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TCP 01-2018 on GCP for ATMPs – Summary 08/02/2019

SUMMARY REPORT OF THE TARGETED STAKEHOLDER CONSULTATION ON THE DRAFT GUIDELINES ON GOOD CLINICAL PRACTICE FOR ADVANCED THERAPY MEDICINAL PRODUCTS

This document provides an overview of the contributions to the targeted Public Consultation. The content of this review should not be regarded as reflecting the position of the Commission.

1. INTRODUCTION

Article 4 of the Regulation (EC) No 1394/2007 on Advance Therapy Medicinal Products (ATMP) requires the Commission to draw up detailed guidelines on good clinical practice specific to advanced therapy medicinal products ("GCP for ATMPs"). The Commission is working together with the European Medicines Agency (EMA) including The GCP Inspectors Working Group (IWG) and The Committee for Advanced Therapies (CAT) and the the expert group of the competent authorities of the Member States on the drafting and finalising of these guidelines.

The aim of the exercise is to adapt GCPs specific to ATMPs. The Directorate General for Health and Food Safety gave an opportunity for concerned stakeholders to express their views on the GCP requirements that should apply to ATMPs, taken into account the recent advances and experience in the field.

The responses of the targeted consultation on this draft which lasted from 1 August until 30 October 2018 will be duly considered by the Commission in the finalisation of the Guidelines.

2. OVERVIEW OF THE CONSULTATION

The number of contributions to the consultation received was 35. The responders came from small and medium-sized enterprises (SMEs) or their representatives (ca one third of the total), academia, hospitals (together one third of the total) and patient organisations. Responses were also received from EU competent authorities and international bodies. It should be noted that some entities are included in two or more separate contributions. The responses which were non-confidential can be found on the DG SANTE website.

The guideline under consultation details only the GCP requirements that need to be adapted or added to ATMPs and the standard principles of ICH E6 GCP applies. The key message was that all the responders were welcoming the approach of having a GCP guideline for ATMP to be read in conjunction with ICH guidelines. Many responders also recognised the high quality of the overall document and its usefulness for the ATMP developers.

Some responders were requesting a reference and alignment to the draft produced in 2009 with reference ENTR/F/2/SF/dn D(2009)35810. In this regard, it is noted that this document has not been adopted by the European commission as it is clearly explained therein. The document is also produced at the time when the experience with ATMPs was very limited. The document under consultation is based on the experience accumulated with ATMPs until now.

3. SUMMARY OF KEY FINDINGS

Majority of contributions recognised the need for a flexible and pragmatic approach with respect to GCP standards relative to the development of these products. However, some responders considered that further adaptations to the specific characteristics of ATMPs in clinical trials were still required, in particular in connection with the following items:

- One of the topics addressed in the GCP for ATMP guidelines is **the long term follow up** of patients (the study subjects) which may be necessary for certain ATMPs. The follow up strategy may need to go far beyond the end of the trial. In this context, some responders addressed that it is necessary to clarify the relationship of monitoring schemes for patients treated with the investigational medicinal product and those monitoring schemes that are imposed after the marketing authorisation is granted.
  While the majority of the responders supported the approach proposed some responders considered that additional guidance should be given on the legal status of the schemes intended to fulfil the long-term follow up obligation. Additionally, the 'general' 15 years follow up requirement for gene-therapy products was seen by some as too strict.

- The issues related to **paediatric populations** and fostering earlier paediatric inclusion in trials was raised by some submitters. Some asked for further guidance of these trials especially related to the early reporting of the adverse events.

- Some responders considered that the tone of the guidance appears to discourage the **use of placebos** and were afraid of that it might result in clinical trials that are difficult to interpret. The current document includes a specific example of intra-subject control which was also considered difficult to interpret by some responders.

- The quality issues for ATMP are in connection with some specific sections in the current document and many of the responders welcomed this approach. Some submitters, though, shared the views that these topics are described in too much detail. The suggestion was that the quality related issues should be removed or only referred to in general terms. There were also suggestions to align better the use of the guidance to some **other** 'clinical trials' guidelines of EMA and commission like the EMA Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products (EMEA/CHMP/SWP/28367/07 Rev. 1 dated July 20 2017).

- Clarification in relation to the content of protocol and the **investigational medicinal product dossier** were requested by some submitters. A few responders requested also additional guidance on the documentation to be submitted in the context of a clinical trial application. In addition, some comments were expressed which are beyond the

scope of the GCP, such as in relation to authorisation requirements for gene therapy medicinal products.

4. NEXT STEPS

The above summary of the responses is not exhaustive but tries to cover the main issues raised. The nature of the responses reflects the complexity of ATMP development. The Commission services will carefully analyse all the responses submitted in consultation with experts in the European Medicines Agency and the Member States when finalising the document.