid overuse in companion animals, which would be beneficial as well to other aspects such as environmental and user safety. Please see also below our answer to the comment to line 143.
4	This draft guideline supports the prudent use of antiparasitic veterinary medicinal products which is much welcome by EGGVP. To avoid confusion and misinterpretations in the final version of the guidance, we have drafted some comments, mainly in regards to the "average" sizes and body weights, and "realistic proportion" as used in the Annex I.	Thank you for the comments. Please see below the answers to specific comments.
5	The FVE experts have reviewed the guideline and had no comments on the proposed guideline.	Thank you for the comments.

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
40-42	3	Comment: Wording is unusual. Also, effective and responsible use is desired whether resistance has evolved or not. The specific resistance focus of the document is covered in the following sentence in line 43/44. Proposed change: delete "in the face of an evolving resistance situation". Alternative wording: "The Summary of Product Characteristics (SPC) is one means to promote effective and responsible use of antiparasitic Veterinary Medicinal Products (VMPs). The aim of this document… "	Partly accepted. The stakeholder flags a potential mixing of the overall aim of an SPC and the focus of this document (resistance); also, speaking of an "*evolving resistance situation*" may not be generally applicable. This can be agreed on. Although the proposed wording has not been used as such, the text has been modified in that sense, simplified, and the wording "*evolving resistance situation*" has been deleted. Please see guideline text, section Executive summary.
44	3	Comment: SPC guidance is not only about resistance. Proposed change: "[…]sections ~~mainly~~ including in relation to antiparasitic resistance […]"	Not accepted. It was the intention of the CVMP that the focus of this revised guideline, like for the initial version, would be on issues linked to antiparasitic resistance, although the link may only be indirect for some recommendations. The word "mainly" has been used to adequately reflect this scope.
51	3	Comment: Antiparasitic resistance development is inevitable, the aim must be to limit the risk of development and slow its progress. Proposed change "to limit the risk of the development of antiparasitic resistance."	Accepted. (as "*the risk of ~~the~~ development of…*")

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53	3	Comment: This is a very general statement. The concern does not extend to all ectoparasite species in all host species. Proposed change: "… which highlights that resistance is of concern in certain ectoparasites as well…"	Partially accepted. "*In ectoparasites*" does not mean "*in all ectoparasites*" (and further information can be found in the Reflection Paper referred to). However, it is suggested to replace "*is*" by "*can be*". Please see guideline text – Executive summary.
59	3	Comment: re "medically justified": is this defined – what does it mean exactly? Proposed change: delete "medically"	Partly accepted. "*Medically justified*" intends to cover not only animals with clinical signs of parasitosis, but also animals with a significant parasitological burden or animals significantly exposed to parasites. Instead of deleting "*medically*", the meaning has been clarified in the guideline (please see guideline text – Executive summary).
67	3	Proposed change: Please amend as follows: "the use of veterinary medicinal products (VMPs) intended for antiparasitic treatment in livestock".	Not accepted. "*based on systematic (…) prophylactic schedules*" may also concern companion/individual animals.
95-96	2	Comment: 'in certain cases' and 'to some extent' are vague terms and do not define which antiprotozoal medicines would fall under the scope. Proposed change: Further clarification of which classes fall within scope should be included in the final document for MAH clarity.	Not accepted. It is not possible at this point to determine which antiprotozoal medicines would fall under the scope of this guideline and for which aspects. The purpose of this text was to let the door open to the use of this guidance in the context of antiprotozoals, where deemed useful and relevant.
94-97	3	Comment: Unclear to us what "certain cases" & "some extent" might be? Proposed change: please consider revising to be clearer.	Not accepted. Please see previous comment.

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101-104	3	Comment: Reference is made to the scope of this guidance: new applications for marketing authorisation or referral and variations that require reconsideration of the overall risk-benefit balance. Assurances that it will not apply to routine variations requiring assessment intended to revise the QRD format to V9.0 is needed in order Proposed change: Please add: "in particular, the revision of the product information for compliance with the latest version of the QRD (V9.0) is not considered as requiring reconsideration of the overall benefit-risk balance."	Not accepted. The wording *"that require a reconsideration of the overall benefit-risk balance"* is considered sufficiently clear to exclude variations that merely concern the format or structure of the SPC. The current wording is the same as for the current Guideline on the SPC for VMPs containing antimicrobial substances (EMA/CVMP/383441/2005-Rev.1).
125	3	Proposed change: consider using the term 'infestation' instead of 'infection' when referring to both ecto- and endoparasites.	Accepted. It would seem from the currently approved SPCs that this corresponds to the most frequent use.
133	3	Comment: Please reformulate more positively. Proposed change: "~~No detailed study results or experimental details should be included in the SPC unless those are relevant for proper product use or are considered essential information for the user.~~ Study results or experimental details should be very brief and concise, if included in the SPC. Those details have to be relevant for proper product use or be considered essential information for the user."	Partly accepted. A slightly different wording has been included, in the spirit of the stakeholder's comment (please see guideline text, section 4).

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139	3	Proposed change: Please amend as follows: "medical and/or epidemiological need".	Accepted.
143	3	Comment: In the scientific guidelines for parasitic treatment (ESSCAP), the use of strategic treatments may advocated as part of a Strategic Treatment schedules. The statement advice for systematic use at defined times of the year seems to exclude that strategy advised in the scientific guidelines. Proposed change: Advice for systematic use at defined intervals or times of the year (unless recommended as part of a Strategic Treatment schedule)	Not accepted. The wording "*strategic treatment schedule*" should be avoided because it has no precise/consensual definition and not everyone may have the same understanding of this. Basically, the decision to re-treat (i.e. to prolong the protection period beyond the claimed efficacy period, or to repeat curative treatment at a given time where re-infection is expected to have occurred) with the same product should be taken considering each particular situation, using general veterinary knowledge and/or "external" scientific guidance (possibly ESCCAP, but not only). Such general recommendation in the SPC might lead to overuse and be promotional. Nevertheless, the guideline still gives the possibility to justify that a recommendation for re-treatment is necessary for a given product and parasitic disease.
146	3	Comment: The statement "evidence-based views" is high-level and it is not clear whether or not the outcome of predictive modelling is regarded as evidence-based scientific views. As resistance is emerging, the benefit of insights provided by predictive modelling is very useful to predict how treatment should be used to prevent antiparasitic resistance development. This has been outlined in	Not accepted. We agree that predictive modelling may be a useful tool to guide antiparasitic use (depending on its level of precision, validation, associated *in vivo* data, etc.); however, we do not see the need to specify this in a guideline concerning the SPC. "Evidence-based" may cover modelling as well, and it can be decided in the context of each application whether

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		scientific literature (*e.g.* D Leathwick's research on sheep and horses). Proposed change: Antiparasitic resistance is an evolving matter, and SPC recommendations should always be based on the most recent, evidence-based scientific views, including insights derived from predictive modelling	data from modelling are appropriate to derive SPC recommendations or information.
162	3	Comment: The text as written may be misleading. There are antiparasitic substances for which resistance has been reported, however there are still populations which are susceptible to the substance. The relevant information is already included in the statements in line 255/256. Proposed change: In accordance with good veterinary practice, a product should not be used in situations where ~~to treat~~ parasite populations are known or likely to be resistant to the concerned product, and therefore, it is not considered appropriate to include the following wording in the indications: "<target parasite species> susceptible to <antiparasitic substance>"	Partially accepted. A slightly different wording is now used compared to that proposed by the stakeholder, notably because the word "populations" precisely refers to a whole species, while here, only *cases* of suspected/known resistance are concerned. Please see guideline text – section 5 -3.2. A very similar text is used in the Guideline on the SPC for VMPs containing antimicrobial substances (EMA/CVMP/383441/2005-Rev.1). The statement referred to at lines 255/256 consists of standard text to warn professionals to consider the probability that the parasites to treat are resistant to some substances, which is distinct from the issue discussed here.
176-179	3	Comment: The clarity of this section could be improved (*i.e.* "Claims of efficacy against parasites that are known to be resistant to another active substance are not accepted in this section"): what if the product to be labelled has a claim of efficacy against such parasites?	Accepted. The following wording has been included: "*The results of clinical studies investigating efficacy in parasite subpopulations resistant to another substance or class should not be referred to in this section, i.e., claims*

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			reading "<parasite a> resistant to <substance x>" should not be included." Please see guideline text – Section 5 -3.2.
183	3	Comment: It is not clear what is meant by serious risk to animal health from resistance. Proposed change: should be moved to special warnings (when clarified)	Not accepted. The intention is to state that in some cases, a contra-indication might stem from a resistance issue, so this should not be moved to section 3.4. Such contra-indication may concern e.g. off-label use in a species where resistance is known to develop readily, with a potential impact on animal or even human health. For example (although these relate to antimicrobials), some paromomycin-containing products are contra-indicated for use in turkeys, because of the high risk of resistance emergence in intestinal organisms. Also, some products containing 3rd - 4th generation cephalosporins are contra-indicated in poultry to avoid development of resistance potentially affecting human health. It is proposed to only clarify that this could concern also public health (please see guideline text – section 5 -3.3).
192-194	3	Comment: The construction of the sentence could be misleading and imply to some that use, e.g., for prevention is not justified when you "only" protect the animal. We think this is not the intention but should	Accepted.

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		probably be reworded. Proposed change: Maybe separate out as a different sentence: "… environment and lifestyle. A further consideration, where relevant, is the zoonotic risk."	
196	3	Comment: is reference to economic perspective appropriate for a CVMP GL? Proposed change: "and may also be beneficial from an environmental ~~and economic~~ perspective."	Accepted, as "…may also be beneficial *e.g.* from an environmental perspective."
198	3	Comment: The principle of leaving parasites unexposed within a herd as refugia should be more acknowledged and widely accepted from a national authority's standpoint. National authorities should be open for scientific models justifying a certain percentage of animals being untreated and should support appropriate recommendations in the product information.	Not accepted. It is unclear what changes to the guideline are expected through this comment. Although there is currently no clear consensus as to the precise criteria to implement such methods optimally on the field, the benefits of leaving refugia are currently widely accepted based on scientific grounds, and therefore it is still considered appropriate to recommend them as a general good practice. Recommendations may be adapted/more elaborated if deemed appropriate by NCAs based on further scientific advances.
200-202	3	Comment: regarding means of diagnostics the situation today is very different across parasite species, host species and across Europe in terms of availability of diagnostics, need to consider practicality… Proposed change: "…encouraging a proper identification of the parasitic species of concern	Accepted with slight modifications (please see guideline text – section 5 -3.4 –(i)). It is noted that this change does not impact the associated standard SPC text.

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		(where appropriate and rapid diagnostics are widely available) and evaluation …"	
211-217	3	Comment: is this really the level of detail that one wants to describe within an SPC? There is a risk for outdated and heterogenous information across SPCs potentially leading to confusion. Proposed change: rather refer to current recommendations of, e.g., national academic institutions	Partly accepted. This comment is on the standard text about refugia/TST in grazing animals. It is unclear what the stakeholder wants to keep or not within that text, and it is deemed that this text remains high-level/general and does not consist in a too high level of detail as is objected. When it is stated in that text that guidance should be sought from the responsible veterinarian, it is expected that this will be based on current scientific data and recommendations, e.g. from national academic institutions, as pointed out by the stakeholder. The stakeholder remarks that "*there is a risk for outdated and heterogenous information across SPCs potentially leading to confusion*"; it is assumed that this rather relates to the recommendation "*More specific guidance can be given where methods for guiding targeted treatment have been established (e.g. through product-specific studies or literature data) for a given indication".* This is acknowledged; indeed, it remains very difficult to say when a particular method to implement TST, potentially among several other possible methods, should be included in the SPC or not, and it would not be easily withdrawn when/if it becomes outdated. Therefore, the text quoted above has been deleted from the revised guideline.

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216	2	Comment: Suggest amended wording for clarity Proposed change: Suggest using 'combined' instead of 'associated'	Accepted.
216	3	Proposed change: please consider using "combined" instead of "associated"	Accepted.
217	2	Comment: Suggest amended terminology to reflect variation in parasite status amongst subgroups within a herd/flock. Proposed change: Change 'herd' to 'management group'	Not accepted. As the responsible veterinarian is rather associated to a herd (meaning more similar to "farm") and not to a subgroup, it is preferred to keep the initial wording. Also, the meaning of "management group" may be questionable to many readers.
223-225	1	Comments: The direct reference to a competing product seems to be inappropriate in a SPC. Proposed change: "Where relevant, more specific information can be given on the possible alternatives ~~and/or on typical situations where an alternative product would be indicated~~.	Partly accepted. "*Alternative product*" (which indeed could let the reader think to a "*competing product*") has been replaced by "narrow-spectrum product" (just as in the standard text) (please see guideline text – section 5 -3.4 – (i)).
243-251	3	Proposed change: We propose at this point to also introduce the nuance provided by the wording of "lack of efficacy", together with "resistance".	Accepted. It is not fully clear what changes are expected. It is acknowledged however that there is an important nuance between "resistance" and "lack of efficacy", in that lack of efficacy is not always attributable to resistance; therefore:

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			- A note has been included in accordance, within section 1. Introduction. - The following paragraph has been included in section 5 – 3.4 –(iii) (resulting also from the next comment below): "*The content of this paragraph should be based on reliable reports of confirmed acquired resistance. It should primarily reflect the European situation, however, information from non-European regions can be relevant (e.g. when claims against exotic parasites are included).*"
246-247	3	Comment: statement is very general and it may be difficult to provide meaningful information that is applicable across EU, more specific information on the other hand may require frequent update Proposed change: refer to national academic institutions for relevant information	Partly accepted. It is acknowledged that it might not be easy in some cases to define the content of this paragraph, and that this concerns an evolving matter. Nevertheless, it is considered insufficient to refer to other sources/institutions, as the purpose of the statement is to directly provide minimum information to the user. Also, referring to other sources may also require update. It is noted in addition that the same types of statements are already required by the current version of the guideline and are consequently used in SPCs. The following paragraph has been included in section 5 –3.4 –(iii): "*The content of this paragraph should be based on reliable reports of confirmed acquired resistance. It should primarily reflect the European situation, however, information from*

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			non-European regions can be relevant (e.g. when claims against exotic parasites are included)."
248	3	Comment: It is not clear what is meant by 'more detailed information on the clinical impact'. Antiparasitic resistance will lead to a lack of efficacy. It is not clear what information is expected here.	Accepted. The wording has been clarified by using "*occurrence*" instead of "*clinical impact*". Please see guideline text – section 5 –3.4 –(iii).
253-256	4	Comment: The standard text is proposed to be used in the case of parasite species for which clinical resistance to the active substance has been reported in the field. Nevertheless, there is no guidance on the resistance information (sources and their validity, e. g. scientific literature, AE reports, the frequency of reports). Proposed change: To provide some guidance in regards to the reports to be considered as reliable/valid to determine the necessity for the inclusion of the proposed advice.	Partly accepted. It is not considered feasible to provide detailed guidance in a SPC on which type of information would be reliable or not and would lead to the inclusion of that statement, all the more that this would be evolving. This issue is considered as appropriately covered by the inclusion in the standard text of the wording "*where available*", as proposed by another stakeholder (see below).
255-256	3	Comment: local information will not be always available and may be hard to obtain Proposed change: Add: "… target parasites, where available."	Accepted (supported also by the comment above). Please see guideline text, section 5 -3.4 –(iii).
259	3	Proposed change: "It is recommended to further investigate cases of lack of efficacy and/or suspected resistance, using an appropriate"	Not accepted. It is deemed unnecessary to lengthen the standard text. This could be a redundancy, as a suspected case of resistance should normally be a case of lack of efficacy (and

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			normally other possible causes of lack of efficacy should have been envisaged when resistance is suspected).
276	3	Proposed change: "The recommended dose should be expressed in mg <u>of</u> active substance per kg bodyweight"	Accepted.
279-280	1	Comments: This proposal is not applicable for a tablet form, which implies a range of target weights, even if the dosage should be at least that indicated in the SPC in mg/kg of active substance. Proposed change: ~~Ranges in dose level 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.~~	Partly accepted. It is necessary to clarify the wording, but the recommendation is still valid and should not be deleted (what should be avoided is a "choice" of doses for the prescriber, not weight bands). The following wording has been included: "*Where ranges in the recommended dose level are proposed, there should be clear guidance for the user as to when to administer the product at the upper or lower limit of the range.*" (Please see guideline text – section 5 -3.9).
282	2	Comment: Suggest amended wording for clarity Proposed change: Change 'Underdosing precludes effective use..' to 'Underdosing can render treatments ineffective….'	Partly accepted. This would possibly change the meaning of the text and be redundant with the second part of the sentence. The following change has been made to the text: *"Underdosing could result in ineffective use…"*.
285	2	Comments: Dosing to the heaviest may not be appropriate when a product has a lower safety index.	Accepted.

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		Need to avoid the impression that underdosing is bad but overdosing is ok. Proposed change: Additional/amended wording should be included to reflect this.	The standard text has not been modified, but an additional sentence reflecting the point made by the stakeholder has been included: *"Also, recommendations may need to be adapted for products with a narrow safety margin, e.g. recommendations to dose based on the heaviest animal may need to be omitted."*
300	3	Comment: It should be possible to keep different dosage regimens, when justified Proposed change: "Recommending different dosing regimens for different parasite species is not acceptable when the concerned species are commonly present as mixed infections, or cannot be readily distinguished under field conditions, unless justified."	Accepted.
300-302	4	Comment: Different dosing regimens are not recommended in cases of mixed infections, or different parasite species cannot be readily distinguished. For some products, different efficacy (persistent) periods against concurrently present parasites (e. g. fleas and ticks) are indicated. While the most common treatment interval may be recommended, for some of indications more frequent intervals may be appropriate (provided that the safety profile remains favourable). Proposed change (if any): The proposed guidance may be modified to distinguish between the dose and	Partly accepted. Actually, this recommendation does not concern the claims for persistent efficacy, which are mentioned in SPCs for each parasite separately based on study results. This is deemed sufficiently clear, as "dosing regimen" is not the same as persistent efficacy periods. Nevertheless, the wording under section 5 -3.2 (Indications) in relation to the claimed durations of persistent efficacy has been amended to better reflect the fact that periods of persistent efficacy are granted separately for each parasite.

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		the treatment frequency (intervals) to avoid confusion.	
318	3	Proposed change: After "killing", please add "anti-feeding", which does not necessarily correspond all the time to "repellency".	Accepted.
339-340	1	Comments: What means "appropriate measures of central tendency for pharmacokinetics parameters" ?	Partly accepted. The wording "*appropriate measures of central tendency*" was kept, as it refers to the use of a suitable measure of the average value of a parameter (e.g. arithmetic mean, geometric mean, harmonic mean, median) depending upon which PK parameter the value relates to. The wording has however been revised to include '*mean*' alongside '*central tendency*' for the purpose of clarity.
344	2	Comments: Suggest inclusion of additional guidance placing onus on the prescriber to supply the most appropriate pack size.	Partly accepted. It is recognized that the prescriber plays an important role in the use of appropriate pack sizes; however, this part of the guidance concerns the pack sizes that should(n't) be marketed by the MAH. The prescription of an appropriate pack size is rather seen as a matter of good veterinary practice, and it is not deemed appropriate to provide SPC recommendations in that regard. Also, a significant number of antiparasitic products can be sold without prescription.

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			Nevertheless, a general statement pointing out to the role of the prescriber in selecting the appropriate pack size has been included under section 5 -5.4.
347	3	Comment: The definitions of infection/infestation and lack of efficacy in the meaning of the Guideline should be added.	Partly accepted. As explained above, it is not considered appropriate to refer to "lack of efficacy" (and to its specific meaning with regard to "resistance") within the guideline recommendations, and therefore no definition of "lack of efficacy" is included. Nevertheless, it is proposed to include a note within section 1. Introduction, to clarify that this is not interchangeable with "lack of efficacy". Definitions of "infection" and "infestation" have been included.
352	3	Proposed change: After the word "parasites", please provide some examples of what is meant by "parasites", for instance in the following fashion: "(e.g. arthropods, nematodes, trematodes, cestodes, etc.)".	Not accepted. The definition given there is that of Regulation (EU) 2019/6, and it is preferable not to modify it. Also, in the context of a document used for professional purposes, is not considered necessary to give examples of "parasites" at a high level. Furthermore, the types of parasites directly concerned by the guideline are defined within section 2 - Scope.
372	3	Proposed change: Please add ", medical/clinical" after "parasitological".	Accepted.
445-447	1	Comments: It is acknowledged that large pack sizes may not be in line with the guideline. Nevertheless, a	Not accepted.

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		pack size that covers antiparasitic treatment for only part of the year, or even a maximum period of one year for an individual, would be more suitable for pets. Moreover, single-dose unit packaging would result in the over-consumption of packaging which seems to be not acceptable from an ecological and societal point of view.	The guidance already allows, where justified, to provide pack sizes containing more than a single-dose unit, i.e. which may potentially cover one season of exposure to a parasite (*"Additional, larger pack size(s) may be justified where it is usually necessary to repeat treatment…"*). The environmental impact of single-dose units may be very limited depending on the material chosen for the outer packaging, while the impact of product leftovers might also be relevant.
445-450	3	Comment: Pack sizes containing more than a single treatment may be required for reasons beyond the need of re-treatment, *i.e*. the treatment of multiple animals within the same household, or for administration by the veterinarian in the clinic Proposed change: "For products primarily intended for animals kept individually, ~~in principle~~ the smallest pack size ~~available should~~ corresponding to one single antiparasitic treatment (of an animal of average size, where applicable) should be available~~. Unless otherwise justified~~. ~~Additional, larger pack size(s) may be made available where it is usually necessary to repeat treatment. In such cases, all substances combined within a product should be considered when assessing the likely necessity for repeated administration.~~ "	Partly accepted. With the wording as proposed by the stakeholder, the guidance would only recommend that single-treatment packages are made available, with no restriction for larger pack sizes. This would clearly limit the impact of the guidance on prudent use of antiparasitics. Nevertheless, the first sentence was adapted as proposed. It is also accepted to add the following (please see guideline text – Annex I): "*…or to treat several animals in the same household*". Furthermore, the guideline has been revised to state in a general manner that pack sizes must be justified based on the intended use, which is considered to cover the issue of products to be used specifically by veterinarians.
445-450	4	Comment: For the treatment of individual animals, the pack sizes should be adjusted to "an animals of	Not accepted.

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		average size" and no further guidance is provided on the "average size." Proposed change (if any): Some clarification and standardisation in regards to the average size would be beneficial (e .g. standard body weights may be referenced as per VOLUME 9B of The Rules Governing Medicinal Products in the European Union – Guidelines on Pharmacovigilance for Medicinal Products for Veterinary Use).	It is not deemed appropriate to refer to a precise/fixed source for the interpretation of "average size". Also, the representative animal size/weight to select depends on the concerned indication. Slight differences in this interpretation are not expected to have a significant impact on the eventual pack sizes selected. It is noted that comparable recommendations, with no precise figures or sources in relation to average size or bodyweight, are given in the recently revised Guideline on the SPC for VMPs containing antimicrobial substances (EMA/CVMP/383441/2005-Rev.1).
451-456	4	Comment: For the group treatment, a subgroup of reasonable size and the realistic minimum proportion of animals to be treated should be considered. No guidance is proposed to determine the realistic minimum proportion. It is acknowledged that a universal recommendation may be challenging to provide (due to differences in host, parasites, products/ingredients, and environment), nevertheless some suggestion would be welcomed. Traditionally close to 100% of the group has been treated (as presented in the guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38, EMA/CVMP/ERA/418282/2005-Rev.1- Corr.) however	Not accepted. Although the concern is understood, the shift from mass treatment to more targeted (selective) treatment is only in progress currently and it is not possible, at this point or in a near future, to establish precise figures for what would be "a reasonable proportion". This would vary also with the parasitic disease considered. As indicated in the guideline text, an estimation should be made "in view of the current best practice recommendations". It is noted that comparable recommendations, with no precise figures in relation to the number of animals to be treated, are given in the recently revised Guideline on the SPC for VMPs containing antimicrobial substances (EMA/CVMP/383441/2005-Rev.1).

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		this may no longer be the case (as per the current guideline). Proposed change (if any): It may be beneficial to initiate a discussion with veterinary surgeons and specialists in the EU member states to determine the realistic minimum proportion. Until the outcome of the discussion, the provision may be omitted.	
456-459	4	Comment: For the group treatment, the maximum pack size is limited to one antiparasitic treatment of the whole group of a typical size (based on the average expected bodyweight of animals). No further information is provided on "average expected bodyweight of animals." Proposed change (if any): Some clarification/standardisation in regards to the average bodyweight would be beneficial (e.g. standard bodyweights may be referenced as per VOLUME 9B of The Rules Governing Medicinal Products in the European Union – Guidelines on Pharmacovigilance for Medicinal Products for Veterinary Use).	Not accepted. It is not deemed appropriate to refer to a precise/fixed source for the interpretation of "average bodyweight". Also, the representative animal size/weight to select depends on the concerned indication. Slight differences in this interpretation are not expected to have a significant impact on the eventual pack sizes selected. It is noted that comparable recommendations, with no precise figures or sources in relation to average size or bodyweight, are given in the recently revised Guideline on the SPC for VMPs containing antimicrobial substances (EMA/CVMP/383441/2005-Rev.1).