



Associazione Farmaceutici Industria
Società Scientifica

L'EVOLUZIONE DEL REGOLATORIO NELLE TERAPIE AVANZATE

WEBINAR

**MERCOLEDÌ 9 APRILE 2025
14:30 - 18:00**

***"From Bench to Bedside: navigating ATMP
complex and evolving regulatory framework interplays"***

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Aptuit (Verona) srl, an EVOTEC company

*From Bench to Bedside:
navigating ATMP complex
and evolving regulatory
framework interplays*





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Agenda

1. EU ATMP Regulatory landscape
2. GMO Directives & ATMP Regulation interplay
3. C&T Directive/SoHO Regulation & ATMP Regulation interplay
4. Medical Device & ATMP Regulations interplay – case study
5. What next



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Advance Therapies Medicinal Products (ATMPs)

ATMPs = DRUGs



HCTs = NOT-DRUGs

- HCTs are generally considered as **established medical procedures** performed in hospitals and follow **different requirements** and **authorization processes**
- **Not** requiring **prospective demonstration of efficacy through clinical trials** and **different quality standards** are applied
- As HCTs present a **lower risk to patients**, they are often covered by other **legal frameworks** such as **transplant regulations**: aimed largely at the **prevention of contamination & disease transmission**
- HCTs are generally **not considered as “medicinal products”** and are not subject to medicinal product/ pharmaceutical registration requirements

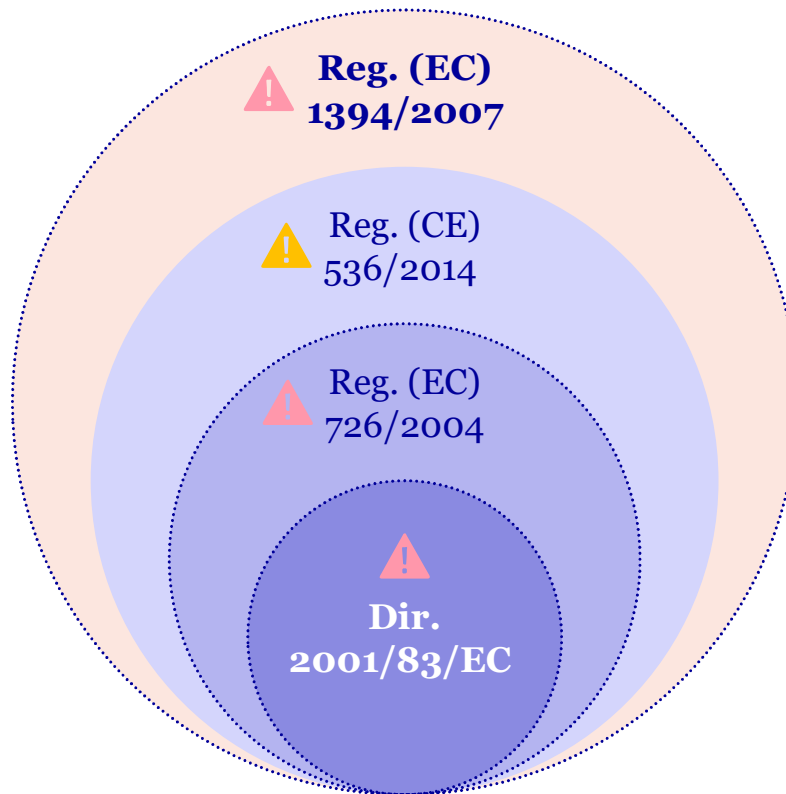


Advance Therapies Medicinal Products (ATMPs)

EU Legal basis and interplays



<i>Orphans</i>	⚠
<i>Pediatrics</i>	⚠
<i>Pharmacovigilance</i>	
<i>Post-approval commitments</i>	⚠
<i>Falsified drugs</i>	
<i>HTA Regulation</i>	⚠
<i>GxP</i>	



“Lex specialis”
for ATMP

Interventional
Clinical Studies

Centralised
procedure

**Medicinal Drugs
(Development &
Registration)**

 Work in progress



Advance Therapies Medicinal Products (ATMPs)

Classification: Art 1 Dir 2001/83/CE; Art.2 Reg 1394/2007



- Products containing exclusively non-viable cells or tissues
- Vaccines against infectious disease

Classificazione ATMP

- What are they **made of**?
- What is their **scope of use**?

Gene therapy (GTMP)

- ✓ **recombinant nucleic acid**
- ✓ to regulate, repair, replace, add or delete a genetic sequence
- ✓ to **treat, prevent** or **diagnose** a disease

Somatic-cell therapy (CTMP)

- ✓ **substantially manipulated cells/tissue**
- ✓ not intended to be used for the same essential function (**non-homologous use**)
- ✓ to **cure, prevent** or **diagnose** a disease (pharmacological, immunological, metabolic action)

Tissue-engineered product (TEP)

- ✓ contain **cells or tissues** that have been **modified** so they can be used to **repair, regenerate** or **replace** human tissue
- ✓ TEP and CTMP differ in the mechanism of action

Combined ATMP

- ✓ it must **incorporate**, as an **integral part of the product**, one or more medical devices



Reg (EU) 1394/2007 – ATMP regulation

Key concepts



10.12.2007	EN	Official Journal of the European Union	L 324/121
REGULATION (EC) No 1394/2007 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004 (Text with EEA relevance)			
THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,		been defined in Annex I to Directive 2001/83/EC, but a legal definition of tissue engineered products remains to be laid down. When products are based on viable cells or tissues, the pharmacological, immunological or metabolic action should be considered as the principal mode of action. It should also be clarified that products which do not meet the definition of a medicinal product, such as products made exclusively of non-viable materials which act primarily by physical means, cannot by definition be advanced therapy medicinal products.	
Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,			
Having regard to the proposal from the Commission,			
Having regard to the Opinion of the European Economic and Social Committee (1),			
After consulting the Committee of the Regions,		(4) According to Directive 2001/83/EC and the Medical Device Directives the basis for deciding which regulatory regime is applicable to combinations of medicinal products and medical devices is the principal mode of action of the combination product. However, the complexity of combined advanced therapy medicinal products containing viable cells or tissues requires a specific approach. For these products, whatever the role of the medical device, the pharmacological, immunological or metabolic action of these cells or tissues should be considered to be the principal mode of action of the combination product. Such	
Acting in accordance with the procedure laid down in Article 251 of the Treaty (7),			
Whereas:			
(1) New scientific progress in cellular and molecular biotech.			

Classificazione
ATMP

Gene therapy
(GTMP)

Somatic-cell therapy
(CTMP)

Tissue-engineered
product (TEP)

Combined ATMP

Definition and Classification



Mandatory Centralised procedure for Access to Market (Reg. 726/2004)

CAT¹ Committee for Advance Therapies to evaluate MAA technical dossier, provide advice on scientific consultation (Scientific Advice), prepare guidelines



Risk: Missing single forum for transversal review across Q, S, E

Incentives: ATMPs Certification (SME-only), ATMP Classification, Fee reductions, Scientific Advice



Define Special Quality Standard and GMP for production
(and enforce traceability system)



Post-Registration Monitoring & Risk Management

Hospital exemption: Art 28.2
Non-repetitive use for **non commercial** ATMP administered under the phisicial responsibility at a specific authorised hospital



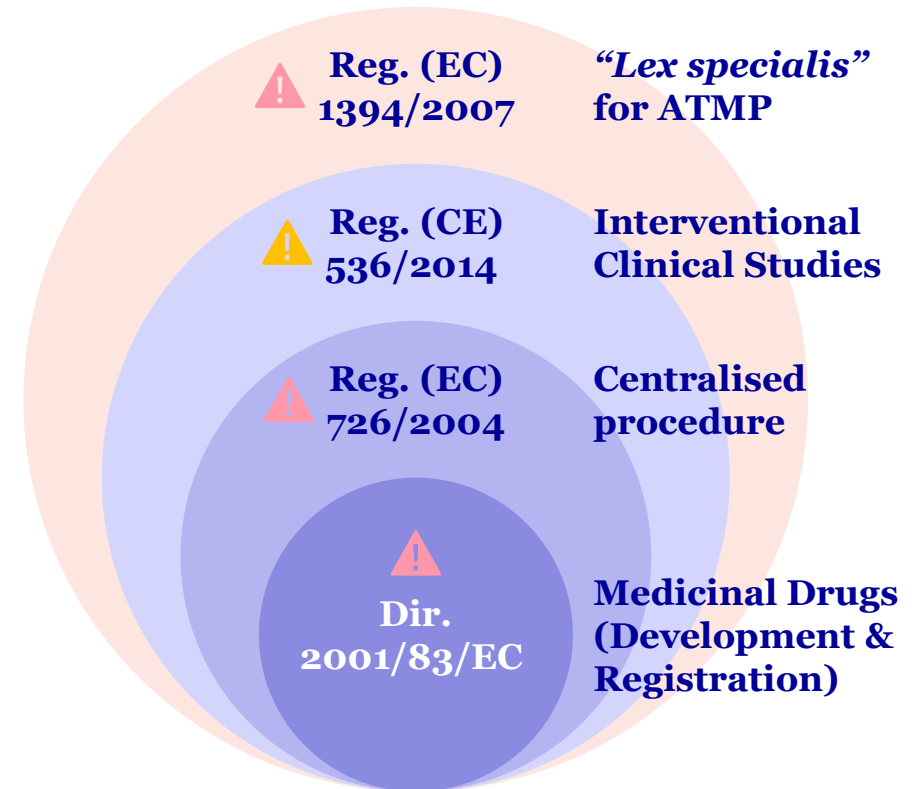
The importance of the ATMP-specific legislation

Dealing with high complexity and multiple evolving legislative interplay

Cells & Tissues Dir. 2004/23/EC & its amendments	
SoHo Reg. 2024/1938 (implemented by 2027)	
Medical Devices Reg. 2017/745	⚠
In vitro Diagnostics Reg. 2017/746	⚠
GMO	Directive 2009/41/EC (contained use) Directive 2001/18/EC (deliberate release)
GMO	Legal framework evolution

General Pharma Strategy Revision: great promise to improve public health, return to being competitive, foster innovation

☐ Work in progress



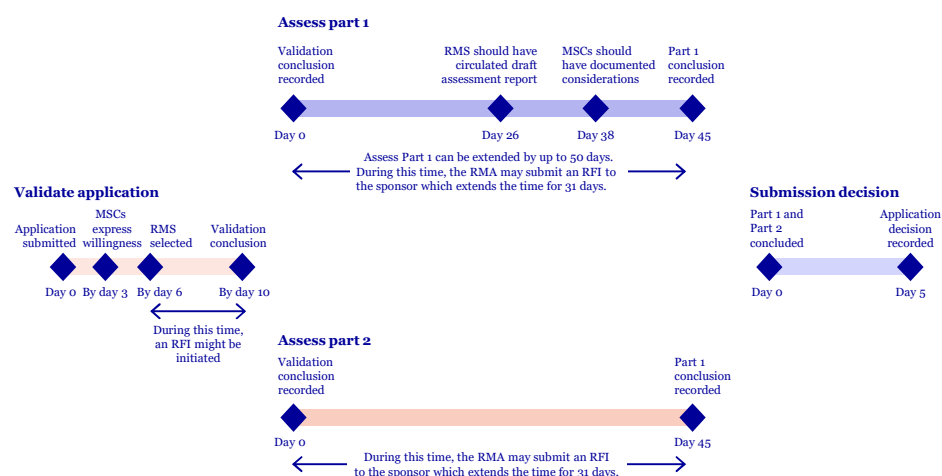
Clinical Trial Regulation EU No 536/2014 (CTR)

Interventional Clinical Studies:

1) CTIS database: CTA submission

2) Clinical Trial Map¹

3) Cross-border Access to Clinical Trials
Recommendation initiative (out for comments)²



- On the **CRITICAL PATH**: **timelines to respond to REQUEST FOR INFORMATION (RFI)**: **only 12 days for PART I**
- Of note: **Extended review timeline for ATMP review (not for RFI)**
 - Still work in progress** (optimization planned)

		Initial application
Validation	# days without RFI	10 days
	# days to respond RFI	10 days ←
	# days to assess RFI	5 days
Part I	# days without RFI	45 days (+50 days for ATMPs)
	# days to respond RFI	12 days ←
	# days to assess RFI	19 days
Part II	# days without RFI	45 days
	# days to respond RFI	12 days ←
	# days to assess RFI	19 days
Decision	# days without RFI	5 days
	# days to assess RFI	



Agenda

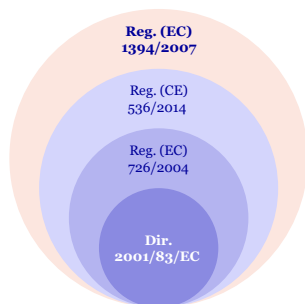
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How to get out of the GMO labyrinth in EU?

National Level conundrum

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Becoming soon SoHo Reg. 2024/1938
Medical Devices Reg. 2017/745
In vitro Diagnostics Reg. 2017/746
GMO Directive 2009/41/EC (contained use) Directive 2001/18/EC (deliberate release)
GMO Legal framework evolution



- **Old legislation** established mainly for applications in **agriculture** (plants and cotton) but extended as an application also to ATMPs
- **2 Separate legal pathways:**
 - Content Use Directive (2009/41/EC)
 - Deliberate Release Directive (2001/18/EC)
- **Heterogeneous requirements:**
 - Implemented at national level
- **Different Competent Authorities/Country:**
 - National authorisation processes (various)
 - **Different expectations/demands for GMO risk assessment**
 - Complexity and possible delays in clinical trials start



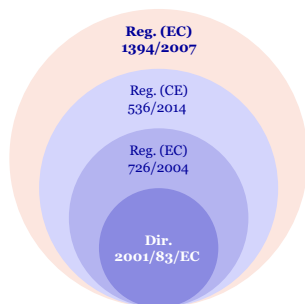
A repository of national regulatory requirements has been created to this effect: https://health.ec.europa.eu/medicinal-products/advanced-therapies/genetically-modified-organism-gmo-aspects-investigational-medicinal-products_en



How to get out of the GMO labyrinth in EU?

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GMO Legal framework evolution



- **Old legislation** established mainly for applications in **agriculture** (plants and cotton) but extended as an application also to ATMPs
- **2 Separate legal pathways:**

In the new **EU General Pharma Strategy revision** there are provisions for:

- **Transferring GMO assessments** from the current regulatory framework to the Medicines regulatory framework
- **Transfer the competences** for the **assessment** of Environmental Impact Dossiers (**ERAs**) to the EMA

One submission & One decision



A repository of national regulatory requirements has been created to this effect: https://health.ec.europa.eu/medicinal-products/advanced-therapies/genetically-modified-organism-gmo-aspects-investigational-medicinal-products_en



Genetic Modified Organism (GMO) Directives

Italian level implementation

Con il **Decreto Legislativo 12 aprile 2001, n. 206**, viene data attuazione in Italia alla Direttiva 98/81/CE, che modifica la precedente Direttiva 90/219/CE sull'impiego confinato di microrganismi geneticamente modificati (MOGM)

Two fulfilments

- a) **MOGM impianto:** the cell factory/hospital holds a valid “notifica di impianto”
- b) **MOGM impiego:** the cell factory/hospital holds a valid “notifica di impiego”

<https://www.salute.gov.it/new/it/tema/biotecnologie-mogm/mogm-microrganismi-geneticamente-modificati/>

[Autorizzazione degli
impieghi confinati di
MOGM e degli impianti](#) ^

Procedura di notifica

Notifiche di impianto

Notifiche di impiego



Agenda

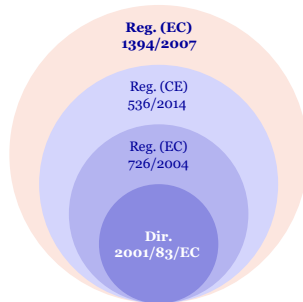
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EU legal framework & regulatory interplay

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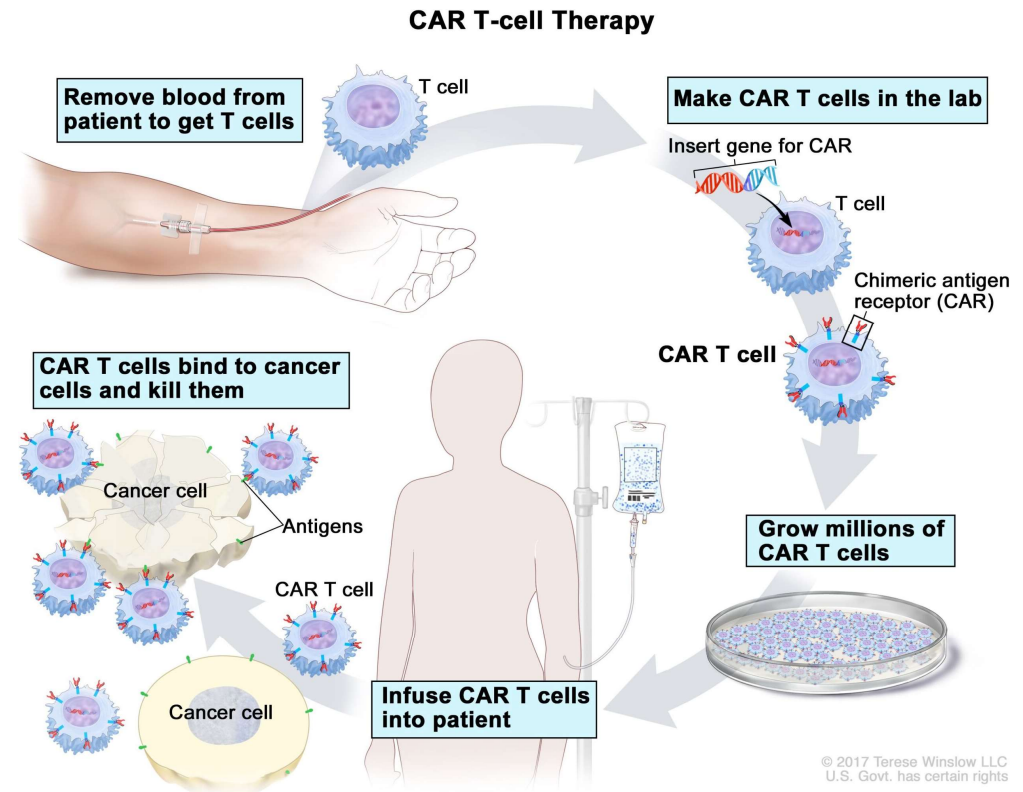
Evolution of the concept form

“One product fits all”

to the concept of

“Personalised medicine”

“Patient at the center of the drug’s production process”

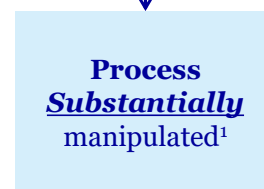
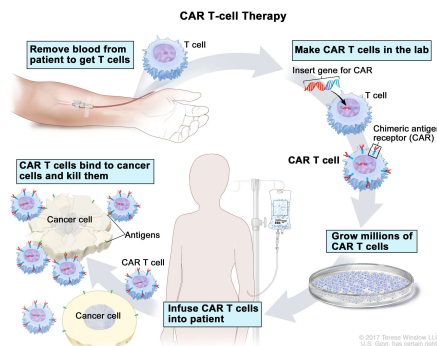
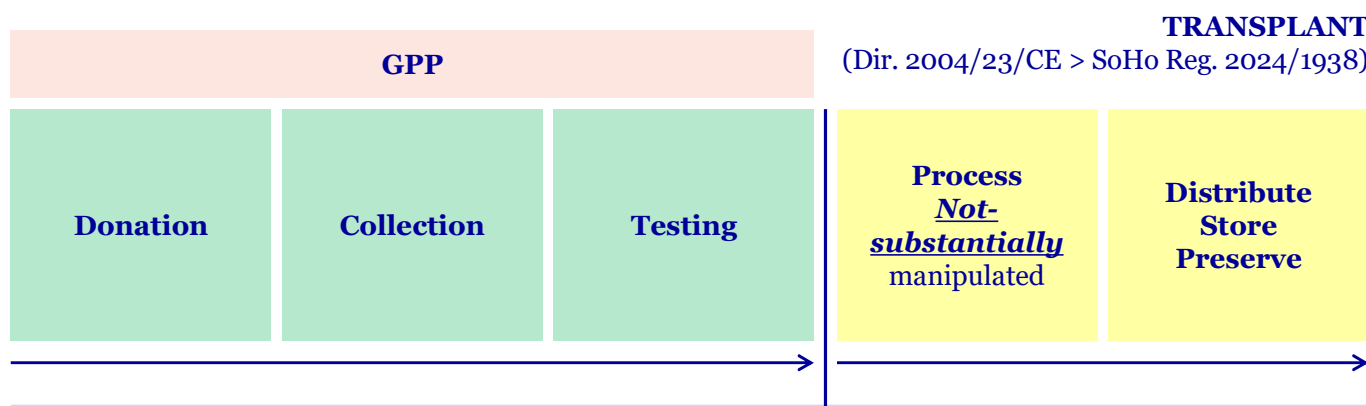
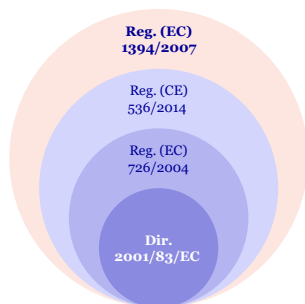




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EU legal framework & regulatory interplay

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**MEDICINAL PRODUCTS
ATMP DRUGs**
(Reg. 1394/2007/CE)

Quality	Safety	Efficacy
GMP	GLP	GCP

Mandatory to define:

- **CoC** Chain of Custody
- **CoI** Chain of Identity

Hospital ws. Manufacturer!



EDQM guide (2022 edition)

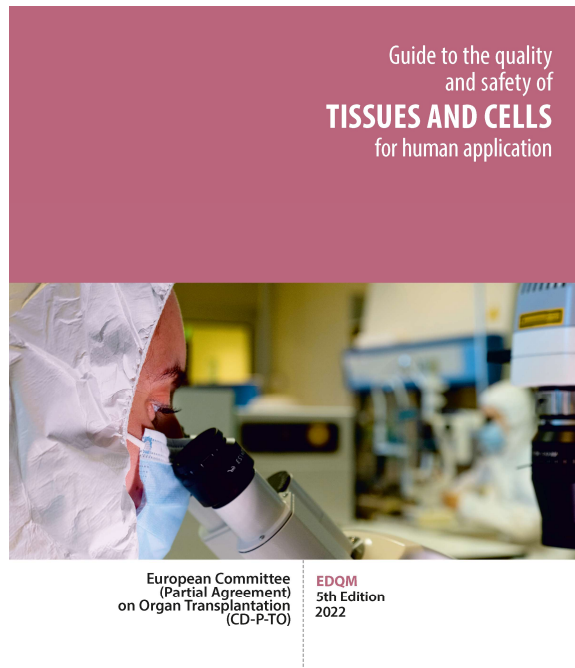
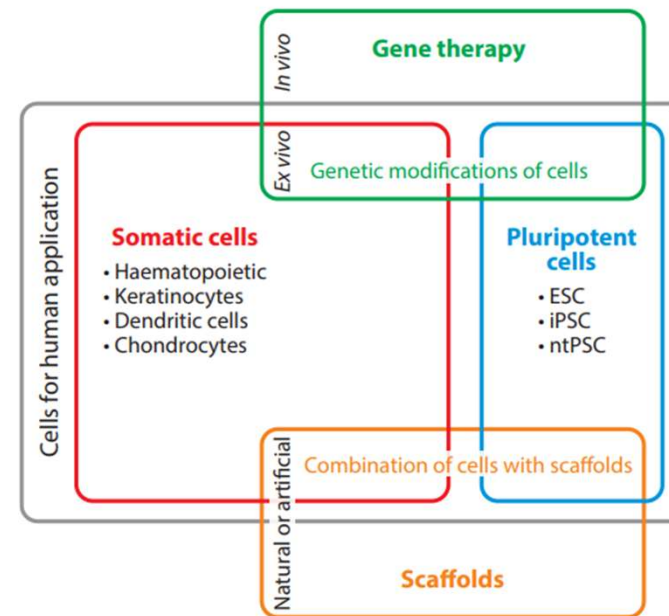


Figure 34.1. Some novel therapies involving human tissues and cells



Note: ESC = embryonic stem cells; iPSC = induced pluripotent stem cells; ntPSC = nuclear transfer pluripotent stem cells.



EDQM guide (2022 edition)



Figure 34.1. Some novel therapies involving human tissues and cells



Tissue and cell collection and processing *versus* ATMP manufacturing and application.

Procurement centre and tissue establishment

Donor selection Procurement

Selection, evaluation, information, consent, collection, packaging, labelling, custody, transport (direct to ATMP manufacturer, if agreed), biovigilance

Processing Release

Reception, evaluation, processing (non-substantial manipulation when required), preservation, storage, release, coding, traceability, **biovigilance**

Directive 2004/23/EC¹

ATMP manufacturer and hospital

ATMP manufacturing

Processing (non-substantial and substantial manipulation when required), storage, QP release, transportation

ATMP administration

Hospital pharmacy or TE under agreement, clinical services, **pharmacovigilance**

EC Regulation 1394/2007



Cells & Tissue Directives 2004/23/CE

EU Human Biological Samples legal framework

	Law #	Law path	Law content
3 main legislative frameworks to be considered	2004/23/EC	Tissues & Cells Directive	To be replaced by SoHO Regulation (2024/23/EC & 2022/98/EC collectively named as “BTC Directives”)
	2002/98/EC	Blood directive	To be replaced by SoHO Regulation (2024/23/EC & 2022/98/EC collectively named as “BTC Directives”)
	2010/53/EC	Solid organs directive	So called “ <i>Translant Organs Legislation</i> ”: remains effective after SoHO implementation
Legislation of relevance for cell-based therapies	2004/23/EC	Tissues & cells directive	Setting standards of quality and safety for donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells
	2006/17/EC	Directive implementing 2004/23	Technical requirements for the donation, procurement and testing of human tissues and cells
	2006/86/EC	Directive implementing 2004/23	Technical requirements for traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells
	2012/39/EC	Directive amending 2006/17/EC	Technical requirements for testing of human tissues and cells
	2015/565/UE	Directive amending 2006/86/EC	Technical requirements for the coding of human tissues and cells
	2015/566/UE	Directive implementing 2004/23	Procedures for verifying the equivalent standards of quality and safety of imported tissues and cells
Effective	2024/1938	SoHO Regulation	New Regulation, repealing the Blood Directive 2002/98/EC and the Tissues and Cells Directive 2004/23/EC and their implementing legislations by 07 Aug 2027 . Solid organs continue to be regulated by Directive 2010/53/EU and are excluded from the definition of this term.



Cells & Tissue Directives 2004/23/CE

DIRECTIVE → Implementation @ NATIONAL level

	Law #	Law path	Implemented in Italy with	
Legislation of relevance for cell-based therapies	2004/23/EC	Tissues & cells directive	Decreto legislativo 6 novembre 2007, n. 191	Definizione di standard di qualità e sicurezza per la donazione, l'approvvigionamento, l'analisi, la lavorazione, la conservazione, lo stoccaggio e la distribuzione di tessuti e cellule umani
			Decreto legislativo 10 ottobre 2012	Modalità per l'esportazione o l'importazione di tessuti, cellule e cellule riproduttive umani destinati ad app
	2006/17/EC	Directive implementing 2004/23	Decreto legislativo 25 gennaio 2010, n. 16	Cellule riproduttive umani destinati ad applicazioni sull'uomo
	2006/86/EC	Directive implementing 2004/23	Decreto legislativo 30 maggio 2012, n. 85	Prescrizioni tecniche relative alle prescrizioni in materia di tracciabilità, notifica di reazioni avverse ed eventi avversi gravi e talune prescrizioni tecniche per la codifica, la lavorazione, la conservazione, lo stoccaggio e la distribuzione di tessuti e cellule umani
	2012/39/EC	Directive amending 2006/17/EC	Decreto del Presidente della Repubblica, 23 agosto 2019, n. 131	Regolamento di attuazione della direttiva 2012/39/UE della commissione, del 26 novembre 2012, che modifica la direttiva 2006/17/CE per quanto riguarda determinate prescrizioni tecniche relative agli esami effettuati su tessuti e cellule umane
	2015/565/UE	Directive amending 2006/86/EC	Decreto legislativo 16 dicembre 2016, n. 256	Requisiti tecnici per la codifica di cellule e tessuti umani
	2015/566/UE	Directive implementing 2004/23	Decreto legislativo 15 novembre 2016	Procedure per la verifica degli standard equivalenti di qualità e sicurezza dei tessuti e delle cellule importati
Effective	2024/1938	SoHO Regulation	Implemented by Aug 2027 (3 yrs implementation period)	SoHO regulation: The new Regulation, repealing the Blood Directive 2002/98/EC and the Tissues and Cells Directive 2004/23/EC and their implementing legislations by 07 Aug 2027 . Solid organs continue to be regulated by Directive 2010/53/EU and are excluded from the definition of this term.



Who can collect, test and import SoHO in EU?

Directive 2004/23/UE > SoHO Regulation 2024/1938

EU Tissue Establishment > Soon becoming SoHO Establishment

Now, let's practice: <https://webgate.ec.europa.eu/eucoding/reports/te/index.xhtml>

Report for EU TE Code IT000690

Name of TE	Laboratorio di Manipolazione e Crioconservazione Cellulare SIMT		
Competent Authority	IT029-Italian National Transplant Center		
Hospital Name	Azienda Ospedaliero Universaria Policlinico di Modena		
Country	Italy		
Address	71 Via del Pozzo 41124 Modena Italy	Phone	0594225551
		E-mail	trasf.labcriobiologia@policlinico.mo.it
		www	
Status	Active		
Competent Authority	IT029-Italian National Transplant Center		
Name of Licence Holder		Last registration update	16-Sep-2019
Type of Authorisation	System site inspection		

End date	Type of tissues/cells	Detail	Activities							
			Procurement Donation	Testing	Preservation	Processing	Storage	Distribution	Import	Export
	Progenitor Cell, Hematopoietic, Bone Marrow	Autologous			A	A	A	A		
		Allogeneic Related			A	A	A	A		
		Allogeneic Unrelated			A	A	A	A	A	A
	Progenitor Cell, Hematopoietic, PBSC	Autologous			A	A	A	A		
		Allogeneic Related			A	A	A	A		
		Allogeneic Unrelated			A	A	A	A	A	A
	Progenitor Cell, Hematopoietic, Cord Blood	Autologous					A	A	A	
		Allogeneic Related					A	A	A	
		Allogeneic Unrelated					A	A	A	
	Mature Cell, T Cell	Autologous								
		Allogeneic Related			A	A	A	A	A	A
		Allogeneic Unrelated			A	A	A	A	A	A

A - Authorized
S - Suspended
R - Revoked
C - Ceased activity

Report for EU TE Code IT000131

Name of TE	Laboratorio Manipolazione e Crioconservazione Cellule Staminali - Servizio di Immunoematologia e Medicina Trasfusionale		
Competent Authority	IT029-Italian National Transplant Center		
Hospital Name	A.O. Spedali Civili di Brescia		
Country	Italy		
Address	1 Piazzale Spedali Civili 25123 Brescia Italy	Phone	030 3996579
		E-mail	camillo.almici@asst-spedalicivili.it
		www	http://www.staminali.brescia.it
Status	Active		
Competent Authority	IT029-Italian National Transplant Center		
Name of Licence Holder		Last registration update	19-Apr-2023
Type of Authorisation	System site inspection		

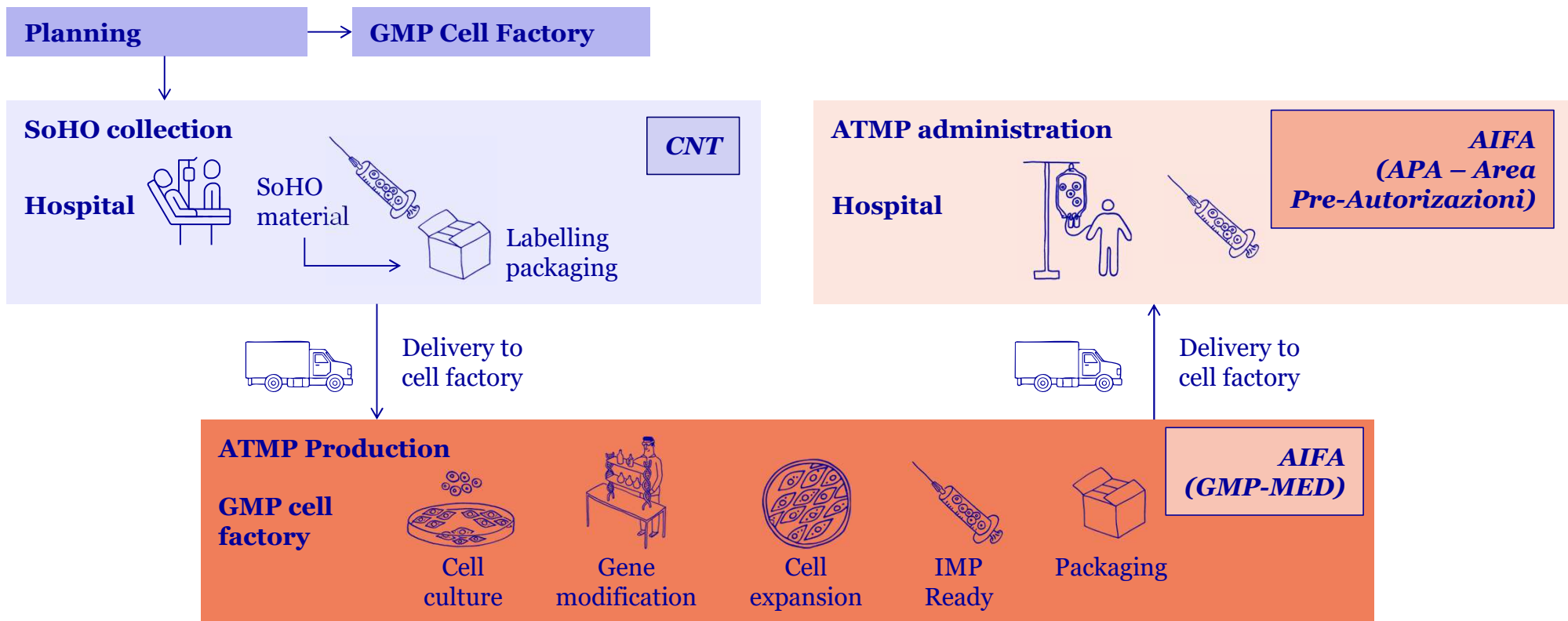
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		Allogeneic Unrelated			A	A	A	A	A	A
	Progenitor Cell, Hematopoietic, PBSC	Autologous			A	A	A	A	A	
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		Allogeneic Unrelated			A	A	A	A	A	A
	Progenitor Cell, Hematopoietic, Cord Blood	Autologous								
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		Allogeneic Unrelated			A	A	A		A	
	Mature Cell, T Cell	Autologous								
		Allogeneic Related			A	A	A	A	A	A
		Allogeneic Unrelated			A	A	A	A	A	A

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Overall supply chain design

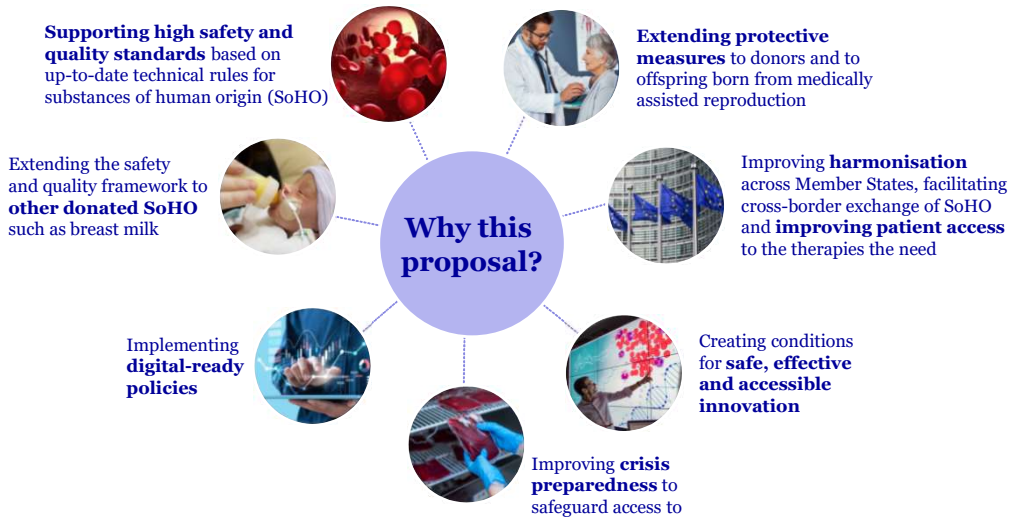
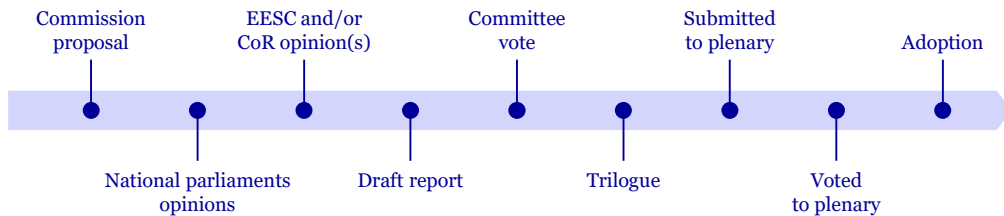
Chain of Custody among parties & competent authorities





SoHO – Subject of Human Origin Regulation

Stronger rules for greater safety and quality of blood, tissues, and cells



- **Published:** on 17 July 2024
- **Effective:** 21 days after publication in EU Official Journal
- **Implementation:** The regulation would apply three years after its adoption (**by Aug 2027**)



SoHO – Subject of Human Origin Regulation 2024/1938

Stronger rules for greater safety and quality of blood, tissues, and cells

*Innovation in SoHO is a big challenge and it is clear there is a need to manage **Quality, Safety and Efficacy** demonstration as well as **management of the associated risks**.*



Strengthened levels of health protection



A wider scope to cover blood, tissues, and cells, together with other SoHO (like human breast milk or faecal microbiota)



High standards for safety and quality, implemented through **technical guidelines** developed mostly by expert bodies¹ based on up-to-date scientific evidence



Renewed commitment to the **principle of voluntary and unpaid donation**, protection donors from exploitation and from risks to their own health without discouraging donations



Improved reporting and follow-up on adverse reactions

Harmonisation, simplification & support



Implementation of risk-based oversight, for more efficient use of resources (for authorising establishments and activities, carrying out of inspections, ...)



Application of **common technical guidelines** while safeguarding Member States' possibility to have more stringent rules



Collection of information on supply, quality and safety of SoHO for oversight, policy and research



EU support to Member States through training for authorities, joint activities and advisory mechanism

Facilitation of innovation



Common EU-wide authorisation procedures for innovative SoHO preparations



Body providing advice on regulatory status of a substance or a product

Digitalization



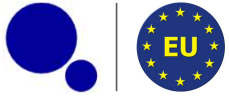
Common IT Platform to facilitate data reporting and information sharing

★ areas of potential impact for ATMP developers



Agenda

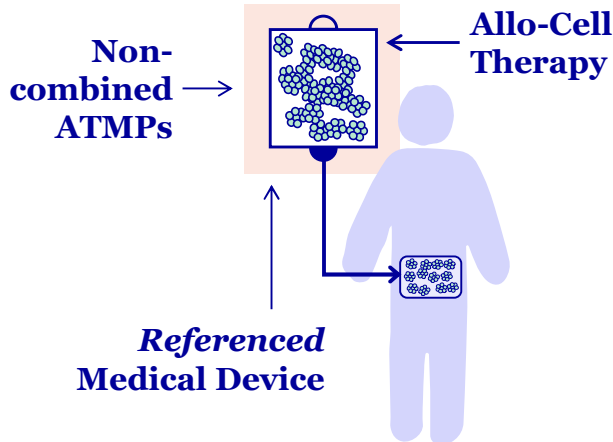
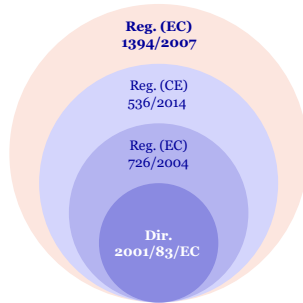
1. EU ATMP Regulatory landscape
2. GMO Directives & ATMP Regulation interplay
3. C&T Directive/SoHO Regulation & ATMP Regulation interplay
4. Medical Device & ATMP Regulations interplay – case study
5. What next



FIH Combined Trial: iCell Therapy + iMedical Device

EU Regulatory Submissions Strategy

Cells & Tissues Dir. 2004/23/EC & its amendments
Becoming soon SoHo Reg. 2024/1938
Medical Devices Reg. 2017/745
In vitro Diagnostics Reg. 2017/746
GMO Directive 2009/41/EC (contained use) Directive 2001/18/EC (deliberate release)
GMO Legal framework evolution



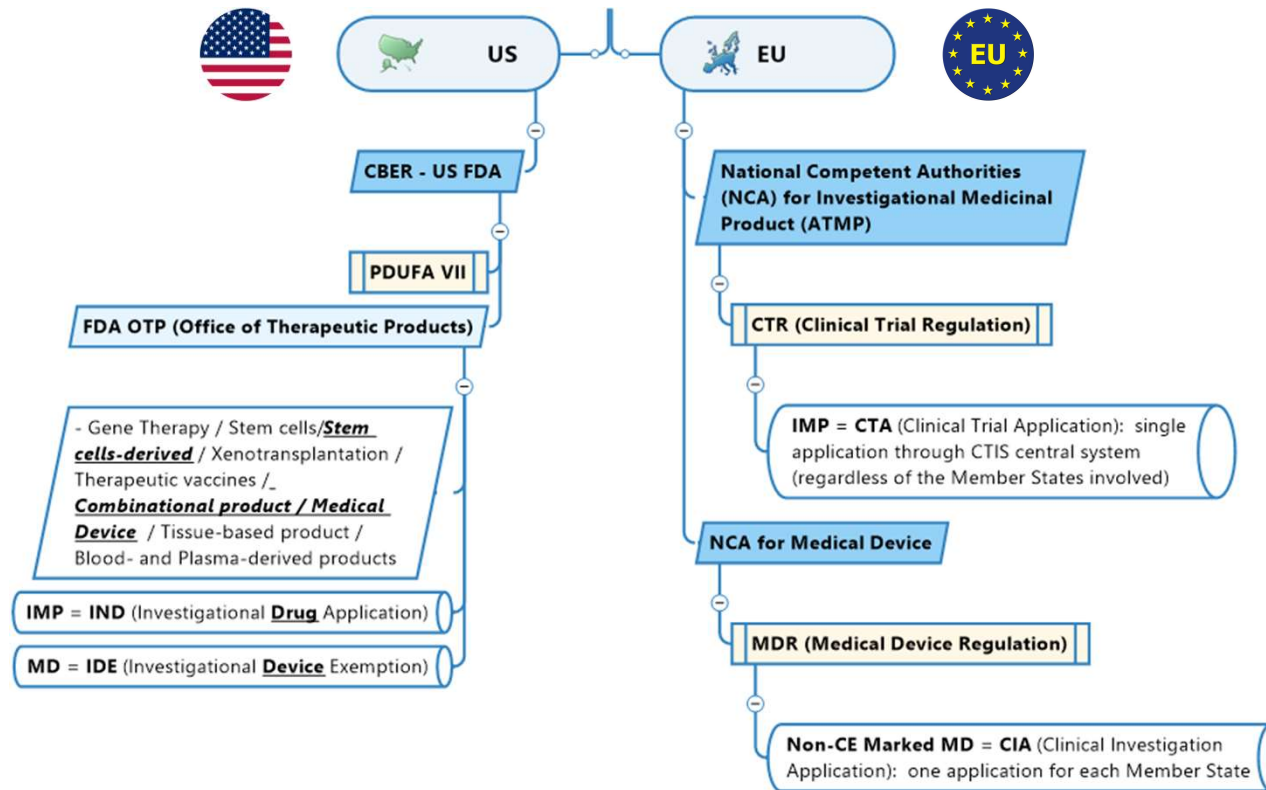
- **Single combined trial: simultaneous investigation** of an ***investigational medicinal product*** and of a ***non-CE marked medical device***
- **Separate legal frameworks** regulates ATiMP & iMD:
 - **Clinical Trial Regulation (CTR 536/2014/CE)**: clinical investigation for the investigational cell therapy (drug) authorized under EU CTR with a CTA (**Clinical Trial Application**)
 - **Medical Device Regulation (MDR 2017/745/CE & 2023/607)**: clinical performance study for the device authorized under EU MDR with a CIA (**Clinical Investigation Application**)
- There is **no dedicated procedure foreseen** in the CTR for “**combined Trials**” and therefore, currently, **no harmonized procedure in place** (hence, procedures to be synchronized)
- There is **no regulatory dependency of drug and medical device laws that require the evaluation of a study to be combined** for the purposes of classification



US vs EU legal frameworks

Implications of different classification

“Combo” Cell Therapy



“Not- Combo” Cell Therapy



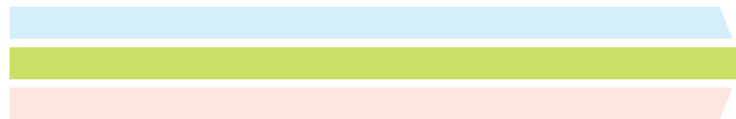
Implementing 3 regulations together ...



Authorisation

CT:

Member States
coordinate using CTIS

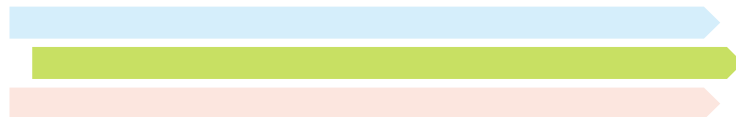


Clinical trial of a medicinal product



No coordination between the 2 sets of authorization processes in the Regulations

MD/IVD: currently
national authorisations,
coordination piloted



Performance study of IVD, e.g. for inclusion of patients



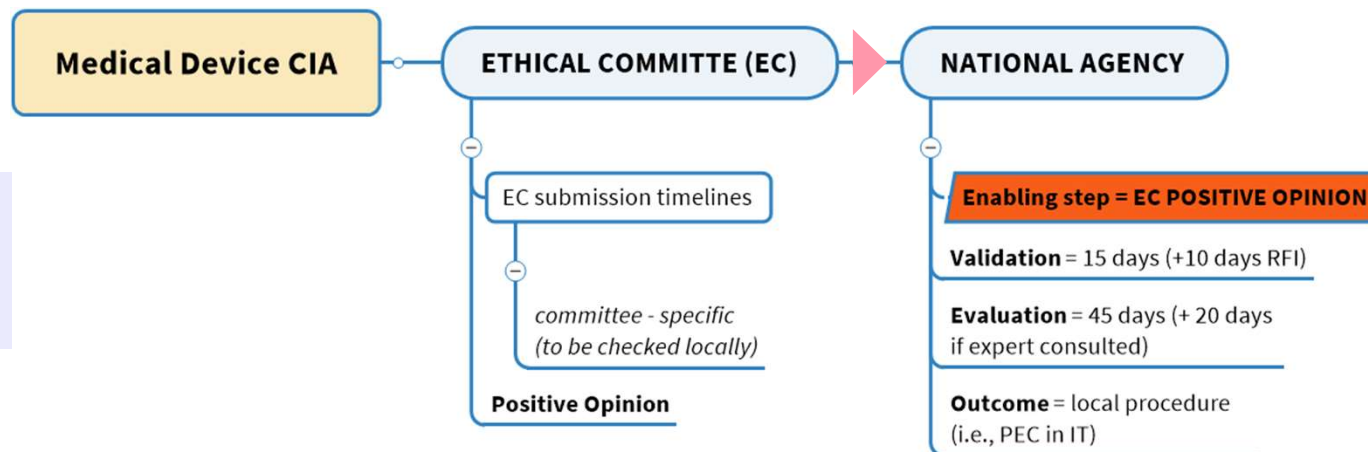
Medical Device Regulation (EU) 2017/745 & (EU) 2023/607

Medical devices (MDR)

Clinical Investigation Application (CIA)

Clinical Investigation procedure & timetable defined at national level:

- **Country by Country**
- CIA VALIDATION *triggered* by a “Non-negative Opinion” on the Clinical Investigation Protocol by the Ethical Committee
- No legal framework for Scientific Advice on Medical Device

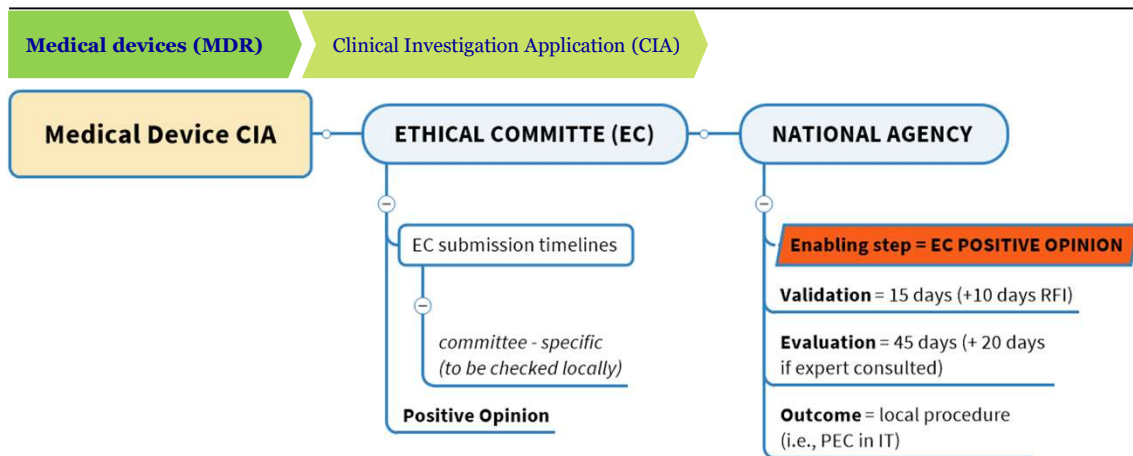


Cell Pouch CIA
Submission
timetable



i-Cell therapy and i-Medical Device: FIH Clinical Trial

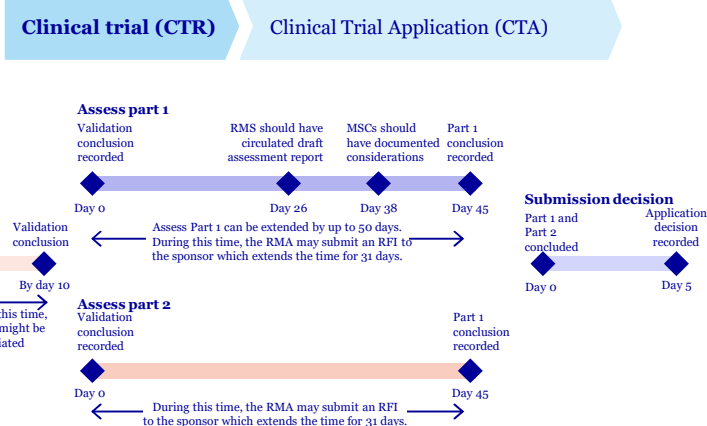
Projected Timelines (EU/US)



- Parallel CIA/CTA not advisable under the new MDR/CTR
- **Sequential approach** is recommended (tbc!)
- Critical: protocol reviewed by 2 different Ethical Committee focused on MD only and on CT only

Complex Clinical Trial Application (iCell Therapy & iMedical Device)

	Duration (days)	
	US	EU
EC Review (initial) for MD	45 - 60	45 - 60
FDA Review (COMBO: simultaneously IMP & MD)	30	na
EU National Competent Authority for MD	na	60 - 90
EU CTA for IMP (CTIS) ¹	na	110 - 156
TOT. US timelines for study start (COMBO)	75 - 90	—
TOT. EU timelines for study start (not COMBO)	—	215 - 306





Agenda

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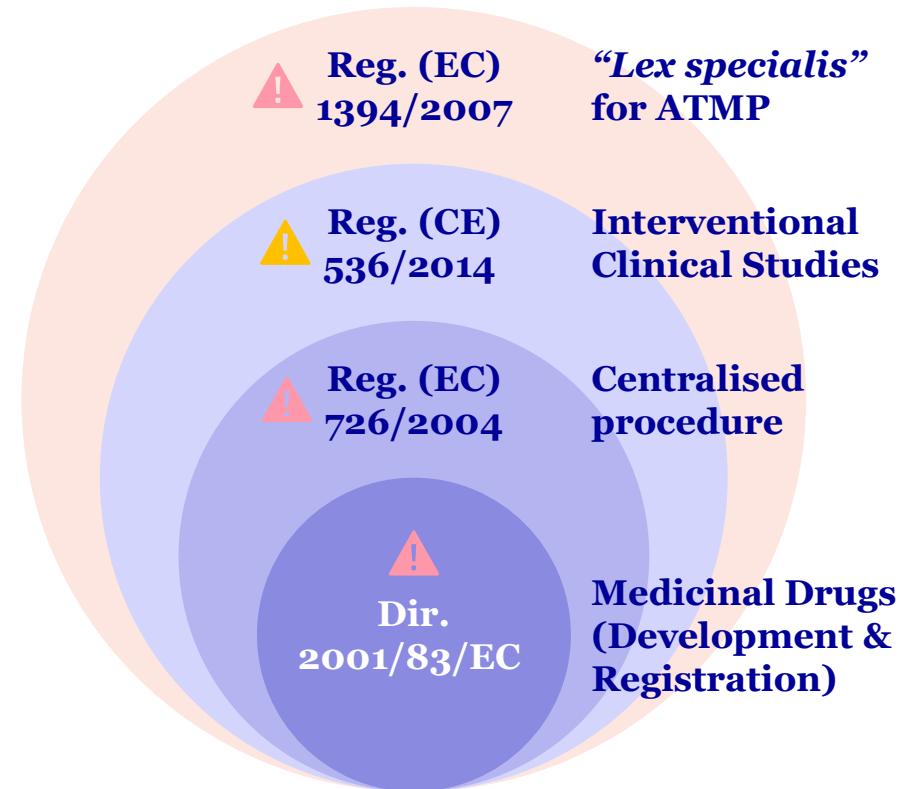
The importance of the ATMP-specific legislation

Dealing with high complexity and multiple evolving legislative interplay

Cells & Tissues Dir. 2004/23/EC & its amendments	
SoHo Reg. 2024/1938 (implemented by 2027)	
Medical Devices Reg. 2017/745	⚠
In vitro Diagnostics Reg. 2017/746	⚠
GMO	Directive 2009/41/EC (contained use) Directive 2001/18/EC (deliberate release)
GMO	Legal framework evolution

General Pharma Strategy Revision: great promise to improve public health, return to being competitive, foster innovation

☐ Work in progress





Evolving Regulatory Pathways

Dealing with uncertainties and opportunities – 1

ATMP special legislation

Dir.2001/83/EC

Reg. (EC) 726/2004

Reg. (EC) 1394/2007



?

Legal framework evolution



Great **promise**

- Speed and flexibility in drug approval
- Foster innovation by decreasing time for approval

Great **uncertainties**

- CAT proposed abolishment:
 - Who will deal with so complex products? Loosing transversal CMC, NC, C dossier review (scientific advice/MAA)
 - Diluting key ATMP expertise into CHMP/WPs
 - Potentially diminishing competencies also at national level (currently knowledge sharing also with EU Countries lacking ATMP expertise)
- ATMP incentives - fee reduction for Scientific Advice abolished in the new EMA Fee Regulation effective Jan 1st, 2025 (exempted only for SME/no-profit/academia)



Evolving Regulatory Pathways

Dealing with uncertainties and opportunities – 2

GMO Directive 2009/41/EC (contained use)
Directive 2001/18/EC (deliberate release)

GMO Legal framework evolution

Cells & Tissues Dir. 2004/23/EC & its amendments

Becoming soon SoHo Reg. 2024/1938

Great **promise**

- Accelerate CTA approval for multinational clinical studies
- If EMA adequately staffed to review ERA on approved clinical trials (not at iso-resource)
- Increase GMO expert resources

Great **promise**

- Higher quality standard, cross-border SoHO movement, technology advancement

Mixed **feeling**

- If CAT abolished and SoHO Coordination Body responsible for classification of ATMP borderline products
- Remains grey area at the legislative interplay:
 - Still National differences for panel testing but also importation conditions (challenge for ALLO ATMP global supply)



Evolving Regulatory Pathways

Dealing with uncertainties and opportunities – 3

Foster Innovation in Drug Development

Platform technology provisions

No Quality DMF for ATMP

Quality DMF for ATMP

Great **promise**

- Accelerating ATMP development by leveraging on consolidated platform knowledge
- Potential for reducing development costs while safeguarding product quality & patient safety
- Utilize fixed and well characterized starting materials and/or reference standards (could ease the process)
- Consolidate product agnostic analytical assays (identity & potency tailored for each drug product, but data from other analytical assays may be leverageable across products when the factors impacting assay output are kept constant (e.g., formulation, storage conditions))
- Invest earlier on industrialization/scalability (for more prevalent indications)



Evolving Regulatory Pathways

Dealing with uncertainties and opportunities – 4

Hospital Exemption provision (Art 28.2)

TBD

- **Art 28.2 Non-repetitive use for non commercial** ATMP administered under the physician responsibility at a specific authorized hospital
- Proposal to give more dignity to this legal tool (still not clear the context)



Conclusions

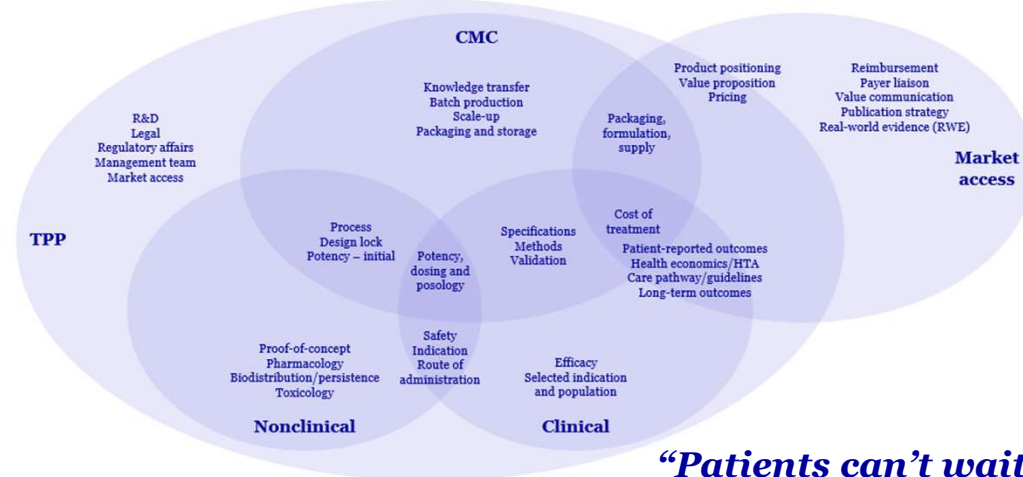


Importance of holistic vision for successful translation



- **Complex products:** different legal frameworks interplay have an impact on Innovative Medicines development
- **Not harmonized legal framework** across different jurisdictions impacting on data expectations, risk-evaluation, authorization procedure's content & timelines
- But are **potentially disease game-changers!**

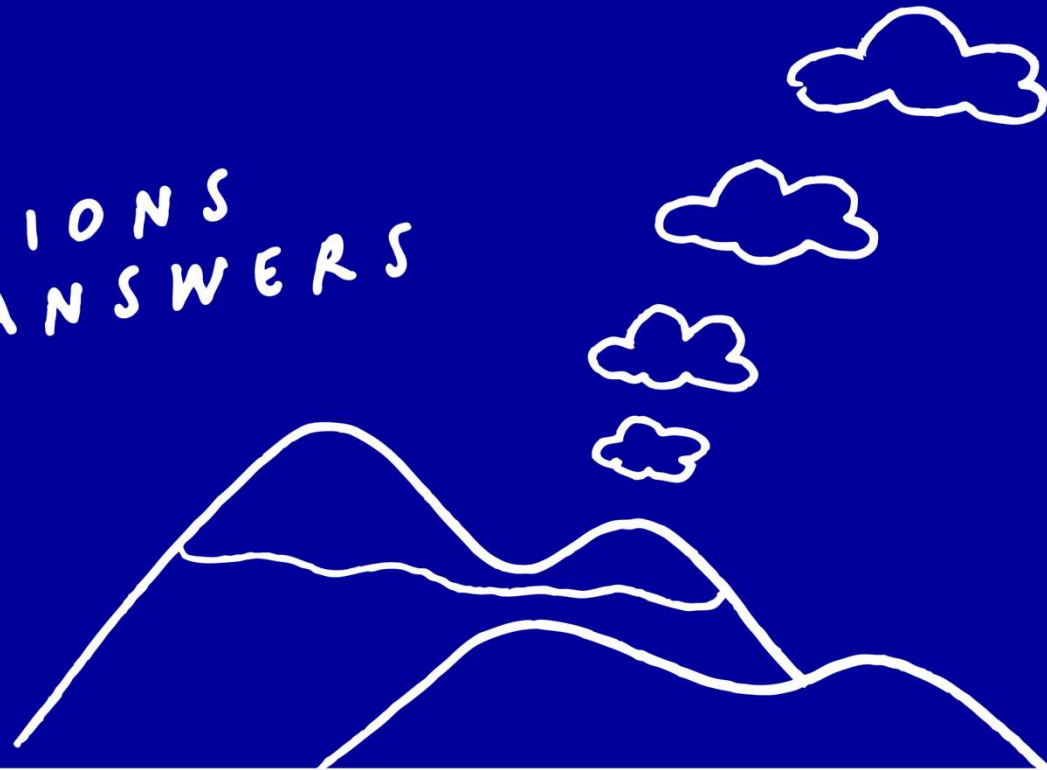
“Start with the end in mind”



“Patients can’t wait!”

- The revision of the EU General Pharmaceutical Legislation is driven by a need to **make EU healthcare systems more resilient, support pharmaceutical innovation, improve patient access** to affordable and safe treatments, and **address public health challenges**. This modernization effort is designed to create a balance between supporting industry innovation and ensuring that medicines are available, accessible, affordable, (and sustainable) across the EU.
- **More to come...**

QUESTIONS
AND ANSWERS





#RESEARCHNEVERSTOPS

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