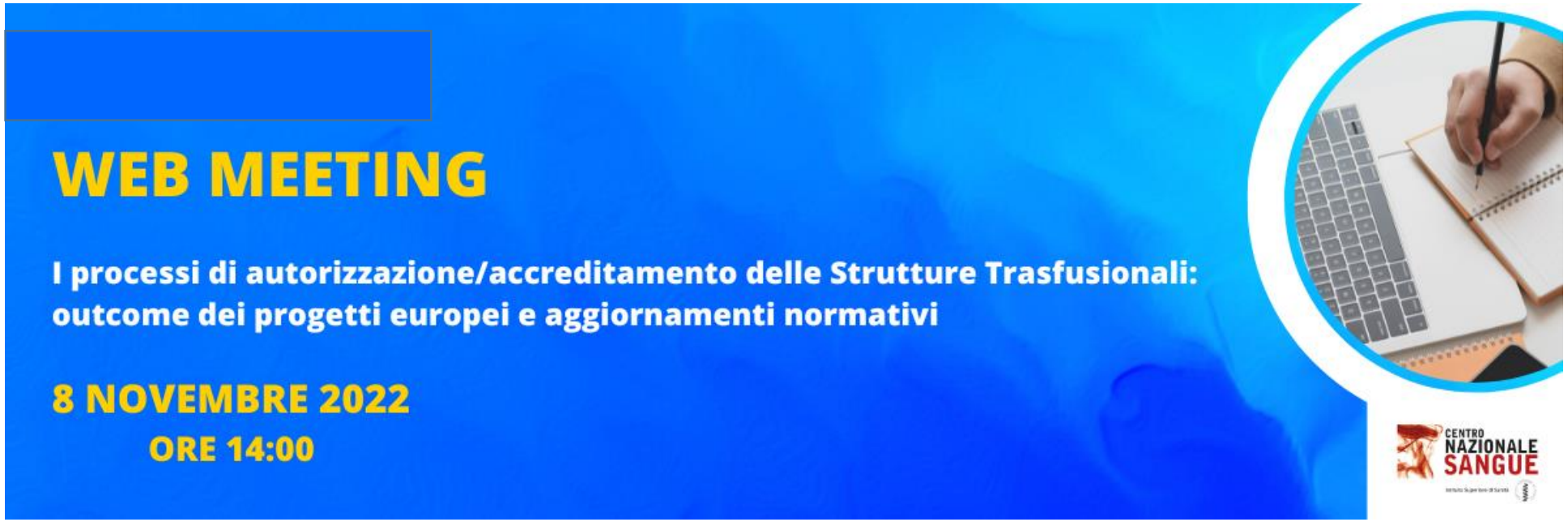


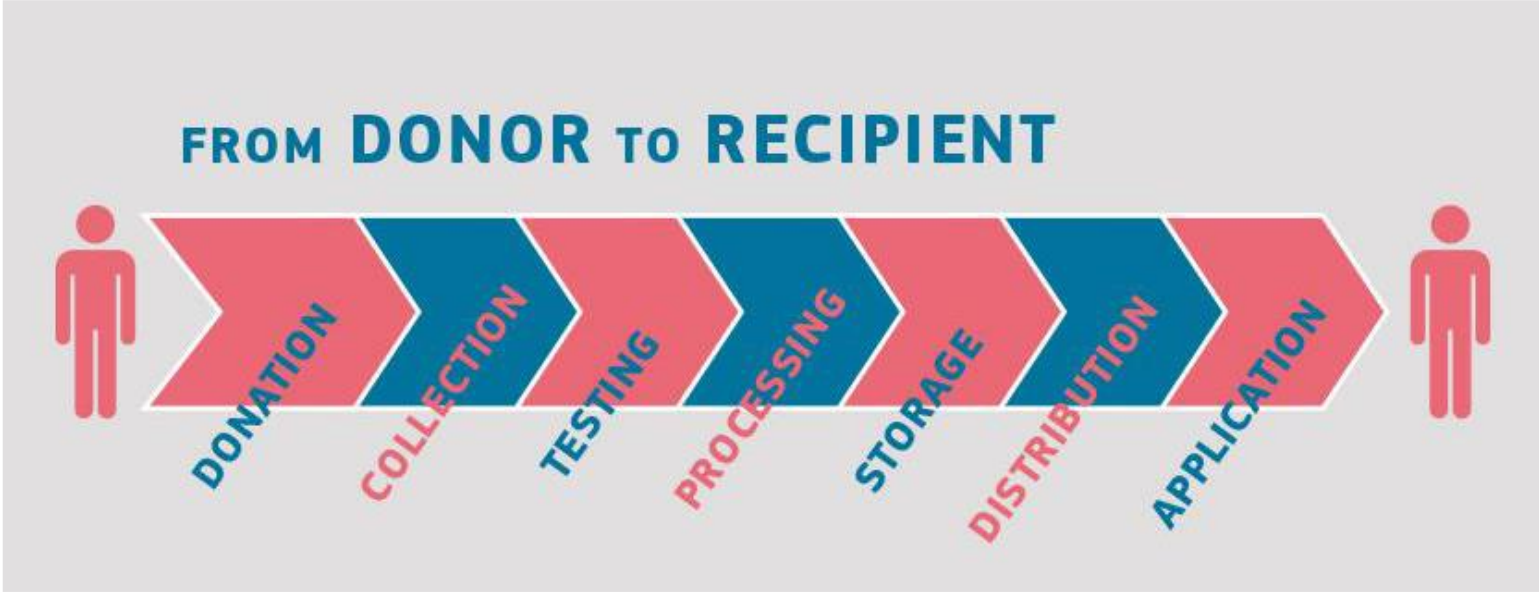
Introduzione alla nuova visione della CE in materia di sangue, cellule e tessuti

Dott.ssa Simonetta Pupella

CENTRO NAZIONALE SANGUE

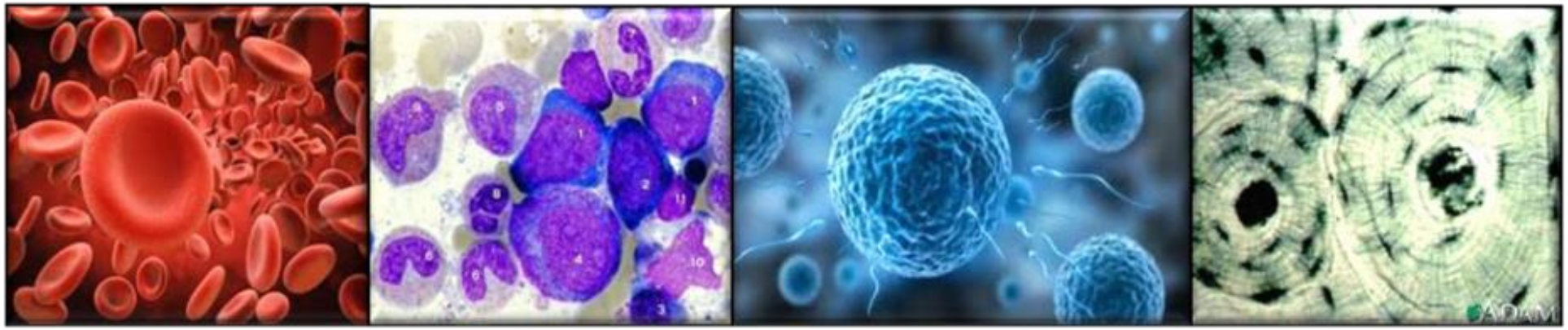
AGENDA

- Impact assessment
- Punti di debolezza delle Direttive vigenti
- La nuova visione della CE in materia di SOHO
- Il nuovo Regolamento europeo



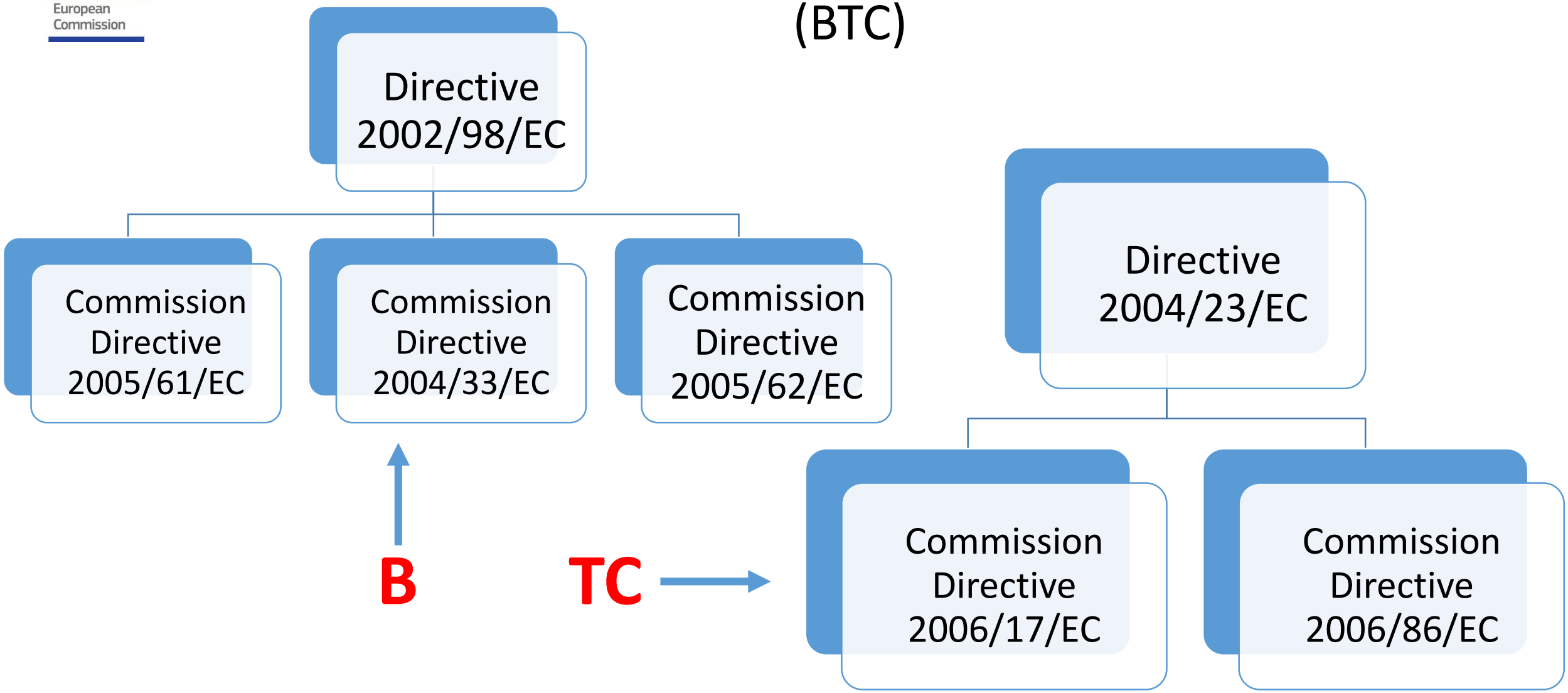
Source: European Commission, DG SANTE website
https://ec.europa.eu/health/blood_tissues_organs/overview_en

La catena dei processi, dal donatore al paziente ricevente, accomuna tutte le sostanze biologiche di origine umana (SoHO)



CENTRO NAZIONALE SANGUE

LA CORNICE REGOLATORIA PER BLOOD – TISSUES AND CELLS (BTC)



THE IMPACT ASSESSMENT,
processo di valutazione di impatto della legislazione comunitaria vigente

PURPOSES and SCOPE

- Define safety and quality requirements for all stages of the chain from donor to recipient;
- Ensure effective regulatory oversight of the sectors;
- Achieve a degree of harmonisation of safety and quality that facilitates inter-MS exchanges;
- Establish a high level of legal certainty at Union level;
- Achieve community sufficiency through the encouragement of voluntary unpaid donations (VUD).

QUALITA' E SICUREZZA

SUPERVISIONE E CONTROLLO

ARMONIZZAZIONE E MUTUO RICONOSCIMENTO

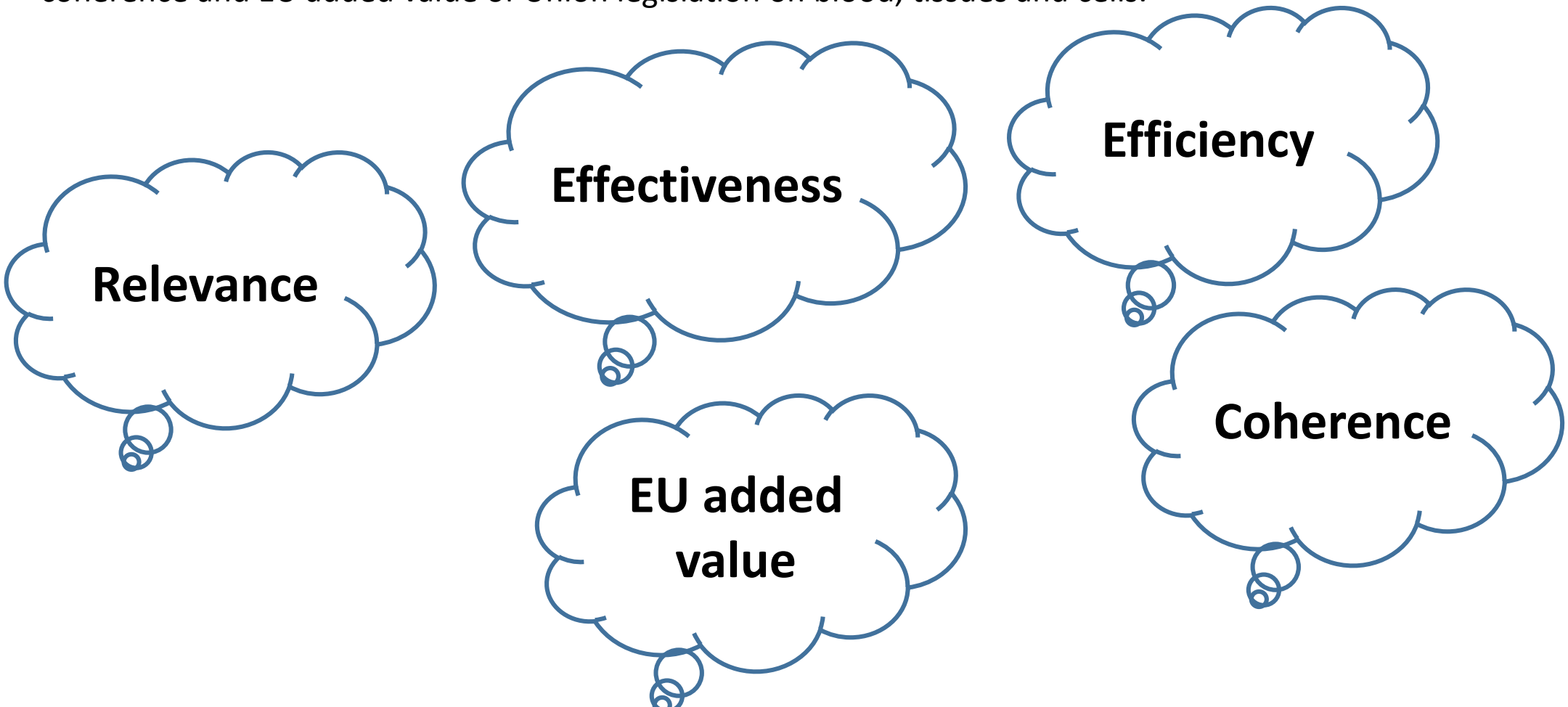
CERTEZZA E COERENZA DELLE NORME

AUTOSUFFICIENZA COMUNITARIA BASATA SULLA VUD

THE IMPACT ASSESSMENT

Data sources and methodology

This study provides evidence that **answers 14 high-level evaluation questions**, defined by the Commission in the Blood, Tissues and Cells Evaluation Roadmap. These questions covered the relevance, effectiveness, efficiency, coherence and EU added value of Union legislation on blood, tissues and cells.



THE IMPACT ASSESSMENT: **Key stakeholders**

EUROPEAN COMMISSION

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

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

EHA EUROPEAN HEMATOLOGY ASSOCIATION

eba EUROPEAN BLOOD ALLIANCE

ISBT International Society of Blood Transfusion

EHC european haemophilia consortium

Blood and blood components sector

IFPA international plasma fractionation association

IPOPI INTERNATIONAL PATIENT ORGANISATION FOR PRIMARY IMMUNODEFICIENCIES

PLUS PLATFORM OF PLASMA PROTEIN USERS

PPTA Plasma Protein Therapeutics Association

Donor and donor Associations
Regulators from third countries (FDA)
International organisations (WHO)

WMDA

European Association of Tissue Banks

eshre SCIENCE MOVING PEOPLE MOVING SCIENCE

Tissues and cells sector

International Society ISCT Cell & Gene Therapy

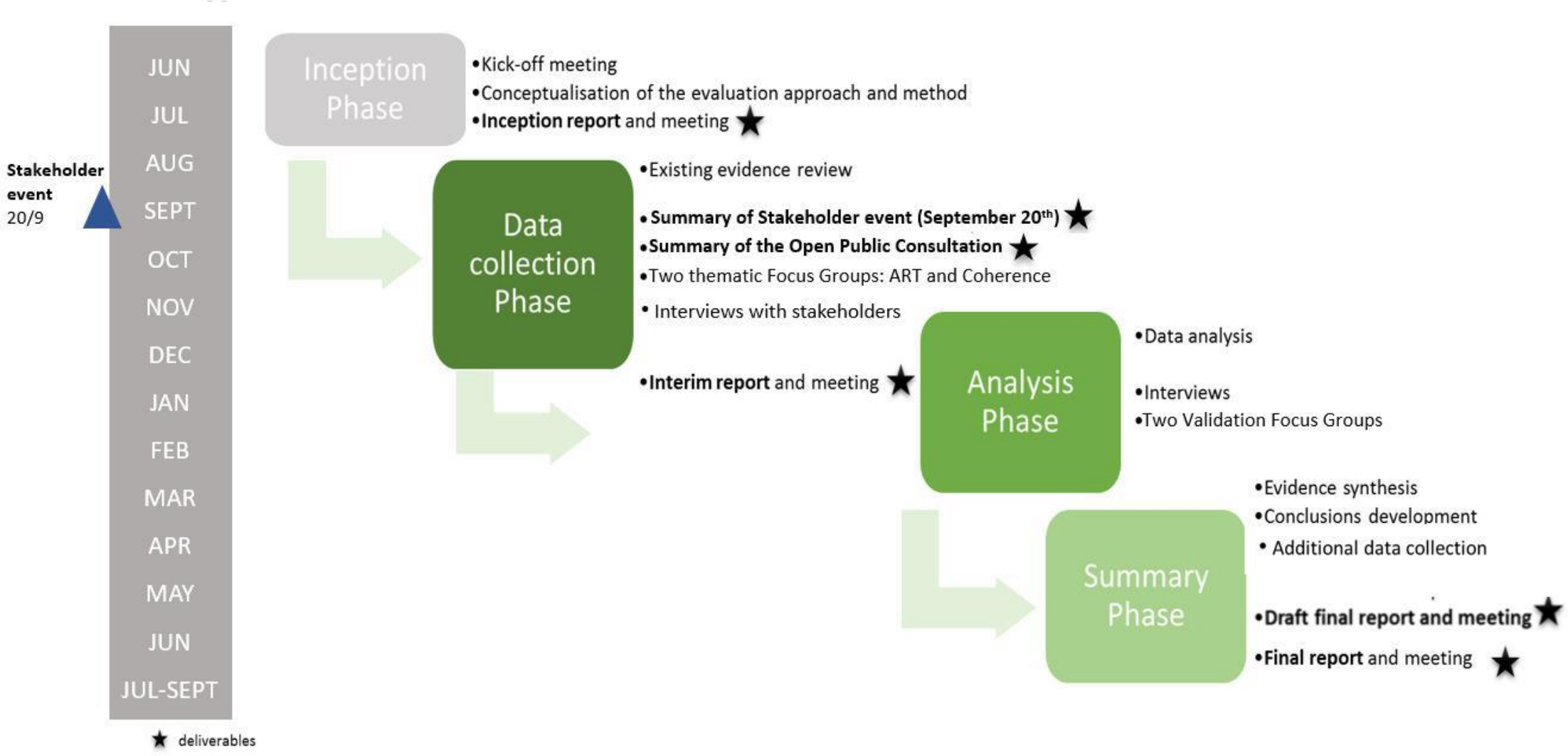
EBMT European Society for Blood and Marrow Transplantation

EEBA

EUROPEAN EYE BANK ASSOCIATION

CENTRO NAZIONALE SANGUE

THE IMPACT ASSESSMENT: **study methodology**



THE IMPACT ASSESSMENT

Relevance

- To what extent is the legislation sufficiently adapted to, adaptable to, and up-to-date with, **scientific, technical, socio demographic and epidemiological developments** in the sectors since it was adopted?
- To what extent is the legislation sufficiently adapted to, adaptable to, and up-to-date with **clinical demand and practice**, commercialisation and internationalisation developments in the sectors since it was adopted?
- Are there any gaps in terms of **substances of human origin and/or activities that are not regulated** by the Directives? Or are there substances and/or activities that are regulated by the Directives but should be removed from them due to changes that have occurred?

A. Substances	**1. Relevant to blood**	**2. Relevant to tissues and cells**
1. Candidates for inclusion	• Autologous or allogeneic serum • Platelet preparations • Autologous cell saver blood	• Human placenta • Breast milk • Urine and faeces
2. Candidates for a separate legislation	• Inclusion of blood components for transfusion & plasma for fractionation in same legislation [No consensus]	• Inclusion of reproductive tissues and cells & non-reproductive ones in same legislation [No consensus]

THE IMPACT ASSESSMENT

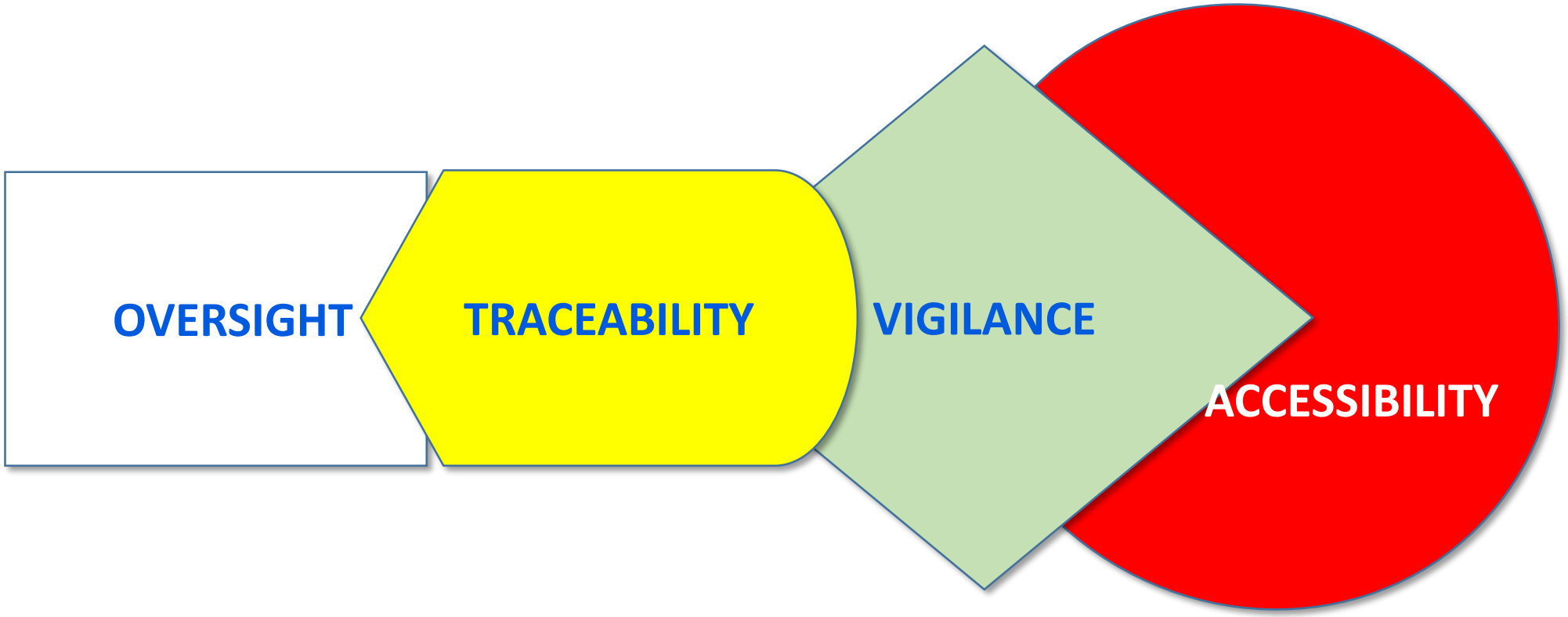
Relevance

Type of developments	1. Developments for BTC	2. Developments specific to blood	3. Developments specific to tissues and cells
A. Scientific and technical	1. Emergence of new donor tests such as Nucleic Acid Technology (NAT) testing. 2. Emergence of procedures to increase safety of BTC	1. New scientific evidence on donor deferral criteria. 2. New evidence on acceptable maximum pH value for platelet concentrates at end of shelf-life. 3. Leukocyte depleted components as standard.	1. New evidence on possibility of less stringent timeframes for donor tests. 2. Technological developments in the tissue and cells field, particularly in the ART sector.
B. Socio-demographic	1. Europe-wide demographic developments, i.e. ageing population, ageing of previous high birth rate cohorts, falling birth rates in many countries. 2. Increased movement of people, especially to/from countries with prevalent pathogens able to cause Transfusion / Transplant Transmitted Infections (TTIs).	1. New scientific evidence on donor referral based on sociodemographic characteristics.	1. Increasing demand for assisted reproductive technologies (ART), especially for Lesbian, Gay, Bisexual and Transgender (LGBT) couples and women choosing to delay conception. 2. High level of cross-border travelling to access ART. 3. Increased possibilities to ship and distribute gametes 4. Genetic screening to prevent transmission of genetic conditions.
C. Epidemiological	1. Emergence of new infectious diseases (e.g. Severe Acute Respiratory Syndrome (SARS)) and changes in distribution of diseases (e.g. Chikungunya) since the adoption of the blood, tissues and cells legislation. 2. Threats to donor bases caused by epidemiological widespread outbreaks (e.g. Zika).		

THE IMPACT ASSESSMENT

Effectiveness

- To what extent has the legislation increased the quality and safety of BTC and achieved a high level of human health protection?
- Has the legislation led to any **unintended effects** (positive or negative)?
- What, if any, have been the **barriers preventing effective implementation of the legislation**?
- Are the **rules on oversight sufficient to address the increased internationalisation**?
- What, if any, are the challenges to maintain compliance with the legislation?
- To what extent, if any, has the legislation **impacted on patient access to BTC**?



THE IMPACT ASSESSMENT

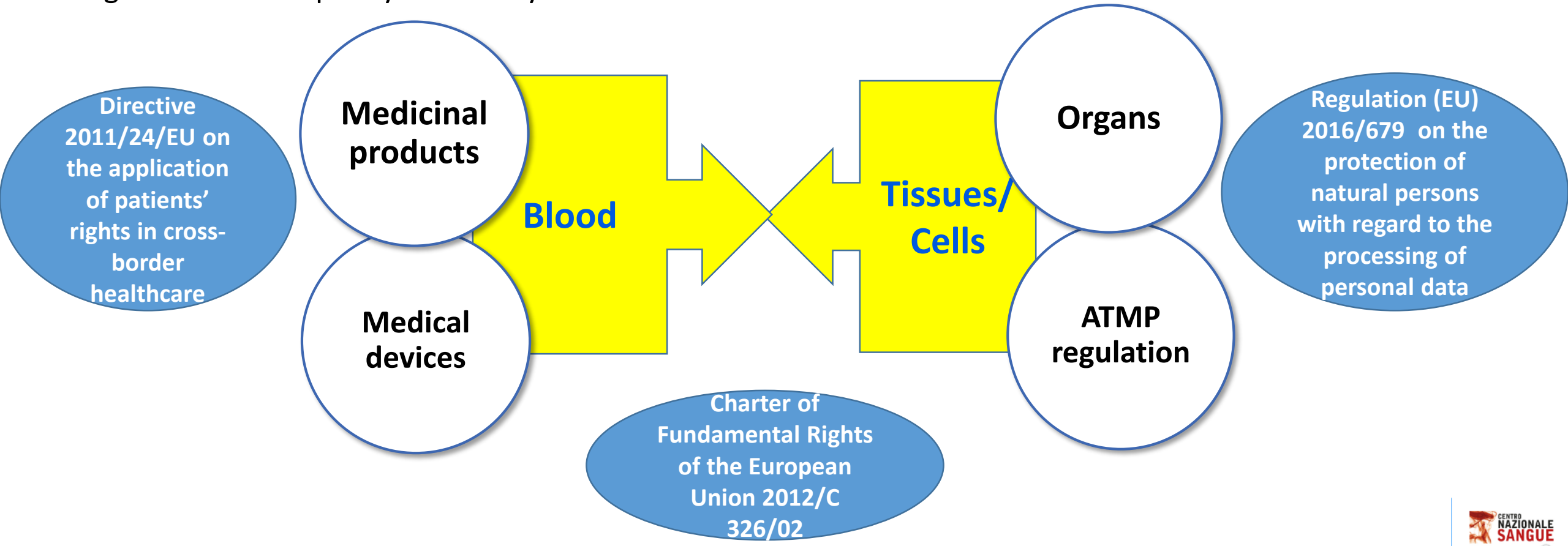
Efficiency

- How cost-effective has the application of the quality and safety requirements in the legislation been for operators (have the benefits outweighed the costs?)?
- Are there particular administrative or other burdens for specific groups of operators, including downstream users of BTC as starting materials for medicinal products?
- To what extent has the legislation resulted in cost implications for hospitals/patients using/receiving BTC?
- To which extent does the oversight required by regulatory bodies pose a burden to public authorities (has the burden been proportionate to achieving the original oversight objectives of the legislation?)?

THE IMPACT ASSESSMENT

Coherence

- To what extent is the legislation on BTC consistent and coherent within its own provisions?
- To what extent is the legislation coherent and consistent with other relevant Union legislation?
- Are the requirements of the Directives suitable when BTC are used as starting materials for the manufacture of medicinal products/medical devices?
- To what extent is the legislation coherent with other relevant international / third country approaches to the regulation of the quality and safety of BTC?



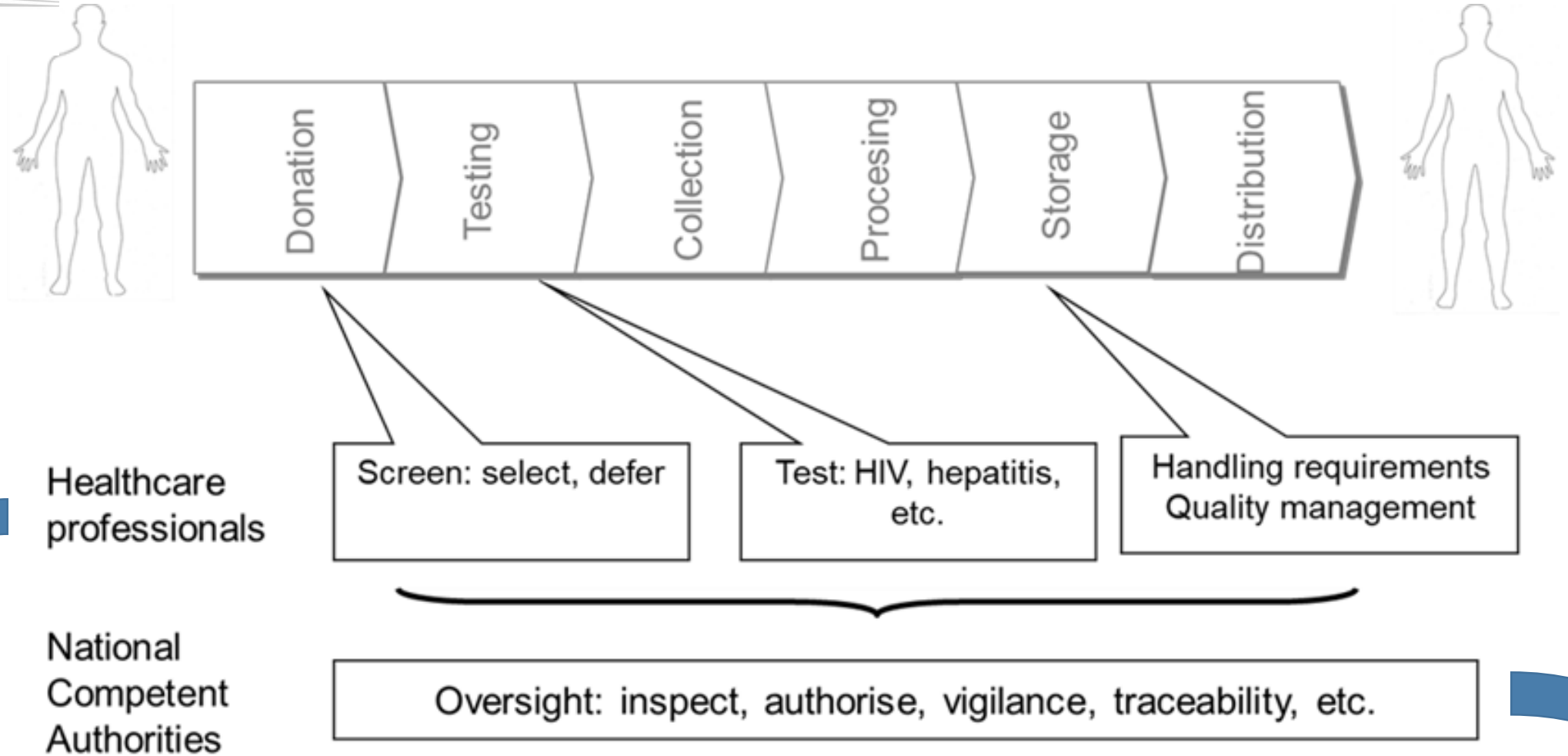
THE IMPACT ASSESSMENT

EU Added Value

- To what extent has the legislative framework at EU level added value to the regulation of BTC across the EU-28 in a manner that could not have been achieved by measures taken at national or global level?
- To what extent do stricter national measures pose an obstacle to exchange of supplies between Member States?

doi: 10.2875/674510

OBIETTIVI DELLE DIRETTIVE BTC



QUALITA' E SICUREZZA

VIGILANZA E CONTROLLO

PUNTI DI DEBOLEZZA DELLA LEGISLAZIONE BTC

i) The legislation effectively increased the level of safety and quality of BTC across the EU
→ **nuove minacce infettive (globalizzazione)**

i) The current rules are no longer up to date with the dynamic BTC sectors
→ **adattamento alle sfide legate agli sviluppi tecnologici e agli scenari epidemiologici**

iii) Key oversight principles are not sufficiently robust
→ **indipendenza, limiti delle autorità competenti**

PUNTI DI DEBOLEZZA DELLA LEGISLAZIONE BTC

iv) Some citizen groups, such as donors and offspring are not adequately protected

→ **protezione donatori di gameti e PMA**

v) The legislation does not keep pace with innovation

→ **nuovi prodotti e nuovi processi senza cornice regolatoria**

v) Requirements are insufficient to support sufficiency and a sustainable supply for all BTC

→ **scarsi strumenti a supporto dell'autosufficienza (PMDP)**

PERCHE' UNA REVISIONE DELLA LEGISLAZIONE BTC

GAP/LIMITI

1. Patients are not fully protected from avoidable risks

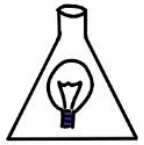
EU safety and quality requirements are incomplete and have failed to remain up to date with frequently changing scientific and epidemiological developments. The outdated provisions are technical in nature

2. Avoidable risks for BTC donors and for children born from donated eggs, sperm or embryos

Donor adverse reactions (including serious ones) are not systematically reported and the requirements for testing egg and sperm donors for genetic conditions are limited.

3. Divergent approaches to oversight cause unequal levels of safety and quality and barriers to the exchange of BTC across the EU

Lack of general principles, provisions for verification of effective implementation of inspection, authorisation, vigilance.



4. BTC legislation lags behind innovation

Limited clinical data on safety and efficacy of new ways of processing donations. Difficulties in defining the borderlines for novel BTC with other regulatory frameworks

5. EU vulnerable to interruptions in supply of some BTC

High dependence on plasma import. Lack of supply monitoring for crisis management

LE POLICY OPTIONS

All policy options:
- **Safety and quality PRINCIPLES to be defined in EU legislation**
- **Rules to protect recipients, DONORS and CHILDREN born from donated gametes/embryos**

Policy option 1:
Strengthened quality & safety requirements defined by blood and tissue establishments with strengthened national inspection, EU audits of national control systems (self-regulation)

Policy option 2:
EU-level safety and quality requirements defined by European Expert Bodies (ECDC, EDQM,…) and strengthened national inspection, EU audits of national control systems, and MS joint inspections (co-regulation)

Policy option 3:
EU-level safety and quality requirements laid down in the BTC legislation with improved national inspection systems, and MS joint inspections (horizontal regulation)

LE ULTERIORI MISURE

Strengthen oversight (gap 3) through:
- stronger principles in EU legislation,
- combined with mutual peer audits, training and guidance

Facilitate innovation (gap 4) by:
- clarifying the BTC scope and provide advice to Member States on scope
- risk-based authorization of novel processes and use, with proportionate collection and assessment of outcome data

All policy options include clarification/extension of scope to include currently unregulated SoHO

Manage supply issues (gap 5) through:
- strengthening supply monitoring
- emergency supply measures

Proposta di

REGOLAMENTO DEL PARLAMENTO EUROPEO E DEL CONSIGLIO

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

CAPO I
DISPOSIZIONI GENERALI

Art.2

a) reclutamento di donatori di SoHO;
b) riesame degli antecedenti dei donatori di SoHO e valutazione dell'idoneità di questi ultimi;
c) controllo dei donatori di SoHO a fini di idoneità o compatibilità;
d) raccolta di SoHO da donatori o pazienti;
e) processazione delle SoHO;
f) prove di controllo della qualità delle SoHO;
g) stoccaggio delle SoHO;
h) rilascio delle SoHO;
i) distribuzione delle SoHO;
j) importazione delle SoHO;
k) esportazione delle SoHO;
l) applicazione di SoHO sugli esseri umani;
m) **monitoraggio degli esiti clinici relativi alle SoHO.**

CAMPO DI APPLICAZIONE

IL NUOVO REGOLAMENTO EUROPEO (BTC)

CAPO II
AUTORITÀ COMPETENTI

- Designazione delle autorità competenti
- Delega di determinate attività di sorveglianza sulle SoHO da parte delle autorità competenti
- Indipendenza e imparzialità
- Trasparenza
- Responsabilità e obblighi generali
- Comunicazione e coordinamento tra autorità competenti per le SoHO
- Obblighi di consultazione delle autorità di altri settori normativi e di cooperazione con le stesse
- Obblighi generali riguardanti il personale delle autorità competenti
- Obblighi in materia di controlli svolti dalla Commissione

CAPO III
ATTIVITÀ DI SORVEGLIANZA SULLE SOHO

- Registro degli enti/centri SoHO
- Sistema di autorizzazione di preparazioni di SoHO
- Autorizzazione di preparazioni di SoHO
- Valutazione delle preparazioni di SoHO
- Valutazioni congiunte di preparazioni di SoHO
- Obblighi specifici riguardanti i valutatori di preparazioni di SoHO
- Sistema di autorizzazione di centri SoHO
- Sistema di autorizzazione di enti SoHO importatori
- Ispezioni sui centri SoHO
- Ispezioni congiunte
- Obblighi specifici riguardanti gli ispettori
- Estrazione e pubblicazione di dati sulle attività
- Rintracciabilità
- Vigilanza
- Allerte rapide relative a SoHO

IL NUOVO REGOLAMENTO EUROPEO (BTC)

CAPO IV
OBBLIGHI GENERALI PER GLI ENTI SOHO

- Registrazione degli enti/centri SoHO
- Persona responsabile del rilascio di SoHO
- Esportazione
- Autorizzazione di preparazioni di SoHO
- Domanda di autorizzazione di preparazioni di SoHO
- Autorizzazione di enti SoHO importatori
- Raccolta e segnalazione dei dati sulle attività
- Rintracciabilità e codifica
- Sistema di codifica europeo
- Vigilanza e segnalazione

"ente SoHO": un'organizzazione legalmente stabilita nell'Unione che svolge una o più delle attività relative a SoHO

CAPO V
OBBLIGHI GENERALI PER I CENTRI SOHO

- Autorizzazione di centri SoHO
- Sistema di gestione della qualità
- Medico

"centro SoHO": un ente SoHO che svolge sia la processazione che lo stoccaggio di SoHO;

IL NUOVO REGOLAMENTO EUROPEO (BTC)

CAPO VI
PROTEZIONE DEI DONATORI DI SOHO

CAPO VII
PROTEZIONE DEI RICEVENTI DI SOHO E DELLA PROGENIE

CAPO VIII
CONTINUITÀ DELLA FORNITURA

CAPO IX
COMITATO DI COORDINAMENTO PER LE SOHO

CAPO X
ATTIVITÀ DELL'UNIONE

CAPO XI
Piattaforma UE per le SoHO

IL NUOVO REGOLAMENTO EUROPEO (BTC)

LE AMBIZIONI

- Rafforzare I requisiti di qualità e sicurezza per tutte le fasi della catena da vena a vena e per tutte le tipologie di donatorI
- Rafforzare le NCA con strumenti a supporto delle misure di oversight
- Ottenere un elevato grado di armonizzazione e di mutuo riconoscimento tra gli SM
- Mettere in coerenza tutte le normative comunitarie in materia di SoHO
- Potenziare le strategie per l'autosufficienza basate sulla donazione volontaria e non remunerata.

CENTRO NAZIONALE SANGUE

Istituto Superiore di Sanità

Grazie dell'attenzione!