Comments to the Good Clinical Practice for Advanced Therapy Medicinal Products from **GCP-Inspectors Working Group**

Line 140: Suggest adding a clarification for the requirements of cells/tissues of animal origin, as equivalent principles should apply for those ATMP compared to ATMPs containing cells or tissues of human origin.

Line 394-398: Suggest adding the text highlighted in blue:
Depending on the characteristics of the ATMP, patient alert cards may need to be provided to subjects participating in ATMP trials, with the objective to inform treating physicians about the product used with a view to facilitate medical care of the patients in case of an emergency and to facilitate reporting of adverse events. This should include information on short and long term safety issues particular to ATMPs such as infections, immunogenicity/immunosuppression as well as on viral shedding and any precautions required for ATMPs involving gene therapy.

Line 416-417: Suggest deleting the text highlighted in blue:
…adverse events) should be adapted to reflect a differentiated causality assessment for each of components of the ATMP (e.g. the cell-based part and medical device part in the case of…

Suggest adding a section 11 on Clinical Trial Master File for ATMPs
It would be preferred to have a section on this included in the guideline.
In addition to the standard requirements that are needed for the reconstruction of the trial and verification of trial conduct, the Clinical Trial Master File (CTMS) for ATMPs should contain any documents related to patients' safety, documentation on the confirmation of the traceability systems (sponsor), the traceability responsibility matrix and the location of the traceability records. In cases where the administration procedure may have an impact on the safety/efficacy outcome, there should be appropriate documentation in respect of the procedure that has been followed. It should be noted that the legal requirement for keeping traceability documents is 30 years.
In addition to the documents laid out in ICH E6E2, the following documents need to be filed in the CTMS:

Sponsor:

- Identification of the manufacturing site and identification of the investigator/institution that used the ATMP together with Batch and/or code number the trial reference code and the trial subject code
- Documentation on the confirmation of the traceability systems
- Traceability responsibility matrix including the details of the process, responsibilities and documentation required to document the link from the donor to the subject receiving the product and vice versa
- Description of the location of the traceability records
    - Reference to the GMO approval, where the ATMPs contains a genetically modified organism (GMO)- Relevant to allow verification that the clinical trial is conducted in accordance with all applicable regulatory requirements.
- The documentation used to determine the follow-up strategy
- The follow up strategy expected for the ATIMP (including follow-up after the end of the trial) with the rationale and objectives based on appropriate risk assessment.

Investigator and institution responsible for human application:

- Certificate of analysis of each ATMP allocated to a subject at the investigator.-- Applicable to ATMPs manufcatured by the investigator site. For all others, it is sufficcinet to file the Certificate of Analysis (CoA) in the CTMF at the sponsor.
- Traceability records linking the manufactured ATIMP delivered to that clinical trial site and from the clinical trial site to the patient code, patient identification and medical file.
- Drug accountability records enabling the allocation of each individual ATMP (Including product name/code, pharmaceutical form, route of administration, quantity of dosage units and strength and batch and/or code number) to the individual patient.
- Documentation of adverse events including a differentiated causality assessment for each component of the ATMP, the application process and, where applicable, any required concomitant medication.
- Follow-up procedures, contact information and data collected, to document the conduct of the clinical follow-up, safety follow-up and efficacy follow-up required.