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 International Society for Cell Therapy and DG SANTE B4

14 June 2018

Summary Minutes

Participants:

ISCT: Andrea Hauser, Ineke Slaper-Cortenbach, Mark Lowdell, Martin Hildebrandt.

DG SANTE (Unit B4 Medical products: quality, safety, innovation): S. Van der Spiegel, D. Fehily, R. McGeehan

1. The meeting participants were welcomed and the organisations represented were introduced. The meeting had been organised in the context of the formal evaluation of the blood, tissues and cells (BTC) legislation that is currently being undertaken by the European Commission[1]. It was explained that the attendees represented the International Society for Cell and Gene Therapy (ISCT), the AGORA Consortium, the ATMP Group of the European Compliance Academy (ECA) and ICCBBA.

   ISCT is a global not for profit organization association promoting the translation of scientific research to deliver innovative cellular therapies to patients. ISCT helps academic, government and biotech/pharma sectors transform research into practice and product.

   ICCBBA is a non-profit organisation that manages the ISBT 128 international information standard for use with medical products of human origin, providing common data structures for information technology, data processing, exchange and transfer, and labelling for these substances.

   The **ECA Foundation** was founded in 1999 as an independent not-for-profit organisation to provide support to the pharmaceutical Industry and regulators to promote the move towards a harmonised set of GMP and regulatory guidelines by providing information and interpretation of new or updated guidances. In 2017, ECA established an ATMP Interest Group to support a Europe-wide network for ATMP developers.

   The **Agora project** ran from 01 September 2013 to 31 October 2015 and was funded by the European Commission (Grant No. 602366). It aimed to build an academic & industrial partnership to facilitate safe and effective delivery of new advanced therapy medicines within the framework of the relevant EU regulations. To avoid the loss of the collected AGORA knowledge ECA and AGORA decided to

[1] https://ec.europa.eu/health/blood_tissues_organs/policy/evaluation_en

transfer the content of the AGORA website at the end of the project (especially the AGORA toolbox) to the website of the new ECA ATMP Interest group.

2. Following the introduction of the participant organisations, DG SANTE explained to the stakeholder representatives that the Commission is not currently working on a revision to any of the blood or tissue and cell Directives. The current initiative is limited to evaluating the existing legislation, with a view to establishing whether it achieved its original objectives and whether it is still fit for purpose. DG SANTE also explained that the process does not cover the scope of the EU legislation on Advanced Therapy Medicinal Products, but it does cover the collection of starting materials for ATMPs and borderlines with ATMPs. DG SANTE updated the stakeholders on progress with the evaluation. In general, the process is on schedule and the final report should be published by the end of 2018 or early in 2019.
3. The participants noted that some of the donor selection and testing requirements of the BTC legislation are applied in different ways in different Member States and are not adapted to the kinds of donors that now donate for cell therapies. For example, a specific concession that allows bone marrow donors to be tested up to 30 days before donation cannot be applied to lymphocyte donors, although they are likely to be the same type of donor. They suggested that to resolve the challenges posed by different selection and testing requirements it would be preferable to have an EU Regulation rather than Directives that are transposed differently in Member States.
4. In relation to starting materials for ATMPS, it was noted that there is a difference between 'standard' and 'non-standard' tissues and cells. The current donor selection and testing requirements should be adapted for 'non-standard' materials such as tumour cells/tissue.
5. The stakeholders noted the ethical challenges that are posed by the commercialisation of ATMPs. They consider that, while the tissue and cell legislation was clearly based on principles of altruistic donation, the commercialisation of the donation, once it becomes classified as a medicinal product, needs to be addressed and transparent information and rules should be in place. They believe that this issue will become more challenging as the technology moves towards the decellularisation of whole organs, with subsequent recellularisation with recipient cells. The current ATMP classification approach would lead to such an organ becoming a medicinal product; a concept that will be difficult to align with the current rules and accepted practices in organ donation and transplantation.[2] This concern had also been raised in ISCT's submission to the Open Public Consultation on the BTC legislation, where they had expressed the view that rules are needed regarding consent and Voluntary Unpaid Donation (VUD) where donated biological material is used for commercialisation of a pharmaceutical product.
6. The stakeholders noted that the organisations developing new cell therapies are already authorised and working as tissue establishments, as many of these processes and therapies are a natural progression from current bone marrow and peripheral blood stem cell transplantation. The degree to which authorised tissue establishments are allowed to provide ATMPs under the 'hospital exemption' varies considerably between Member States. In some Member States, these centres are already required to work to GMP so the additional effort is not significant. In some Member States there are national rules that make it more difficult, e.g. in the UK, procurement sites must be

[2] One of the participants has given a TED talk that introduces this topic, see https://www.youtube.com/watch?v=qP7k35KNdY4

individually authorised. This often means giving a license to an operating theatre. Clinical trials in these countries are more complicated as they require contracting, educating and auditing procurement sites. However, other countries have a simplified approach towards this, like The Netherlands where procurement sites for HSC are subject to JACIE accreditation which is recognized by the authorities. The stakeholders consider that legislation should be adapted to support ATMP development and cross-border exchange that is safe for the donor and the recipient.

7. Overall, stakeholders believe that ATMPs are subject to the same risks as tissue/cell transplants, in particular the transmission of infectious diseases. The stakeholders consider that more stringent rules should apply where risks are higher. An important factor is the number of recipients from a single donor/donation. If there will be multiple recipients then the rules should be more stringent.
8. DG SANTE described the new GAPP Joint Action that will work on the authorisation of novel processes and applications of tissues and cells, including guidance on the conduct of clinical studies to demonstrate effectiveness. The stakeholders noted that a significant factor for new therapies is the 'learning curve' associated with changes in surgical procedures. This needs to be taken into account in the evaluation of clinical outcomes.
9. On the topic of traceability of tissues and cells when they are used to manufacture ATMPS, the stakeholders consider that the SEC should be required also on the ATMP product to facilitate tracking over the entire chain all down to the tissue establishment and donor. Also, the use a label indicating whether a collected tissue/cell is "for clinical administration" or "for further processing" can be helpful to ensure appropriate requirements are used on the right graft.
10. As described in the ISCT submission to the Open Public Consultation, the group considers there should be a mechanism for requesting classification of new therapies that is not limited to seeking advice from the Committee for Advanced Therapies (CAT). In their view, CAT recommendations generally result in a classification as an ATMP, with the consequence of greatly increasing cost and reducing patient access. In cases where the processing of cells does not involve substantial manipulation, it is often identical to that already performed for transplanted cells (only the therapeutic target is different). ISCT do not consider it logical that different safety and quality standards apply and consider the tissue and cell legislation to be adequate in those circumstances.
11. The Stakeholders discussed whether substances subject to the 'same surgical procedure' exemption should be brought into the scope of the Tissues and Cells legislation. Their original exemption dates from a time when many of the clinical procedures that currently exist were not available. Authorisation of such procedures would need to be adapted and minimal compared to the full authorisation of a tissue establishment.
12. DG SANTE thanked the stakeholders for their contributions to the meeting and to the BTC evaluation in general.