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Submission of comments on Consultation Document 'Risk proportionate approaches in clinical trials'

Comments from:

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1. General comments

EUCROF	General comment (if any)	Outcome (if applicable)
	We welcome the opportunity to provide comments on the Consultation Document 'Risk proportionate approaches to clinical trials'. We would like to suggest using abbreviations in a consistent manner. For example, in line 60, the meaning for the abbreviation IMP is given, however in the subsequent text, the abbreviation is not used consistently (see, for example, lines 114, 116, 118, 119)	

2. Specific Comments Consultation Document Text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder No.	Comment and rationale; proposed changes	Outcome
67		Comment "… participants in trial subjects and the quality and integrity of the trial outcome." Proposed change (if any): to replace the first "and" with "as well as" in order to make it clear that it is about the two goals of GCP	
75, 76		Comment "This guideline applies to all sponsors, commercial as well as academic and all types of clinical trials..." There could be other non-commercial sponsors than academic ones, for example, patient organisations or authorities. Although most of the non-commercial clinical trials are initiated by academia, this guideline should not be limited to those. Proposed change (if any): To replace "academic" with "non-commercial"	
78-79		Comment "Thus it is addressed both to those clinical trials that are intended to be included in the application for a marketing authorization for the medicinal product under investigation, clinical trials with novel IMPs and to trials using only IMPs with a marketing authorization, …"	

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder No.	Comment and rationale; proposed changes	Outcome
		The word "both" anticipates two options, however three options are given. The logic of the sentence is strange. Maybe what is meant is: " **..., <u>i.e.</u>** clinical trials with novel IMPs …" ?	
82, 83		Comment "In this document, more explanations and examples of the areas …are provided" More than where? The reader can guess but it is not totally clear.	
127		Comment " … or other appropriate evidence." Another important aspect is the publication of individual treatment attempts. It would be helpful to mention this possibility as well.	
215, 216		Comment ", as well as pharmacists and research nurses." Replace with: ", as well as pharmacists, research nurses and laboratory experts."	
218		Comment "(e.g.SOPs, pharmacy manuals, (e)CRF manual, (e)TMF manual)" Replace with: "(e.g.SOPs, pharmacy manuals, (e)CRF manual, (e)TMF manual, laboratory manuals)"	
251-253		Comment	

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder No.	Comment and rationale; proposed changes	Outcome
		"As a general rule, any adverse event considered by the investigator as being potentially related to the IMP, and therefore representing an adverse reaction, should be reported to the sponsor, unless justified in the protocol and supported by the risk assessment outcome" The above sentence is a bit confusing as the "real" general rule is actually that the investigator has to report all adverse events and not only all adverse reactions. As a consequence, the risk-based approach has to start with considering all adverse events and subsequently - if justified - defining the exemptions of reporting all adverse events.	
272, 273		Comment "This applies in particular, but not only, to marketed products …" EUCROF is of the opinion that it should not be encouraged not to collect all AEs in clinical trials with IMPs without marketing authorisation. This seems to be high risk. With "but not only" the door is opened too wide. Proposed change (if any): Delete "but not only"	
342		Comment "For these IMP's" is not clear which IMPs are meant as above there are 2 options listed. Are "these IMPs" only those which are provided directly or also those which are provided through the supply chain? Please clarify.	
366		Comment	

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder No.	Comment and rationale; proposed changes	Outcome
		"Other risk factors, like the stability of the active ingredient that impact the management of IMP …" In fact there might be risk factors coming from the AMP – AMP should not be left out when considering risk factors with medication required by the trial protocol. Proposed change (if any): "Other risk factors, like the stability of the active ingredient that impact the management of IMP or AMP …"	
388, 389		Comment "On-site monitoring remains relevant in certain types of clinical trials, as it is instrumental for verification of several critical aspects at the trial site, for e.g. the informed consent process, source data verification and IMP handling on site." EUCROF thinks that the above sentence gives the wrong priority. In fact, on-site monitoring is relevant for almost all clinical trials. Not to perform any on-site monitoring should remain the exception and should be duly justified (as already explained in ICH-GCP 5.18). Proposed change (if any): Change above sentence to: "As a general rule, on-site monitoring remains relevant in clinical trials, as it is instrumental for verification of several critical aspects at the trial site, for e.g. the informed consent process, source data verification and IMP handling on site. Not to perform any on-site	

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder No.	Comment and rationale; proposed changes	Outcome
		visits should be duly justified."	
426,427		Comment "Monitoring activities that do not require visits to individual sites such as telephone contacts with the site, web-enabled training;" The term "remote monitoring" could be introduced here. This term is often used in the wrong way (e.g., it is used synonymously with centralized monitoring) and it would be helpful to provide clarification. Proposed change (if any): add onto above sentence. "Monitoring activities that do not require visits to individual sites such as telephone contacts with the site, web-enabled training (remote monitoring);"	
447-449		Comment • Combining of documents: one document serves multiple purposes (job descriptions, curriculum vitae); • Objectives achieved by other means It is not clear what is really meant. How can a CV and a Job Description be the same document? And what is meant with the second bullet point? Note to Files? Please clarify.	