Impatto sul processo di produzione e utilizzo degli emocomponenti

Vincenzo De Angelis

Centro Nazionale Sangue – ISS

ROMA

Il sottoscritto, in qualità di Relatore
dichiara che

nell'esercizio della Sua funzione e per l'evento in oggetto, NON È in alcun modo portatore 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.

Gazzetta ufficiale dell'Unione europea

IT
Serie L

2024/1938

17.7.2024

REGOLAMENTO (UE) 2024/1938 DEL PARLAMENTO EUROPEO E DEL CONSIGLIO

del 13 giugno 2024

sui parametri di qualità e sicurezza per le sostanze di origine umana destinate all'applicazione sugli esseri umani e che abroga le direttive 2002/98/CE e 2004/23/CE

With the permission of DG-SANTE SoHO team

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

X

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

X

DONATION / COLLECTION

PROCESSING / APPLICATION

SoHO – transfusion, transplantation, assisted reproduction

Medical devices

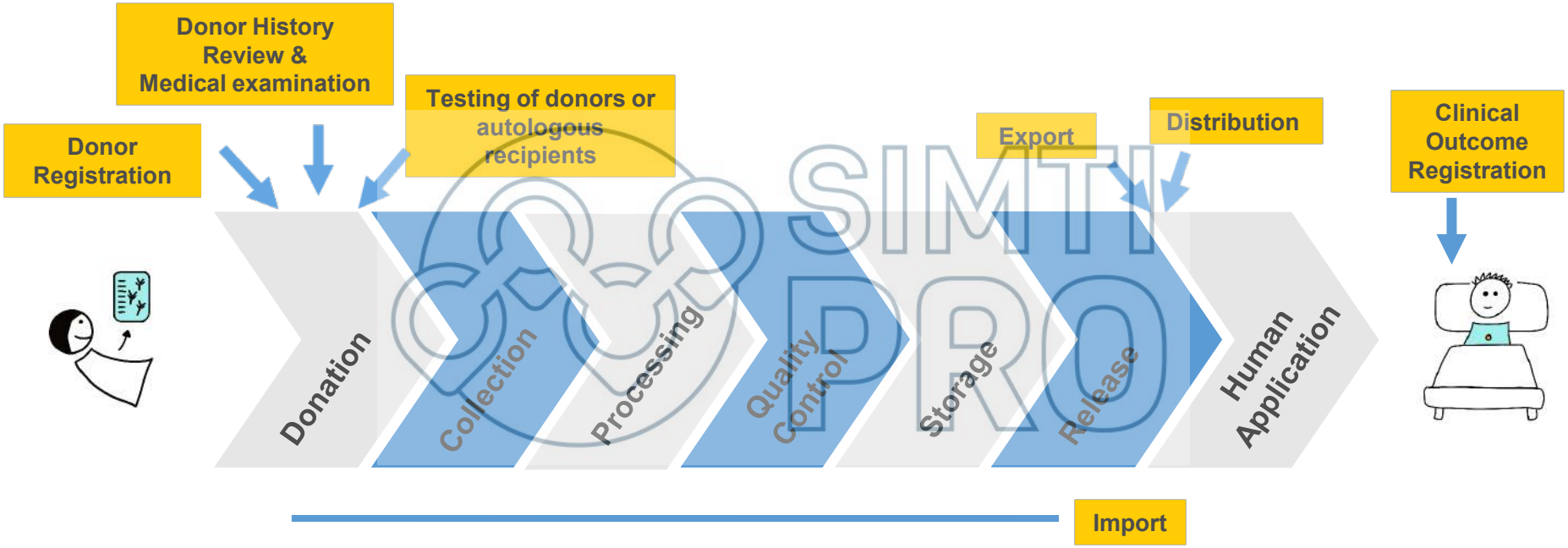
Medicinal products

Commission Directive 1214/2016

Provisions still valid; absorbed into EDQM guidelines (GPGs)

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

COMPETENT AUTHORITY (CA) OBLIGATIONS



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

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

Approccio risk-based e strumenti di risk assessment in ambito autorizzativo

Articolo 8

Responsabilità e obblighi generali delle autorità competenti per le SoHO

1. Le autorità competenti per le SoHO sono responsabili, all'interno del loro territorio, delle attività di sorveglianza sulle SoHOal fine di verificare l'effettiva conformità:

a) degli enti SoHOai requisiti stabiliti nel presente regolamento; e → **Enti SoHO = enti + centri SoHO**

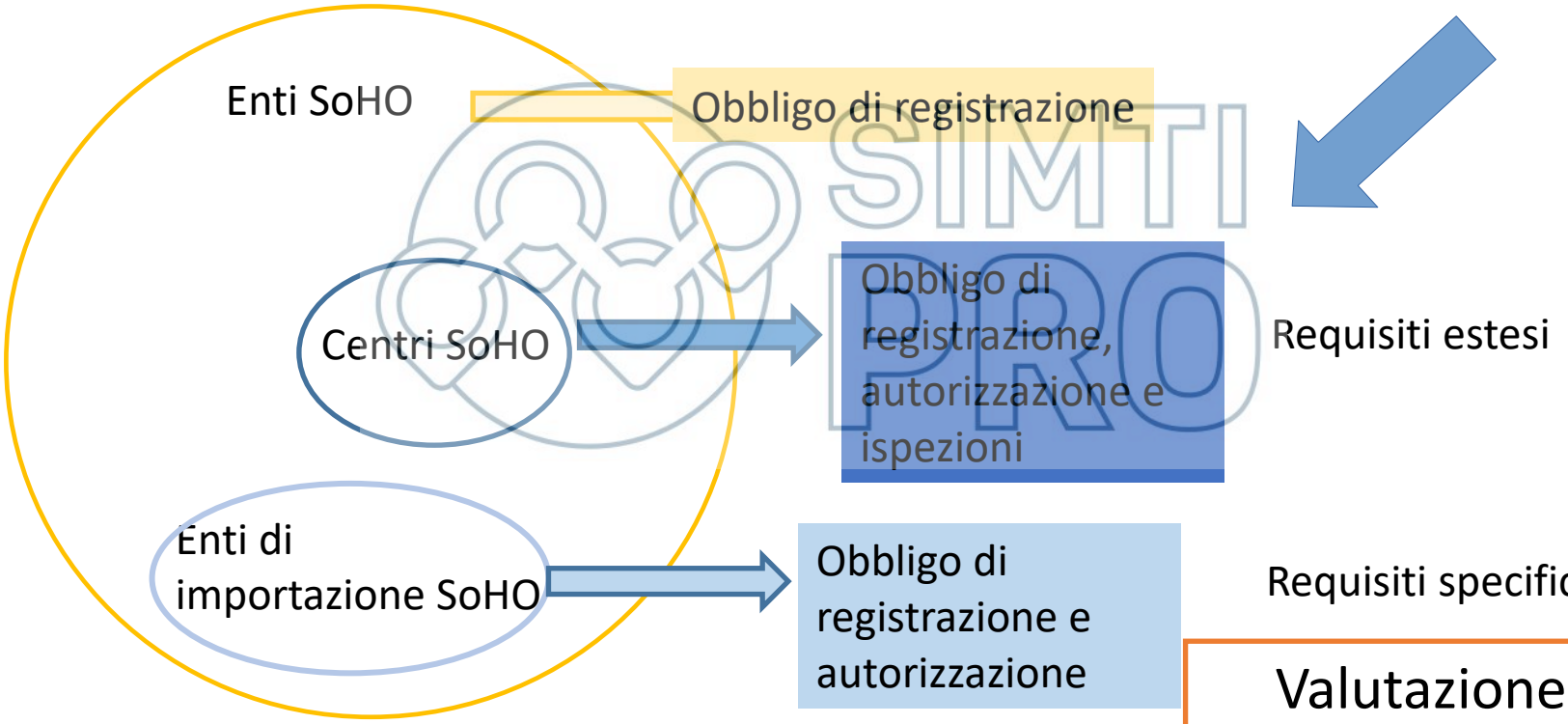
b) delle preparazioni di SoHO alla corrispondente autorizzazione.

a) Autorizzazione/accreditamento/misure di controllo (attività ispettiva)

a) Autorizzazione delle preparazioni SoHO

Approccio risk-based e strumenti di risk assessment in ambito autorizzativo

Enti SoHO e Centri SoHO



Quality Risk Management Tool: Intrinsic risk

- Two factors
  - Complexicity of the site, processes and products.
  - Criticality of the products, services, etc.

A total score of 1 or 2 represents a **Low** Intrinsic Risk
A total score of 3 or 4 represents a **Medium** Intrinsic Risk
A total score of 6 or 9 represents a **High** Intrinsic Risk

Criticality: - → +

Complexity: - → +

Complexity	1	2	3
1	1 (Low)	2 (Low)	3 (Medium)
2	2 (Low)	4 (Medium)	6 (High)
3	3 (Medium)	6 (High)	9 (High)

CAPO III

ATTIVITÀ DI SORVEGLIANZA SULLE SOHO

Articolo 18

Sistema di autorizzazione di preparazioni di SoHO

1. Le autorità competenti per le SoHO istituiscono e mantengono un sistema per concedere l'autorizzazione di preparazioni di SoHO agli enti SoHO presenti sul loro territorio. Tale sistema comprende la ricezione e l'elaborazione delle domande e l'approvazione dei piani di monitoraggio degli esiti clinici al fine di generare le prove richieste per l'autorizzazione, ove necessario, e consente la sospensione o la revoca delle autorizzazioni.

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**

CAPO III

ATTIVITÀ DI SORVEGLIANZA SULLE SOHO

Articolo 18

Sistema di autorizzazione di preparazioni di SoHO

Il Regolamento richiama le autorità competenti a tenere conto **delle migliori prassi pertinenti**.

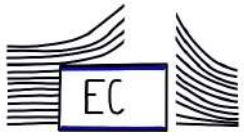
Le autorità competenti per le SoHO possono utilizzare il canale di comunicazione sicuro sulla piattaforma UE per le SoHO per scambiare, con il centro SoHO, documenti relativi alla domanda di autorizzazione.

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

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 -

Guide to the preparation, use and quality assurance of **BLOOD COMPONENTS**

European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS)

EDQM
21st Edition
2023

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

COUNCIL OF EUROPE
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- CHAPTER 5 Principles of blood component MONOGRAPHS
1. Definition and properties
2. Preparation
3. Requirements and quality control
4. Storage and transport
5. Labelling
6. Warnings

SIMTI

ESTM
EUROPEAN SCHOOL OF TRANSFUSION MEDICINE

Manuale applicativo delle "Good practice guidelines" (GPGs) per i Servizi Trasfusionali, richieste per la conformità con la Direttiva Europea 2005/62/CE

(messe in forza dalla Direttiva Europea 2016/1214)

Guide to the preparation, use and quality assurance of

BLOOD COMPONENTS

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Blood component monographs

Part A. Whole Blood components

Part B. Red cell components

Guide to the preparation, use and quality assurance of

BLOOD COMPONENTS

European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS)

EDQM
21st Edition
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European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

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Blood component monographs

Part C. Platelet components

Guide to the preparation, use and quality assurance of

BLOOD COMPONENTS

European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS)

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Blood component monographs

APPENDICE 2 - SCHEDE TECNICHE DI PRODOTTO

NOMENCLATURA IN LETTERATURA

CB-PG: Gel Piastrinico da Sangue Cordonale (cord blood)
CB-PRP: Plasma Ricco di Piastrine da Sangue Cordonale (cord blood)
LP-PRP: Plasma Ricco di Piastrine Povero di Leucociti
LR-PRP: Plasma Ricco di Piastrine Ricco di Leucociti
PC: Concentrato Piastrinico
PG: Gel Piastrinico (platelet gel)
PL: Lisato Piastrinico
PLT: Piastrine
PRF: Fibrina arricchita di Piastrine
PRP: Plasma Ricco di Piastrine
PRP gel: Plasma Ricco di Piastrine coagulato dopo Attivazione

PREPARATION PROCESS AUTHORISATION

Taking into account any relevant EDQM monograph

1 Systematic Benefit:Risk Assessment to determine the evidence available o… 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

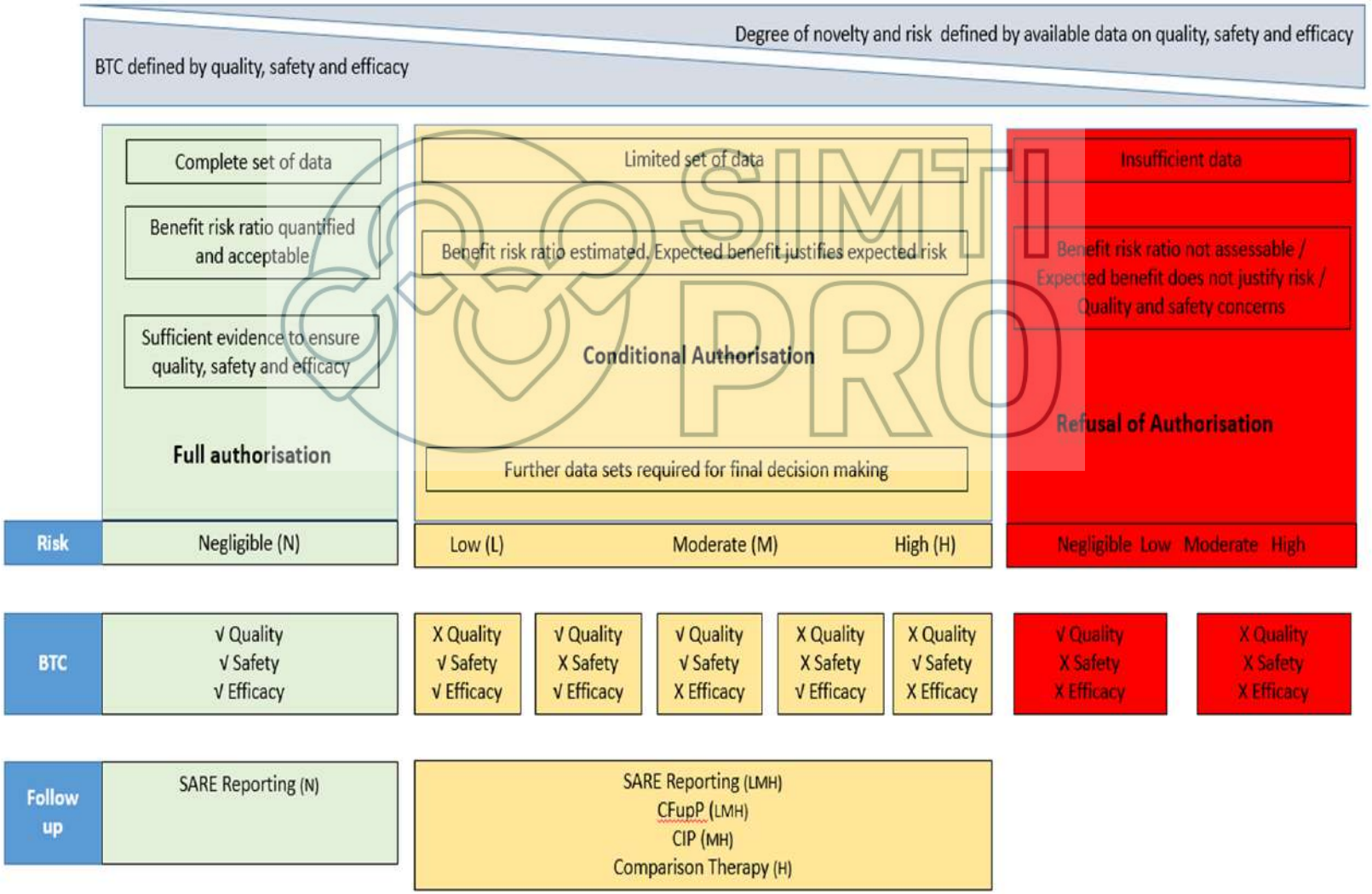
3 Assessment of the application by the competent authority

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

Risk/benefit balance



CLINICAL OUTCOME MONITORING PLAN

Positive expected benefit/risk

Risk-based approach

\+ comparison to standard therapy

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

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

No clinical outcome monitoring required

Negligible Risk	Low Risk	Moderate Risk	High Risk

OR

Sufficient evidence of positive benefit:risk

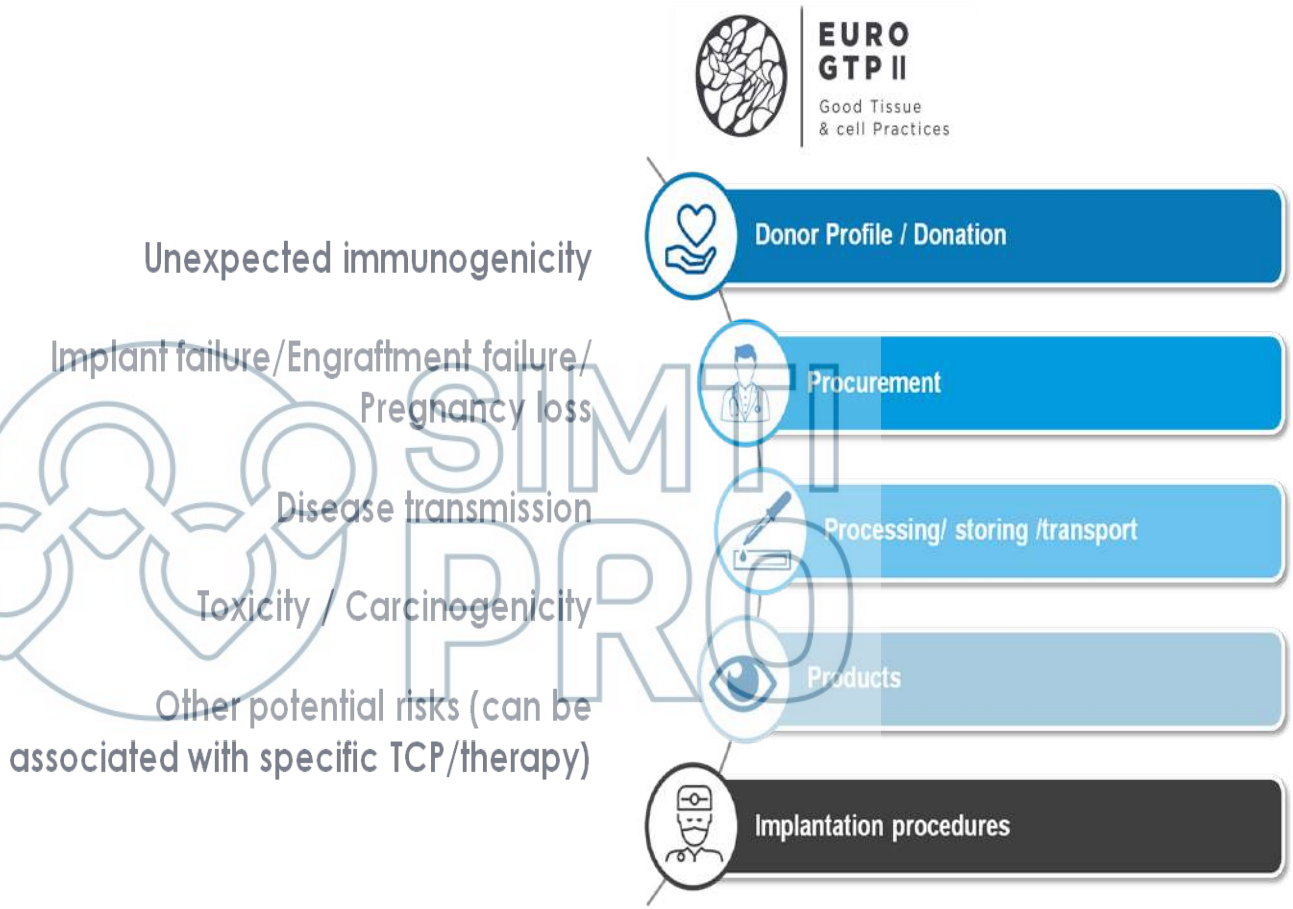
Evidence of ethics committee approval

Studies registered on SoHO Platform prior to commencement

Risk assessment tool: EUROGTP II

The **Euro GTP II** Methodologies and Interactive Assessment Tool (IAT) have been developed to assist professionals involved in the provision of BTC to:

- Determine if a BTC or preparation process has any novelty (Step 1)
- Assess the risks associated with the BTC or preparation process (Step 2)
- Determine the extent of any studies and/or follow up required to assure the safety and efficacy of BTC (Step 3)

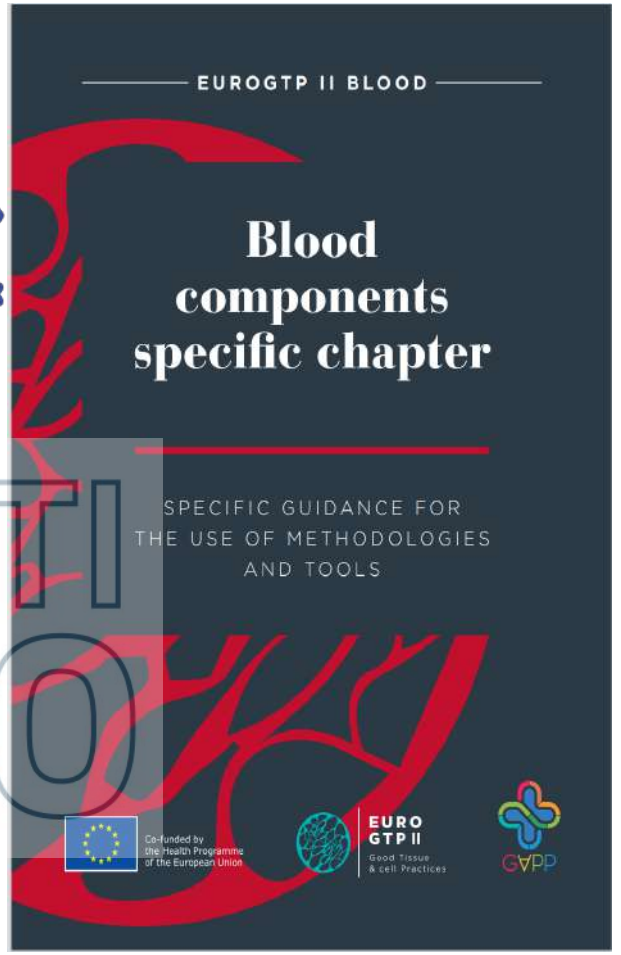


Details available on the website:
https://tool.goodtissuepractices.site/

Adopted by EDQM for guidelines implementation
https://soho-guides.edqm.eu/home/

EURO GTP II
Good Tissue & cell Practices

Co-funded by the Health Programme of the European Union



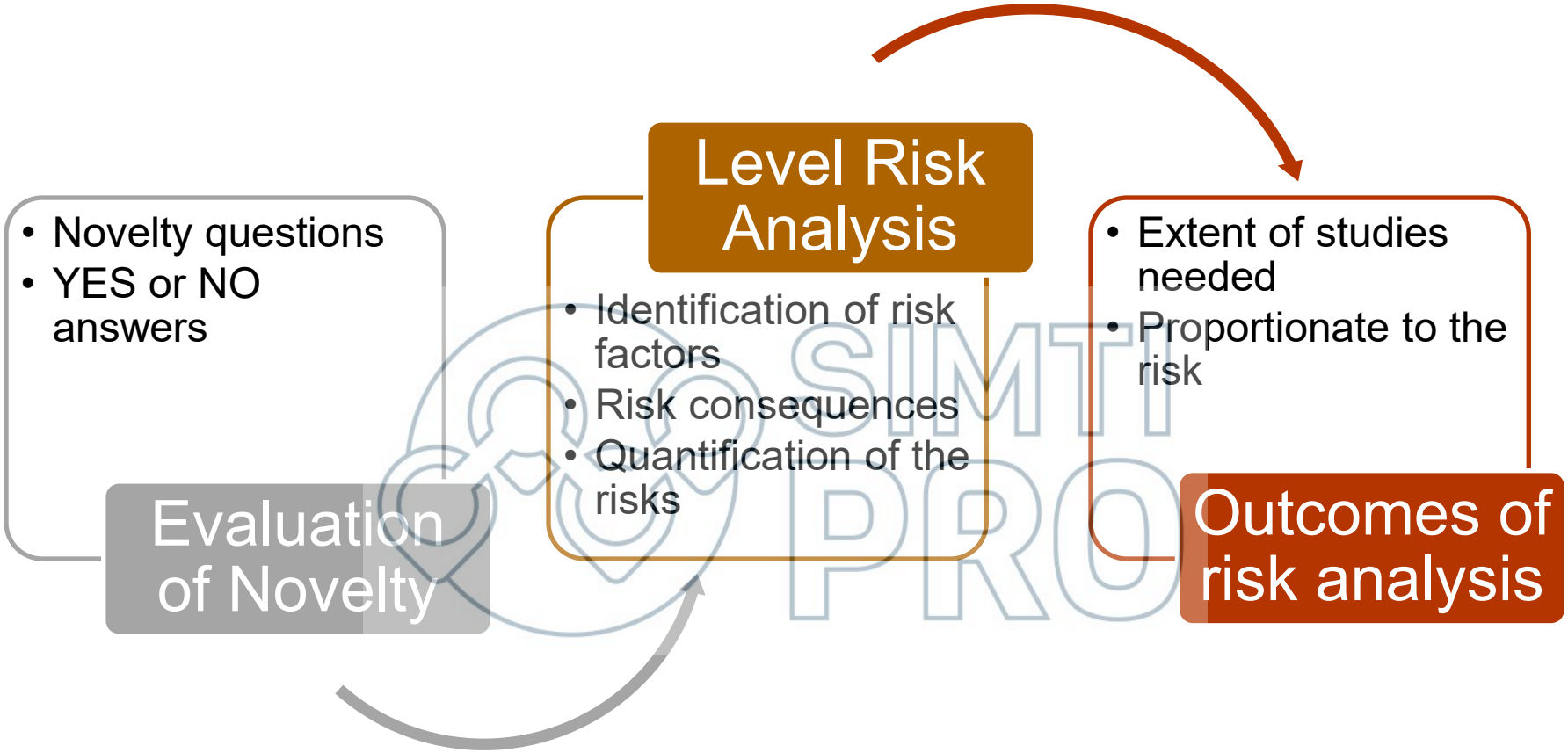
- Guide
- Interactive Assessment Tool
- Training

EuroGTPII@bst.cat

http://www.goodtissuepractices.eu/

http://goodtissuepractices.eu/images/docs/EuroGTPII_Blood_INT.pdf

EUROGTP II TOOL – BLOOD: metodologia



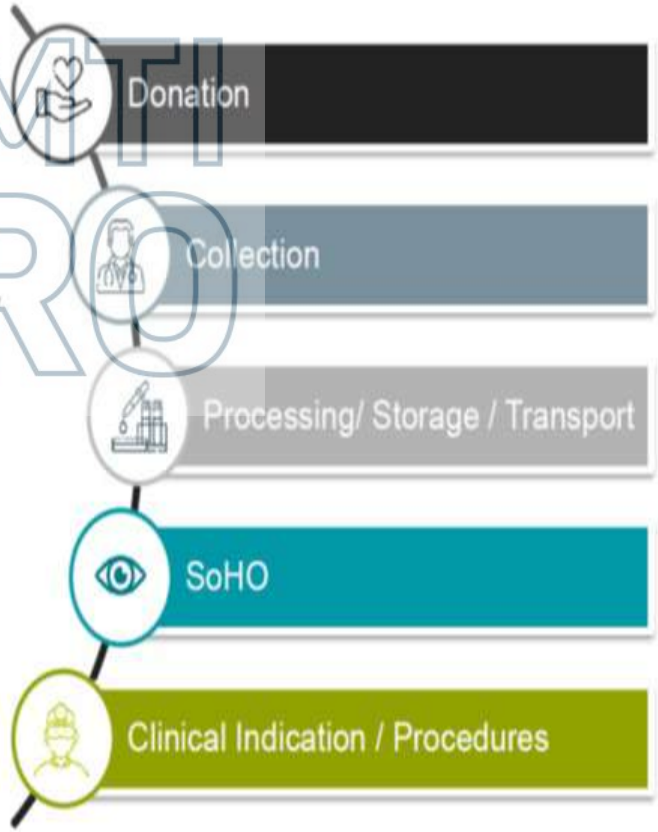
NOVELTY QUESTIONS: step 1

	YES	NO	NA
A. Has this type of BTC* previously been collected, processed/prepared and issued for clinical use by your establishment?			
B. Will the starting material used to prepare this BTC be obtained from the same donor population previously used by your establishment for this type of BTC*?			
C. Will the starting material for this BTC be procured/collected using a procedure used previously by your establishment for this type of BTC*?			
D. Will this BTC be prepared by a procedure (processing/preparation, decontamination/pathogen reduction and preservation) used previously in your establishment for this type of BTC*?			
E. Will this BTC be packaged, stored and distributed using a protocol and materials used previously in your establishment for this type of BTC*?			
F. Will this type of BTC* provided by your establishment be applied/infused clinically using an application/transfusion/infusion method used previously?			
G. Has your establishment provided this type of BTC* for the same clinical indication or for application/transfusion/infusion into a same anatomical site?			

LEVEL RISK ANALYSIS – step 2a

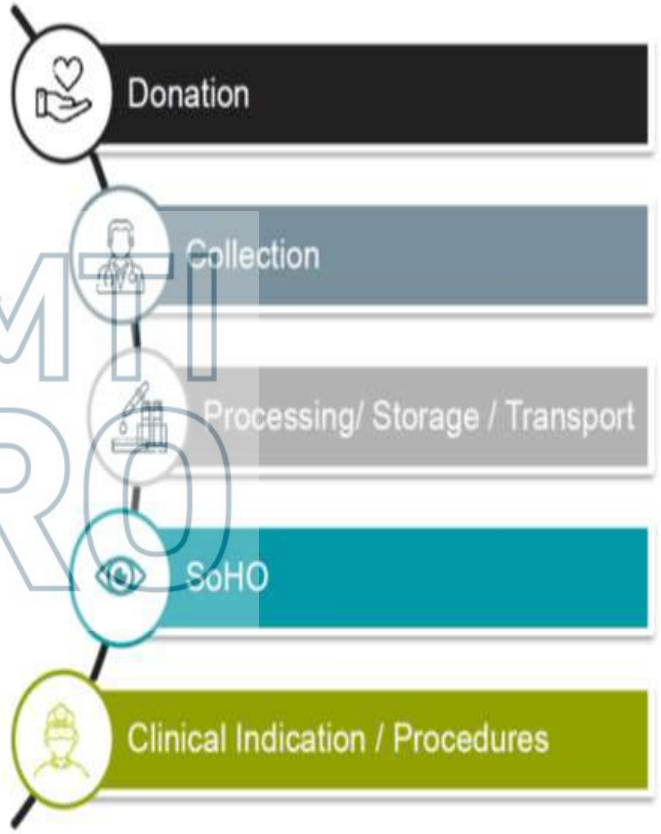
Identification of risk factors

i) Donor Characteristics
ii) Collection process and environment
iii) Processing and environment
iv) Reagents/Added components
v) Reliability of Testing
vi) Storage Conditions
vii) Transport Conditions
viii) Presence of unwanted residues
ix) Clinical indications



LEVEL RISK CONSEQUENCES – step 2b

i) Unexpected immunogenicity
ii) Failure to perform clinically
iii) Disease transmission
iv) Toxicity/Carcinogenicity
v) Other



LEVEL RISK SCORING – step 3

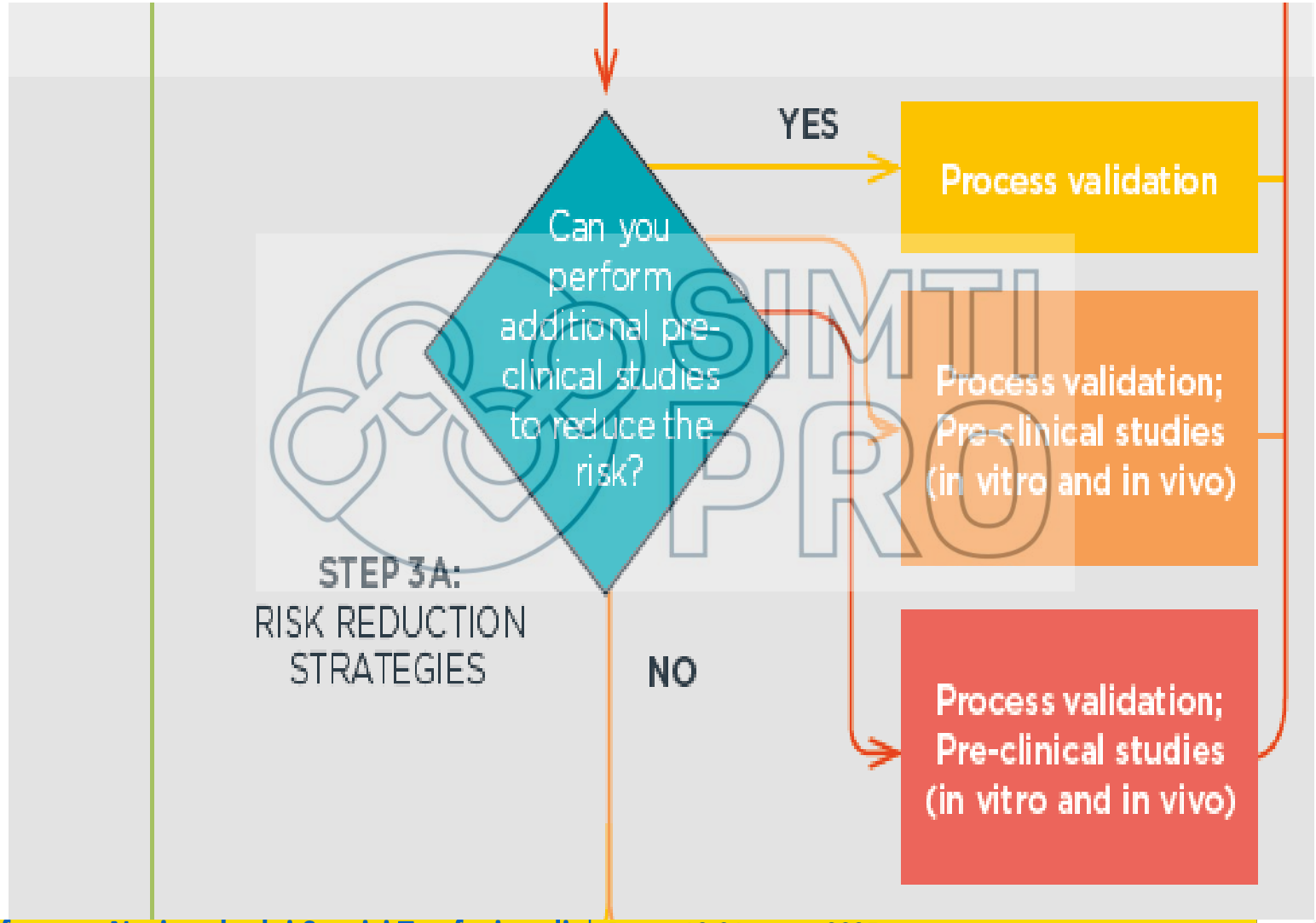
LEVEL OF PROBABILITY
1 - Rare
2 - Unlikely
3 - Possible
4 - Likely
5 - Almost certain

LEVEL OF SEVERITY
1- Non-serious
2- Serious
3- Life-threatening
4 - Fatal

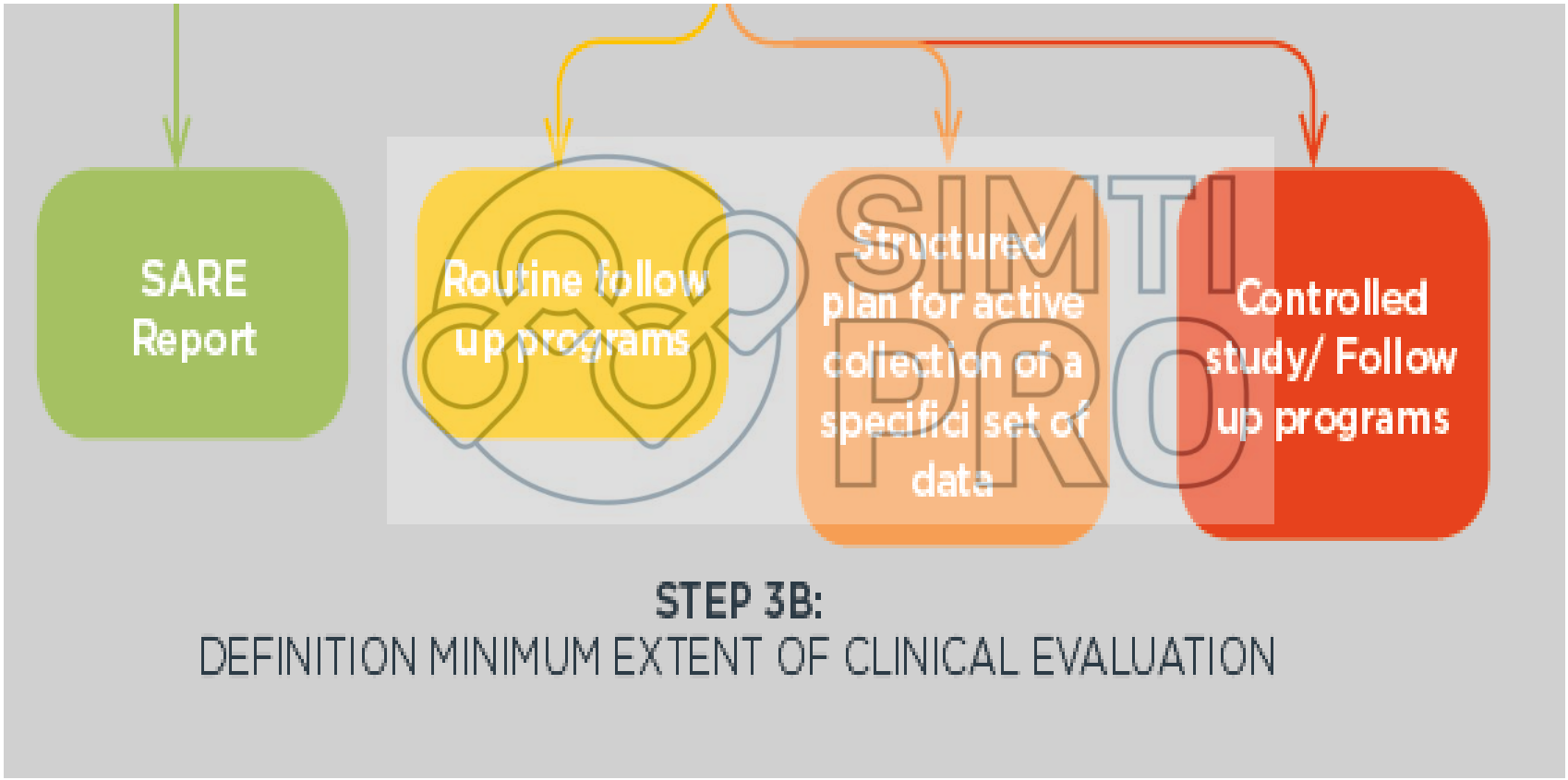
LEVEL OF DETECTABILITY
1 - Very high
2 - Moderatefy high
3- Low
4 - Very low
5 - Cannot be detected

PERCENTAGE RISK REDUCTION	
0	None
25	Limited
50	Moderate
75	Substantial
95	Extensive

LEVEL RISK REDUCTION – step 3a



LEVEL EXTENT CLINICAL EVALUATION – step 3b




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

CAPO II

AUTORITÀ COMPETENTI PER LE SOHO DEGLI STATI MEMBRI

Articolo 5

Designazione delle autorità competenti per le SoHO

1. Gli Stati membri designano l'autorità o le autorità competenti per le SoHO cui affidano la responsabilità delle attività di sorveglianza sulle SoHO. L'autorità o le autorità competenti per le SoHO designate sono indipendenti da qualsiasi ente SoHO.

Articolo 6

Indipendenza e imparzialità

Articolo 7

Trasparenza

Regioni/PPAA

CNS

- Sufficienti risorse umane e finanziarie
- Capacità operativa e competenza anche tecnica
- Organizzazione – SGQ – piani di continuità
- Capacità di offerta formativa interna e esterna

VALUTAZIONE DI IMPATTO

Articolo 18

Sistema di autorizzazione di preparazioni di SoHO

1. Le autorità competenti per le SoHO istituiscono e mantengono un sistema per concedere l'autorizzazione di preparazioni di SoHO agli enti SoHO presenti sul loro territorio. Tale sistema comprende la ricezione e l'elaborazione delle domande e l'approvazione dei piani di monitoraggio degli esiti clinici al fine di generare le prove richieste per l'autorizzazione, ove necessario, e consente la sospensione o la revoca delle autorizzazioni.

Autorizzazione delle preparazioni SoHO:

- Impatto organizzativo (procedure)
- Risorse
- Competenza tecnica/clinica

SOCIETÀ SCIENTIFICHE !

Grazie per l'attenzione!