45° Convegno Nazionale di Studi di Medicina Trasfusionale
Rimini | 29-31 maggio 2024
SIMTI

Nuovo regolamento SOHO e potenziale impatto sul sistema trasfusionale

Simonetta Pupella

Centro nazionale sangue, ISS

CENTRO NAZIONALE SANGUE
Istituto Superiore di Sanità

La sottoscritta, Simonetta Pupella in qualità di Relatrice
dichiara che

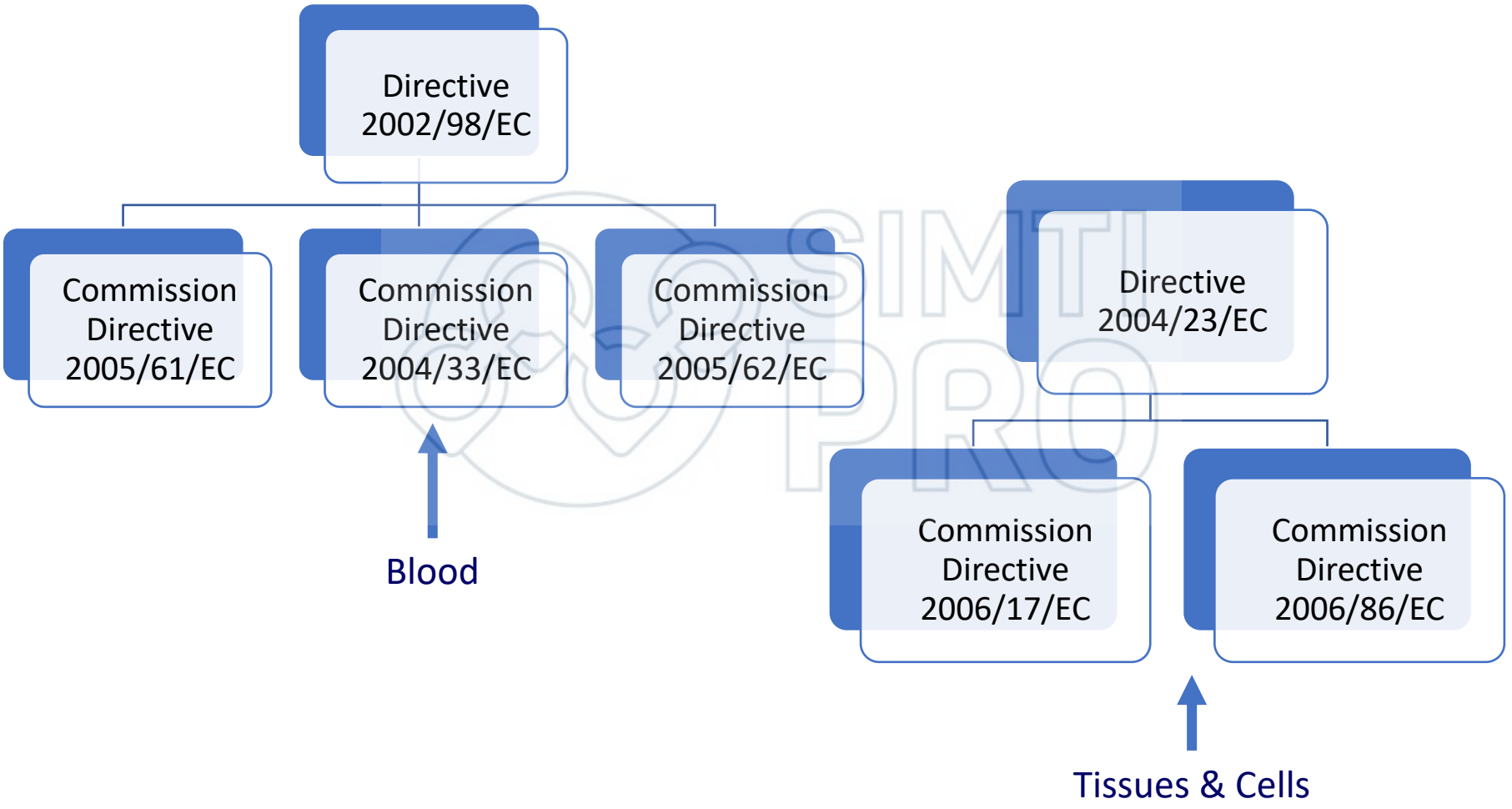
nell'esercizio della Sua funzione e per l'evento in oggetto, NON È in alcun modo portatrice di interessi commerciali propri o di terzi; e che gli eventuali rapporti avuti negli ultimi due anni con soggetti portatori di interessi commerciali non sono tali da permettere a tali soggetti di influenzare le sue funzioni al fine di trarne vantaggio.

NEW REGULATION

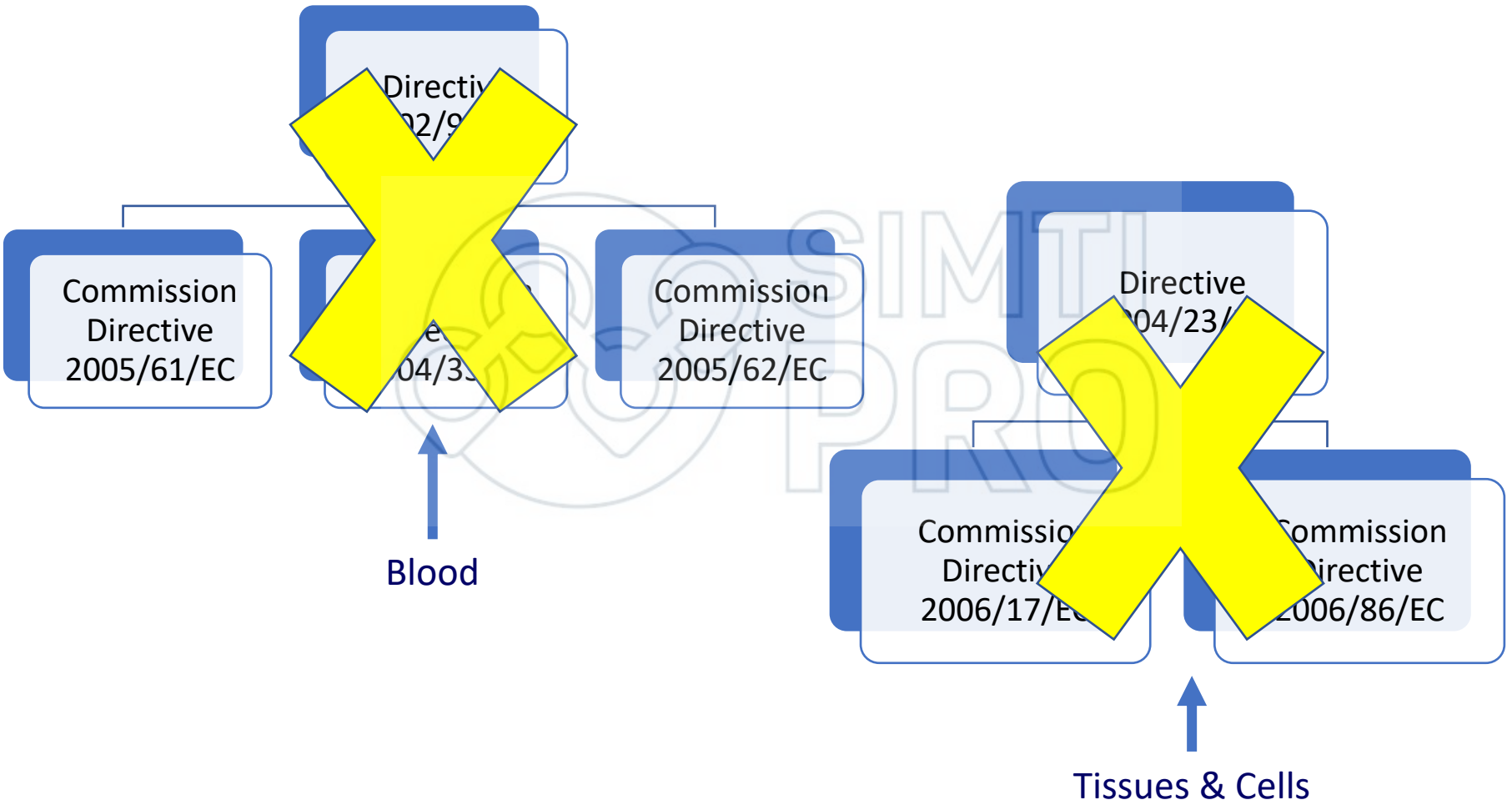
- Scope and advice
- SoHO activities, entities and establishments
- SoHO Preparations and their authorisation
- Standards and hierarchy of technical guidelines
- Donor Protection and Voluntary Unpaid Donation
- Recipient and offspring protection
- Vigilance
- Supply continuity
- Digitalisation – the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

With the permission of DG-SANTE SoHO team

CURRENT REGULATORY FRAMEWORK



CURRENT REGULATORY FRAMEWORK



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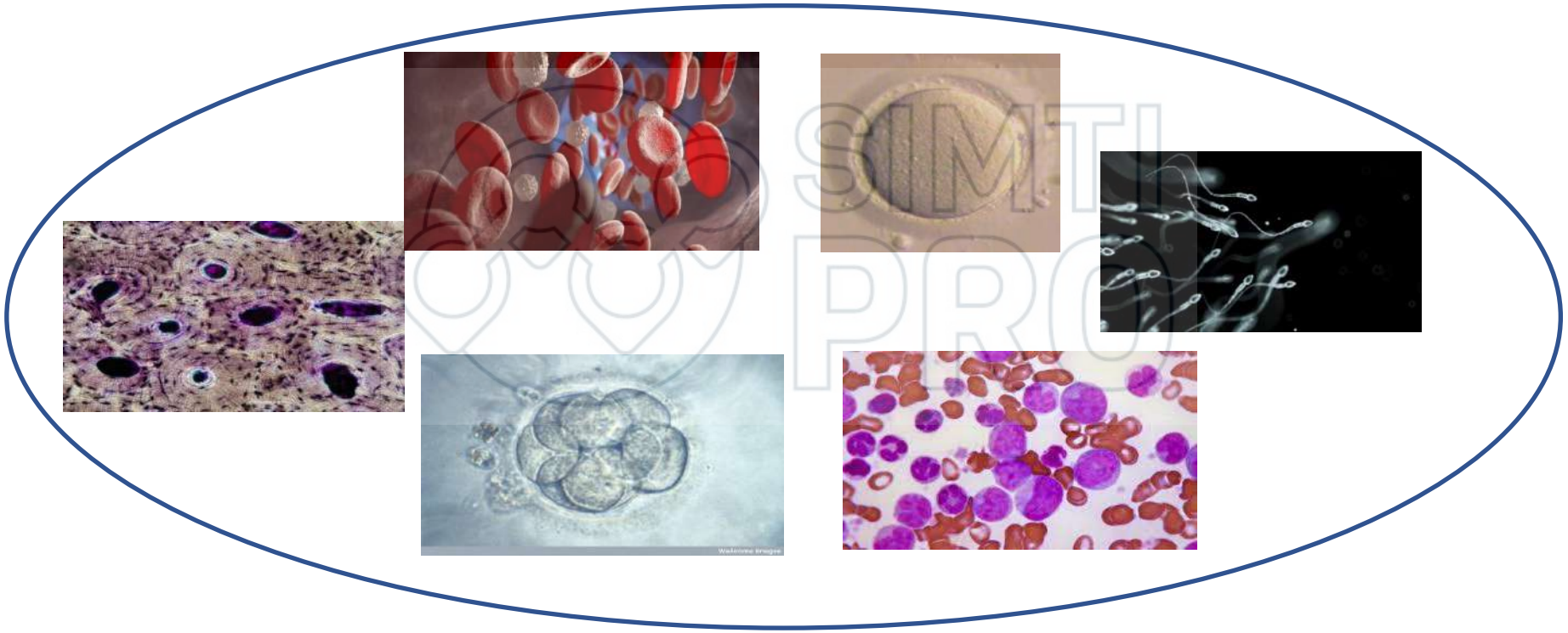
NEW REGULATION

SCOPE: set high standards of quality and safety for all SoHO intended for human application and for activities related to those substances.



Including **«new»** products such as **breast milk, microbiota, biological eye drops**

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

Publication obligations – national security or defence

- Breast milk for own child
- Organs
- Private situations
- Autologous bedside (closed systems)

DONATION / COLLECTION

PROCESSING / APPLICATION

SoHO – transfusion, transplantation, assisted reproduction

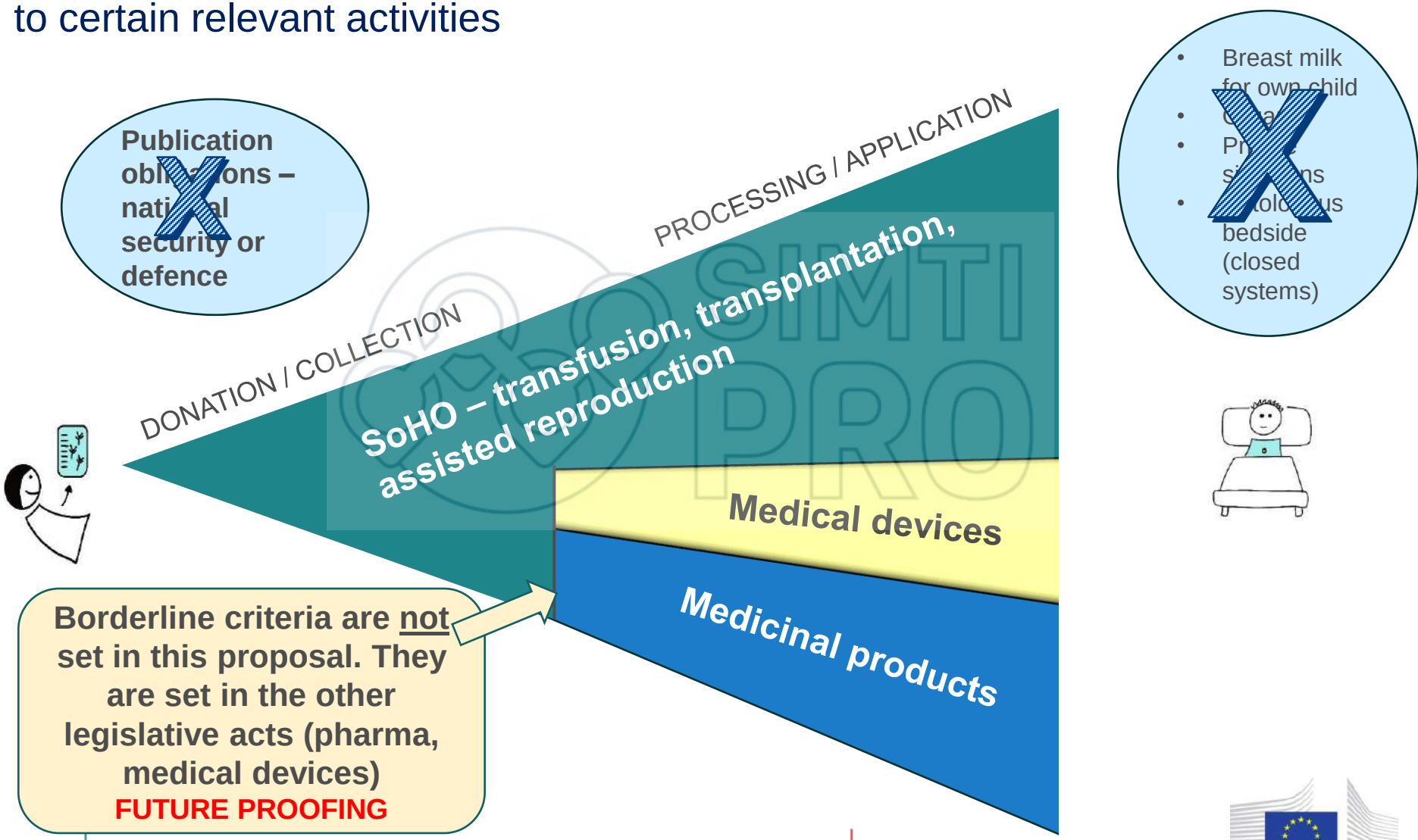
Medical devices

Medicinal products

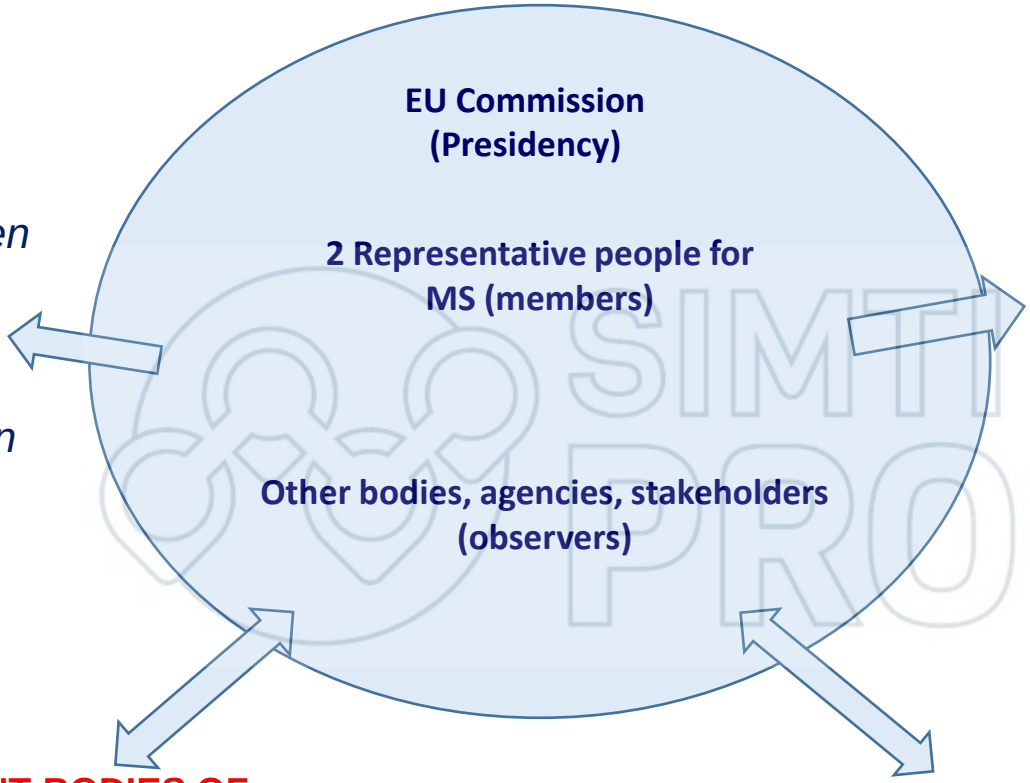
Borderline criteria are not set in this proposal. They are set in the other legislative acts (pharma, medical devices)

FUTURE PROOFING

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



SoHO COORDINATION BOARD (SCB)



To promote coordination between MS concerning the implementation of Regulation and to facilitate cooperation with stakeholders in that regard

TASKS:
preparing opinions at the request of CAs;
exchanging and documenting best practices;
liasing with EDQM and ECDC and EMA;
collaborating for the organisation of joint inspections and joint PPA;
giving advices on classification of new SoHO products;
…….

CONSULTANT BODIES OF OTHER REGULATORY FRAMEWORKS

ECDC/EDQM EXPERTS

INTERACTIONS

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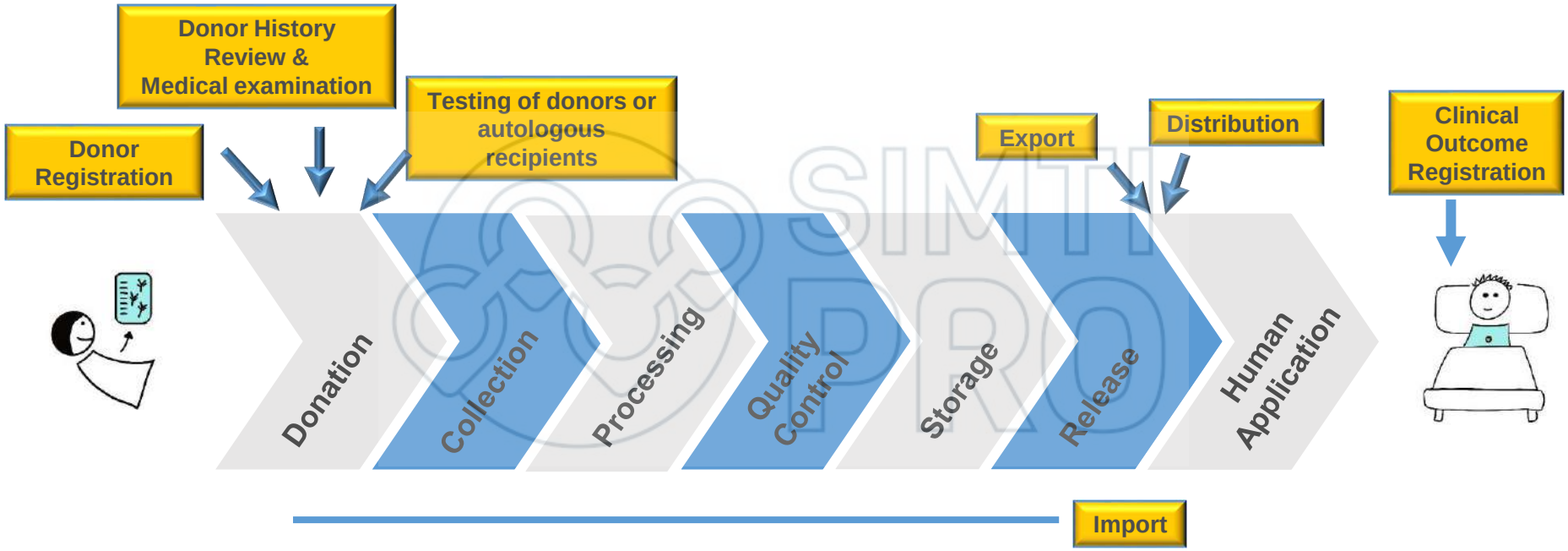
COMPETENT AUTHORITY (CA) OBLIGATIONS

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

SoHO entity means an entity legally established in the Union that carries out one or more of the SoHO activities

SoHO Establishment means a SoHO entity that carries out *at least:*

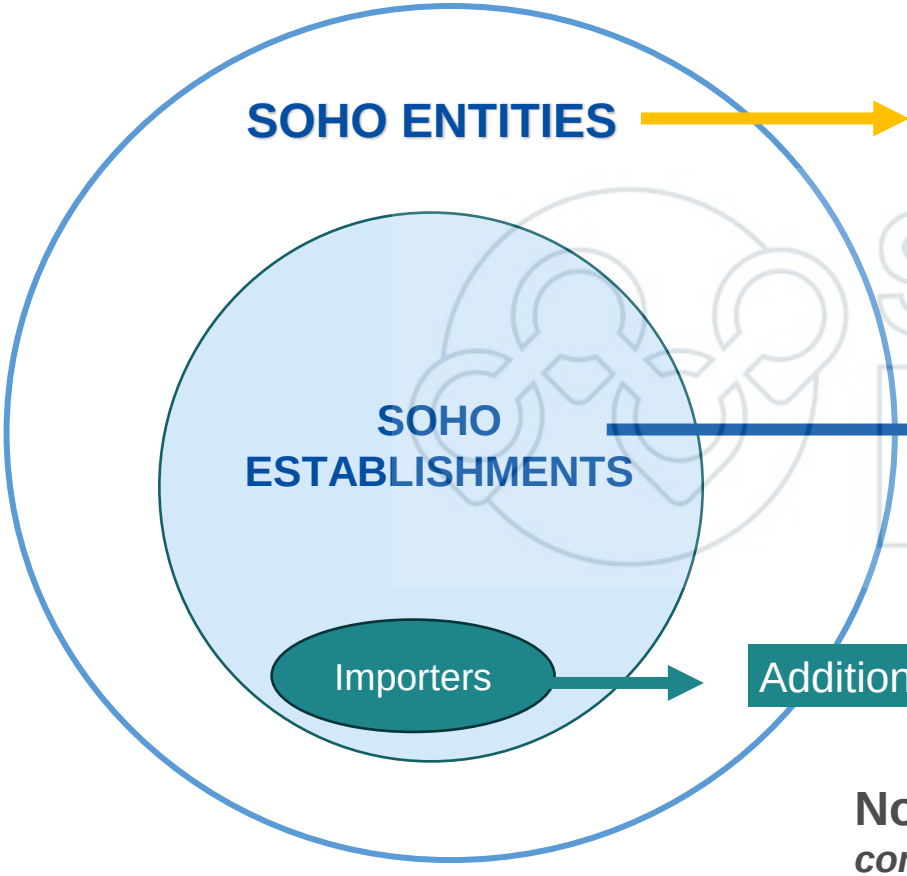
a) *Both processing and storage, or*
b) *Release, or*
c) *Import, or*
d) *export*

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).***

Risk-based approach

OVERIGHT ACTIVITIES GRADED APPROACH

- high level of transparency -



SoHO entities must be registered

- **Responsible person (+/- as today)**
- **Releasing officer(s)**
- **Nominated physician**

Must be registered, authorised, and **inspected regularly**

Additional specific authorisation requirements

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

- **Responsible person (+/- as today)**

Article 36

Responsible person

SoHO entities shall appoint a person responsible, within their entity, for ensuring that SoHO activities carried out by the SoHO entity comply with the requirements of this Regulation applicable to those SoHO activities.

- **Releasing officer(s)**

Article 49

Releasing officer

In cases where a SoHO establishment releases SoHO, it shall appoint one or more releasing officers.

'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***;

- **Nominated physician**

Article 50

Physician

shall be responsible for at least the following tasks:

a) development, review and approval and supervision of procedures
   - SoHO donor eligibility criteria,
   - SoHO collection
   - criteria for the allocation of SoHO;

b) supervision of the implementation of procedures referred to in point (a) when they are carried out by SoHO entities contracted by the SoHO establishment;

c) the clinical aspects of investigation of suspected adverse reactions in SoHO donors, SoHO recipients

d) design and supervision, in collaboration with treating physicians, of clinical outcome monitoring plans to generate evidence required to support applications for SoHO preparation authorisations

e) other tasks of relevance to the health of SoHO donors, SoHO recipients in relation to SoHO collected or supplied by the SoHO establishment

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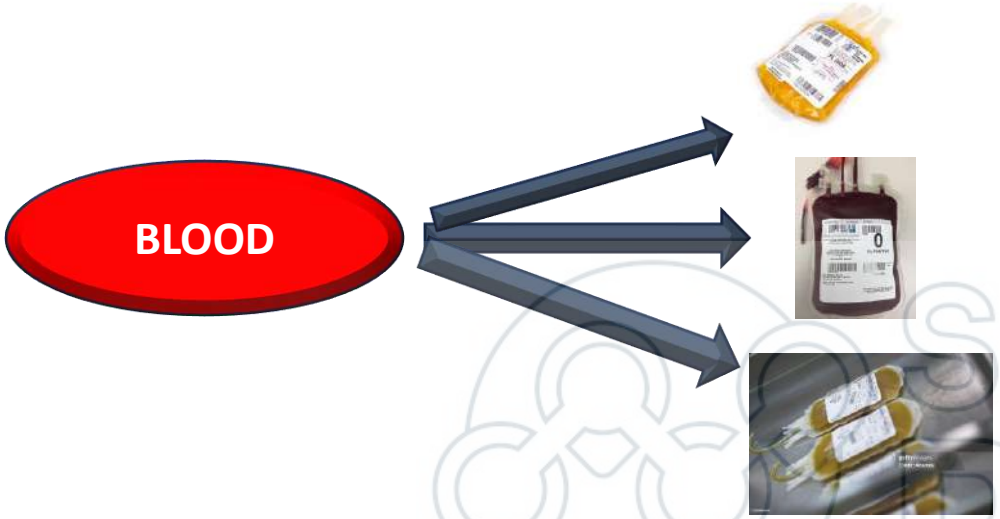
PREPARATION PROCESS AUTHORISATION

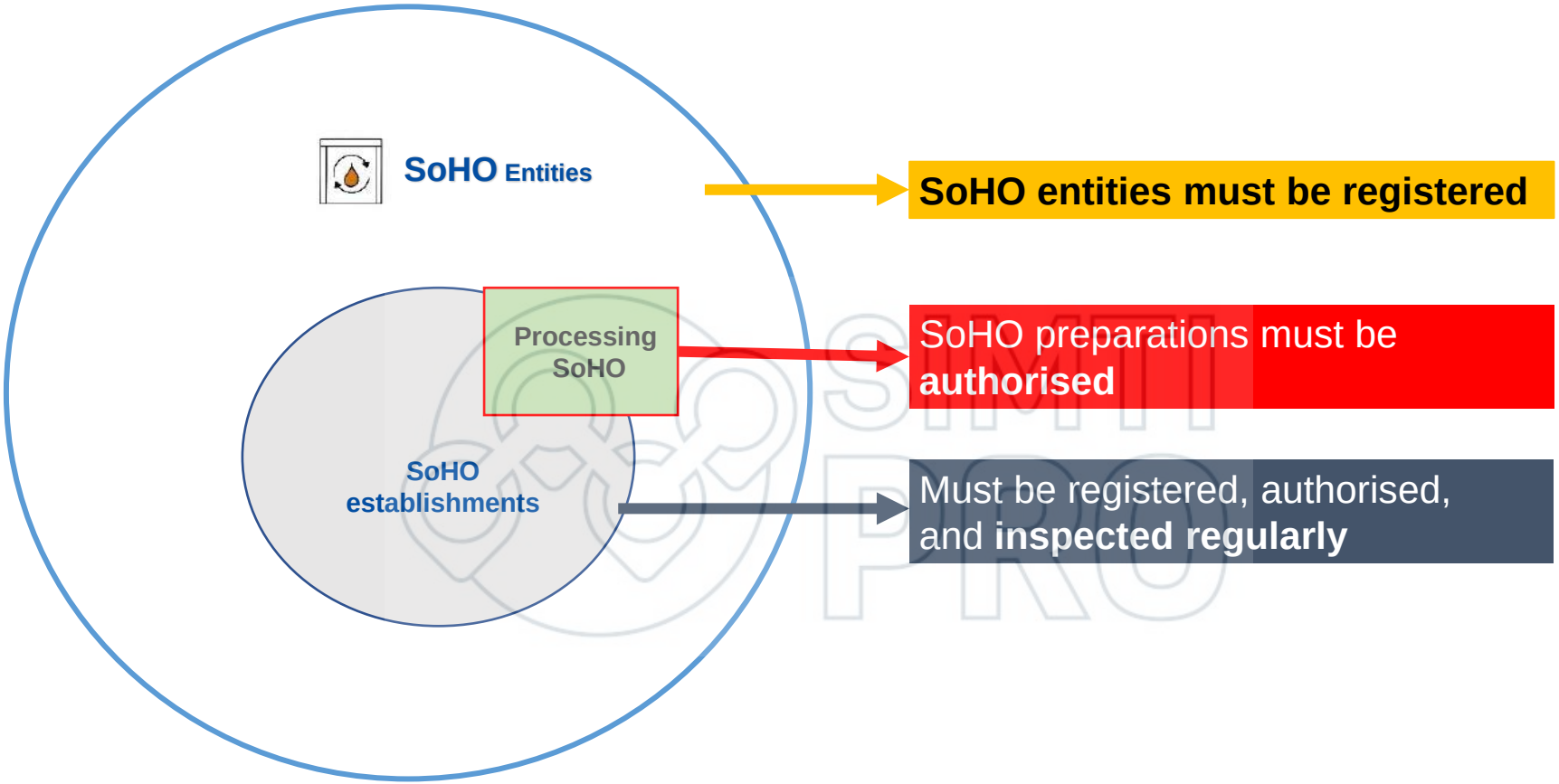
SoHO Preparation



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

→ Must be **authorised**

PREPARATION PROCESS AUTHORISATION



CA obligations: supervision of all SoHO Activities that directly impact safety, quality or effectiveness

PREPARATION PROCESS AUTHORISATION

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

PREPARATION PROCESS AUTHORISATION

Taking into account any relevant EDQM monograph

1. Systematic Benefit:Risk Assessment to determine the evidence available on 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
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Grant authorisation **OR** Refuse authorisation

CLINICAL OUTCOME MONITORING PLAN

Positive expected benefit/risk

\+ comparison to standard therapy

\+ clinical investigation study with appropriate number of patients and pre-defined clinical endpoints

No clinical outcome monitoring required

Clinical follow-up of a defined number of patients is required

Negligible Risk | **Low Risk** | **Moderate Risk** | **High Risk**

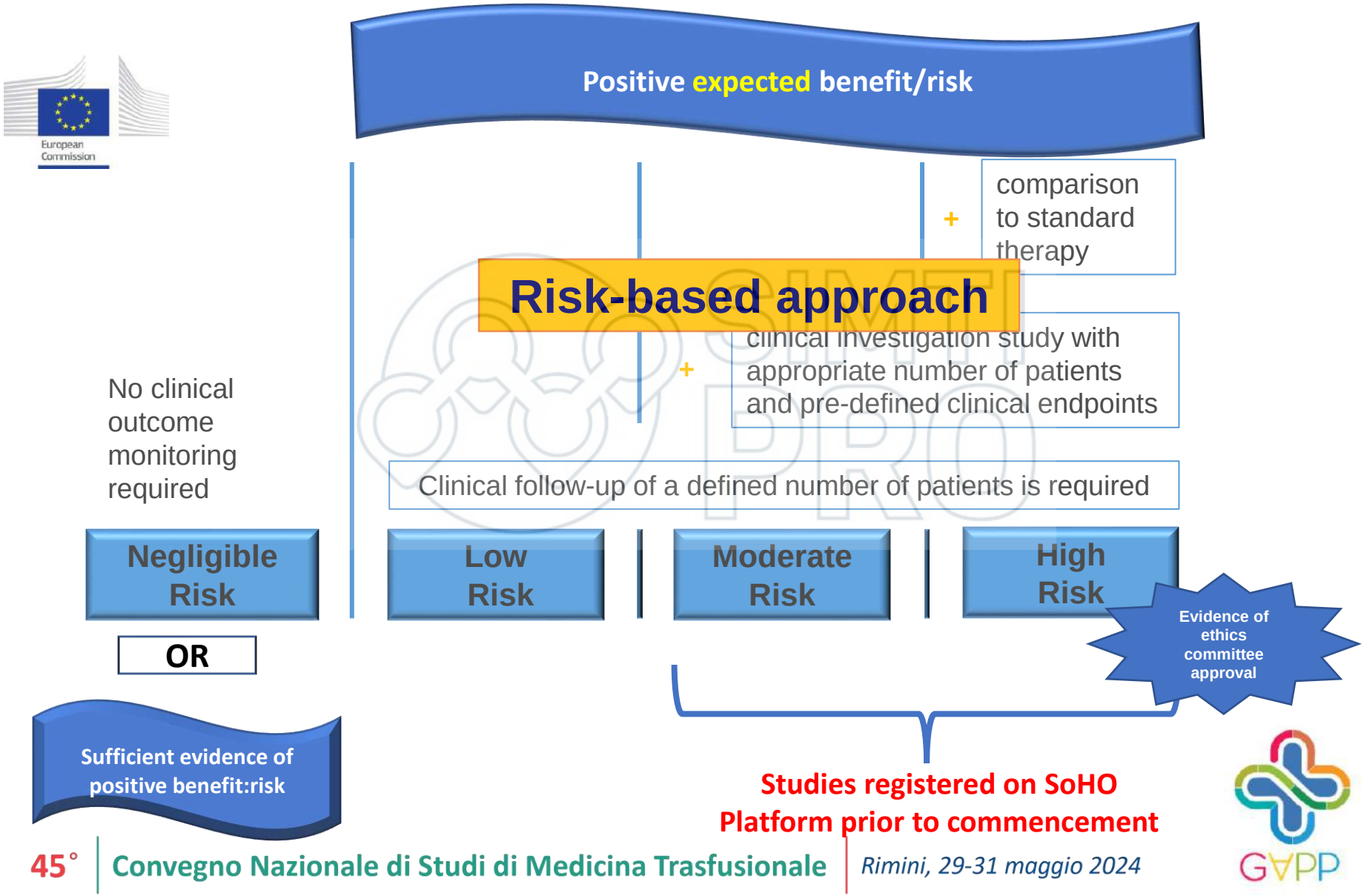
OR

Sufficient evidence of positive benefit:risk

Evidence of ethics committee approval

Studies registered on SoHO Platform prior to commencement

CLINICAL OUTCOME MONITORING PLAN



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EU SoHO PLATFORM

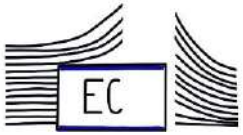

Registry of entities and their authorisations
Compendium of authorised SoHO preparations + List of ongoing Clinical studies
Member State National and other competent authorities
The EU SoHO Platform
Technical guidelines for implementation of standards
SoHo Coordination Board Membership and compendium of advice given
Supply flows and shortages monitoring
Supply alerts
Vigilance reporting
Rapid alerts

HIGH LEVEL STANDARDS THROUGH TECHNICAL GUIDELINES

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

Level 1

Commission Implementing Legislation → "where the Commission deems necessary"



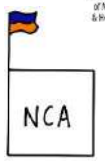
If none:

Level 2

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

OR:

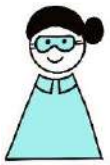
"Equivalent" Guidance → Deemed by CAs to achieve equivalent standards



If none:

Level 3

Other guidelines or methods based on international standards or scientific evidence



– staying up-to-date with the science in an agile way -

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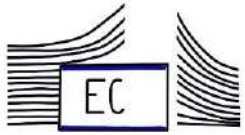

If none:

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

– staying up-to-date with the science in an agile way -

HIGH LEVEL STANDARDS THROUGH TECHNICAL GUIDELINES

Shall establish, maintain and update a **Quality Management System**, that is appropriate, taking into account their SoHO activities, and that achieves a high level of quality of SoHOs.

SoHO entities shall take into account the technical guidelines for quality management published by the EDQM, together with the **EDQM Good Practice Gguidelines**, as indicated ion the EU SoHO Platform.

Alternative approaches to the design of the quality management system may be applied where SoHO entities can demonstrate to their SoHO competent authorities, that they achieve an **equivalent level of quality**.

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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

New article!

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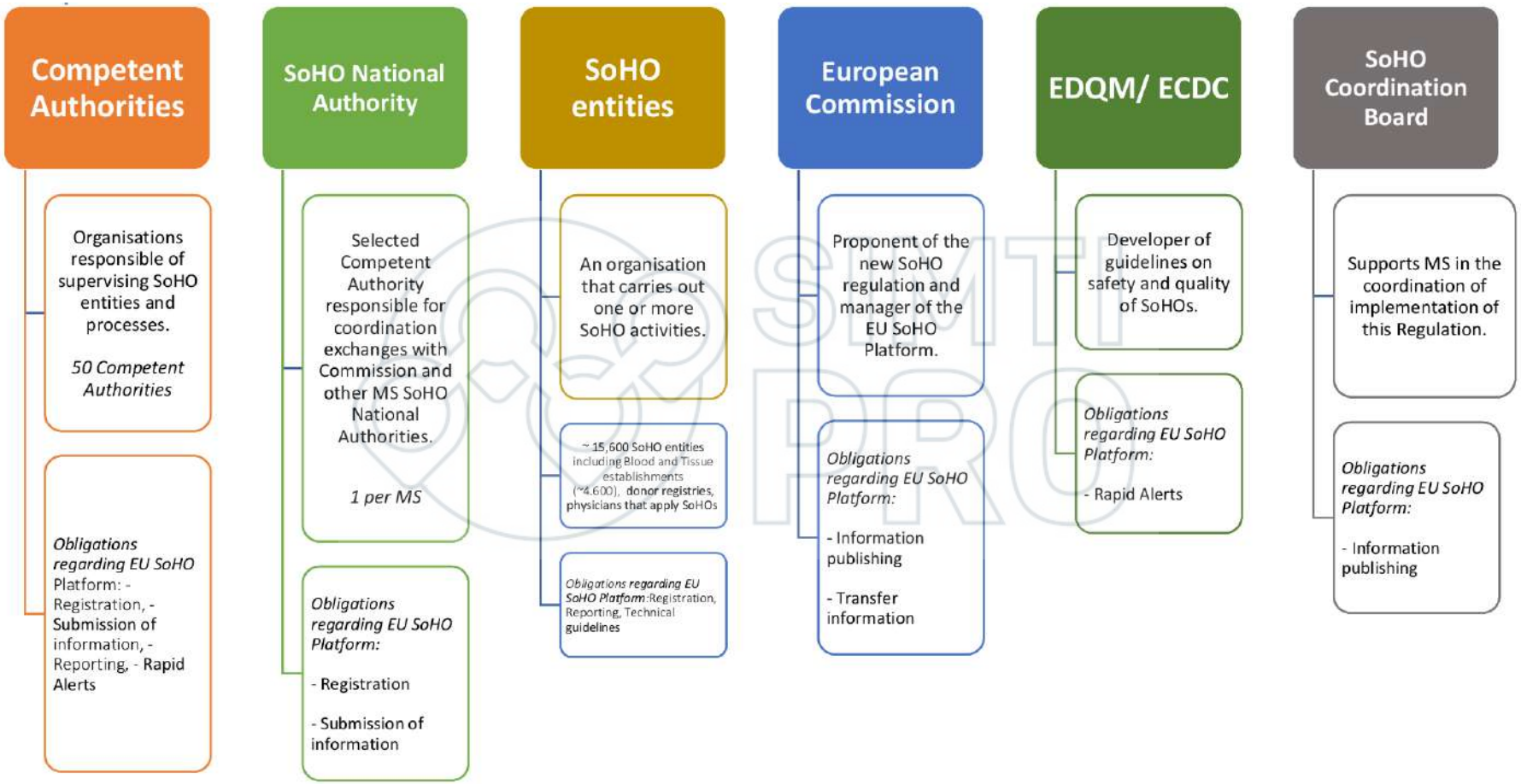
Not substantially changed

NEW REGULATION

ACTORS



Grazie per l'attenzione

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