This document aims to describe the views of the European Association of Tissue and Cells Banks (EATCB) and its sister Association – *Asociación Española de Bancos de Tejidos* (AEBT) – on the *Proposal for a Regulation of the European Parliament and of the Council on standards of quality and safety for substances of human origin intended for human application and repealing Directives 2002/98/EC and 2004/23/EC*. Thus, this analysis represents the position of European professionals involved in the collection, processing, and distribution of human tissues and cells for human application, who are responsible for the provision of such SoHO to the public health systems of the different Member States, and which govern their activities pursuant to the principles, shared with CoRe SoHO of:

- -Not-for-profit/non-financial gain;
- -Voluntary and altruistic donation;
- -Sufficiency;
- -Cost efficiency / patient accessibility to health care

The EATCB and the AEBT supported the EC in the process of revising the current EU legislation and welcome the definition of a new SoHO regulation, reaffirming once again the principles stated in the *CoRe SoHO statement welcoming the proposed Regulation on standards of quality and safety for substances of human origin (SoHO) intended for human application*.

We also endorse the position of the Rapporteur Nathalie Colin-Oesterlé in reference to her support for the current regulatory proposal: "*The **European Commission's proposal is good and comes at just the right time.** It will contribute to the overall target of building a strong Europe of Health that is able to offer EU citizens the best health security in the world and is prepared to tackle any future pandemics*"

Moreover, we see the proposed Regulatory Framework for SoHO as a great opportunity to improve quality and safety by:

- Including in its scope the tools for the correct **assessment of clinical outcomes**, by allowing the implementation of Clinical Investigational Plans (CIP) to assess safety and efficacy of SoHO innovations, under **conditional (temporary) authorisations**, issued based on the results of **standardized risk assessments**;
- **Improving transparency associated with the activities of National Competent Authorities**;
- **Refining technical competence and optimizing the use of resources available at Union level**, through the validation of collaborations and synergies between the different stakeholders in the field (namely external experts (professionals), NCAs, EDQM, ECDC, etc);
- **Promoting the evolution of current registries and mean of communication exchange** between NCAs and professionals, by developing the new SoHO-X Platform;
- **Improving the classifications of innovative SoHO**, based on technical knowledge and transparent and impartial assessments by the *SoHO Coordination Board* (SCB);

We also support, in principle, the majority of conclusions stated by the EC in the recitals of the Proposal for a Regulation.

However, it is noticeable that some generalization was applied in order to fit all SoHO in the same regulatory instrument, and this has created significant regulatory gaps for the activities associated with human tissues. Our three main concerns are highlighted in the present document:

1. **Complete lack of references related with the promotion of SoHO donation within the Union:** Instead of promoting the development of the European Health system and rely on the European society to increase the availability of SoHO, the proposal leaves the solution for the access to treatment and sufficiency, dependent on the supply performed by companies whose primary goal is financial gain and could result in a situation of unfettered distribution of SoHO with (potentially) inferior quality and safety, from 3rd countries.
   In 2019, 4.653.033 persons died in the EU, who are potential donors. This shows that despite of opting in or out models some Member States are lacking the necessary resources and organisation to convert potential donors into actual donors.
2. **Reliance on 3rd countries to supply our health systems: Absolut dependence on SoHO imported from 3rd countries**, for which the proposal defines **inappropriately relaxed safety and quality requirements** (compared with the requirements that are proposed to be imposed to the European Establishments in the current regulation).
   This impacts directly the sustainability of public health systems that currently support the activity of the Tissue Establishments in the different MS, as well recipients' health who might potentially receive SoHO collected and processed with lower safety and quality requirements.
   We propose to establish requisite criteria that must be met prior to the authorisation of import of SoHO preparations, namely:
   - The importation of SoHO will only be authorized if the following circumstances apply:
     a) There is a proven clinical benefit in the use of the SoHO that are intended to be applied.
     b) In cases SoHO preparations which are usually processed in the SoHO establishments of the Union, there is no availability of said SoHO preparations (self-sufficiency) at the time.
   - All imported SoHO preparations must be authorized under Article 21 prior to importation

   There is a clear intention of relaxing the criteria to import SoHO into the Union. It is not obvious why this has been defined this way. However, this impacts significantly (in a negative way) in the sustainability of tissue establishments in Europe. We consider that SoHO entities that aim to introduce SoHO or SoHO preparations according the harmonized EU criteria, must be limited in their distribution (i.e. individual authorisations per Member State, or case by case authorisations).

3. **Unsuitable and vague definitions, which potentially lead to a dubious definition of scope and confusion with the activities developed by the pharmaceutical sector**. We consider that definition should be done by intent. The definition of when a SoHO crosses a regulatory boundary and becomes a medical device or a medicine has always been challenging. For tissue allografts, this has been done historically by defining a list certain named processing activities, for example washing and cutting, as being out with the definition of substantial manipulation. This list will always be subject to omissions as knowledge and processes evolve. We propose that going forward, this definition be based on the **intent** of the process, that is to say if the process is not intended to alter the fundamental biomechanical or biological properties of donated SoHO that the resultant graft should be classed as a SoHO.

Other concerns, raised from the interpretation of the regulatory proposal are:

- The **lack of tools/methodologies to effectively assess the absence of financial gain (financial neutrality):** it is not clear how the EC and NCA will assess and ensure that SoHO Entities do not pursue financial gain associated with SoHO activities. EATCB and AEBT would welcome a clearer definition of criteria to define non for profit (financial neutrality) of entities dealing with SoHO. These criteria must impose rules to correctly ensure transparency (publicly available and proved financial information) of all organisations associated with SoHO activities.

- Missing rules for the **exchange of SoHO and SoHO preparations among MS** (as proposed in recital 47 of the current proposal). To address this concern, the new regulation should seek the "*Harmonisation of national systems to facilitate cross-border exchanges"* by considering:

    - Evolution of existing authorisation procedures among MS;
    - Harmonisation of practices of BE and TE;
    - Consensus definitions and classification of novel SoHO according the opinions of the newly proposed SoHO Coordination Board;
    - Economics and capacity of the different Health care Systems

- The tasks defined in **the Articles 51 and 61 are not compatible with the role of a physician in the current practices and structure of SoHO establishments**: A physician shall be responsible only for the protocols and policies covering the anamnesis procedures associated with SoHO collection, particularly, when the procedure may represent any risk for the donor.
  All the tasks described in Article 51 should be carried out by the Responsible Person and a physician must be **involved and consulted whenever there is impact for the safety of donor or patients**.