Harmonised requirements for non-investigational medicinal products in CTA submissions

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COMMENTS FROM - F. Hoffmann-La-Roche, Basel

GENERAL COMMENTS

F. Hoffmann- La Roche appreciate the proposal for harmonised requirements for NIMP and also the details included on case by case basis. We would like to suggest below some further comments which are either for clarification of some missing points or to improve the exact understanding of the text. Thanks for providing us the opportunity to comment.

General Question- In the clinical trials can the background therapy be defined as " investigators best choice" without defining the exact therapy [brand name] or 2-3 choices [generic names]? This could be particularly the case for Oncology trials where standard of care choices for chemotherapy could differ in the member states? Any comment and if appropriate and eventual inclusion in the guidance will be appreciated.

SPECIFIC COMMENTS ON TEXT

GUIDELINE SECTION TITLE

Section/Line no. + paragraph no. Or the item No.	Commission position	Suggestion/Proposed change
Section 2. General principles	1. End of paragraph 1- documents submitted to the competent Authority may be submitted in English. 2. …the sponsor should implement a system allowing traceability of medicinal products which allows adequate reconstruction of NIMP movements and administration, taking into account the	1. It is not clear if more then one country is involved in the trial, English documents are recommended and acceptable. 2. **This comment is not very clear.** What is actually expected? Not clear how to manage this principle at a site level. Labeling is not foreseen for a Non IMP. Additional requirements for the site pharmacy could have an impact on the trial costs and on the site selection.

	purpose of the trial and trial subjects' safety. It has at least to include a procedure, established with the investigator and if applicable, with the hospital pharmacy, to record which patients received which NIMPs during the trial with an evaluation of the compliance."	
Section 3.1.1	*Background Therapy* *Second sentence-….Background treatment is generally considered to be the current standard of care for a particular indication in the member state concerned.*	Standard of Care may not be identical in all the member states involved in the trial. Please confirm that this is OK. Suggestion- ……..Background treatment is generally considered to be the current standard of care[SOC] for a particular indication in the member state concerned although the SOC may not be identical in all the countries involved in the trial.
Section 3.1.2	*Rescue Medication* . ……..when the efficacy of the IMP is not satisfactory, **or the effect of the IMP is too great ……..**	Suggestion- In some trials some medications are given prophylactically already to avoid too great effect of the IMP and potential damage. So one can add a comment about such medications given prophylactically also under rescue medication section.
Section 3.2.1	*NIMP is a marketed medicinal product in the concerned Member State* Simplified dossier is required containing… copy of SmPC	Is there a need for English translation or the country language version is sufficient?? Please clarify.
Section 3.2.2,	1. *NIMP is a marketed medicinal product in an other EU Member State* 2. Simplified dossier is required containing… Copy of the SmPC	1. Correction from an other to another in 3.2.2 Title and bullet point 4 *NIMP is a marketed medicinal product in another EU Member State. This comments applies to several places in the document.* *2.* SmPC from other country- and translation into English is sufficient?? i.e. no translation in local language is not necessary. Please clarify in the text.
Section 3.2.3	*1. bullet 1 - Evidence of its regulatory….* *2. bullet 5- importers authorization*	*1. what kind of evidence is needed? Will registration date and copy of SmPC [is sufficient? Please specify what is expected.*

	3. bullet 6- *an other EU Member State* 4. last bullet- Confirmation of reduced testing (e.g. identity) by analytical testing or an alternative appropriate method	2. - *importers authorization into EU* 3. *in another EU Member State* 4. generally the evidence of GMP compliance [manufacturers authorization/QP certification for non-EU sites is provided and no any other testing is done. So is this a new additional requirements? Please clarify.
Section 3.2.5	1. Gap in the second sentence and an other	1, Delete the gap and add another
Section 3.2.6	If particular brand is not specified in the protocol, information should go in the cover letter.	This is fine. What should be mentioned in the protocol, a generic name? Can we add this in the first paragraph Suggestion- …… generic name is included in the protocol but brand name is not specified in the protocol
Section 4.2.1 and 4.2.2	Simplified dossier is required containing… Copy of the SmPC	SmPC from other country- and translation into English is sufficient?? i.e. no translation in local language is not necessary. Please clarify in the text.
Section 4.2.2	*bullet 1 - Evidence of its regulatory….*	*what kind of evidence is needed? Will registration date and copy of SmPC is sufficient? Please specify what is expected.*
Section 4.2.4, and 4.2.5	1. ……NIMP….in a trial conducted in the concerned Member state…	1. is it correct to assume this can not be applied if the trail is conducted in another member state in the EU? Clarify or confirm.
Section 4.2.4, 4.2.5	"…*or where a letter of access to the data from the sponsor of the previous trial is available*"	In Italy *full dossier* is required in this case. Letter of access is not applicable in the majority of the cases since, due to the multiplicity of the competent bodies, it is not common to have the same coordinating bodies of a previous trial involving the same product. How this will be handled ?
4.2.6	Title …….active moiety has been previously administrated to humans……	…….administrated in humans in which countries ?All-EU, ICH, countries with MRA ? please specify?