EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

16th October 2018

Submission of comments on "Guidelines on Good Clinical Practice for Advanced Therapy Medicinal Products"

Comments from:

Name of organisation or individual
International Society for Cell & Gene Therapy

On behalf of the International Society for Cell & Gene Therapy (ISCT), please find attached consolidated comments prepared by the ISCT Europe Legal & Regulatory Affairs (EU LRA) Committee and the ISCT Europe Regional Executive Committee. The members of these Committees represent the collective voice of academic hospitals, institutions, biopharmaceutical, and manufacturing companies of all sizes operating in Europe. Comprised of over 1300 members globally, ISCT currently has over 280 European members. For more information, please visit www.celltherapysociety.org.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	Despite the fact that some recommendations represent a challenge and will demand a great effort from clinical trial sponsors and all involved in their implementation, we certainly believe that they will effectively contribute to improve not only the quality of clinical research with ATMPs but also the safety of patients.	

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)*
Line 95-105		In this paragraph, the document specifies the need for additional safeguards in cases of paediatric population or foetuses (in utero treatment). A precise definition of those additional safeguards and their scope is needed in addition to the aspects that differentiate this guidance from the already present ICH E11 guidelines. For example, in the case of in-utero gene therapy, additional risk minimization measures for mother and future offspring should be considered.	
Line 118-122		Proposed change: It might be added: "When the control group patients have been exposed to invasive procedures for collection/extraction of their cells/tissues, and once the placebo-controlled trial has finished, they should be offered the ATMP treatment, provided there is evidence supporting the safety and efficacy of the treatment."	
Line 151-154		Proposed change: It might be added: "without prejudice that those specifications are also included in the IMPD and Investigator's Brochure."	
Line 162-164 (+ line 401-413)		The high variability of product specification in the case of ATMPs especially in the autologous settings could affect the outcome of the trial. We encourage the clarification of specific situations, for example, specifying a range of product specification (Cell dose, transduction efficiency etc…) at which the patient should be included in the final analysis. Another option could be categorizing patient population into subpopulations according to the product specifications	

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)*
		received. Products that did not fall into any of the specifications could be administered when the benefits of administration outweigh the risks in cases of autologous use or allogenic matched donors.	
Line 167-172		Proposed change: It might be added: "This is irrespective of the fact that information related to the risks associated to the process of taking biopsies/extracting cells as well as the potential impact on the quality and safety of the product should be included in the inform consent."	
Line 173-177		Due to the administration difficulties of ATMPs, ensuring a standardized administration process is a necessity and it can influence the final outcome of the trials as well as the safety of the study participants. Information about the training received by investigators should be duly described in the product dossier when specific or novel administration procedure is introduced, especially in the case of multi-center trials, where the activities could not be closely monitored.	
Line 193-197		Concerning the in utero gene therapy, a special consideration should be made to the mother in case of long-term follow up.	
Line 304-310		The impression received from the paragraph indicates that the presence of a sponsor or a representative during the administration of the product is not advised. However, the administration of ATMPs is a complicated process that may require the presence of supervision. We suggest that the language be more welcoming for such supervision.	
Line 312-333		We suggest including the possibility of tracing any cellular or tissue products that came in contact with the product during	

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)*
		the manufacturing process (production of viral vectors, generation of feeder cells, etc…).	
Line 362-372		The implementation of a registry system should be mandatory for ATMPs. Due to the small sized studies usually conducted using ATMPs and the targeting of orphan diseases; the collection of real world evidence is becoming more significant. The availability of such registries will also allow the secondary use of clinical data by the EMA and researchers, which will give the scientific community as well as regulator a better understanding of the long-term safety and efficacy of these products.	
Line 374-383		More elaboration is needed regarding the remote follow-up system, particularly with the long-term follow up demanded by the EMA for ATMPs, which could extend for very long periods of time up to 15 year.	