Targeted stakeholder consultation on the draft Guidelines on Good Clinical Practice for Advanced Therapy Medicinal Products (TSC 01/2018 on GCP for ATMPs)

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This response is submitted by Gary L.A. Jones (admin@europeaneyebanks.org) on behalf of the *European Eye Bank Association* (EU Transparency Register Identification Number: 840527028525-56), in conjunction with *Fondazione Banca degli Occhi del Veneto ONLUS* (EU Tissue Establishment Code IT001313).

Clear and unambiguous guidelines are necessary tools for the comprehension of Good Clinical Practices (GCPs), as well as to facilitate their application in the context of clinical trials. Very important aspects have been well addressed in the proposed draft document including:

- the GMP concordance;
- the need for specific instructions and training for clinicians;
- the need for long-term follow-ups;
- the traceability;
- compliance with the EU Directives on tissues and cells (with respect to procurement and retrieval).

Nevertheless, even if considered as pharmaceutical drugs, ATMPs are different from standards medicinal products. For this reason, we are raising a few comments that might help clarify doubts that are present in the Consultation document.

1. **General principles (section 1.2):** it would be important to clearly define which products are referred to as ATMPs in accordance with Article 2 of Regulation No.1394/2007;
2. **Clinical Trial Design (section 2):** it would be useful to identify the personnel involved and the roles/responsibilities assigned to them (for example the head of pharmacovigilance, etc.);
3. **Clinical Trial Design (section 2(i)):** in the examples shown, the categories of people "most at risk" (elderly, pregnant women, people with disabilities) are not taken into consideration. It might be useful to explain what to do in these cases and whether to include them in the study population only after the collection of data from the "average" adult population;

EUROPEAN EYE BANK ASSOCIATION

European Eye Bank Association
Via Paccagnella n. 11 - Padiglione Rama
30174 Zelarino – Venice (Italy)
Tel: +39 041 9656422
Fax:+39 041 9656421
admin@europeaneyebanks.org
www.europeaneyebanks.org
Fiscal code: 90111850278

4. **Clinical Trial Design (section 2(vii)):** whenever possible a statistical analysis should be implemented in order to understand the minimum number of subjects/patients needed (considering the dropout percentage) or if a pilot study is necessary before initiating the trial (when dealing with ATMPs it is not always possible to have high numbers of subjects);
5. An important phase of any Clinical Trial Design is the identification of the inclusion and exclusion criteria and the identification of the duration of the recruitment period. This should be pointed out;
6. **Application dossier (section 3(ix)):** little information is given about the Medical Devices (MD). Should the class of the MD be specified? Should any information be given about the presence/absence of the CE mark, Eudramed code etc.? Are MD-ATMP compatibility studies necessary/advisable to minimize risk? These points should be clarified;
7. **lines 288-90:** in case of temperature deviations, no guidelines are given about what to do. Is some tolerability margin acceptable? Does the ATMP need to be discarded? Should a case-by-case be evaluated?;
8. **Informed consent (section 8.1):** the informed consent should always be accompanied by an informative letter for the patient's personal physician. This should be pointed out. Furthermore, indications about the insurance coverage should always be indicated unambiguously;
9. Actions to take in case of adverse events should always be identified and clearly indicated in the protocol;
10. There is no section on data management, document conservation (how and for how long?) and on people/institutions that have access to the data;
11. Very often sera/products of animal origin are used in the preparation of ATMPs. Should specific actions be implemented? Should safety tests be performed?;
12. It would be useful to explain how the label and the data sheet of the study product should be formulated.

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