Regulation on standards of quality and safety for substances of human origin intended for human application (SoHO Regulation) – summary for professionals in the field of medically assisted reproduction

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On 6 August 2024, Regulation 2024/1938 on standards of quality and safety for substances of human origin intended for human application (the SoHO Regulation) entered into force. This Regulation will provide the legal framework for the quality and safety of all Substances of Human Origin (SoHO), including oocytes, sperm and embryos, in the European Union (EU) and European Economic Area (EEA).

Most of the rules in the SoHO Regulation will become applicable on 7 August 2027. From this date on, the EU Tissues and Cells Directive (2004/23/EC) and its implementing acts[1] will no longer apply, since they are repealed by the SoHO Regulation. More information on the difference between a Directive and a Regulation is provided in the info box below.

This document aims to help MAR professionals navigate the SoHO Regulation by providing a summary of the key aspects of relevance to professionals in MAR clinics. Sections of the Regulation that ESHRE does not consider relevant for the MAR sector are thus not included in this summary. Any interpretations of the legal text are solely ESHRE's views. To ensure compliance with the legal framework, please consult the full SoHO Regulation as published in the Official Journal of the European Union, which can be accessed here.

Info box: Directive vs. Regulation

Directive: A type of EU law that is binding to Member States regarding the objectives that need to be achieved. Directives need to be "transposed" into national law, i.e., when the EU adopts a new Directive, each Member State has to adopt a law in its national legislation to achieve the objectives of the EU Directive.

Regulation: A type of EU law that is directly applicable and binding in all Member States without transposition into national law. Regulations usually ensure greater harmonisation in the rules that apply across the EU than Directives.

[1] Commission Directives 2006/17/EC, 2006/86/EC, 2015/565, 2015/566, 2012/39/EU and Commission Decisions 2010/453/EC and C(2015) 4460

Contents

Abbreviations

MAR	Medically Assisted Reproduction
SoHO	Substance(s) of Human Origin
EU	European Union
EEA	European Economic Area
IUI	Intrauterine insemination
IVF	In-vitro fertilisation
SCB	SoHO Coordination Board
SAR	Serious Adverse Reaction
SAE	Serious Adverse Event
ECDC	European Centre for Disease Prevention and Control
EDQM	European Directorate for the Quality of Medicines and Healthcare

Scope - what is covered by the Regulation?

➢ Referring back to article 2 and article 3(3), (7), (9), (14) and (15)

The SoHO Regulation applies to all substances of human origin (SoHO) intended for human application, except for solid organs (e.g., uteri) and breast milk when not processed and if only used for feeding one's own child. **Sperm, oocytes, ovarian and testicular tissue, and embryos are covered by the Regulation under the term "reproductive SoHO".**

The SoHO Regulation applies to SoHO donors, recipients and offspring, aiming to ensure the protection of these three groups. In the context of MAR, the use of reproductive SoHO between persons with an intimate physical relationship is referred to as **"within-relationship use"**. The partners in this setting are not considered donors. Only **third-party donors** are covered by the standards for donor protection of the Regulation. However, the person to whom SoHO are applied in within-relationship use (i.e., the female partner having an IUI or embryo transfer) is considered a **recipient**.

Lastly, the Regulation lists a number of **SoHO activities** that are considered to have a direct impact on the quality, safety or effectiveness of SoHO and are therefore covered by the Regulation:

- SoHO donor registration
- SoHO donor history review and medical examination
- testing of SoHO donors or of persons from whom SoHO are collected for autologous or within-relationship use
- collection
- processing
- quality control
- storage
- release
- distribution
- import
- export
- human application
- clinical-outcome registration

Info box: Definitions of SoHO activities (SoHO Regulation article 3 (19)-(31))

'SoHO donor registration' means recording in a registry, and transferring to other registries, where appropriate, information on a SoHO donor that is essential for identifying a match with a prospective SoHO recipient

'collection' means a process by which SoHO are obtained from a person, including any preparatory steps, such as hormone treatment, needed to facilitate the process at, or under the supervision of, a SoHO entity

'processing' means any operation involved in the handling of SoHO, including, but not limited to, washing, shaping, separation, decontamination, sterilisation, preservation and packaging, except for the preparatory handling of SoHO for immediate human application during a surgical intervention, without the SoHO being removed from the surgical field before they are applied

'quality control' means performing a pre-defined test or set of tests or checks to confirm that pre-defined quality criteria are met

'storage' means the maintenance of SoHO under appropriate controlled conditions

'release' means a process through which it is verified that a SoHO meets defined quality and safety criteria and fulfils the conditions of any applicable authorisation, before distribution or export

'distribution' means providing, within the Union, released SoHO:

(a) intended for human application to a specific SoHO recipient in the same or in another SoHO entity;
(b) intended for human application in general, without the prior identification of a specific SoHO recipient, in the same or in another SoHO entity;
(c) intended for the manufacture of products regulated by other Union legislation, as referred to in Article 2(6), to a manufacturer of such products

'import' means activities carried out to bring SoHO into the Union from a third country before their release

'export' means activities carried out to send SoHO from the Union to a third country

'human application' means being inserted, implanted, injected, infused, transfused, transplanted, ingested, transferred, inseminated or otherwise added to the human body in order to create a biological interaction with that body

'clinical-outcome registration' means the management of a clinical registry where information on the results from the implementation of a clinical-outcome monitoring plan are recorded, including transferring such information to other registries

The SoHO landscape

The SoHO Regulation describes several different actors in the SoHO landscape, who will each have specific obligations.

SoHO entities

➢ Referring back to articles 3(33), 35, 36, 37

Any legal entity carrying out one or more of the SoHO activities listed above is a SoHO entity. This includes all MAR clinics, but also other entities like laboratories analysing blood samples of potential donors or of persons from whom SoHO are collected for within-relationship use. If an entity is not sure whether their activities fall under the definition of one the SoHO activities, they can request an opinion from their local SoHO competent authority.

All SoHO entities have to:

- **register themselves** in a register of SoHO entities. It is up to the SoHO national authorities to decide whether they will establish a registry in their country themselves or whether they will ask SoHO entities to register directly on the EU SoHO platform
- **designate a responsible person** who will be in charge of ensuring that the entity complies with the Regulation
- put a **quality management system** in place that is appropriate to their activities and achieves a high level of quality of SoHO

SoHO establishments

➢ Referring back to articles 3(26) and (35), 45, 46, 47, 48, 49, 50, 60, 81

A SoHO establishment is a SoHO entity that carries out at least one of the following:

- Both processing and storage of SoHO
- SoHO release
- SoHO import
- SoHO export

Most entities that currently operate as tissue establishments under the Tissues and Cells Directive will match this definition. Typical examples of SoHO establishments are IVF laboratories and gamete banks. Moreover, competent authorities can decide that certain SoHO entities that do not match this definition, for instance laboratories performing serological or genetic testing, also have to follow the obligations of SoHO establishments, in particular if they have significant influence on the quality and safety of SoHO due to the scale, criticality or complexity of their activities, or if they carry out SoHO activities in connection with multiple SoHO establishments.

SoHO establishments will be subjected to **regular inspections** by their competent authorities. In addition to the general obligations of SoHO entities, SoHO establishments have the following obligations:

- to **apply for a SoHO establishment authorisation**. Tissue establishments who are already designated, authorised, accredited or licensed under the Tissues and Cells Directive are automatically deemed authorised SoHO establishments under the Regulation
- to appoint a **physician** who shall be responsible for tasks requiring clinical expertise, including the definition of donor eligibility criteria, investigations of suspected serious adverse reactions (SAR), and the design and supervision of clinical outcome monitoring for SoHO preparation authorisations. The physician needs to work in the same Member State, but does not need to be employed by the establishment
- **if they release SoHO:** to appoint one or more **releasing officers** at the establishment who are responsible for verifying that the SoHO meets defined quality and safety criteria. A formal release step is not needed for intrauterine insemination (IUI) with partner sperm if the sperm is used immediately without storage.
- **if they import SoHO** from outside the EU/EEA:
    - to apply for a specific authorisation for importing SoHO establishments
    - to put in place written agreements with suppliers

SoHO competent authorities

➢ Referring back to articles 5, 6, 7, 8, 9, 16, 18, 24, 27, 28, 29

Member States shall designate one or more competent authorities to carry out the supervisory activities in their country, aimed at verifying effective compliance by SoHO entities with the requirements of the Regulation. SoHO competent authorities are bound to independence, impartiality and transparency. Some of the tasks of competent authorities can be delegated to "delegated bodies" based on a written agreement with those bodies.

Competent authorities have to:

- establish and maintain the **register of SoHO entities** in their country. They may make use of the EU SoHO platform for this task, but they can also establish a separate national registry. In this case, competent authorities need to submit the information on registered entities to the EU SoHO platform themselves.
- establish and maintain a system for **authorising SoHO establishments**, which also allows for suspension and withdrawal of authorisations
- carry out **inspections of SoHO establishments** in their Member States.
    - On-site inspections shall be carried out **before granting an authorisation to a SoHO establishment**. After that, some inspections can also take place virtually or by remote document review.
    - The frequency of inspections shall take a risk-based approach, but in any event, there needs to be an **on-site inspection at least once every four years.**
    - Competent authorities also have the **right to inspect SoHO entities that are not SoHO establishments** or any third parties contracted by SoHO establishments if necessary and proportionate to the risks associated with the activities carried out by those entities.
    - **Joint inspections** can be carried out with the participation of inspectors from other Member States, particularly if an entity performs SoHO activities in more than one Member State or if specialist technical expertise from another Member State is required for the inspection.

SoHO national authorities

➢ Referring back to articles 5, 8, 12,13

Each Member State shall designate a single SoHO national authority among its competent authorities. If a country only has one competent authority, that authority is automatically considered the SoHO national authority.

The obligations of SoHO national authorities are:

- to ensure efficient and effective **coordination between SoHO competent authorities** in their Member State
- to manage information exchanges with the **European Commission**
- to manage information exchanges with SoHO national authorities of other Member States
- to manage communication with **authorities of other regulatory sectors**, e.g., pharmaceuticals or medical devices

The European Commission

➢ Referring back to articles 70, 71 and 72

The European Commission is responsible for supporting and overseeing the implementation of the SoHO Regulation at the EU level.

The Commission will have the following obligations:

- to provide **trainings to personnel of competent authorities** on the implementation of the Regulation
- to organise programmes for the exchange of competent authorities' personnel between Member States
- to perform **"Commission controls"**, aimed at confirming whether Member States are adhering to the requirements of the Regulation
- to provide the secretariat and technical, scientific and logistic **support to the SoHO Coordination Board (SCB)** (more details below)
- to establish, manage and maintain the **EU SoHO Platform** (more details below)

SoHO Coordination Board (SCB)

➢ Referring back to articles 68 and 69

The SCB is composed of two permanent members and two alternate members from each Member State, representing their SoHO national authority and, where the Member State chooses so, the Ministry of health or other relevant authorities. The SCB may invite experts and observers, e.g., from professional societies like ESHRE, to attend its meetings.

The main aim of the SCB is to promote coordination between Member States and to assist competent authorities in the implementation of the SoHO Regulation, for instance by documenting and publishing best practices on supervisory activities. These best practices should be taken into account by competent

authorities when carrying out their tasks. They may cover very specific topics, e.g., what to include in certain application and reporting templates, but also broader topics such as how to organise inspections.

The SCB also has a role in determining the **regulatory status of a substance**, product or activity that is at the borderline between the SoHO Regulation and other frameworks (e.g., organs, pharmaceuticals or medical devices) by providing an opinion and consulting the equivalent EU level advisory bodies of those other frameworks.

The EU SoHO Platform

➢ Referring back to articles 73 and 74

The EU SoHO Platform is a **digital platform** that is planned to facilitate efficient and effective exchange of information concerning SoHO activities in the EU. It will have a public part and a part with restricted access.

The public part will provide access to information on:

- the registration and authorisation status of SoHO entities
- the list of national authorities
- the SCB: members, rules of procedure, agenda and minutes of each meeting
- the list of approved SoHO clinical studies and authorised SoHO preparations (further details below)
- the annual Union SoHO activity report and annual Union SoHO vigilance report (further details below)
- relevant best practices on supervisory activities documented and published by the SCB
- technical guidelines published by the European Centre for Disease Prevention and Control (ECDC) and the European Directorate for the Quality of Medicines and Healthcare (EDQM) for the implementation of donor, recipient and offspring protection standards
- the SoHO compendium: a compendium of opinions of the SCB on the regulatory status of substances, products or activities that are at the borderline with other frameworks
- more stringent measures adopted by Member States

The restricted part is aimed to provide a secure channel of information exchanges between:

- competent authorities within a Member State
- national authorities of different Member States
- national authorities and the European Commission
- national authorities and the SCB
- national authorities and the ECDC
- SoHO entities and their respective competent authorities, if the competent authority chooses to use the EU SoHO Platform for such exchanges

The European Commission will provide instructions, materials and training on the correct use of the EU SoHO Platform.

SoHO preparation authorisations

➢ Referring back to articles 3(23), 18, 19, 20, 21, 22, 38, 39, 40, 82

SoHO that have been subjected to processing and have a specific clinical indication are called SoHO preparations. Processing is defined as "any operation involved in the handling of SoHO, including, but not limited to, washing, shaping, separation, decontamination, sterilisation, preservation and packaging [...]" (Article 3(23)).

SoHO entities are only allowed to release SoHO preparations (or prepare and immediately apply them, in case of IUI with partner sperm) if they have a SoHO preparation authorisation. If a SoHO entity has previously been designated, authorised, accredited or licensed to perform a tissue and cell preparation process under the Tissues and Cells Directive, they are automatically considered to hold a SoHO preparation authorisation for the resulting preparation under the SoHO Regulation.

If a SoHO entity aims to introduce a new SoHO preparation into its practice, it has to submit an **application for a preparation authorisation** to its competent authority. If the **SoHO preparation was already authorised in another SoHO entity** in the same or a different Member State, it is sufficient to verify that the steps of processing are carried out in such a way that the quality, safety and effectiveness of the SoHO preparation will be equivalent to where the preparation was first authorised. However, competent authorities may choose not to take SoHO preparation authorisations granted in other Member States into account.

Applications: Competent authorities will have to provide more detailed guidelines and templates for applications, but applicants will have to provide at least the following information:

- details on the applicant SoHO entity
- **details on the SoHO that are used** and the activities performed for the preparation, such as donor eligibility criteria, collection procedure, processing steps, quality control parameters and clinical indications for applying the preparation
- results of a **benefit-risk assessment**. Four risk categories are defined: negligible, low, moderate and high. If a non-negligible risk was identified without a significant expected benefit, the application will be rejected.
- a proposed plan for clinical-outcome monitoring, depending on the results of the benefit-risk assessment:
    - in case of negligible risk and an expected positive benefit risk-assessment, no clinical-outcome monitoring is required
    - in case of **non-negligible risk or unknown benefit**, at least pro-active clinical follow-up of a pre-defined number of SoHO recipients is required. In addition:
        - in case of a **moderate risk** and an expected positive benefit-risk assessment, a clinical study of a pre-defined number of SoHO recipients is required to be able to assess pre-defined clinical end-points
        - in case of a **high risk** and an expected positive benefit risk assessment, or if the risk or benefit are not evaluable due to a lack of evidence, a clinical study with comparison to standard therapy is required

Competent authorities have to **register approved clinical studies** on the EU SoHO platform. If a preparation authorisation is granted, competent authorities are obliged to submit **information on the SoHO preparation, including a summary of the evidence used for the authorisation, to the EU SoHO platform**, where it will be publicly available.

Competent authorities of different Member States also have the option to assess applications for preparation authorisation together in a **joint assessment**.

There are some exceptions when SoHO preparations can be released without a preparation authorisation:

- within an **approved clinical-outcome monitoring plan** as part of a preparation authorisation application
- in **health emergency situations**, if it is in the interest of public health (likely not applicable to reproductive SoHO)
- if a specific recipient has **no therapeutic alternative**, the treatment cannot be postponed, and the SoHO preparation can reasonably be assumed to be safe and effective based on available clinical data. In this case, the SoHO entity needs to request an exceptional authorisation from the competent authority and the recipient needs to be fully informed about the lack of a preparation authorisation.

Activity data reporting

➢ Referring back to articles 31 and 41

SoHO entities will have the obligation to send an **annual report with summary data** on their SoHO activities to their competent authorities via the EU SoHO platform before 30 June of the subsequent year. Competent authorities can also allow SoHO entities to send their data to them **via a national or international registry**.

Reporting of summary data is mandatory for SoHO entities carrying out the following activities:

- SoHO donor registration
- collection
- distribution
- import
- export
- human application

The exact parameters on which data needs to be reported will be described in a further legal document.

The European Commission will compile all reports and prepare an **annual Union SoHO activity report**, which will be made publicly available after review and approval by national authorities.

Info box: The EuMAR registry

ESHRE is currently building the EuMAR registry, a European cycle-by-cycle registry of MAR treatments. This registry is hosted by ESHRE and separate from the EU SoHO platform. Data submission to EuMAR will not be mandatory, but EuMAR might be able to take over the mandatory activity data submission for MAR centres in the future, if competent authorities in their Member State allow this.

For more information on EuMAR, please visit www.eshre.eu/EuMAR

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Vigilance

➢ Referring back to articles 3(45-47), 33, 34 and 44

The vigilance system under the SoHO Regulation remains mostly unchanged compared to the Tissues and Cells Directive. SoHO entities have to have a system for detecting, investigating and recording information concerning adverse reactions and events, and have an obligation to report any **serious adverse reactions (SAR) and serious adverse events (SAE)** to their competent authorities.

The new definitions of SAR and SAE are presented in the info box below. One novelty is that it will also become **mandatory to report SAR related to the SoHO collection in third-party donors (e.g., severe OHSS in oocyte donors)**. In within-relationship use, only SAR related to the application of the SoHO (IUI or embryo transfer) need to be reported. *(Note: The SoHO Regulation does not oblige SoHO entities to report any complications during SoHO collection (e.g., OHSS or bleeding) in within-relationship use, but it is possible that Member States choose to impose such an obligation in addition to the requirements of the Regulation.)*

Info box: Definitions of serious adverse reactions and events (SoHO Regulation article 3 (45) and (46))

'serious adverse reaction' or 'SAR' means an adverse reaction that results in any of the following:

a) death;
b) life-threatening, disabling or incapacitating condition, including transmission of a pathogen or of a toxic substance that might cause such condition;
c) transmission of a genetic disorder that:
    i. in the case of medically assisted reproduction with third-party donation, resulted in pregnancy loss or might result in a life-threatening, disabling or incapacitating condition in the offspring from medically assisted reproduction; or
    ii. in the case of medically assisted reproduction in the context of within-relationship use, resulted in pregnancy loss or might result in a life-threatening, disabling or incapacitating condition in the offspring from medically assisted reproduction, due to a pre-implantation genetic test error;
d) hospitalisation or prolongation of hospitalisation;
e) the need for a major clinical intervention to prevent or reduce the effects of any of the results referred to in points (a) to (d);
f) prolonged sub-optimal health of a SoHO donor following single or multiple SoHO donations;

'serious adverse event' or 'SAE' means an adverse event that poses a risk of any of the following:

a) inappropriate SoHO distribution;
b) a defect posing a risk to SoHO recipients or SoHO donors is detected in one SoHO entity that would have implications for other SoHO recipients or SoHO donors because of shared practices, services, supplies or critical equipment;
c) loss of a quantity of SoHO that causes human applications to be postponed or cancelled;
d) loss of highly matched SoHO or SoHO for autologous use;
e) a mix-up of reproductive SoHO in such a way that an oocyte is fertilised with sperm from a person other than the intended person, or reproductive SoHO are applied to a SoHO recipient other than the intended SoHO recipient;
f) loss of the traceability of SoHO

SAR/SAE notification and investigation

➢ Referring back to article 44(2),(3),(4) and (7)

When a SoHO establishment (IVF laboratory or cryobank) detects or suspects a SAR or SAE, it has to submit a **notification to its competent authority** with a description of the suspected reaction or event, any immediate steps taken to limit harm, a preliminary assessment of the seriousness of the consequences and, for adverse reactions, a preliminary assessment of the likelihood that the suspected SAR was associated with the SoHO collection or application (imputability).

Following the notification, the SoHO establishments have to investigate the suspected SAR or SAE and submit an **investigation report** including a full description of the investigation, the final assessment of imputability and seriousness, a risk assessment of the likelihood of recurrence (where relevant), and a description of the actions taken to limit harm or prevent recurrence.

SoHO entities that are not SoHO establishments should communicate adverse reactions and events to the SoHO establishment who distributed the SoHO to them or for which they are carrying out their activities. The SoHO establishment will then be responsible for the investigation and, if the adverse reaction or event is considered serious, notification to the competent authority.

MAR clinics offering treatments with third-party donation are asked to encourage recipients of such donations to inform the clinic in case any **serious genetic conditions emerge in the offspring**. In this case, the SoHO establishment (IVF laboratory or gamete bank) that released the gametes shall be informed immediately and shall investigate whether the condition was transmitted from the donor.

Sharing SAR/SAE information to allow risk mitigating actions

➢ Referring back to articles 34 and 44(8)

If a SoHO entity detects a SAR or SAE that is **of relevance to other** entities, it has to inform these other entities and provide them with the information that is necessary and appropriate to take risk mitigating actions. For instance, if a gamete bank detects a serious genetic condition in a donor, it has to inform all clinics to which it has distributed gametes from this donor to allow them to discontinue the use of this donor's gametes, in accordance with national law.

If a SAR or SAE is **of relevance to other EU Member States**, e.g., if gametes from a donor were distributed to one or more other countries, the competent authority who received the notification has to inform its SoHO national authority, who shall launch a **rapid alert** on the EU SoHO platform. The rapid alert will go the SoHO national authorities of all EU Member States and the European Commission. If the rapid alert concerns a communicable disease, the ECDC will also be informed.

Annual Union SoHO vigilance report

➢ Referring back to article 33(13) and (14)

SoHO national authorities have to send an annual summary of the confirmed SAR and SAE in their countries to the EU SoHO platform. The European Commission will aggregate the data from all countries and publish an **annual Union SoHO vigilance report**.

Traceability

➢ Referring back to articles 3(53), 32, 42, 43

SoHO entities shall have a traceability system in place to be able to **link each person from whom SoHO were collected to the SoHO collected from them at any point**. They shall keep the data necessary to ensure traceability, in electronic or paper form, for at least 30 years.

In the case of third-party donation, or if SoHO for within-relationship use are moved between SoHO entities, a code needs to be applied that is unique within the EU and does not reveal the identity of the person from whom the SoHO were collected. This code should be machine-readable, unless this is not possible due to the size or storage conditions of the SoHO. The code should be on the labels applied to the SoHO or on the documents accompanying the distributed SoHO, where it can be guaranteed that such documents will not be separated from the SoHO or will be kept digitally linked to the SoHO concerned. If SoHO for third-party donation are moved between entities, the code additionally needs to comply with the requirements for the **Single European Code (SEC)**, which the European Commission will set out in another legal document.

Donor compensation

➢ Referring back to article 54

The SoHO Regulation aims to ensure **financial neutrality** for donors, i.e., donors should have no substantial financial gains or losses from their donation.

Donors may receive a reimbursement of their expenses and/or a financial or non-financial compensation for other losses. However, it is up to the Member States to decide whether they allow such a compensation in their country. If Member States allow for donor compensation, they have to establish the conditions for it in national legislation, including by setting an **upper limit**.

Promotion and publicity activities to advertise for donations are not allowed to refer to compensation.

The rules for donor compensation also apply to **SoHO donation for research**.

Donor protection

➢ Referring back to articles 52, 53 and 55

While the Tissues and Cells Directive focused on the quality and safety of SoHO for recipients, the SoHO Regulation also has the **objective to ensure donor protection**, particularly by ensuring respect for the dignity and integrity of donors and a high level of safety of the donation.

For this purpose, SoHO entities are obliged to adhere to the following **high-level standards**:

- meeting consent or authorisation requirements in force in their Member States
- ensuring **full informed consent**, including information on the risks of the donation, the intended use of the SoHO, and anonymity rules in donation for MAR
- safeguarding the **donor's rights** to physical and mental integrity, non-discrimination, privacy and the protection of their personal data
- ensuring that the donation is **voluntary and unpaid** in line with the rules on donor compensation
- conducting a **donor health evaluation** that is aimed at verifying the eligibility of donors and minimising any risks that the donation may pose to their health. The results of this donor health evaluation need to be documented and clearly explained to the donors

- identifying and **minimising any risks** to the health of donors during the collection procedure
- in cases where a frequent donation might have a negative effect on the donor's health (e.g., oocyte donation) verifying, by means of entity-level, national or recognised international registries, that donors are not donating more frequently than what is indicated as safe for the particular type of donation, and monitoring relevant health indicators
- in cases where the donation involves a surgical procedure or intake of medication (e.g., oocyte donation), developing and implementing a plan for **monitoring the donor's health after the donation**

For the implementation of these high-level standards, the SoHO Regulation refers to technical guidance, as further explained in the chapter on technical guidelines below.

Recipient and offspring protection

➢ Referring back to articles 57 and 58

To ensure the protection of recipients and offspring, the SoHO Regulation sets the following **high-level standards** for SoHO entities:

- mitigating the risk of **communicable disease transmission** from donors by:
  - ➢ testing donors for communicable diseases
  - ➢ taking other measures that reduce or eliminate potential communicable pathogens when feasible (e.g., sperm processing)
  - ➢ where risks cannot be minimised by testing, deferring donors with a high risk of transmitting a communicable disease based on their health, travel or behavioural history
- mitigating the risk of **transmission of serious genetic conditions** (defined as potentially life-threatening, disabling or incapacitating conditions) from donors to offspring in MAR by:
  - ➢ reviewing the donor's health and family history and deferring donors that carry a risk of transmitting a serious genetic condition
  - ➢ routinely testing donors for certain serious genetic conditions
  - ➢ where donor gametes are to be used in combination with the recipient's own gametes and the recipient has a family history of a serious genetic condition, testing the recipient and the donor to ensure matching that prevents the condition from occurring in the offspring *(Note: while the SoHO Regulation only mentions the combination of donor gametes with the recipient's own gametes, it may be advisable to apply the same measures in the context of oocyte donation if donor oocytes are combined with partner sperm, even though the partner is not considered a recipient under the Regulation)*
- mitigating the risk of **contamination of SoHO** from other SoHO from different persons or from the environment, personnel, equipment or materials
- mitigating the risk that any **reagents and solutions added to SoHO** might be transferred to recipients and have a harmful effect on their health
- mitigating the risk that any SoHO activity performed **reduces the clinical effectiveness** of SoHO (i.e., in MAR, the chances of a pregnancy and live birth)
- mitigating the risk that SoHO cause an **unexpected immune reaction** in recipients

- mitigating **any other avoidable risk** to the recipient or offspring health and dignity, in accordance with national law
- complying with **national legislation on limits to the number of offspring from MAR,** to be monitored by donor registries, in accordance with national law
- using technologies that reduce the risk of human error

The SoHO Regulation also lists a number of **things that SoHO entities shall not do:**

- apply SoHO preparations to recipients **without proven benefit**, except in an approved clinical-outcome monitoring plan in an application for preparation process authorisation
- apply SoHO preparations **unnecessarily**
- advertise or promote particular SoHO using **misleading information**
- use allogeneic SoHO (i.e., SoHO from a person other than the recipient) for purposes other than the prevention or treatment of a medical condition or for MAR

Like for the standards on donor protection, the SoHO Regulation refers to technical guidance for the implementation of these standards, as further explained in the chapter on technical guidelines below.

Implementation of donor, recipient and offspring protection standards – the role of technical guidelines

➢ Referring back to articles 27, 56 and 59

The European Commission has the right to adopt further legal acts with binding rules on the implementation of any particular standard on donor, recipient or offspring protection.

In the absence of further legal acts, SoHO entities shall take into account:

- the most recent **technical guidelines from the ECDC** for the prevention of communicable disease transmission and the most recent **technical guidance from the EDQM** for the implementation of all other standards. These technical guidelines will be indicated on the EU SoHO Platform.
    - ➢ If SoHO entities can demonstrate during inspections that they are following these guidelines, **inspectors shall consider the standards of the Regulation to be met.**
- **other guidelines adopted by the Member State** as adequate to achieve compliance with the standards in the Regulation. Member States have to publish these guidelines on the EU SoHO platform.
    - ➢ If SoHO entities can demonstrate during inspections that they are following these guidelines**, inspectors shall consider the standards of the Regulation to be met.**
- other guidelines or technical methods
    - ➢ In this case, **SoHO entities need to provide a justification during inspections** that these guidelines or methods are adequate to achieve the level of quality and safety set out in each specific standard for which they decided to follow other guidelines or technical methods. This justification may be based on a demonstration of equivalence with ECDC/EDQM guidelines.

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 ca. 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.

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