



EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

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

Brussels,
SANTÉ

Meeting between the European Society for Human Reproduction and Embryology (ESHRE) and DG SANTE B4

3 May 2018

Summary Minutes

Participants:

ESHRE EU Affairs Committee members

DG SANTE (Unit B4) representatives of the Substances of Human Origin team

Background

ESHRE had invited DG Santé to this meeting to discuss the following topics:

- ESHRE's involvement in EU related activities
- The on-going Commission evaluation of the blood, tissue and cell (BTC) legislation
- Future actions of the ESHRE committee
- ESHRE Survey on ART in Europe

DG Santé aimed to use the meeting to validate their findings in the BTC evaluation to date, of relevance to the ART sector and, in particular, to ask if any gaps were noted by the Committee.

Discussion points:

1. ESHRE is currently actively involved in many European collaborative activities. They are currently participating in EU Joint Actions (JA) and EU funded projects as well as Council of Europe (CoE) activities. The meeting began with a joint review of those activities.

European Union activities:

ESHRE is currently participating in the following:

- VISTART (EU Joint Action) - This JA aims to strengthen the oversight of authorities with regard to inspections, vigilance, traceability and authorisation of novel processes.

- ARTHIQS (EU Joint Action) – This JA aims to strengthen the oversight of authorities with a focus on the specific fields of ART and cord blood banking.
- EURO GTPII (EU funded project) – led by, and aimed at, professionals in the fields of tissues, cells and ART, this project is developing practical tools for assessing the risks associated with changes to any step from donor selection to supply and clinical application. ESHRE has developed a template to assess ART technologies, which is still in a testing phase to see whether members would grade and assess novelties in the same way. The project will propose the kinds of studies that should be conducted to mitigate any residual risks following process validation in tissue establishments.
- GAPP (EU Joint Action) - this new JA targets competent authorities with an aim of developing guidance and best practice for the authorisation of preparation processes for tissues and cells (for transplant and for ART) with exchange of know-how and information on the authorisations granted.
- Transpose (EU funded project) – this project aims to agree common EU approaches to the selection and protection of donors of blood, tissues and cells, taking into account the need to select donors that can provide safe substances for recipients but that also will not be put at risk themselves through donation.
- Registries – ESHRE has participated in a meeting with other sectors running donor or recipient registries such as for bone marrow (EBMT) and corneas (ECCTR). ESHRE has a well-established registry, in which data is stored that could, for example, help answer questions on the effectiveness of novel preparation processes prior to authorisation. ESHRE aims to implement significant enhancements to its registry in the future, funding permitting.

Council of Europe activities:

- CD-P-TO (CoE) – This committee oversees the work of the Council of Europe in the areas of organs, tissues and cells and approves for publication the widely used guides for safety and quality in these fields. ESHRE informed the Commission that they now have a representative in this committee where they are working on issues such as activity data reporting and donor protection.
- EDQM Tissue and Cell Guide (CoE) – ESHRE participates in an expert group under CD-P-TO that is revising this guide. ESHRE leads on the ART related chapters and contributes to the generic chapters.
- DH-BIO (CoE) – An ESHRE representative has participated in the committee on Bio-ethics that recently developed a paper on Prohibition of Financial Gain by donors of substances of human origin.

ESHRE noted that this level of interaction with EU and Council of European groups is new to the society and involves considerable investment in time and effort. DG Santé expressed strong support for the engagement of ESHRE in these European initiatives, stressing the importance of ensuring that the view and perspective of the professionals is taken into account in the development of European regulations and guidance. The participants agreed that only in this way can it be guaranteed that the rules and guidance are feasible to implement and optimal to ensure safety and good patient outcomes.

2. DG SANTE explained the process of the BTC evaluation and summarised progress to date. The two main work streams comprise an independent study by an external contractor and a series of stakeholder consultation activities organised directly by the Commission services. Both streams aim to assess the five Better Regulation criteria – relevance, effectiveness, efficacy, coherence and EU added value – to build a sound evidence base to answer evaluation questions under each of these criteria. The work of the external contractor focuses on gathering evidence from published reports, articles, meeting minutes etc. and from interviews and focus groups with key experts. In parallel, DG Santé has organised an Open Public Consultation and a series of bilateral and multilateral meetings with stakeholder organisations, including a major stakeholder event in September 2017 where ESHRE had been invited to make a statement and had participated actively in the discussions. The combination of all these activities will ultimately feed into a final Commission Evaluation Report due for publication towards the end of 2018. DG SANTE stressed that no decision on a need for amending the legislation could be considered until after the completion of the evaluation.
3. The Commission presented to the ESHRE representatives the main ART-related outcomes from its Open Public Consultation (OPC) and invited the Board members to elaborate or clarify any particular messages or fill any gaps that they considered important.

Submissions from the ART sector had been received from ESHRE and from many other ART associations and societies as well as from individual ART clinics and from national competent authorities. Some emerging messages were presented and discussed. The following were key discussion points:

- There is a call for clearly requiring the reporting of genetic conditions in children born after ART with non-partner donation as serious adverse reactions (SAR).
- Given the developments in genetic testing since the legislation was adopted, rules for non-partner donor testing are lacking. It was noted that interpretation of genetic test results and accurate communication to donors and patients is challenging.
- ESHRE does not support the view of some national associations that argue that inclusion of gametes and embryos in the scope of the tissues and cells legislation is inappropriate. They consider that the inclusion of this sector has had a positive effect but noted that the specificities of the field need to be appropriately reflected in the legislation.
- ESHRE Board members agree with an emerging message that the air quality of IVF laboratories (in terms of particle counts) is not a key factor in achieving good outcomes in ART. They noted that contamination of embryos originating from the air in the laboratory has not been reported, to their knowledge. Reported contaminations in IVF clinics originated from people, usually the donor. There is, however, some evidence that Volatile Organic Compounds (VOC) in polluted air may affect the embryo's development and should be taken into account in defining laboratory requirements. Some expressed the view that having a defined minimum requirement of air quality is necessary. ESHRE agreed to work on this topic and develop updated recommendations.
- ESHRE agrees with the many stakeholders that argue that the legislation has not been easy enough to adapt when new risks and new technologies emerge. They pointed to a

- high degree of innovation, with associated risks, and cited the recently published development of blastocyst-like structures generated solely from stem cells¹ as an example. ESHRE would welcome a legal framework that in an appropriate way takes account of clinical outcomes as part of the authorisation of novel laboratory techniques.
- They agreed that the legislation led to higher costs but it also brought benefits that justified the costs, although in the ART field both the donor testing requirements (particularly testing frequency requirements for partner donors) and air quality requirements have been raised as exceptions to this.
 - The legislation is considered coherent within its own provisions, however not with some other relevant EU legislation such as medical devices and medicinal products but also with the EU charter on human rights in regards to the unclear definition of Unpaid Voluntary Donation (VUD).
 - Finally, the legislation has helped increase safety and quality, harmonisation and confidence, although the EU added value is limited by more stringent national requirements, which hinder to reach one standard across the EU.
4. In the light of remaining evidence gaps, particularly relating to quantitative information regarding costs, the external contractor conducting a study for ESHRE had sent a questionnaire to the participants of this meeting, asking for specific quantitative data, where available, to fill those gaps. The Commission encouraged ESHRE to provide whatever data they could and the representatives agreed to respond to the request in the time period requested.
 5. ESHRE representatives presented the preliminary results from a Survey on ART in Europe, specifying that the data referred to the 31st December 2017. The survey included 41 participating countries around Europe, some of which had not previously participated in the EIM registry (ESHRE registry of ART activities). The main topics addressed national rules for access to ART treatment. Access is limited by public funding and reimbursement and rules allowing or prohibiting non-partner donations. The questionnaire also collected information on the existence of national registries. So far, the main conclusions are that a wide disparity between the countries exists regarding funding/reimbursement policies as well as legal availability and access to ART. Furthermore, it seems that access to non-partner donation is influenced largely by cultural factors. ESHRE has concluded that there is a need for better and more robust registers.
 6. Future actions that ESHRE perceives important in the ART field in Europe would be to have a more comprehensive European IVF registry including donor information and follow-up of donors and of children born. The registry should be capable of tracking cross-border activity accurately and should provide unique identification of each donor and recipient. It would be fed by professionals working in the field and primarily used by the same group, however could attract attention of other international actors and authorities due to its big data

¹ Rivron, N., Frias-Aldeguer, J., Vrij, E. et al. (2018). Blastocyst-like structures generated solely from stem cells. *Nature* 557, 106-111 (2018) doi:10.1038/s41586-018-0051-0

characteristics. ESHRE would wish to see the provision of data to this registry as a mandatory requirement in EU legislation. The Commission informed ESHRE representatives of the digital healthcare financial programme that could be of interest due to its Real World Data subcategory.

7. Closing remarks:

- In terms of *preparation process authorisation*
 - The work on GAPP and on registries is independent from the evaluation and will continue to move forward. ESHRE's collaboration and participation is highly appreciated.
- In terms of the *BTC Evaluation*
 - ESHRE will send data on identified gaps to the external contractor, as requested.
 - As the evaluation will be finalized at the end of 2018, the next meeting between the Commission and ESHRE should be planned for October/November 2018.
- The participants were thanked for the open and informative meeting.