



15 July 2019

Submission of comments on ICH guideline E8 (R1) on general considerations for clinical studies (EMA/CHMP/ICH/544570/1998)

Comments from:

Name of organisation or individual

International Society for Clinical Biostatistics, ISCB

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 <i>(To be completed by the Agency)</i>	General comment (if any)	Outcome (if applicable) <i>(To be completed by the Agency)</i>

2. Specific comments on text

Line number(s) of the relevant text <i>(e.g. Lines 20-23)</i>	Stakeholder number <i>(To be completed by the Agency)</i>	Comment and rationale; proposed changes <i>(If changes to the wording are suggested, they should be highlighted using 'track changes')</i>	Outcome <i>(To be completed by the Agency)</i>
Lines 606-611		<p>EK Comment: In the lines 606-611 it is described what the analysis plan should contain. As the term "statistical analysis plan" is used in the text before, it may seem that the description of the statistical methods given (method of treatment allocation, the analysis population, handling of intercurrent event etc.) can be given in the statistical analysis plan which is often a stand-alone document that is not formally approved by regulatory authorities during the CTA. I consider the information mentioned in the lines 606-611 as information that should be contained in the study protocol and therefore I consider the term "analysis plan" in line 606 misleading.</p> <p>Proposed change (if any):</p> <p>The statistical methods section of the study protocol analysis plan should describe the analytical methods for the estimation and tests of hypotheses about the drug effect, addressing the method of treatment.... The plan should address the handling of intercurrent events, such as treatment discontinuations, use of rescue medication, missed visits, and other protocol violations should be also addressed there.</p>	
Lines 765-766		EK Comment: Here again, the term "statistical analysis plan" is used maybe in a general meaning of planning the	

Line number(s) of the relevant text <i>(e.g. Lines 20-23)</i>	Stakeholder number <i>(To be completed by the Agency)</i>	Comment and rationale; proposed changes <i>(If changes to the wording are suggested, they should be highlighted using 'track changes')</i>	Outcome <i>(To be completed by the Agency)</i>
		<p>statistical methods but it may be misleading.</p> <p>Proposed change (if any): The statistical methods analysis plan is are pre-specified and are defines the analysis methods—appropriate for the endpoints and the populations of interest.</p>	
Line 786		<p>EK Comment: In the table in line 786 (annex 3) a sign that resembles a radical sign was used. Use of a different tick symbol (e.g. ☑) would be preferred.</p> <p>Proposed change (if any): Use ☑ instead of √.</p>	

Please add more rows if needed.