ESHRE position paper on the revision of the European Union legislation on Blood Tissues and Cells

June 2021

INTRODUCTION

The European Society of Human Reproduction and Embryology (ESHRE) welcomes the initiative of the European Commission to conduct a revision of the current Blood, Tissues and Cells (BTC) legislation of the European Union (EU). We take this opportunity to express our views on some identified shortcomings in the current legislation and to put forward recommendations for consideration in the revision process.

ESHRE is a European non-profit organisation with international membership, whose main mission is to promote the study and research of reproductive science and medicine as well as the treatment of infertility. Established in 1984, the Society now comprises of more than 10.000 members and has become the leading Society in reproductive science and medicine worldwide. Our members are medical professionals, scientists and researchers working in reproductive science, reproductive medicine and embryology. We work in close partnership with the patient organisation Fertility Europe, supporting their annual campaign Fertility Week and other activities.

All efforts undertaken by ESHRE target one main and important goal: to help people affected by infertility to have children. We do this by continuously applying, promoting and advancing Medically Assisted Reproduction (MAR), in Europe and beyond.

The result of these treatments is the birth of new human beings, a major specificity not adequately covered in the current legislation. Infertility affects approximately 25 million citizens in the EU. From a demographic perspective, the EU is in a phase of population decline. According to a recent policy audit, the highest fertility rate in a sample of nine EU countries remains below the stabilising rate indicated by Eurostat as necessary for generational renewal[1]. In 2009, the World Health Organisation (WHO) designated infertility a disease with multiple possible causes[2].

As the 'voice' of human reproduction and embryology professionals towards the EU institutions, the views expressed in this position paper are based on evidence and input gathered from scientists, academics, medical professionals and researchers across Europe.

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[1] *A policy audit on fertility: Analysis of nine countries, Fertility Europe and ESHRE, March 2017*
[2] *World health Organization (WHO), Internal Classification of Diseases, 11th Revision (ICD–11) Geneva, 2018*

1. DEFINITIONS AND TERMINOLOGY

In the field of human reproduction, the use of the terms “donor” and “donation” within a couple having an intimate physical relationship, and where only their own gametes are used is not appropriate. In fertility treatment for these couples, their own gametes are being used, just as in a conception without medical intervention. Therefore, we propose a revision of the definition of “donor” and “donation” for couples using their own gametes. This is also highly valid for patients who are cryopreserving their own reproductive tissues and cells for fertility preservation purposes, for example egg freezing and sperm freezing. When the gametes and embryos of partners within a couple are handled outside the body, we agree this should be regulated. However, ESHRE is of the view that these couples should not be regarded as donors and recipients towards each other in the same context as donation of blood or other types of non-reproductive cells.

In addition, in the current directive 2006/86/EC on tissues and cells (Art. 2, b) the term “intimate physical relationship” refers to heterosexual couples. In reality, a couple may be formed of transgender or same sex partners who need to undergo MAR interventions to become parents and this aspect must be reflected in the revised legislation. Following consultation with experts in human reproduction and embryology, we propose the following options for consideration:

- In a couple with an intimate physical relationship, where one person supplies own oocytes and the other supplies own sperm, the term “donation” should be replaced by “within-couple use”.
- For individuals that are cryopreserving their own gametes for fertility preservation, the term donation should not be used.

In every other circumstances, for couples which can be heterosexual, same sex or transgender - and for single women -, in which third-party donation is performed, the terminology “third-party donor” and “third-party donation” should remain unchanged.

2. QUALITY AND SAFETY

Although the current BTC legislation addresses reproduction-related issues, some details need more specific consideration. In what concerns quality of cells, the experience in the field shows that transferring a morphologically suboptimal embryo may lead to the birth of a healthy child, with no increased risk of adverse outcomes for mother or child. Therefore, we consider that the criteria for defining “cell quality” and “release of cells” are neither applicable nor valid in MAR.

In addition, the existing requirements concerning air quality are too stringent for the field of MAR. Reproductive medicine professionals have long recognised that the requirement to ensure a sterile environment in the treatment room is not necessary for MAR procedures and does not result in better treatment outcomes. In a MAR procedure, the sperm or embryos are transferred through a non-sterile environment (the vagina), and the risk of transmitting an infection to the woman via this procedure or the embryo is, as far as known, non-existent. In the current directive, there are exceptions that allow the handling of reproductive cells under less stringent environmental conditions (Dir. 2006/86, Annex I Art. 3, D4) but this is not clearly specified in the legislative text, which leads to inconsistent interpretations in the inspections of MAR clinics. Therefore, we propose that the exceptions that allow procedures under less stringent air quality conditions are clearly made applicable to MAR procedures in the revised legislation on BTC.

As regards the protection and vigilance of donors and offspring, ESHRE recommends including requirements that foresee mandatory reporting. Equally important is the reporting of adverse reactions in donors and offspring for cross-border treatments, as well as the follow-up and protection of the treated recipients, donors and offspring.

3. DATA COLLECTION AND REGISTRIES

The current legislation fails to provide recommendations for national robust and harmonized data collection which can be shared between countries. Member States have different regulations and policies in the MAR field regarding safety, for example concerning ovarian hyperstimulation and multiple births.

The absence of a European registry in the context of cross-border care presents risks of bypassing quality and safety measures, including increased health risks for women and future children. However, given the EU General Data Protection Regulation, it is difficult to create an open and transparent EU registry for MAR and to link data on an international level. This leads to barriers in ensuring traceability of patients, gametes and embryos. Some EU Member States collaborate on data sharing and have also made efforts towards (more) data harmonisation. We therefore invite the Commission to identify and propose solutions with regards to development of an EU-wide registry on MAR treatments.

4. INSPECTION AND AUTHORIZATION OF BTC ESTABLISHMENTS

First, we would like to highlight that the existing provisions for the inspections of BTC establishments are not implemented by Member States in a harmonised manner. Some are very flexible while others are very rigorous. This calls for the consideration of standards with minimum requirements and it is therefore also important to clarify aspects like environmental standards and screening, including genetic testing. Efforts should also be made to achieve a higher level of harmonisation of inspections' quality and content, both among the Member States and within each Member State, especially in countries divided into regions and/or with multiple inspectorate bodies.

Furthermore, we suggest clarifying the 'Harmonisation in the evaluation methods of inspection findings", more precisely how the inspectors should evaluate what they are inspecting. Despite a lot of efforts, the evaluation methods by competent authorities and inspectors are still very different, for instance concerning air quality in rooms where reproductive tissues and cells are handled and serious adverse reactions and events (SAREs) that should be reported. The EU legislation on BTC should include clearly defined criteria for the selection and regular evaluation of inspectors. In the selection process, it should be ensured that the selected inspectors have the necessary understanding and knowledge required to perform this profession within the field of MAR.

Our recommendation is that inspectors in the field of MAR should be provided with adequate education programmes and experts from professional associations should be involved in preparing the training programs for inspectors and authority officials. In particular, we would like to emphasize the need of financial resources to support competent authorities and inspectorate bodies. Additional resources could be made available through an EU financial scheme or dedicated budget.

5. EU BODIES DECISION MAKING AND INVOLVEMENT OF MAR PROFESSIONALS

Since the adoption of the current EU legislation on BTC, ESHRE has been following the various fora and expert-level discussions in the field of MAR. We are pleased that professional societies such as ESHRE are now increasingly consulted by EU bodies.

We believe that decisions for the enforcement of the EU legislation on BTC must be taken with the direct contribution of experts in the different fields, and namely MAR. Therefore, we strongly recommend that professionals from all relevant fields are actively invited to participate directly in expert committees of EU bodies and in Advisory Groups/Expert Groups of the European Commission. Their expertise can bring great contribution to the development and update of future legislation in accordance with scientific and technological developments. Professional and scientific associations must continue to define their standards independently and those standards should be taken into account by the bodies mandated for setting the rules within the EU.

We would also like to draw policy-makers' attention to the fact that giving authority only to bodies such as EDQM may imply some potential risks since this is a body formed by representatives of EU Member States and non-EU Member States. The outcome of EDQM's work is thus based on the expertise and experience of professionals also from non-EU countries, who may not be sufficiently aware of the situation in EU countries and may base their contribution only on the experience from their own countries. Given the differences in scientific advancements and in approaches to science between EU countries and non-EU countries, we see a risk of having rules/guidance for the EU decided by professionals who are not embedded in the EU Member States' realities. The outcome may be either diluted or not fully suitable to EU countries. Considering the above, we recommend that the EDQM maintains an advisory role instead of being given more powers in issuing guidance that is binding on the EU Member States.

6. INNOVATION

We want to emphasize that overly strict legislation in BTC, particularly in the area of MAR, should be avoided, since it restricts innovation to patient benefit and will soon become obsolete. However, while ESHRE fully acknowledges and supports the importance of advancing science and moving forward in discovering new methodologies, we strongly recommend limiting the sale of assisted reproduction technologies/add-ons (i.e. that the patients pay extra for), that are not (yet) validated for efficacy. Specifically, we recommend restricting the use of new MAR technology/methodology until efficacy and safety studies have been carried out, except when performed in approved experimental settings. In addition, new or modified reagents such as freezing media or culture media should only become available if information about the exact content is clearly disclosed to users.

In summary, the legislation needs to strike a balance between stimulating innovation and ensuring that only safe new technologies are placed on the market. Harmonising authorisation and estimated risks at EU level, as developed by Euro GTPII and GAPP joint projects, remains of utmost importance in the field of MAR.

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