Proposal for a Regulation on standards of quality and safety for substances of human origin intended for human application

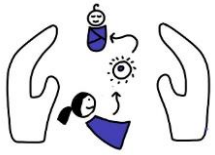
SoHO oversight system: a focus on inspection and authorisation process at national and EU level
28 March 2023

Health

2019 Evaluation

Existing legislation **improved safety and quality** of blood, tissues and cells in the EU – but short-comings identified

1. Rules to protect patients don't keep pace with changing risks and new technologies



2. Insufficient measures to protect donors and children born from donated gametes and embryos

3. Member States have divergent approaches to oversight – barriers to exchange

4. Sub-optimal framework to support safe and effective innovation

5. Vulnerability to supply interruptions

CoVID confirmed problems

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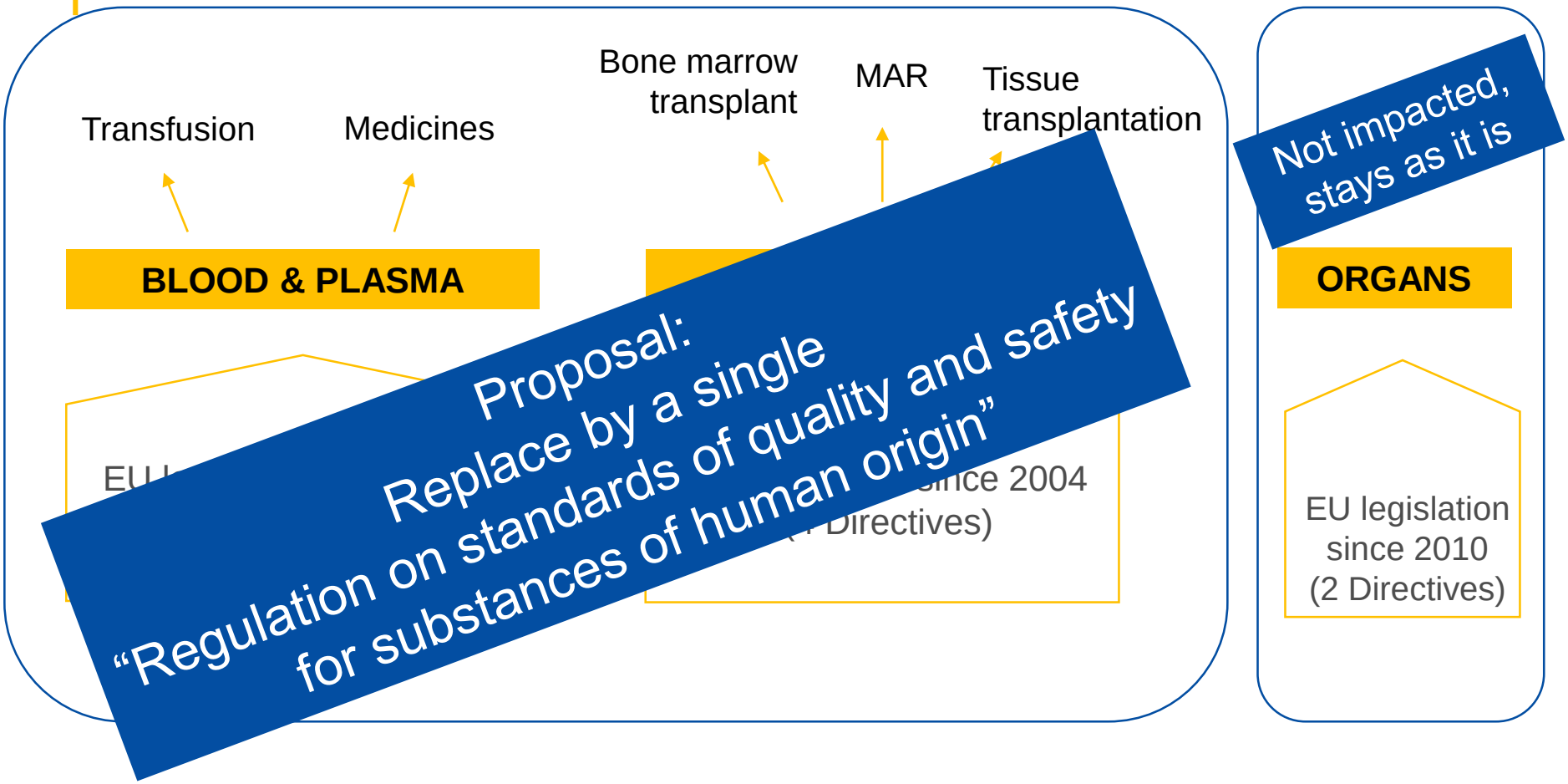
Current EU SoHO legislation on safety and quality



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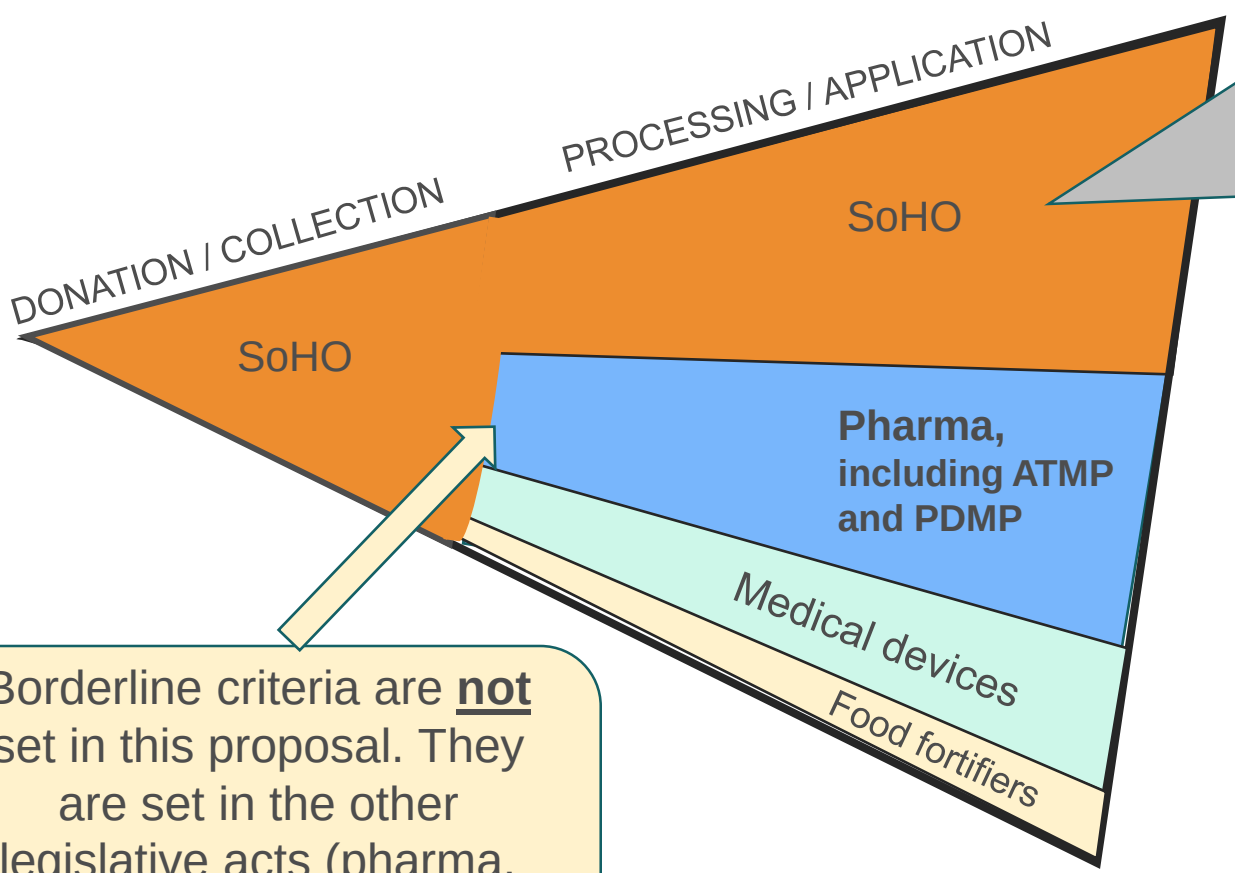
Proposal for a Regulation published in July 2022

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

Key new and changed concepts

- **Scope**
- **Risk based-approach to SoHO supervisory activities**
  - **SoHO activities**
  - **SoHO entities and SoHO establishments**
- **SoHO Preparations and their authorisation**
- **Competent Authorities, Commission controls and the SoHO Coordination Board**
- **Standards and hierarchy of technical guidelines**
- **Donor Protection and Voluntary Unpaid Donation**
- **Resilience of supply**
- **Digitalisation – the SoHO platform**

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 donation and collection (or just collection for autologous)



Including BTC for transfusion, transplantation, medically assisted reproduction as well as currently unregulated SoHO (FMT, breast milk, …)

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

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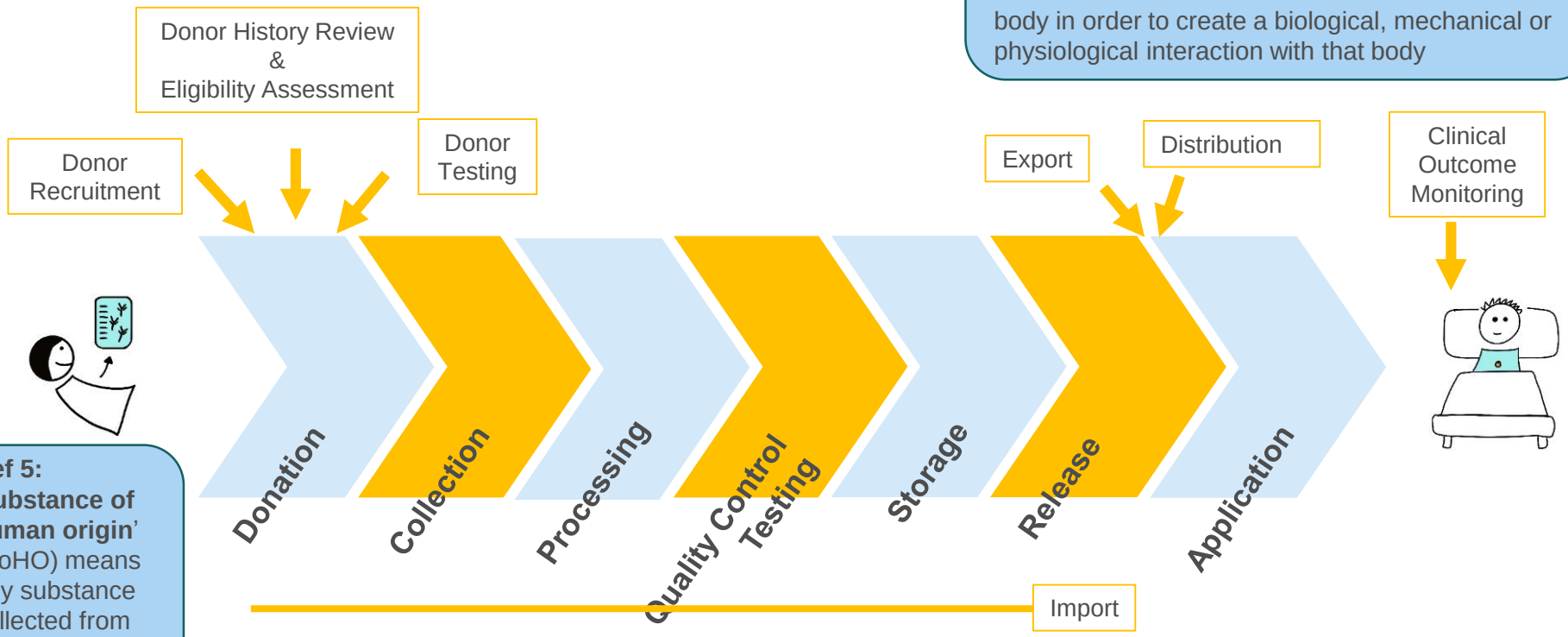
Supervision of all SoHO Activities that directly impact safety or quality

Def 6: '**human application**' means inserted, implanted, injected, infused, transfused, transplanted, ingested, transferred (as in transfer to the uterus or fallopian tube of a woman), inseminated or otherwise added to the human body in order to create a biological, mechanical or physiological interaction with that body



Def 5: '**substance of human origin**' (SoHO) means any substance collected from the human body in whatever manner, whether it contains cells or not and whether those cells are living or not.

Requires registration with the Competent Authority

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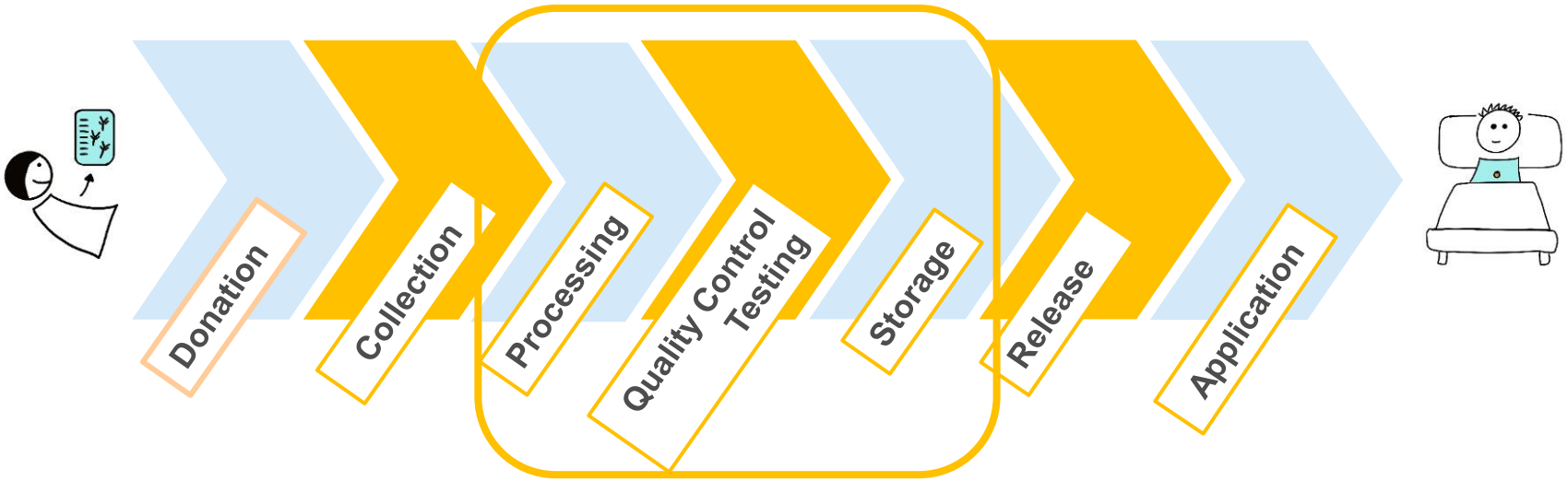
….but risk based measures for efficient use of authority resources

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

A **SoHO establishment** carries out at least **processing and storage**



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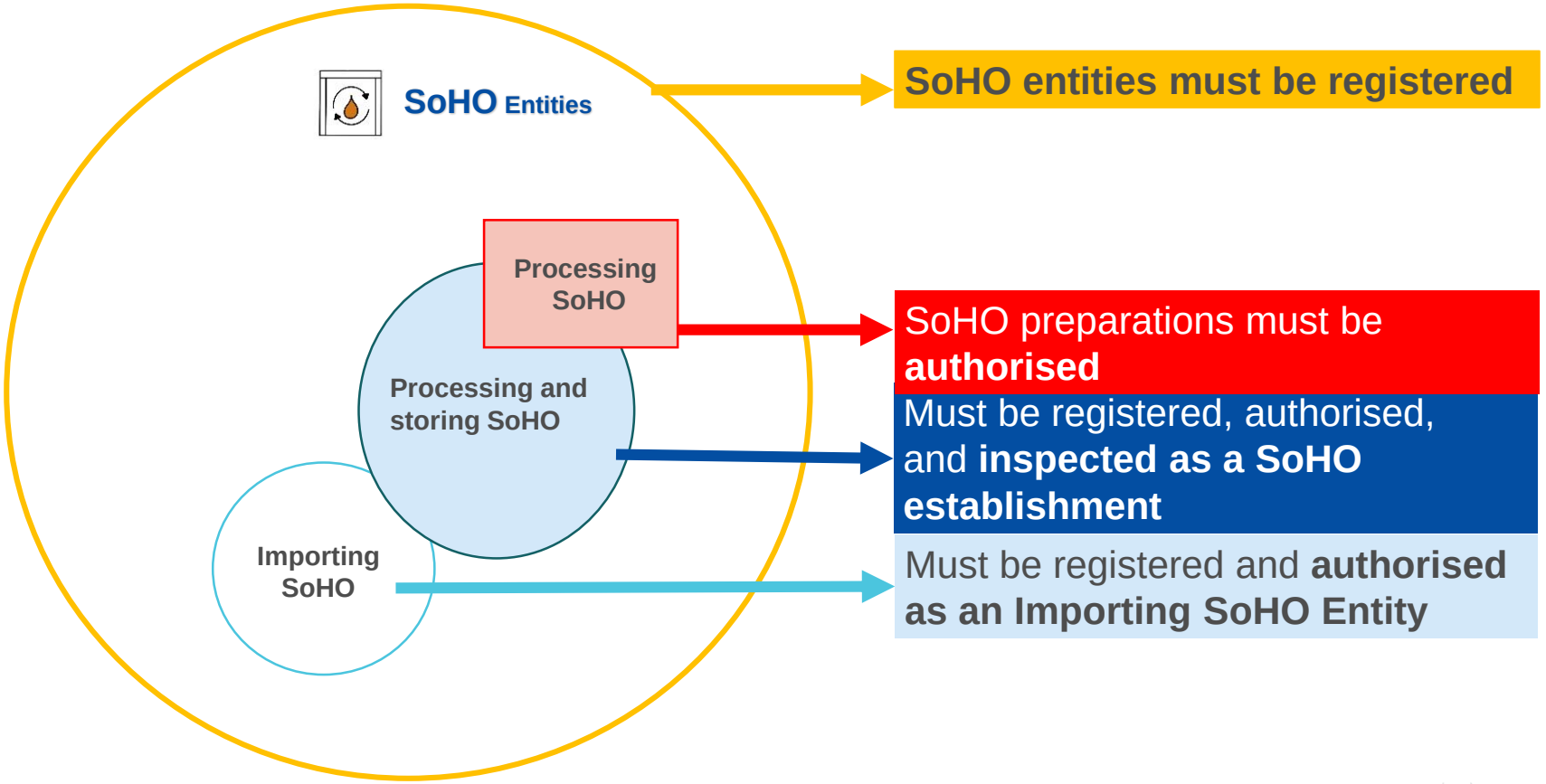
The concept of **SoHO entities** and **SoHO establishments:** graded approach to oversight - high level of transparency



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SoHO Preparation Authorisation – robust evidence of safety and efficacy

What is a 'SoHO Preparation'?

A particular SoHO that has been **subjected to one or more SoHO activities, including processing,** with **pre-defined specification** and **specific clinical indication**

→ Must be **authorised**

Example:

SoHO → **SoHO Preparation**

Blood → Plasma

Blood → Red blood cells

Blood → Platelets

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SoHO Preparation Authorisation

Taking into account any relevant EDQM monograph

1 Systematic Risk Assessment to determine the requirements for authorisation

2 Submission of an application dossier, including laboratory validation and, where relevant, a clinical outcome monitoring plan proportionate to risk

3 Assessment of the application by the competent authority

Grant authorisation **OR** Grant of a **conditional** authorisation to allow evidence gathering **OR** Refuse authorisation

4 Assessment by the competent authority of evidence gathered

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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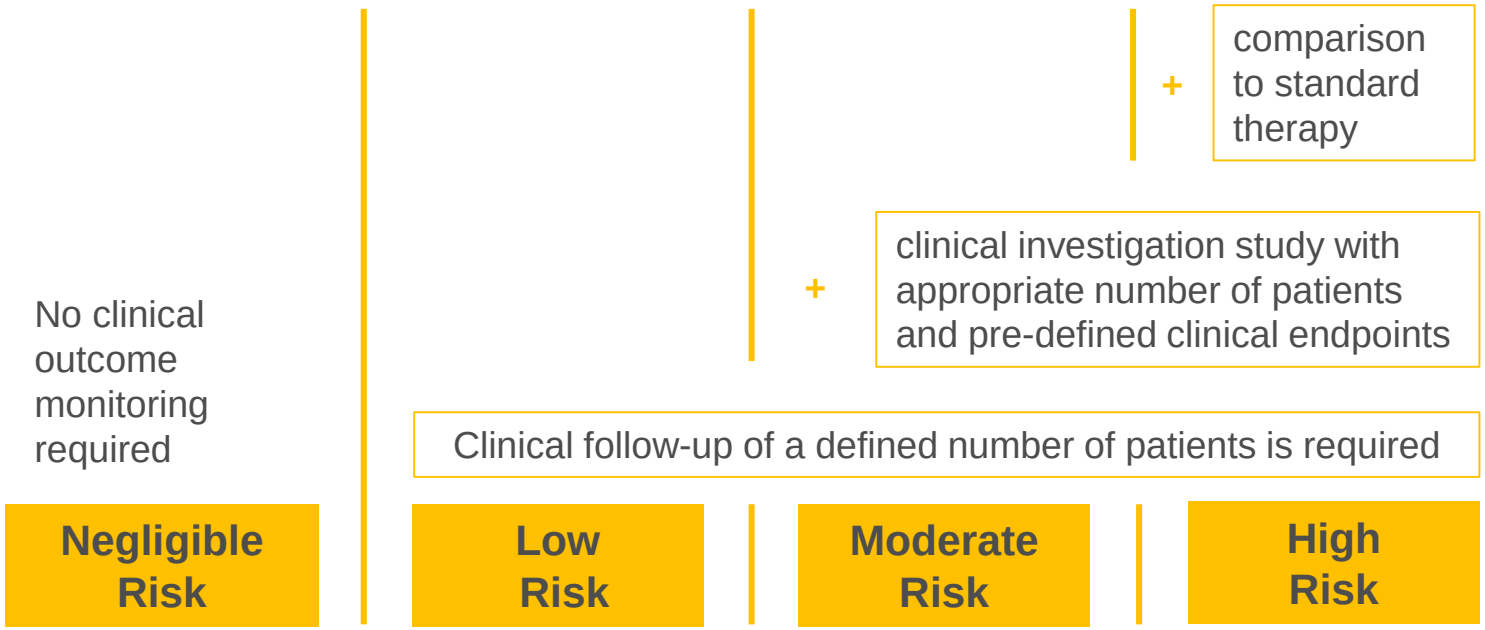
Clinical Outcome Monitoring Plans for Conditional authorisation



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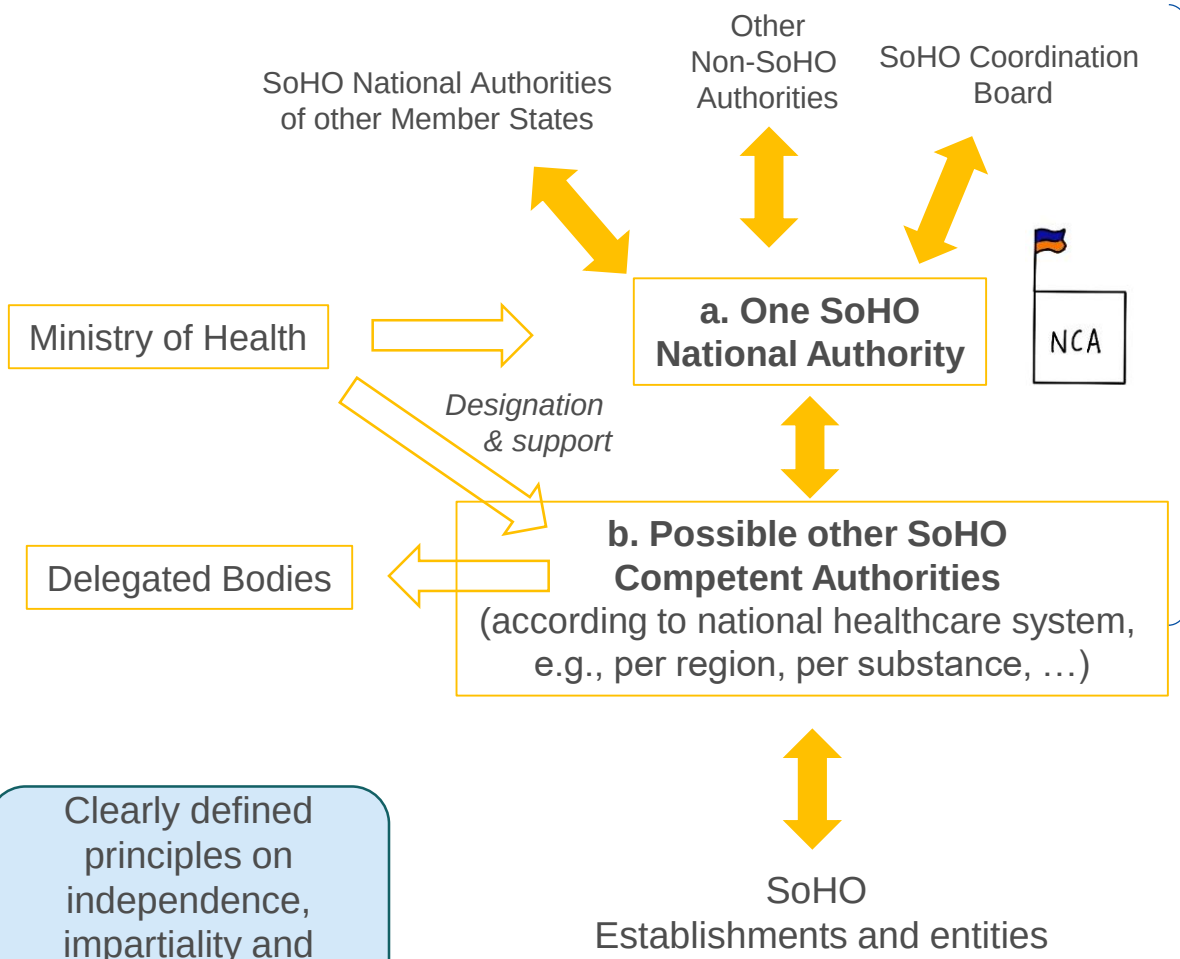
Competent Authorities – working together for improved oversight

2 Main Roles:



a. Liaison & Cooperation

b. SoHO Supervisory Activities

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Commission Controls to increase inter-MS confidence and exchange

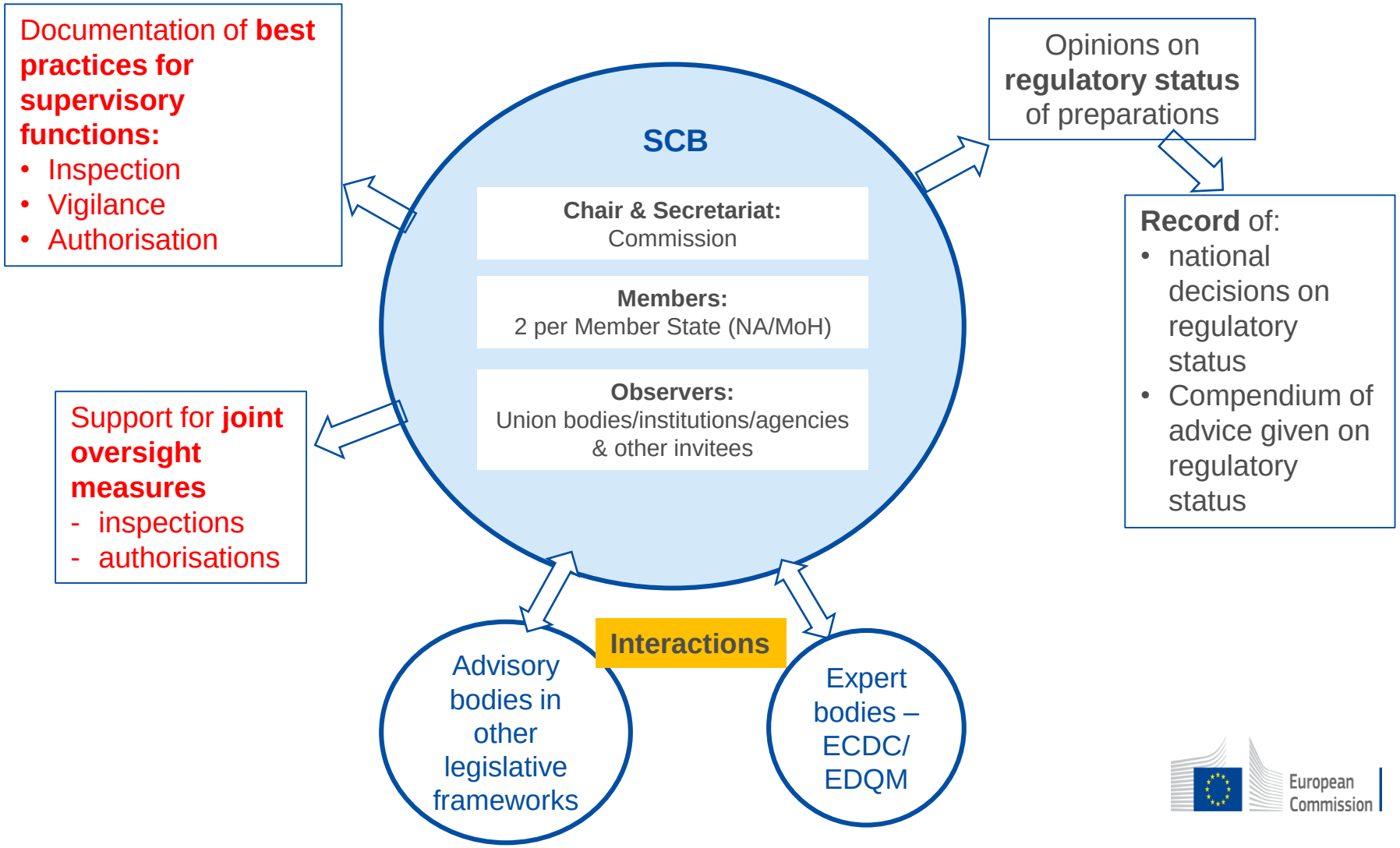
Based on similar Commission controls in the Food, Medical device and clinical trial fields

The Commission shall perform controls/audits in Member States (Art.70)

Topics covered: requirements for competent authorities and delegated bodies, SoHO supervisory activities, and notification and reporting requirements

Organisation: based on best practices collected by SCB, aiming to avoid unnecessary administrative burden, and may include Member State experts

The SoHO Coordination Board (SCB) - supporting MS to implement the Regulation



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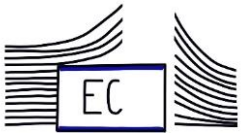
Implementation of high level standards through technical guidelines – staying up-to-date with the science in an agile way

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 & upda by ECDC/EDQM

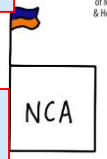
"Inspectors shall accept"

edqm
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

OR:

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

"Entities shall demonstrate equivalence to inspectors"



If none:

Level 3

Methods based on international standards or scientific evidence

"Entities shall demonstrate equivalence to inspectors"

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SoHO Donor Protection – significantly strengthened

SoHO entities shall ensure high levels of safety of SoHO living donors (…) before, during, and after the donation. (Art. 52)

Standards for Donor Protection (Art. 53)

- Including for donations by relatives
- Information & consent
- Data protection & safeguarding of anonymity
- Donor health evaluation
- Risk-proportionate approach to donor monitoring: registration of donors subject to
  - surgical procedures,
  - hormone treatment,
  - frequent or repeated donations.

+ Donor adverse occurrence reporting requirements
+ Possibility for self reporting
(Art. 35 and 47)

Voluntary & Unpaid Donation

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

SoHO entities shall not provide financial incentives or inducements to SoHO donors or their relatives or any persons granting authorisation on behalf of the prospective donors, in accordance with national legislation (Art. 54)

SoHO entities may compensate or reimburse SoHO donors as provided for by their competent authorities (…)

- **Compensation** or reimbursement for losses related to donation are permissible
- Based on fixed-rate allowances within **an upper limit set by Member State**
- Allowances must be **financially neutral** and consistent with standards for VUD

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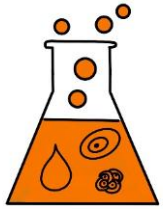
Resilience of Supply



Critical SoHO

‘Critical SoHO’ are SoHO that for which an insufficient supply will result in serious harm or risk of harm to patients (Art. 3)

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 patients (Art. 3)

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

- **Activity data collection** and reporting (Art.44)
- Supply **alerts** (Art. 63)
- National **SoHO emergency plans** & SoHO Entity emergency plans (Art. 62 & 66)
- **Derogations** and additional measures in emergency situations (Art. 64 & 65)

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Digitalisation – efficiency, transparency, monitoring

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Impact on Member States

Changes for Competent Authorities

New Tasks

- Registration of new entities: checking if SoHO establishments or critical SoHO entities or if SoHO preparation authorisation is needed – large number (upfront implementation only)
- SoHO preparation authorisation systems including assessment of outcome data (many already do this)
- National emergency plans (where not existing)
- Co-ordination with CAs in other sectors (many already do this or are even the same organisation).

Reducing the workload

- Many establishments become entities – stop mandatory inspections
- Inspection scheduling risk based instead of every 2 years – efficiency
- The digital platform provides several support tools that authorities can use for national oversight tasks (registration, preparation authorisation, data collection)
- Opportunities for authorities to use each other's expertise (e.g., joint inspections, joint assessments)
- Opportunities to obtain expert advice from bodies like EDQM/ECDC
- Training by COMM

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Thank you

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