10 September 2010

Submission of comments on:

Draft revised guidance on the collection, verification and presentation of AE reports arising from clinical trials on medicinal products for human use ('CT-3')

Comments from:

Name of organisation or individual
AESGP (Contact: Christelle Anquez-Traxler)

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).

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1. General comments

Stakeholder number ***(To be completed by the Agency)***	General comment (if any)	Outcome (if applicable) ***(To be completed by the Agency)***

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)***
2.2.2 'serious event', life-threatening:		We would like to keep the definition of life-threatening which was in annex 1 of the previous version of CT-3: "***Life-threatening in the definition of a serious adverse event or serious adverse reaction refers to an event in which the subject was at risk of death at the time of event; it does not refer to an event which hypothetically might have caused death if it were more severe.***" Please re-include it.	
2.3.2 Non-immediate reporting (#20)		"*…the investigator shall report within the appropriate timeframe taking account of the specificities of the trial and of the serious adverse event,…"* Because of Non-immediate reporting we think it should be written "…***and of the adverse event***", instead of "…the serious adverse event". Would it be possible to concretize the appropriate timeframe? Then, we think that the reference "see section 2.3" should be "see section 2.2 and 2.3".	
4.2.3 'Unexpectedness' (# 34)		Comment: We would recommend listing the reference safety information (IB or SmPC etc.) at this point already.	
4.3.2 Causality (#39)		Comment: What is a 'reasonable causal relationship'? Chapter 3A1 of ICH E2A states that" The expression	

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		"reasonable causal relationship" is meant to convey in general that there are facts (evidence) or arguments to suggest a causal relationship". Is it "an at least possible causality" according to WHO criteria?	
4.5 Adverse reactions not to be reported (#48)		Comment:Should the sponsor inform the marketing authorization holder of the non-IMP about SUSAR supposedly caused by its non-IMP?	
4.5 Adverse reactions not to be reported (#48)		Should the sponsor inform the marketing authorization holder of the non-IMP about SUSAR supposedly caused by its non-IMP?	
4.6 Interface with safety reporting of authorised medicines under Pharmacovigilance rules (#52)		We understand that the scope of this guidance is that of Directive 2001/20/EC i.e. interventional trials. However, we'd like to take the benefit of this consultation to ask how should adverse reactions occurring in non-interventional trials be reported?	
4.7.1.2 Content of initial reporting (#60)		The text should make clear that the 'relevant information' is called the minimum reporting criteria.	
4.7.2.1 timelines for follow-up information (# 63)		For clarity it should be added that the receipt date of the most recent information is to be provided in addition to the date of initial report as described in 4.7.1.1, otherwise it will not be possible to clearly demonstrate that the follow-up information was provided within the additional 8 calendar days as required.	

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4.7.2.2 Content of reporting of follow-up information (#69)		It may be worth précising: downgrades from the investigators	
4.10. Informing the investigator (#91)		To be consistent with section 94 it should be made clear that investigators should preferably be kept blind, i.e. receive blinded line listings.	
4.11.2 SUSARs associated with active comparator or placebo (#98)		According to the previous version of 'CT-3' should the MAH be informed about the notification to the competent authority?	
5. Yearly reporting of suspected serious adverse reactions by the sponsor (#105)		Is our understanding correct that the DSUR replaces the annual safety report described in the previous version of CT-3?	

3. Other comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	By comparing the new version with the old it seems that some special points are missing: *Revision 2 of CT-3 from April 2006:* 4.2.1 The sponsor is responsible for arranging systems and written standard operating procedures to ensure that the necessary quality standards are observed in every step of the case documentation, data collection, validation, evaluation, archiving and reporting. 5.1.1.2 Other safety issues requiring expedited reporting Points a) and c) are missing. 5.1.6.3 Format of the SUSARs reports The current version of MedDRA or the previous one to it should be used for the coding of adverse reactions terms. Lower level terms should be used. 5.1.6.4 Form and format of the reports about other important safety issues also qualifying for expedited reporting This information is missing.	

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	5.1.6.5 How to inform the Ethics Committee? Point a) is missing. The annexes like Data Elements for SUSAR report are missing.	