15 November 2010
EMA/CVMP/SWP/513604/2010
Committee for Medicinal Products for Veterinary Use (CVMP)

Overview of comments received on draft guideline on data to be provided in support of a request to include a substance in the list of substances considered as not falling within the scope of Regulation (EC) No 470/2009 (EMA/CVMP/516817/2009)

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

Stakeholder no.	Name of organisation or individual
1	IFAH-Europe

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1. General comments – overview

Stakeholder no.	General comment (if any)	Outcome (if applicable)
1	IFAH-Europe appreciates that the CVMP approach is not to be overly prescriptive in the information expected to be submitted in support of pharmacological non-activity, that the applicant is not required to conduct new studies and that not all applications will require formal scientific advice. Thus IFAH-Europe would support the proposed guideline. However, the very existence of the application template may lead to questions on blank or incomplete fields and we can only comment on the application of "a pragmatic approach" once the guideline is in force and we have real examples. As some requirements are imprecise, especially in the case where data packages (toxicologgy, pharmacodynamics, pharmacokinetics) might be minimised ('no need to complete the section… in detail…'), it is understood that no absolutely complete data list can be named here. Nevertheless, such wording is likely to lead to further requests and consequently to delay of the procedures. Please find below our specific comments on the document.	The SWP/CVMP appreciates IFAH-Europe's support and hopes that the application of a pragmatic approach will be demonstrated in due course. Currently the CVMP receives a significant number of requests for clarification in relation to data requirements for inclusion of substances in the list of substances considered as not falling within the scope of Regulation (EC) No 470/2009. It is anticipated that through publication of this guidance the process will be made clearer and there will less need for companies to seek clarification on the relevant data requirements. The CVMP would like to highlight that, in the context of this guideline, when it refers to the need for data the intention is not for the company to necessarily perform new studies. Where information exists in the literature companies are encouraged to provide these

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
Lines 51-52	1	Comments: Do colouring agents fall under the scope of this guideline? The addition of a footnote for definition of *excipient* would be helpful to define the limits of the scope (e.g. as described by the European Pharmacopoeia*"Excipient (auxiliary substance): Any constituent of a medicinal product that is not an active substance. Adjuvants, stabilisers, antimicrobial preservatives, diluents, antioxidants, for example, are excipients."*	Unless accounted for by an existing entry in the Annex to Commission Regulation (EU) 37/2010 or by an existing entry in the list of substances considered as not falling within the scope of this regulation a colouring agent would fall under the scope of this guideline. Accepted. A footnote will be added to section 2, providing the definition of excipient as described in the European Pharmacopoeia.
Line 89-91		Comments: How will be handled the aspects of GLP requirements in the case of data from the literature? Does the need to generate new data by companies imply any kind of data protection?	The CVMP does not expect that all literature data provided will be GLP compliant and will give due consideration to non-GLP literature data. The following will be added to the last paragraph of section 4 of the guideline: "*It should be noted that old data that do not comply with current guidelines and standards may be submitted and will be given due consideration. However, in reaching its conclusion the CVMP will, of course, take the quality of the data submitted into account.*" An entry in the list of substances considered as not falling within the scope of Regulation (EC) 470/2009 can be referred to by any prospective Marketing Authorisation Holder, and not only by the company that generated the data on which that entry is based. However, the same commercially confidentiality rules will apply to the data on which the entry was based as

			apply in other MRL-related areas.
Lines 112-115		Comments: In order to keep the *'pragmatic approach'* suggested in the introduction of the GL, we would be rather supportive of a proposed template for submission of data than of a fixed template that can be easily interpreted as mandatory data to be submitted for the evaluation.	Not accepted. The CVMP anticipates that the submission of requests in a standard format will facilitate the evaluation process and so increase the number of requests that can be dealt with outside of the scientific advice process. It therefore considers that there is value in maintaining a fixed template. With regards to the possibility that a company may consider the sections and subsections of the template to represent mandatory data requirements, the CVMP would like to highlight that in section 5 of the guideline it already states that "*The template outlines types of data that may be considered relevant and should be completed as comprehensively as possible. Where no data are available for a particular section, the impact of this should be addressed in the overall evaluation*." However, these sentences will be revised as follows: "*The sections and subsections included in the template do not represent mandatory data requirements. Rather, the template outlines types of data that may be considered relevant and should be completed as comprehensively as possible. Where no data are available for a particular section, the impact of this should be addressed in the overall evaluation.*" Furthermore, in sections 7 and 8 of the template it is stated that there may be no need to complete subsequent sections in detail. The CVMP considers that the reader will understand that the template does not provide a list of mandatory data requirements.
		Additionally, it is not clear if the initial application should already follow the procedure of the formal scientific advice and thus would require the fees accordingly. Proposed change: *"However, companies are advised to*	Partially accepted. The following change will be made: *"However, companies are advised to submit the initial request along with the completed template (provided in Annex I) to the EMA for presentation to the CVMP. The initial request will be handled outside of the scope of the scientific advice procedure.*

		submit the initial request along with all information that is deemed relevant by referring, as necessary, to the completed suggested template (provided in Annex I) to the EMEA for presentation to the CVMP. The initial request will be handled out of the scope of the scientific advice. A first assessment of the CVMP will then clarify if a formal scientific advice procedure is necessary. At this point in time the applicant can withdraw the application if he does not intend to initiate a full procedure and incur the fees thereof. In the case of particularly straight forward enquiries the CVMP may be able to reach a conclusion without the need for a formal scientific advice procedure."	*The CVMP's response to the initial request will clarify whether a formal scientific advice procedure is necessary. Following the CVMP's initial response the applicant can withdraw the request if it does not intend to initiate a full scientific advice procedure. Fees will only be charged in those cases where formal scientific advice procedures follow and will be in line with standard scientific advice fees. In the case of particularly straight forward enquiries the CVMP may be able to reach a conclusion without the need for a formal scientific advice procedure.*
Line 118		Comments: Please see comment above. Proposed change: *"SUGGESTED TEMPLATE TO BE COMPLETED…"*	Not accepted. See response above.
Line 125		Comments: Would it be considered sufficient to provide information on origin and chemistry of the substance by referring to current European Pharmacopoeia?	Partly accepted. Reference to information in the Ph Eur may be acceptable in relation to the chemical make-up of the substance
Lines 173-207		Comments: We would like to suggest changing the order of these two paragraphs (*8. Pharmacokinetics and residue depletion* and *9. Toxicology*), as we would then look at the potential risk in a first step. In turn, these data would further justify the absence of residue depletion data when substances are not supposed to have a toxicological effect. We would also like to see at the end of the paragraph on *Toxicology*, the sentence mentioned at the end of paragraph 7: "*then there may be no need to complete the subsequent sections on pharmacokinetics in detail, although these data could be regarded as useful*	Partly accepted The order in which the data are provided is not considered to be critical. While IFAH's view can be accepted it can also be argued that if pharmacokinetic data demonstrate that no residues will reach relevant tissues, then there would be no need for toxicology data. Nevertheless, the order of sections 8 and 9 of the guideline have now been reversed. Partly accepted. The following sentence will be added to the end of the section on Toxicology: *"Note that if results of toxicology studies are provided, and the company is arguing that, based on this evidence alone, it can be concluded that the substance does not represent a*

		supporting information." Otherwise, applicants may be requested to provide residue depletion for excipients that are not yet classified as out of scope, but for which it is already known that there is no need for data as regards toxicological profile. In this case, such a request would not be in line with the pragmatic approach presented in the core document.	*consumer safety concern even if high levels of residues do gain access to relevant animal tissues after the intended use of the substance, then there may be no need to complete the section on pharmacokinetics and residue depletion in detail, although these data could be regarded as useful supporting information."*
Line 193-207		Comments: Especially old preservatives will have very limited toxicology data available and may not comply with the current requirements and standards. Considering the 3Rs and animal welfare, it does not make sense to generate data for substances used since decades. It should be clearly stated that full and recent toxicology documentation is not mandatory.	Partly accepted. The following will be added to the last paragraph of section 4 of the guideline: "*It should be noted that old data that do not comply with current guidelines and standards may be submitted and will be given due consideration. However, in reaching its conclusion the CVMP will, of course, take the quality of the data submitted into account.*"