19 March 2019

Submission of comments on 'Guideline on safety and efficacy follow-up and risk management of Advanced Therapy Medicinal Products Draft' (EMEA/149995/2008 rev.1)

Comments from:

Name of organisation or individual
TEDDY Network - European Network of Excellence for Paediatric Clinical Research

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)*
	This guideline does not include paediatric issues and specificities. Accordingly, in these guidelines the EMA and ICH paediatric provisions (e.g. ICH Topic E11, the 2007 EMEA Guideline on pharmacovigilance for medicines used by the paediatric population EMEA/CHMP/PhVWP/235910/2005- rev.1) are not mentioned and feedback from PDCO has not been requested. Given the increasing number of ATMPs tested and administered to children and the genetic nature of many paediatric diseases, these issues should be addressed. Therefore, the feedback from PDCO seems necessary and therefore should be envisaged. These considerations also apply to the Guidelines on GCP specific to ATMPs (ENTR/F/2/SF/dn D(2009) 35810) and maybe to the upcoming Guideline on quality, non-clinical and clinical aspects of investigational ATMPs.	

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)*
Lines 115-156		Comment: Reference should be made to ICH Topic E11 and the 2007 EMEA paediatric pharmacovigilance guidelines in 3. Legal basis and relevant guidelines section in order to correlate this guidance with the specific requirements needed for paediatric safety as set by paediatric guidelines. This is applicable both in the context of clinical trials and in the post-authorisation phase. Proposed change (if any): - ICH Topic E11 Clinical Investigation of Medicinal Products in the Paediatric Population (CPMP/ICH/2711/99) - ICH E11(R1) guideline on clinical investigation of medicinal products in the pediatric population (EMA/CPMP/ICH/2711/1999) - CHMP Guideline on conduct of pharmacovigilance for medicines used by the paediatric population (EMEA/CHMP/PhVWP/235910/2005- rev.1)	
Lines 273-288		Comment: Paediatric diseases should be mentioned. Proposed change (if any): to add the following point: "• Treatment/diagnosis/prevention of paediatric/neonatal diseases"	

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Lines 353-362		Comment: Age-appropriate educational material for children should be suggested. Proposed change (if any): "• Where applicable, educational material for children appropriate for their maturity and age. The use of visual help is encouraged (drawings, pictures, cartoons), but also other media and formats (such as DVD's, computer programmes) may be used."	
Lines 382-9		Comment: For the paediatric population, the need for sufficient long-term S&E data mentioned (lines 384-9) is even more relevant, considering the growth and development and organs maturation. Therefore, 8. Efficacy and safety follow-up section should address this topic and provide guidance on safety and follow up when ATMPs are used in paediatrics. Furthermore, ad hoc pharmacovigilance plans should be designed when ATMPs are used in paediatrics according to EMEA paediatric pharmacovigilance guideline (EMEA/CHMP/PhVWP/235910/2005- rev.1). This should be mentioned in 8.1 section. Proposed change (if any):	
Lines 443-5		Comment: The document states that "as part of the marketing authorisation application, applicants are to consider measures to ensure the follow-up of efficacy of ATMPs and of adverse reactions thereto". This is true especially in the paediatric	

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		setting. Proposed change (if any): -	
Lines 467-471		Comment: Another issue relates with the number of the population. Not only orphan, but also paediatric diseases should be mentioned while referring to 'small populations'. Proposed change (if any): "When a subset of exposed patients is used, scientific justification should be provided. A subset is normally not acceptable for medicinal products in orphan diseases due to the low number of exposed subjects. In many cases, ATMPs are developed in indications for which there are a limited number of patients. For these cases the principles described in the guideline on clinical trials in small populations should be carefully considered (CHMP/EWP/83561/2005). Subsets may be needed if a paediatric indication is concerned. Furthermore, it should be considered that up to 5 different subsets may be necessary for paediatric studies. Case by case opinion provided by the Paediatric Committee could help to approach these cases"	
Lines 482		Comment: The need for an adequate duration of the follow-up should be also referred to children in the 'Duration of follow-up' sub-section that recognises that a 15-year follow-up should envisaged for gene therapy. It should be considered that a child considerably changes and grows from a	

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		physiological, intellectual and pharmacological point of view. Proposed change (if any): [….] up to 15 years. Noticeably, in the paediatric setting, the follow up should consider the physiological and intellectual grow occurring in 18 years and the related modifications of the individual pharmacotoxicological parameters.	
Lines 603-621		Comment: Reference to the need for following specific paediatric pharmacovigilance procedures should be included in this section. Proposed change (if any): to add the following point: "•Specific paediatric pharmacovigilance procedures should be followed in compliance with the relevant requirements and provisions".	

Please add more rows if needed.