A new EU Regulation on standards of quality and safety for substances of human origin intended for human application

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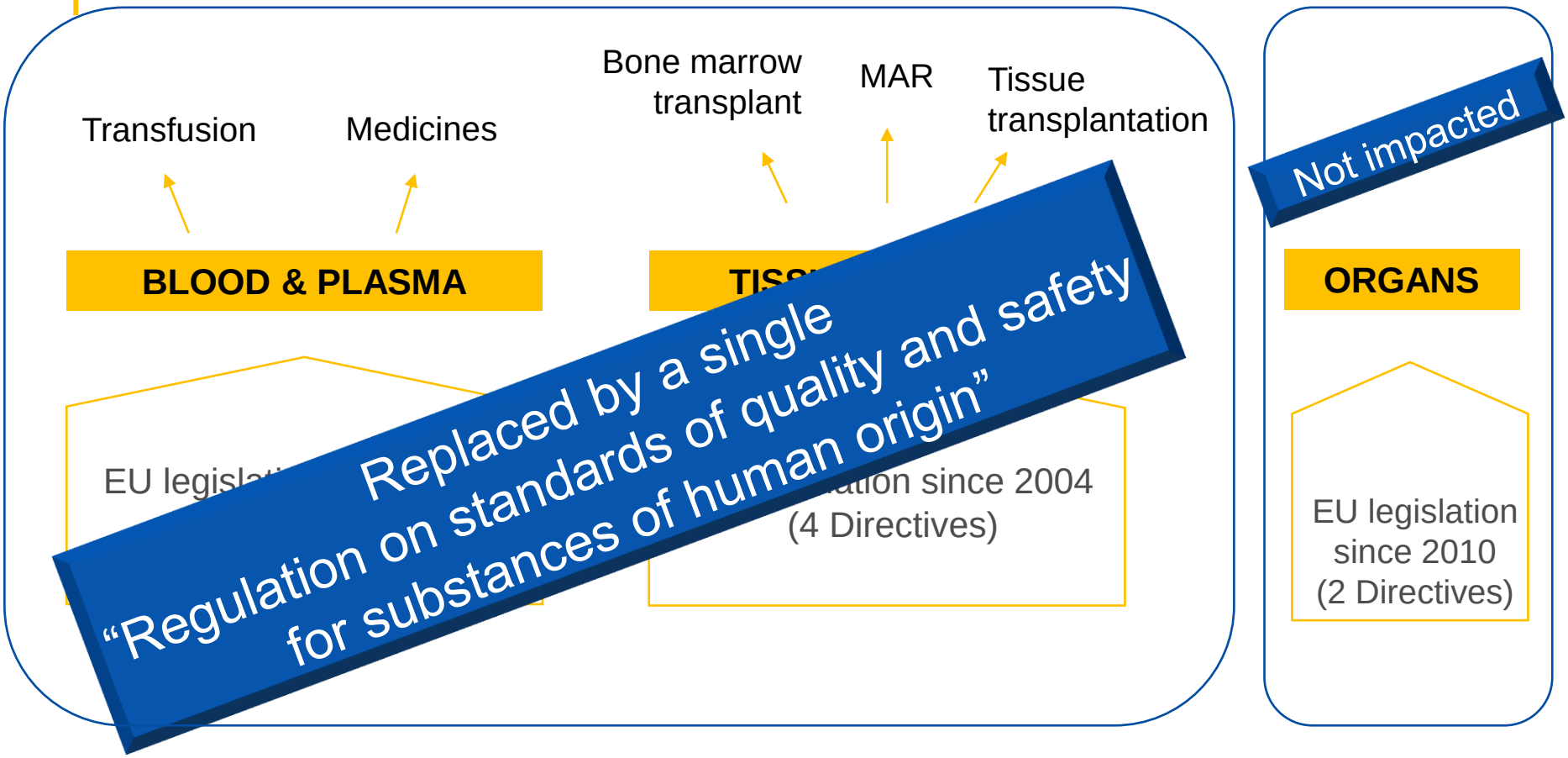
FAMHP symposium on vigilance
05/02/2024

Health

Disclaimer

- Political agreement reached on 14 December 2023 between the European Parliament and the Council on the Commission Proposal for a Regulation on the safety and quality of substances of human origin (SoHO).
- The proposal was published by the Commission in July 2022 and was amended through negotiations between the co-legislators during 2022 and 2023.
- The European Parliament and the Council must formally adopt the new Regulation during 2024. Until this happens, the text cannot be considered as final and is not presented here as legal text.
- **This presentation explains the concepts in the Regulation, as proposed by the Commission and amended during negotiations. The agreed text between the Council and the European Parliament is still subject to legal-linguistic revision.**

Current EU SoHO legislation on safety and quality



https://health.ec.europa.eu/blood-tissues-cells-and-organs/overview/proposal-regulation-substances-human-origin_en

English

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Proposal for a Regulation on substances of human origin

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On 14 December 2023, a political agreement was reached on the Commission's proposal for a Regulation on standards of quality and safety for substances of human origin intended for human application.

- Press release
- Factsheet

The Proposal was tabled in July 2022.

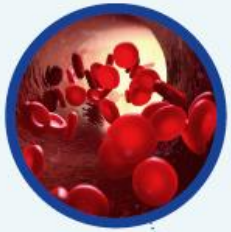
- Press release
- MEMO

By repealing the Blood Directive (2002/98/EC) and the Tissues and cells Directive (2004/23/EC) (both evaluated in 2019), the proposed Regulation concludes the revision of the legal framework for blood, tissues and cells, which was included in the REFIT Annex (#37 p.15) of the Commission's Work Programme for 2021.

Key improvements

NEW OR STRENGTHENED PROVISIONS

Supporting high safety and quality standards based on up-to-date technical rules for substances of human origin (SoHO)



Extending protective measures to donors and to offspring born from medically assisted reproduction

Extending the safety and quality framework to **other donated SoHO** such as breast milk

Improving **harmonisation** across Member States, facilitating cross-border exchange of SoHO and **improving patient access** to the therapies they need

Implementing **digital-ready policies**

Creating conditions for **safe, effective and accessible innovation**

Improving **crisis preparedness** to safeguard access to therapies

Key new and changed concepts

- **Scope and advice**
- **SoHO activities, entities and establishments**
- **SoHO Preparations and their authorisation**
- **Standards and hierarchy of technical guidelines**
- **Donor Protection and Voluntary Unpaid Donation**
- **Recipient and offspring protection**
- **Vigilance**
- **Supply continuity**
- **Digitalisation – the SoHO platform**

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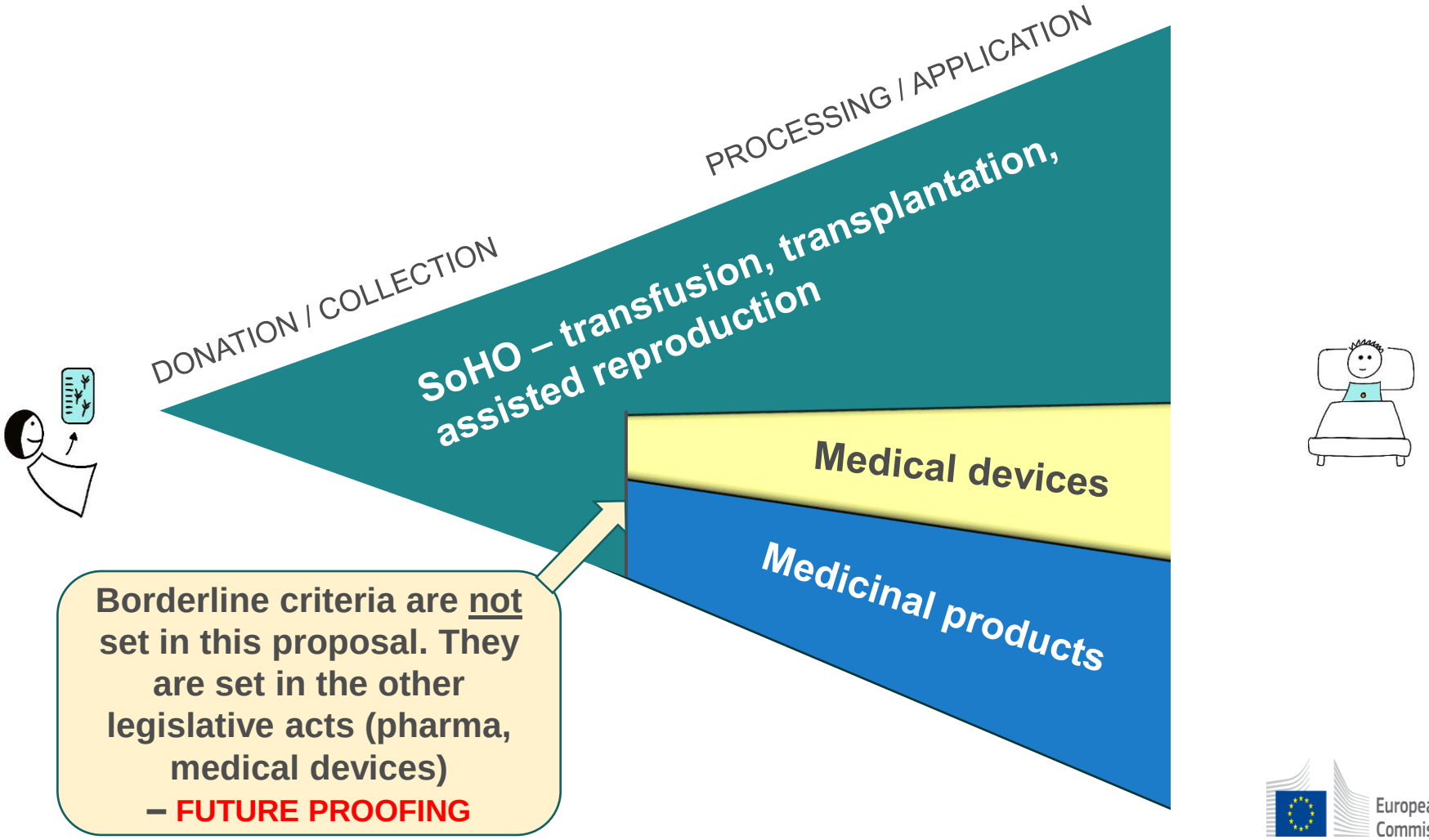
Scope: Regulation covers all steps for all SoHO (some limited provisions for autologous SoHO), unless processing or application steps fall under scope of other EU frameworks (art 2.3) – then SoHO regulation is restricted to certain relevant activities



Borderline criteria are not set in this proposal. They are set in the other legislative acts (pharma, medical devices) – FUTURE PROOFING

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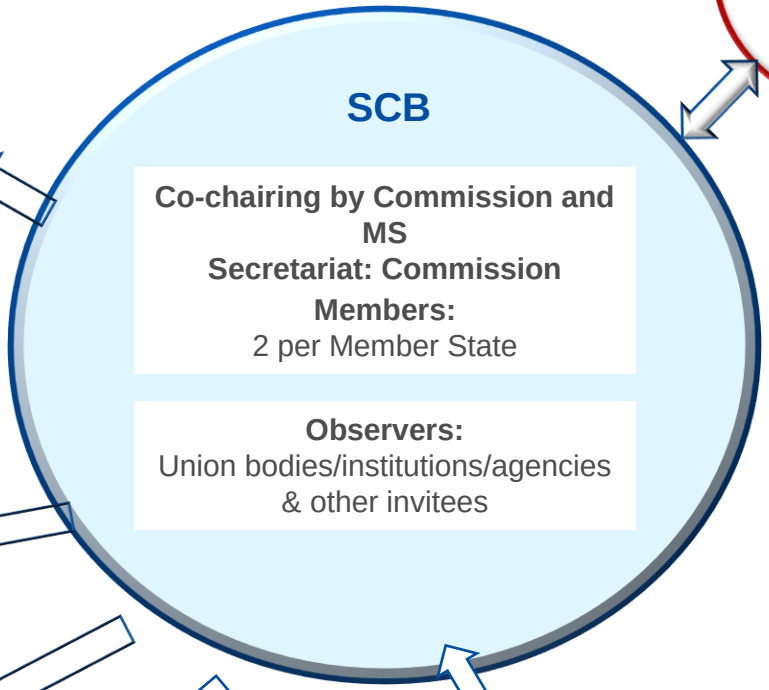
The SoHO Coordination Board (SCB) - supporting implementation in MS

Documentation of
- **best practices** for
  - supervisory functions
  - compensation conditions;
- **Indicative criteria** for critical SoHO and critical SoHO entities

Support for **joint oversight activities**
- inspections
- Preparation assessments

Support for **coordination during emergencies**

Support to COMM on the specifications for the **SoHO Platform**



Advisory bodies in other legislative frameworks

Opinions on **regulatory status**

Record of:
- national decisions on regulatory status
- Compendium of advice given on regulatory status

Exchanges on good practices with Expert bodies – ECDC/ EDQM and with EMA

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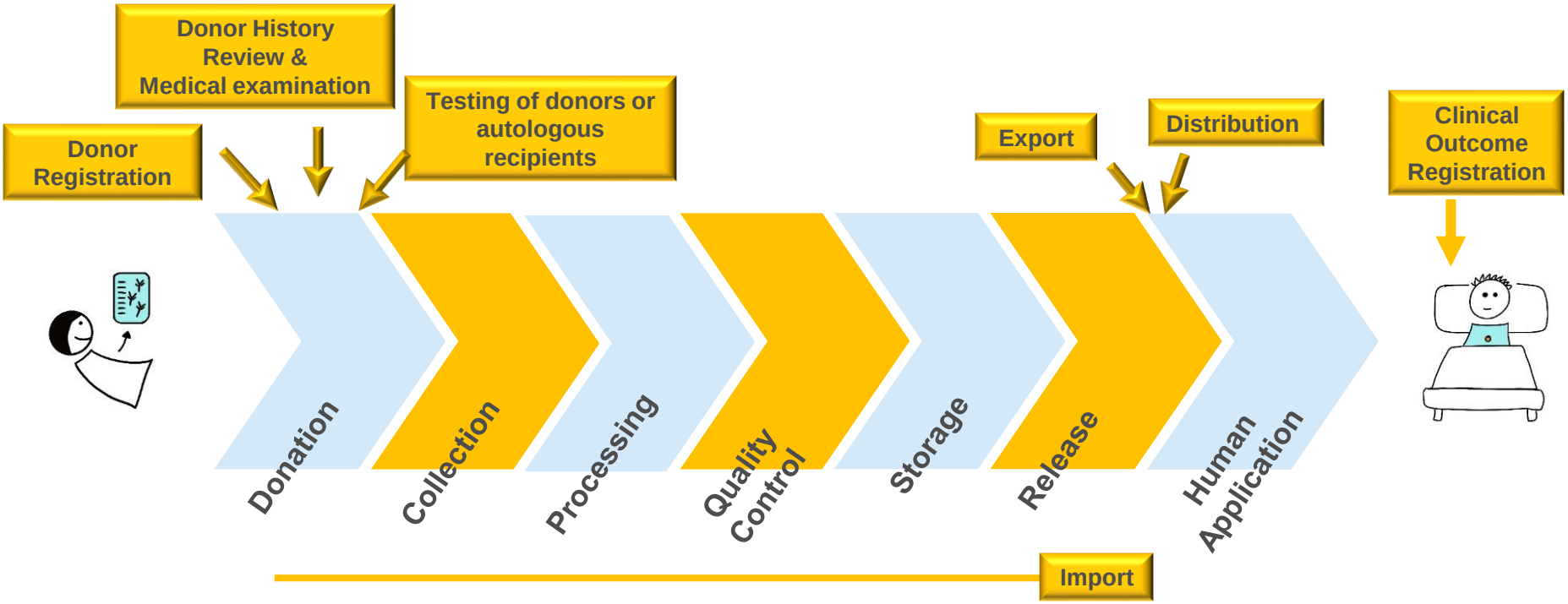
Supervision of all SoHO Activities that directly impact safety, quality or effectiveness



Any actor organising one or more SoHO activity/ies needs to register as SoHO entity with the Competent Authority

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….but risk-based authorisation, ensuring efficient use of authority resources

A **SoHO entity** carries out **one or more SoHO activities**

A **SoHO establishment is a SoHO entity that** carries out at least

- **Both processing and storage, or**
- **Release, or**
- **Import, or**
- **Export**

Note: ***CAs may regulate a SoHO entity as a SoHO establishment, even if it does not meet the criteria above, if it considers that the entity has a particularly important impact (e.g. a testing laboratory that tests donors for a whole region or country, a register that identifies and selects donors for one or more Member States).***

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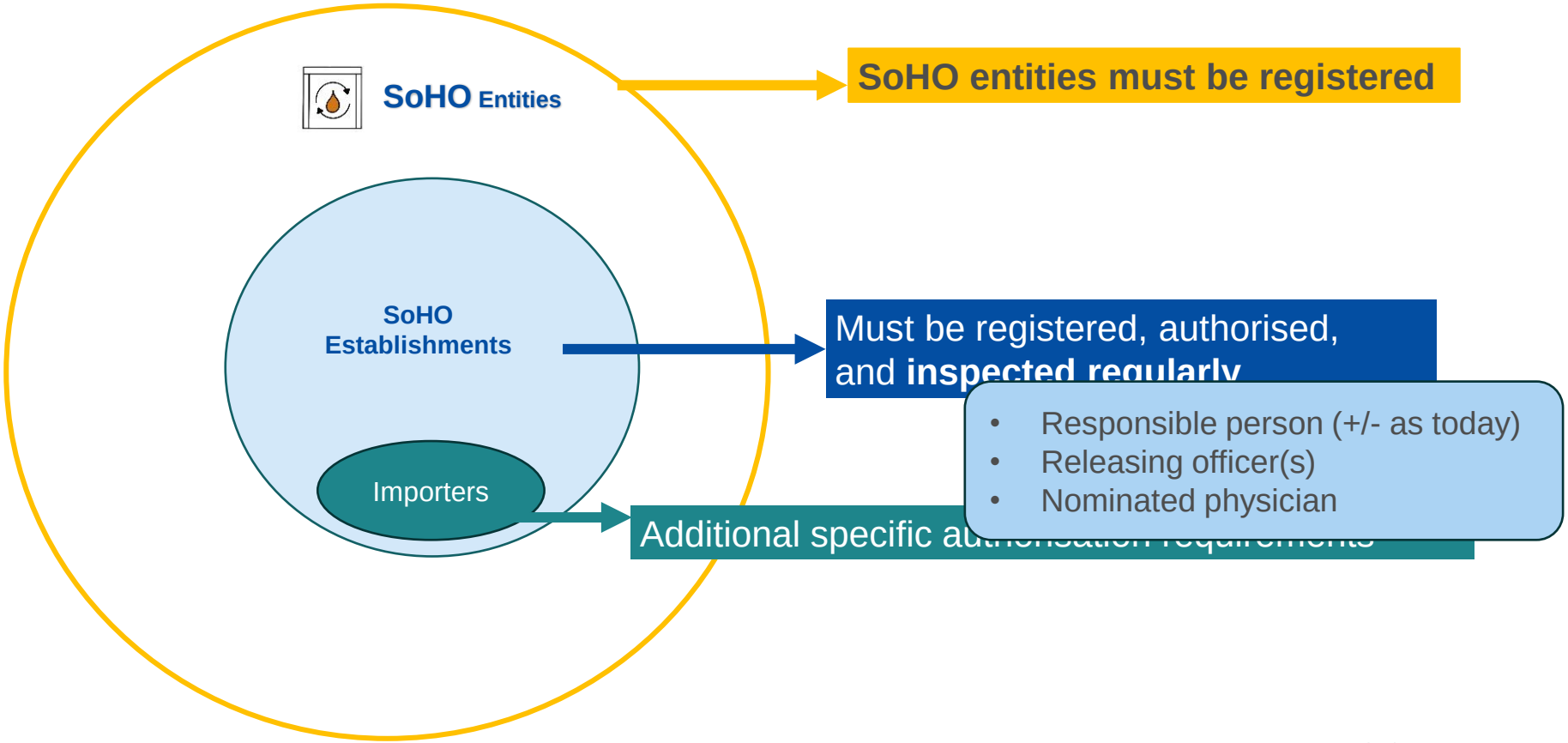
The concept of **SoHO entities** and **SoHO establishments:** graded approach to oversight - high level of transparency



Note: ***CA may inspect any SoHO entity, as it considers necessary and may upgrade an entity to establishment status***

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SoHO Preparation Authorisation – robust evidence of safety and efficacy

What is a 'SoHO Preparation'?

A particular SoHO that has been **subjected to processing,** and where relevant other SoHO activities, **has a specific clinical indication and is intended for immediate application to a recipient or for distribution.**

→ Must be **authorised**

EXAMPLE

SoHO	**SoHO Preparations**	
Blood	Plasma	
	Red blood cells	
	Platelets	

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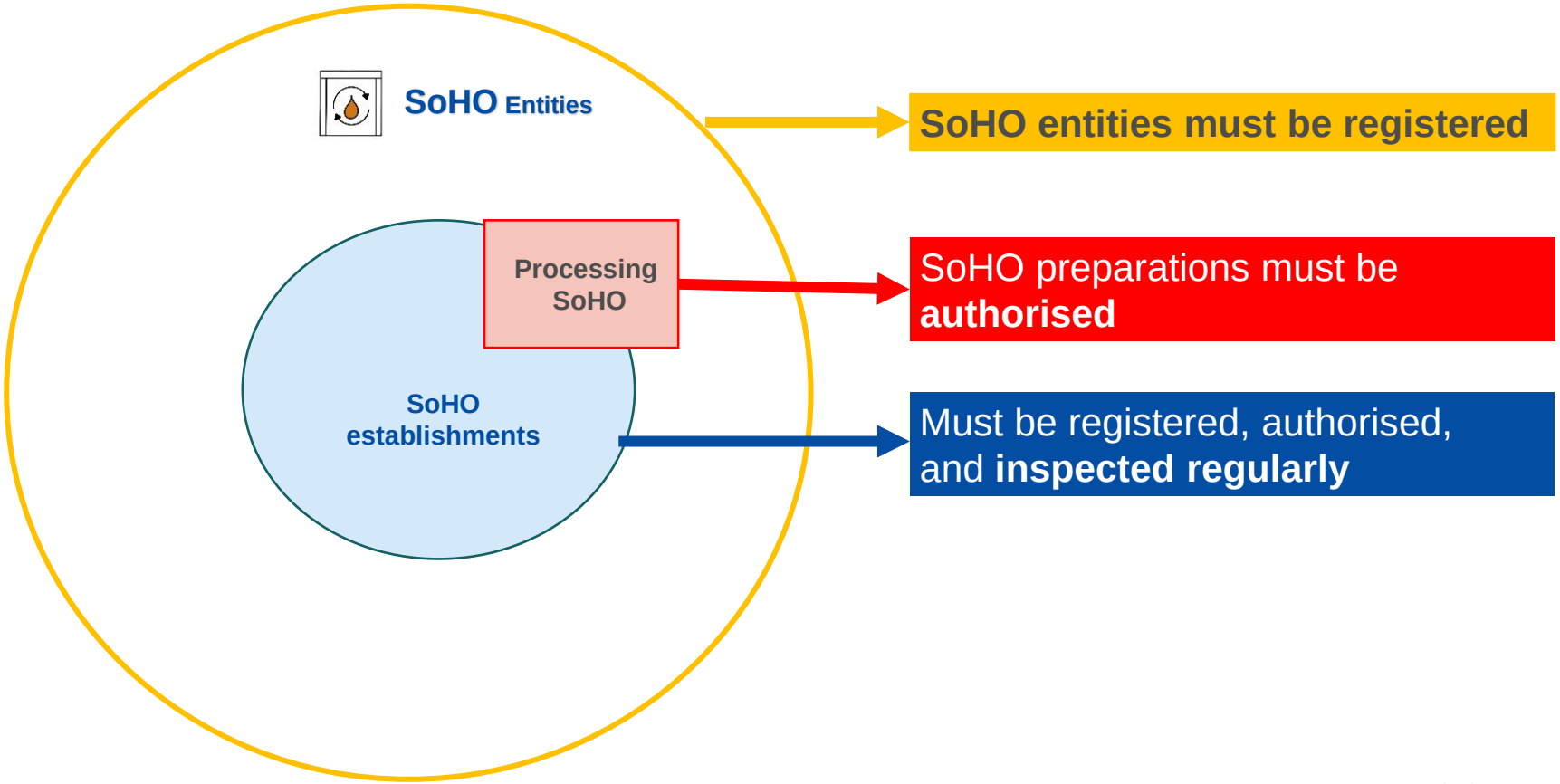
The concept of **SoHO entities** and **SoHO establishments:** graded approach to oversight - high level of transparency



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SoHO Preparation Authorisation

Taking into account any relevant EDQM monograph

1 Systematic Benefit:Risk Assessment to determine the evidence available on safety, quality and effectiveness

2 Submission of an application, including laboratory validation and other safety, quality and effectiveness data and, where relevant, a clinical outcome monitoring plan proportionate to risk

3 Assessment of the application by the competent authority

- Grant authorisation for the SoHO preparation
- **OR**
- Grant of an approval of the Clinical Outcome Monitoring plan
- **OR**
- Refuse authorisation

4 Assessment by the competent authority of evidence of safety, quality and effectiveness data gathered in clinical outcome monitoring

- Grant authorisation
- **OR**
- Refuse authorisation

Based on preparatory work done by GAPP Joint Action
(incl. stakeholders from 17 countries: 15 CAs & professional associations)

GAPP

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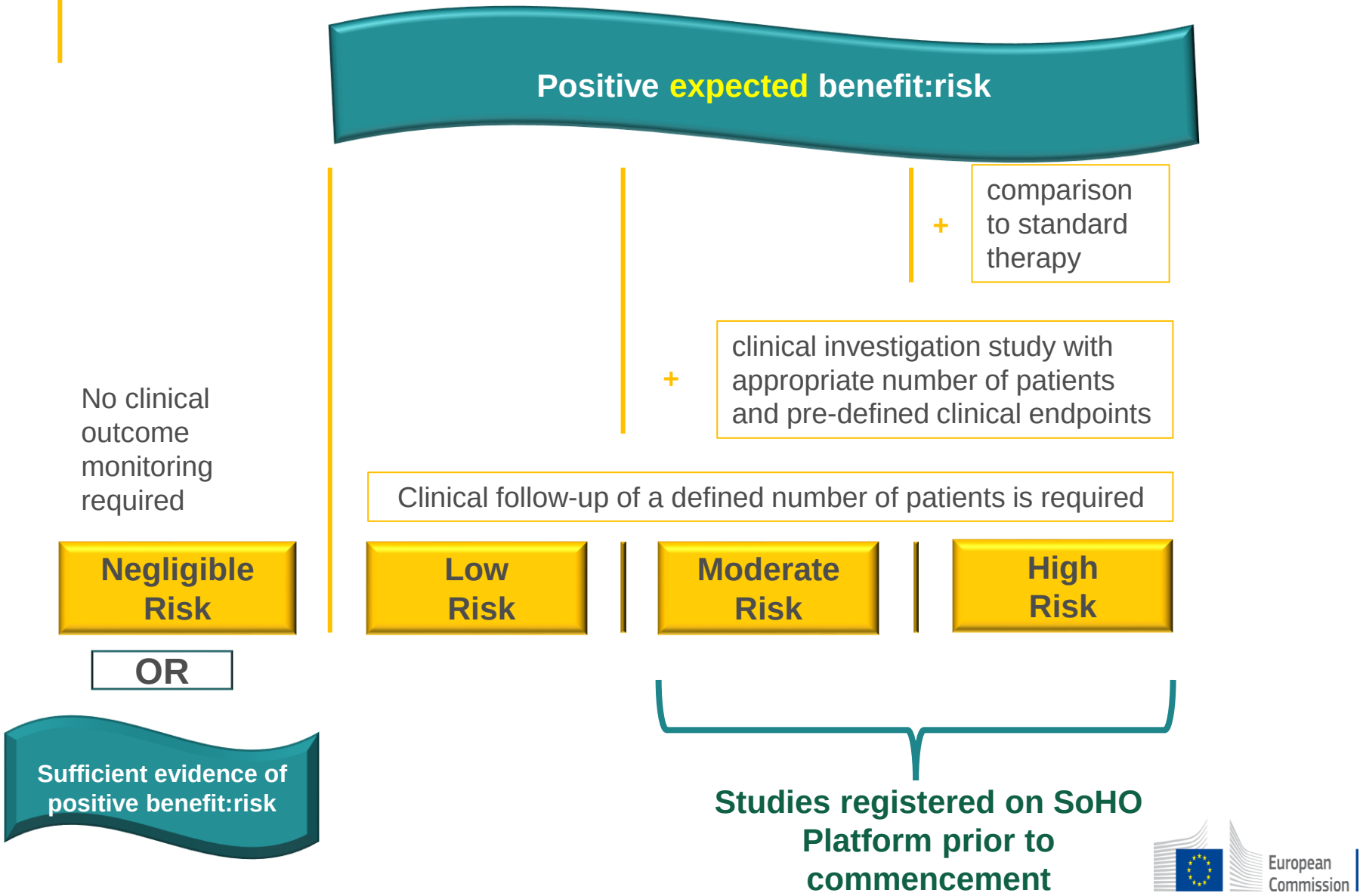
Clinical Outcome Monitoring Plans for gathering further evidence of safety and effectiveness in recipients



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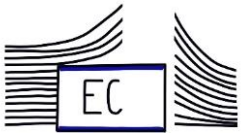
Implementation of high level standards through technical guidelines – staying up-to-date with the science in an agile way

SoHO entities shall follow the highest available levels of standards (Art. 56 & 59):

Level 1

Commission Implementing Legislation → "where the Commission deems necessary"



If none:

Level 2

Technical Guidance on the EU SoHO Platform → Published & updated by ECDC/EDQM

Inspectors shall deem the standards to be met

OR:

"Equivalent" Guidance → Deemed by CAs to achieve equivalent standards

MS shall demonstrate compliance with standards – may do so by demonstrating equivalence to ECDC and EDQM

If none:

Level 3

Other guidelines or methods based on international standards or scientific evidence

Entities shall demonstrate equivalence to inspectors – may do so by demonstrating equivalence to ECDC and EDQM

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SoHO Donor Protection – significantly strengthened

Protection of SoHO living donors before, during, and after the donation

- Including for donations by relatives
- Information & consent
- Physical and mental integrity, non-discrimination, data protection & safeguarding of anonymity (with some exceptions e.g. ID of MAR parents when allowed or obliged in MS)
- Donor health evaluation
- Risk-proportionate approach to donor monitoring: registration of donors subjected to
    - surgical procedures,
    - medicinal product treatment,
    - frequent or repeated donations implying risk to health
- Required reporting of serious adverse reactions in donors

Protection of the dignity and integrity of SoHO deceased donors

- Information & consent by relatives, when applicable

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Voluntary & Unpaid Donation

Principle maintained
Based on Recommendations of the Council of Europe Committee on Bioethics

- **NO financial incentives or inducements** to donate
- **Compensation** of living donors for losses can be allowed in accordance with the principle of VUD
- When a Member State allows compensation – **upper limit to be set in national legislation** – transparent criteria based on best practices established by the SCB
- Compensation conditions set in MS to be **shared** with the other MS via the SCB
- Donation **promotion and publicity activities** must not refer to compensation (without prejudice to national laws on information provision)

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Recipient and offspring protection

- Identification and mitigation of risks from **transmissible infectious, genetic, malignant diseases**
- Identification and mitigation of risks from **toxins, contaminants** from the environment, other donations, the personnel, the equipment, reagents etc.
- Identification and mitigation of risks of **detrimental effects on inherent properties of the SoHO concerned**
- Identification and mitigation of risks of **harmful immune reactions**
- Application of national rules regarding the **maximum numbers of offspring** from one SoHO donor
- **No application of SoHO unnecessarily** or in cases where there is no proven benefit
- No promotion of SoHO application based on **misleading information**
- No human application of SoHO without therapeutic or assisted reproduction objective (i.e. **no cosmetic or exclusively nutritional applications**)

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Vigilance overview – largely unchanged

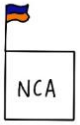
SoHO Entities

Send SAR/SAE notification & SAR/SAE investigation report to their CA

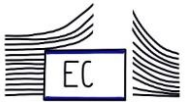
Competent Authorities

- Verify info of SAR/E notifications & investigation reports, assess the results of the investigation, inform the entity
- Send annual summary of SAR/E notifications & investigation reports received to their **SoHO National Authority**
- Launch **SoHO rapid alerts**

Communication with CAs from other frameworks



- Submits annual summary to the **EU SoHO Platform**
- Publishes aggregated summary for their MS



- Aggregate the summaries from the **SoHO National Authorities**
- publish annual SoHO vigilance report

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Vigilance enhancements

- Inclusion of SAR reporting requirement for SAR in **living SoHO donors**
- Clarification that **SAR/E detected during clinical outcome monitoring** must be reported
- Obligation for reasonable efforts to encourage recipients of MAR donations to communicate information on **genetic conditions in offspring** – when serious these are reportable as SAR
- **Role of ECDC** for SAR concerning infectious disease transmissions
- Formalisation of **communication** requirements with **CAs in other sectors**, when appropriate
- Clarification that **loss of SoHO** constitutes an SAE in defined situations
- CAs to provide **guidance and templates** to professionals and to **inform relevant SoHO entities of Rapid Alerts** received

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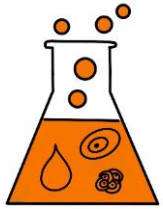
Resilience of Supply



Critical SoHO

'Critical SoHO' are SoHO that for which an insufficient supply will result in serious harm or risk of harm to patients or a serious interruption in manufacture of critical products regulated by other legislation.

A '**critical SoHO entity**' is a SoHO entity that carries out activities contributing to the supply of critical SoHOs and the scale of those activities is such that a failure to carry them out cannot be compensated by activities of other entities or alternative substances or products for recipients.

Supply of **critical SoHO** is protected by:

- **Obligations on Member States** to ensure a sufficient, adequate and resilient supply
  - Facilitate donation
  - Communication and education
  - Optimal use
- **Activity data collection** and monitoring
- Supply **alerts**
- National **SoHO emergency plans**
- SoHO Entity **emergency plans**
- **Derogations** and additional measures in emergency situations

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Digitalisation – efficiency, transparency, monitoring

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Next steps
Entry into Force and Date of Application

- Review and editing by lawyer linguists
- Translation into the EU official languages
- Formal approval by the Council and the European Parliament
- The Regulation will enter into force 20 days after its publication in the Official Journal of the European Union – during **2024**
- 3 years before the provisions become applicable – **2027** - (an additional year for some provisions)

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Thank you

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