Responsible Innovation
in Medically Assisted Reproduction

Position Paper — May 2022

Over the past decades, the field of Medically Assisted Reproduction (MAR) has evolved thanks to innovation and many people affected by infertility benefited from new technologies and treatments. However, a considerable proportion of patients/couples still remain childless after MAR treatment, which demonstrates the need to continuously develop more effective treatment approaches and improve existing technologies and treatments. Even incremental advancements are important for increasing patients' chances of having children. Another driving force for innovation is the need to constantly improve the safety of MAR treatments.

The development of innovative MAR treatments and technologies must be, as in other fields, conducted in a research setting with appropriate monitoring, safety precautions and preceding ethical approval. Following completion of the research phase, tissue and cell based treatments in the European Union (EU) need to be authorised by the national Competent Authorities for tissues and cells[1].

This paper outlines several challenges related to innovation in MAR and puts forward recommendations for responsible innovation, aiming to improve access to innovations for MAR patients, while at the same time ensuring the efficacy and safety of treatments.

BRINGING INNOVATIVE MAR TREATMENTS TO PATIENTS: SOME CHALLENGES IDENTIFIED

The European Society of Human Reproduction and Embryology (ESHRE) has identified several issues in the current system of bringing innovative MAR treatments to patients, which are outlined below:

- Regulatory requirements or insufficient funding for research and development in MAR may in some countries impede innovation.
- There is sometimes no clear distinction made to users between validated treatments and non-validated treatments. Some non-validated treatments may still be in a clinical research phase, others may even have already been shown to be non-effective. However, they are still offered to patients within clinical practice as "add-on" treatments, often at an additional cost for the patient[2].
- Not all national Competent Authorities have sufficient capacity and expertise in MAR to be able to evaluate innovative MAR treatments.
- High-quality data collection on MAR is not available in all countries, precluding Europe-wide overarching data collection systems to draw robust conclusions or achieve a comprehensive analysis of innovative treatments.
- Cross-country recognition of validated innovative procedures is still problematic in Europe, contributing to inequalities in access to treatments.

RECOMMENDATIONS

In order to tackle the identified challenges, ESHRE puts forward several recommendations for the EU institutions and for the Member States.

1. INNOVATION IN THE FIELD OF MAR SHOULD BE STIMULATED

Innovation needs to be stimulated by health and research legislation and should not be hindered by overly rigid regulatory requirements. Moreover, the EU should allocate sufficient funding for research and development. Funding is not only required for efficacy studies, but also for safety studies whose costs are often higher since they need to cover a longer time period to

[1] *Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.*
[2] *Harper et al., 2012. When and how should new technology be introduced into the IVF laboratory?. Human Reproduction 27(2).*

study long-term outcomes in the children born from MAR and require a larger number of participants to be able to detect adverse reactions that occur with a low probability.

2. TESTING, VALIDATION AND AUTHORISATION OF INNOVATIVE MAR TREATMENTS SHOULD BE ORGANISED IN A CLEAR AND COMPREHENSIVE FRAMEWORK

A clear framework for the testing, validation and authorisation of MAR treatments is essential, focusing on establishing the efficacy and safety of innovative treatments. In the EU, tools for risk assessment were defined and included within a framework for authorisation of innovative tissue and cell treatments, recently developed in the Joint Action FacilitatinG the Authorisation of Preparation Process for blood, tissues and cells (GAPP)[3]. We recommend that the framework developed by GAPP is implemented in practice, and where relevant also used as an example for innovations that do not constitute tissue and cell preparation processes. Any existing or future framework for testing, validation and authorisation of innovative MAR treatments should be subject to constant evaluation with the involvement of professional societies.

3. EXPERTS SHOULD BE CONSULTED IN THE EVALUATION OF INNOVATIVE MAR TREATMENTS

The authorisation of innovative treatments requires highly specialised expertise for proper evaluation of the available data from research studies, biological rationale and related safety issues. This expertise cannot be guaranteed by all Competent Authorities in the EU Member States. Thus, we recommend that Competent Authorities systematically consult (national) MAR experts when reviewing applications for authorisation of innovative MAR treatments. ESHRE as a professional society can offer solid expertise to Competent Authorities, for instance through trainings on MAR and by providing expert opinions on specific issues.

4. RESPONSIBLE INNOVATION REQUIRES HIGH-QUALITY DATA ON MAR TREATMENTS

An EU-wide registry with detailed data on MAR treatments allowing long-term follow-up of MAR patients, donors and children can be a valuable resource for the evaluation of both established and innovative treatments. An expanded legal basis for data collection on MAR treatments in the revised EU legislation on blood, tissues and cells would strongly support the development of such a registry.

5. VALIDATED INNOVATIVE TREATMENTS SHOULD BE EQUALLY ACCESSIBLE TO PATIENTS THROUGHOUT THE EU

Currently, the availability and affordability of innovative MAR treatments varies widely between EU countries. ESHRE believes that, once innovative MAR treatments are validated and authorised in one country, the information gathered in the process should be used to facilitate authorisation in other EU countries to create similar access to MAR treatments for patients from all EU countries. A more harmonised authorisation process at EU level would secure more comparable access to innovative MAR treatments. This would contribute to reducing the need for cross-border treatments, while at the same time strengthening the rights of patients from different European countries.

ABOUT ESHRE

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 more than 8.000 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.

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[3] https://www.gapp-ja.eu/