Targeted Stakeholder consultation on the draft Guidelines on Good Practice for Advanced Therapy Medicinal products

Etablissement Français du Sang (EFS)

The French Blood Establishment is the only operator that is responsible for the collection and testing of human blood or blood components, processing and distribution of blood products when intended for transfusion in France. Thus we play an active role in health monitoring and in many fields linked to transfusion and transplants, as well as lead the production of medical biology laboratory reagents in France. **We play also an important role in the field of clinical research as a manufacturer or around 10 investigational ATMPs in our 5 ATMP manufacturing sites in France**. Finally we ensure blood, tissues and cells procurement and the supply of these products as starting materials for ATMP to many pharmaceutical companies. We would therefore like to thank you very much for the opportunity you gave us to comment the draft Guidelines on Good Practice for Advanced Therapy Medicinal products.

We firstly **welcome the global approach and the wording of this guideline that recognizes the specific characteristic of Advanced Therapy Medicinal Products**. We are for instance very pleased that specificities such as intrinsic variability of the starting material is highlighted (162) and welcome the possibility to use photographs or copies of the label in case a sample of the investigational product can't be kept (347) as well as your approach regarding the administration of out of specification products (401). The global wording of the text will undeniably allow the Advanced Therapy Medicinal Products sector to move forward.

However **we are very concerned about the lack of definitions/mentions of the body responsible for the blood tissues and cells procurement**. Indeed, the current wording seems to only encompass investigators, sponsors and medical hospital but nothing could be possible without the body involved in the procurement of substances of human origins (blood, tissues and cells) and the production of research and clinical batches which might be performed by other actors such as the French Blood establishment**. The role played by the responsible for procurement of substances of human origins and production and quality control of the manufacturing processes should therefore be defined in the text to ensure that no actors are left out and that the whole process is performed under the best standard of safety**. This is particularly important regarding the special nature of substances of human origins involved and the Good Manufacturing Practices requirements for batch certification. For example both manufacturers, investigators and sponsor's representative are committed by specific constraints under the retrieval procedure and need to be defined accordingly.

Besides this major concern, we would like to raise your attention on the following additional comments:

- *Follow-up strategy of subjects* (L193-198): we broadly support the use of a risk assessment strategy. We entirely agree that in some cases, this strategy may need to go beyond the end of the trial, especially for some gene therapy medicinal products. However, we think that the wording should be narrowed in order to clarify that for some others ATMP such as autologous adult stem cells such long term follow-up is not expected.

- *Reconstitution* (L240-254): we welcome the training requirement for those involved in the reconstitution process as mentioned in line 253. We would suggest to extend this requirement, where appropriate, to the thawing process unless the thawing process is clearly included in the definition of reconstitution.

- Labelling issues are not addressed by the proposal, yet it is extremely difficult to match GMP requirements for products stocked in liquid nitrogen (-196°C). We would suggest to implement a dual labeling system where the essential information (patient identity, date, investigators, etc.) would be written on the product and the additional one would available on an external certificate accompanying the product.

- It should be specified that all the services involved (pharmacy, clinical services, etc.) must obtain any appropriate authorization required by the legislation before manipulating ATMP.

- It should be specified that ATMP with a short shelf life can be delivered directly to the patient by a qualified person and, in some cases bypass the hospital pharmacy step.