2 September 2016

Submission of comments on **Summary of Clinical Trials Results for Laypersons** – Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use

Comments from:

Name of organisation or individual
AESGP

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).

1. General comments

Stakeholder number ***(To be completed by the Agency)***	General comment (if any)	Outcome (if applicable) ***(To be completed by the Agency)***
	The current version of the Consultation Paper consists of 3 parts: the main part (Sections 1 to 11) and 2 Annexes. In the main part there is no comment on the status of the Annexes. We suggest assigning different statuses to the 2 parts. While the main part may serve as a guideline, the Annexes should be clearly marked as examples to support implementation. The wording in the Annexes is often very prescriptive, e.g. the column heading in Annex 2 is "Promotional Language - DO NOT USE!". This language is inconsistent with the nature of the document (a guideline) and should be softened.	
	The Consultation Paper contains some conflicting or even contradicting recommendations. For example, in Annex 1, the Consultation Paper requests information on "the primary endpoint(s) and results by study arm, patient relevant secondary endpoints and results by study arm, Key patient reported outcome measures (PROMS) or other quality of life indicators of interest to patients". The descriptions of these endpoints will have to use numeric information. At the same time, (Number 7 numeracy in the main part) it is requested to follow the principles of numeracy. A key recommendation on numeracy is to limit the amount of numerical information provided. Thus, if the guideline is followed, the principles	

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	of numeracy cannot be attained. EMA is requested to provide clearer guidance.	
	The Consultation Paper does not address the central aspect of harmonisation with other regulatory documents. According to the EU regulation, the lay summary will be posted together (and in the vicinity) with the scientific/technical summary and the (redacted) clinical study report. The lay summary should contain links to other documents. As interested lay persons are likely to also consult these other documents, harmonisation between documents becomes important, in particular in regards to the presentation of numerical data. This aspect should be included in the guidance.	
	The actions arising out of the draft document would be much too far and wide for sponsors increasing the additional burden unnecessarily. It would be considerably less effort if the system would consider using the Lay Summary from the EudraCT database and take them over unchanged.	
Annex 2 introduction and title of the left column	We disagree in general to the allegation that wording as "... proved to be superior ..." or "... confirmed to be superior ..." were considered "promotional". They rather describe correct in a scientific manner the procedures in confirmatory clinical trials and are therefore in such studies technically correct (but would be incorrect in	

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	exploratory studies).	

2. Specific comments on text

Line number(s) of the relevant text ***(e.g. Lines 20-23)***	Stakeholder number ***(To be completed by the Agency)***	Comment and rationale; proposed changes ***(If changes to the wording are suggested, they should be highlighted using 'track changes')***	Outcome ***(To be completed by the Agency)***
84		**Comment:** **Proposed change (if any):** Text should be changed to "***Writing for lay audience requires a special skill in the use of language and the ability to understand the source documents, ie the clinical study reports. Therefore it is recommended that lay summaries are written by medical writers experienced in writing for a lay audience***."	
87-139		**Comment:** The description of people's reading ability is repetitive. Both Sections 5 and 6 cover this topic. We suggest shortening this information and confine it to one Section only.	
161-241		**Comment:** This information could be placed into an Annex and be summarised in a table. Its current location disturbs the flow of the guideline.	
249-262		**Comment:** The example for visuals provided in the Template Section 4.2 showing a pie chart for 'baseline demographics, sex' is not useful as this particular information is more easily conveyed in	

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		a table or as text. We suggest adding a more meaningful example in Annex 1 - Templates (e.g. primary endpoint result).	
Annex I (templates)		**Comment:** The first sentence of the second paragraph says that 'the wording of the ten elements cannot be changed…'. We strongly object to this recommendation as the headings in Annex V are not appropriate for lay language readers. Sponsors need to be given leeway in transforming the requirements into an appropriate lay language document. This needs to be expressed in the main part of the guideline.	
Annex 1 – 3.1. Where the trial was conducted		**Comment:** The requirement to list individual countries is given in Sections 3.1 and 4.1; please confine it to one location in the document (we suggest 4.1).	
Annex 1 – 5. Investigational medicinal products used		**Comment:** The use of all brand/trade names in the text will make the text unreadable. Therefore we suggest using only the INN in the text. A list of brand names could be provided at the end of the document.	
Annex 1 – 6. Description of adverse reactions		**Comment:** There is still some confusion in regards to seriousness and severity of adverse reactions.	

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and their frequency		The reference to the European Commission's Readability guideline is not helpful and should be deleted. It is stated that "The most serious adverse reactions need to be listed first, …". How should 'most serious' be judged (medical judgment, intensity of AE?)? Serious Adverse Reactions are covered by a later bullet point but the description does not seem to refer to Serious Adverse Events according to the definition in ICH E6, but rather to adverse reactions that are considered to be medically "serious". Clarification on this issue is requested. **Proposed change (if any):** We suggest to state: Serious adverse events need to be listed first and (non-serious) adverse events should be presented separately in a table sorted by frequency.	
Annex 1 – 7. Overall results of the clinical trials		**Comment:** There should be a clear recommendation on how many secondary endpoints should be presented. Given that the description of many secondary endpoints will make it impossible to attain low numeracy levels, recommendation should be given to limit the description to 1 or 2 secondary endpoints in addition to the primary endpoint. In the endpoint table several definitions need improvement (e.g. non-inferiority, surrogate). We suggest adding superiority as a concept to this section. Descriptions of OS and PFS: The example data presentations	

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		for PFS and OS are misleading. These endpoints are often evaluated using a hazard ratio. Both endpoints are related to time alive (example given for OS) and the percentage of patients with certain outcomes (example given for PFS), but providing percentages does not accurately reflect PFS or OS analyses. All key efficacy assessments in oncology are based on time-dependent estimates, thus the representation of these endpoints in percentages is incorrect and misleading. We suggest including better wording or leaving it up to sponsors to develop appropriate descriptions.	
Annex 1 – 8. Comments on the outcome of the clinical trial		**Comment:** There is a lot of emphasis on subgroup analyses in this section, but their relevance for lay persons is unclear. Many trials do not include any subgroup analysis, or present subgroups that are often too small to make any valid statements. Therefore the recommendation to include results of subgroups should be deleted.	

Please add more rows if needed.