Brussels, 22/05/2023

Dear Member of the ENVI Committee,

We are writing to you on behalf of the European Society of Human Reproduction and Embryology (ESHRE) to express our position regarding some of the amendments that have been suggested in response to the European Commission's proposal for a Regulation on standards of quality and safety for substances of human origin intended for human application (SoHO Regulation).

Ensuring proper inclusion of reproductive cells, tissues and embryos under the SoHO Regulation

As mentioned in our position paper from January 2023, the **Commission's legislative proposal does not account for embryos** in its definition of a "substance of human origin", so we are pleased to see that embryos have been explicitly included in **amendment 433**, which replaces the term "reproductive cells" by "SoHO for reproduction". However, we suggest extending the definition of "SoHO for reproduction" by "reproductive tissues" (i.e., ovarian and testicular tissue) to ensure that this term covers all SoHO applied in the field of Medically Assisted Reproduction (MAR). We also support the explicit addition of a mix-up of embryos in the definition of serious adverse occurrences (SAO) in **amendment 403**. In contrast, we do not agree with the re-definition of "reproductive cells" in **amendment 432**, since this definition also does not include embryos.

We further oppose **amendment 129**, which aims to limit the scope of the SoHO Regulation to only include **embryonic stem cells** if they have been derived from postnatal embryonic remnants. In our expert opinion, the proposed regulation should apply to all embryonic stem cells, also those derived from pre-implantation embryos.

Avoiding uncertainty in the MAR field: the vital role of accurate and clear definitions

We strongly oppose **amendment 335**, which **re-defines "cells"** by stating that "a typical cell [...] has been generated directly through mitosis". This definition does not consider cells that are created through meiosis, and thereby introduces uncertainty regarding the regulatory status of reproductive cells.

Moreover, **amendments 355-358**, which seek to revise the **definition of "medically assisted reproduction"**, raise concern. In our opinion, the definition originally proposed by the Commission should be retained. It is comprehensive, consistent with scientific consensus, and encompasses all procedures and techniques to be regulated.

We strongly support **amendments 360 and 361**, removing the term "foetuses" from the **definition of "offspring from medically assisted reproduction"**. The term "offspring" should only describe individuals that have already been born following MAR. Thus, we disagree with **amendment 359**, which also defines embryos as "offspring", as well as with **amendment 362**, which introduces the term "unborn offspring from medically assisted reproduction".

We further disagree with **amendment 376**, which suggests removing "preparatory steps, such as hormone treatment" from the **definition of "collection"**. In our view, hormone treatment should be considered a part of the collection process, for instance to ensure that complications arising from ovarian stimulation in third-party oocyte donors are recorded in the SAO reporting.

Diminishing protection of offspring born from MAR is unacceptable

The **protection of offspring** from MAR is of utmost importance, and we thus strongly object to **amendments 681, 684-686 and 738**, which suggest removing legal provisions aimed at offspring protection. In this context, we also disagree with **amendments 682 and 711**, which suggest allowing gamete donation without genetic screening of the donor, as this would expose offspring to an unacceptable risk of transmission of genetic conditions.

Getting the language right: consensus among experts should take the lead

With regard to **amendments 120-122, 159, 164, 308, 312, 359, 571, 675, 680, 733 and 737**, which suggest **replacing the term "medically assisted reproduction"** by "reproductive techniques" or "fertility treatments", we would like to emphasise that there is a consensus of international experts in the field to use the term "medically assisted reproduction"[1]. To the best of our knowledge, this term is also accepted and preferred by patient representatives. Thus, we see no valid reason for replacing this term throughout the regulation and strongly oppose these amendments.

We further disagree with **amendments 160, 207 and 678**, which propose **replacing the term "offspring"** by "children". Since an individual retains the status of an "offspring" even after reaching adulthood, we consider this term to be more accurate.

Moreover, we noted that **amendments 597 and 598** propose allowing "embryologists" to perform tasks of the "physician", as specified in article 51. While we appreciate that also other professionals from the MAR field are taken into consideration, we are concerned that these amendments might create uncertainty in the application of the SoHO Regulation, since there is currently no uniform or widely accepted definition of an "embryologist". To ensure that responsibilities are clear, health professionals should be described using unambiguous terms.

Unfairly targeted: high standards must apply to all SoHO fields, not just MAR

We also object to **MAR being singled out as a particularly problematic field** in **amendments 121, 122, 164, 274, and 384**. All SoHO treatments should be subject to high ethical, quality and safety standards, and we see no need to focus on MAR specifically in this regard. In this line of thought, we are particularly alarmed by the connection made between MAR and "eugenic abuses" in **amendment 384**.

Addressing donor anonymity in MAR: a complex issue beyond the SoHO Regulation's scope

We further noted that there are several amendments aiming to remove **donor anonymity** in MAR, namely **amendments 295, 571, 675**. Since the EU only has legal competency with regard to the quality and safety of SoHO, we consider these amendments to be outside the scope of this regulation. We do, however, support **amendments 296 and 734** stating a need to inform donors of reproductive cells about the possibility of ID release, since full donor anonymity can no longer be guaranteed in light of the increasing use of direct-to-consumer genetic testing[2].

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[1] European Directorate for the Quality of Medicines & HealthCare (EDQM) (2022). Guide to the quality and safety of tissues and cells for human application, 5th edition. https://www.edqm.eu/en/guide-to-the-quality-and-safety-of-tissues-and-cells-for-human-application1

[2] Joyce C. Harper, Debbie Kennett, Dan Reisel, The end of donor anonymity: how genetic testing is likely to drive anonymous gamete donation out of business, *Human Reproduction*, Volume 31, Issue 6, June 2016, Pages 1135–1140, https://doi.org/10.1093/humrep/dew065

Hierarchy of guidelines: the status of ECDC and EDQM guidelines should not be undermined

Like the professional societies in the Consortium Common Representation of Substances of Human Origin (CoRe SoHO), we are concerned that **amendments 225, 226, 596, 668 and 672** all dilute the position of ECDC and EDQM guidelines in the hierarchy of applicable guidelines. These proposed amendments go in the opposite direction to the common objective of harmonising standards across the EU, one of the main goals of this regulation. The hierarchy of applicable guidelines is a critical component of this regulation, and although we believe that it should remain possible to use national and/or professional guidelines, these guidelines need to be aligned with the standards by the EDQM and ECDC.

Comprehensive data collection and registries: a critical role in improving MAR outcomes

We find it alarming that **amendments 215, 533 and 582** suggest removing the **possibility to use existing clinical data registries** for clinical outcome monitoring. These amendments diminish the role of clinical data registries and go against the aim to reduce doubling of efforts in data collection. The suggested obligation to record clinical studies in the EU SoHO platform in these amendments does not contradict with the possibility to use existing data registries in those studies.

On the other hand, we are pleased to see that there are several amendments aiming to align the new SoHO framework with the **European Health Data Space (EHDS)** and improve interoperability of the EU SoHO platform with other IT systems and databases. Thus, we support **amendments 286, 289, 301, 410 and 845**, which will facilitate data sharing for research and other important purposes.

Stakeholder representation matters: health professionals and patients need a seat at the table

We strongly support the aim to increase the **involvement of stakeholders**, including health professionals and patients, in the formulation of technical guidelines, as well as in the SoHO Coordination Board in **amendments 221, 222, 227, 234 and 665, 804 and 806**.

We remain at your disposal should you wish to discuss the aforementioned points in more detail.

Sincerely,

Dr. Cristina Magli

Chair of ESHRE's EU Affairs Committee