EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Directorate B - Health systems, medical products and innovation
B4 – Medical products: quality, safety and innovation

Meeting between the Committee (Executive Board) of the European Eye Bank Association and DG SANTE B4

26 January 2018

Summary Minutes

Participants:

European Eye Bank Association (EEBA): The President, Executive Officer and Committee Members

European Commission: DG SANTE (Unit B4)

Introduction and Background

In the context of the ongoing Evaluation of the EU legislation on blood, tissues and cells, DG Santé met with EEBA. The meeting was held as part of the EEBA Committee Meeting, immediately prior to the official opening of their annual conference in Coimbra, Portugal.

The consultation submission by EEBA had been reviewed by DG Santé before the meeting, along with those from other stakeholders with a particular interest in ocular tissue donation, processing and transplantation. The latter included submissions from the European Association of Tissue Banks, the Swedish Eye Banking Association, the University Hospital of Uppsala (Eye Bank), the Common Representation for Substances of Human Origin (CoReSoHO), the University of Tampere (Eye Bank), the Medical Faculty of the Technical University of Dresden (Eye Bank) and the Munich Eye Bank.

Some of the messages from EEBA had been reflected in many of the other submissions from other professional groups. The following points were summarised at the beginning of this meeting and were not then the focus of the subsequent discussions as the background was already well documented and understood:

i. A view that it has been impossible for the legislation to keep pace with this rapidly developing field and a consequent call for less detail in legislation and more cross-referencing to appropriate up-to-date technical guidance;

ii. A lack of regulation under the tissues and cells legislation of the processing of tissues and cells used in autologous 'same surgical procedures' – considered to be a gap;

iii. A view that many existing provisions are not evidence based, including those relating to air quality requirements for processing facilities and some donor selection criteria;

iv. A proposal to incorporate risk-based approaches to the regulation of the sector, including a perceived need for cost benefit analysis for all legal requirements;

v. A view that borderlines with ATMPs are not adequately clear;

vi. A consideration that the absence of requirements for inspectors to have an adequate technical knowledge of the sector is a gap.

The group proceeded to review and discuss a series of points that had been raised uniquely, or particularly strongly, in the submissions of the eye banking community as follows:

1. EEBA pointed to the lack of quality criteria in the legislation (the focus being on safety), a point particularly important for this sector, noting that in ocular transplantation the quality criteria for the transplanted tissue are well defined in published literature and among professionals. The absence of any reference to them in the legislation is considered a significant gap that results in wide variation in the quality of ocular tissue transplanted in the EU. The EEBA Committee confirmed that they would want to see EU legislation that includes cross references to quality criteria developed by other organisations, such as EDQM, with appropriate and timely updating as the technology develops.

2. The lack of a requirement to demonstrate clinical efficacy and safety for new/modified preparation processes was considered of particular importance by EEBA for this sector. The EEBA Committee confirmed that they consider that, in the case of ocular tissue, this should be extended to long-term patient outcome monitoring through participation in international registries. They consider that demonstration of efficacy should be a legal requirement for authorisation by competent authorities but raised a caution that any such oversight by authorities should take into account the surgical learning curve observed with the introduction of any new surgical procedure; this should not hamper the authorisation of innovative therapies in ocular tissue transplantation. It was also said that the authorisation procedures should not slow down innovation and that the use of a Preparation Process Dossier (from the Commission's Operational Manual for Tissue and Cells Competent Authorities) sometimes causes delays in the delivery of new therapies.

In this context, EEBA is currently participating in two EU-funded projects addressing the topic of patient outcomes, EuroGTP II for the development of practical tools to support the definition of technical requirements for the assessment and verification of the quality, safety and efficacy of therapies with human tissues and cells and ECCTR for the implementation of a European Registry of outcome data in corneal transplantation.

3. The Association is strongly committed to the principle of voluntary unpaid donation (VUD), considering that payments to living donors or the families of deceased donors could result in the

withholding of critical medical or behavioural risk information with a consequent risk to the safety of recipients.

4. EEBA considers that, to avoid that human tissue donations are a source of financial gain and commercial competition, the legislation should ensure that costing models applied to calculate service charges to users are transparent, reasonable and justified.

5. The EEBA considers that the vigilance obligations that are defined in the legislation should be extended beyond the tissue establishments to apply also to the organisations responsible for human application in a clearer and legally binding manner. Similarly, they consider that procurement organisations should be the subject of clear legal obligations to monitor and report adverse incidents. The EEBA Committee confirmed that they consider the limited scope of the legislation to be inadequate and called for its extension to the early and later parts of the donation-transplantation chain, with reasonable expectations placed on procurement and transplant centres for their participation in monitoring and reporting.

6. Linked with the previous point, the EEBA considers that on an EU level, clinical centres should be authorised by the competent authority to carry out tissue transplantation, as currently happens in Spain, Portugal and Italy. They consider the absence of such a requirement in the current legislation to be a gap and that having such an authorisation system would improve the effectiveness of data reporting, vigilance and long term patient outcome monitoring.

7. The Association considers that the requirement to test donor blood samples taken up to 24 hours after death to be without scientific justification and they point to significant losses of donations and reduced patient access resulting from this provision. They agreed to provide published evidence to demonstrate the appropriateness of using blood samples taken up to 48 hours after death. [Publications were submitted subsequently and have been added to the evidence folders for the DG Santé Evaluation].

8. EEBA Committee Members highlighted the negative impact of Article 17 of Directive 2004/23/EC that defines the minimum qualifications of the 'Responsible Person' of a tissue establishment. They explained that a number of highly experienced technical experts had been prevented from being responsible for compliance of an eye bank with the legislation due to this provision. The topic has resulted in a court case in Germany and it is considered that the provision is not applied in a harmonised way across Member States. The Association considers that the legislation should allow for the acceptance of equivalent experience in those cases where a highly experienced technician does not have a diploma or degree.

9. The Association considers that the references to the achievement of sufficiency for patients in the current legislation are not adequately supported by provisions that oblige Member States to promote donation and to ensure equal access to treatment with donated tissues for patients. This comment was made in the context of a significant level of importation of ocular tissue from the US.

10. In relation to point v. above (regarding the borderline with ATMPs), many EEBA members have the particular experience of being in a position to supply limbal stem cell therapy to patients but, in many Member States, not being allowed to do this now that a commercial limbal stem cell

product has been centrally authorised. They point to an overall reduction in the number of patients receiving treatments due to the high cost of the commercial product whilst their member tissue banks could have provided a safe and effective treatment at an affordable cost as was, in some cases, being done in the past. They noted that the ATMP legislation is being implemented differently across the Member States, where the conditional marketing authorization granted to Holoclar by the European Medicines Agency in 2015 has stopped the provision of limbal stem cell grafts by tissue banks in some countries whilst in others the supply continues. They call for harmonization on this point. As the number of patients is limited and many of the organizations wanting to provide limbal stem cell grafts are from academia or are non-profit, they consider that Article 28 of Regulation 1394/2007 should be implemented for this treatment to improve patient access.

11. It was noted that EEBA data demonstrates that around 40% of donated corneas cannot be used for transplantation because they do not meet the standard quality and safety criteria – this is a normal finding in cornea banking. The community considers that corneas that cannot be transplanted represent a highly valuable resource for research and teaching and they consider that EU legislation should promote their use for ethically responsible non-therapeutic uses such as research, education and surgical training. In that context, the EEBA Committee confirmed their view that the exclusion of this aspect of donation and tissue use from the legislation is an important gap.

The EEBA Committee expressed its appreciation for the open and accessible process of evaluation being conducted by DG Santé and for the opportunity to have this focused discussion. DG Santé also thanked EEBA for this meeting and their constructive engagement in the process.