

Regulatory Procedures for Organoids- and Organs-on- Chips (OOoCs)

WHERE WE STAND AND WHERE WE ARE HEADED

Adrien Bottacci, UMR 7268 ADES, CDSA – UMR 7318 DICE, CERIC, CNRS – Aix-Marseille Université

Overview of the presentation

Applicable regulatory procedures

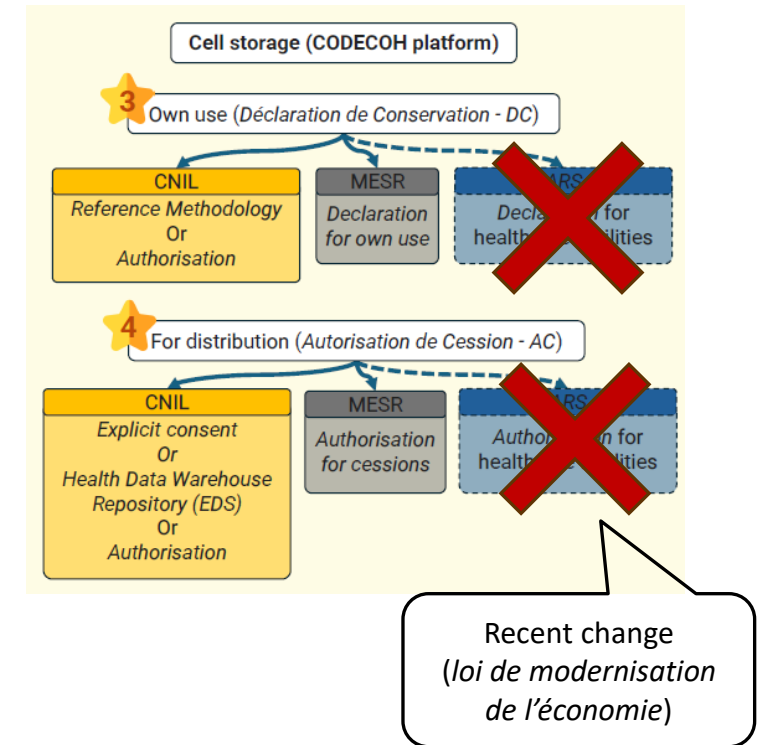
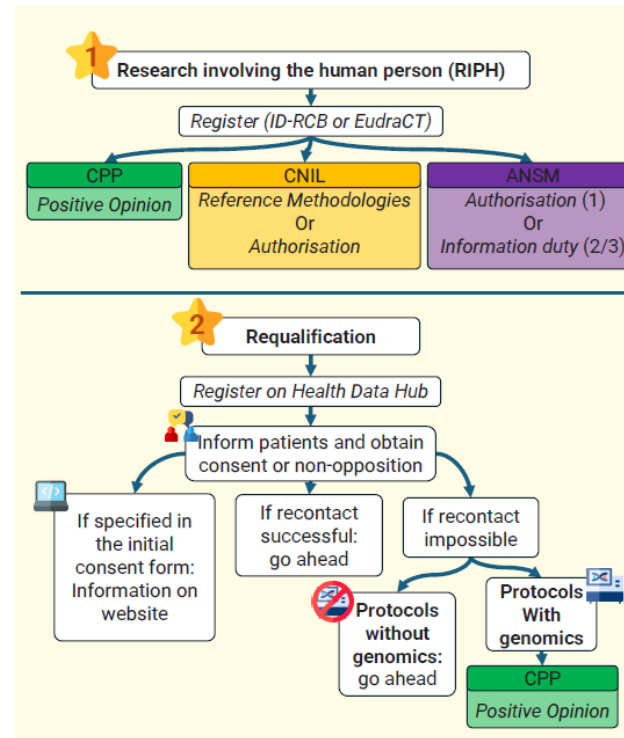
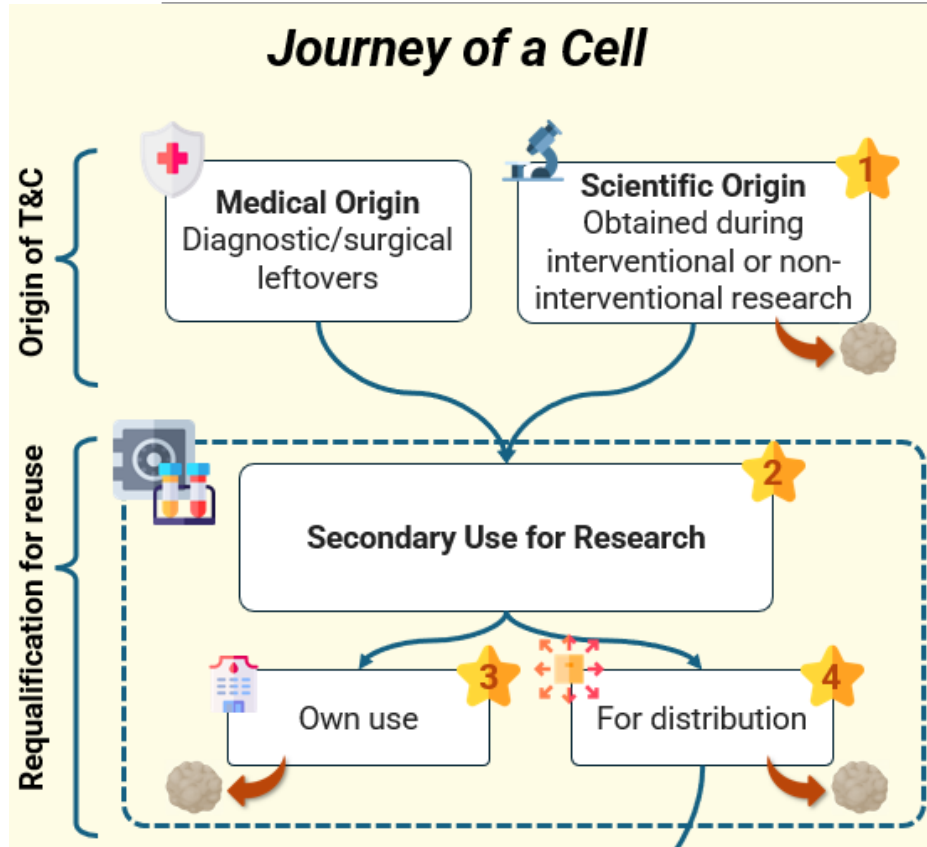
- Biological material procurement and storage (type of cells, mode of procurement, genomics...)
- Data regulation (sensitive medical data, RGPD applicable when data is not fully anonymised)
- End-products categorisation: Advanced Therapy Medicinal products (ATMPs), Medical devices (MDs), In vitro Diagnostic Medical devices (IVDMD), new alternative methods (NAMs)...

News and legislative evolutions

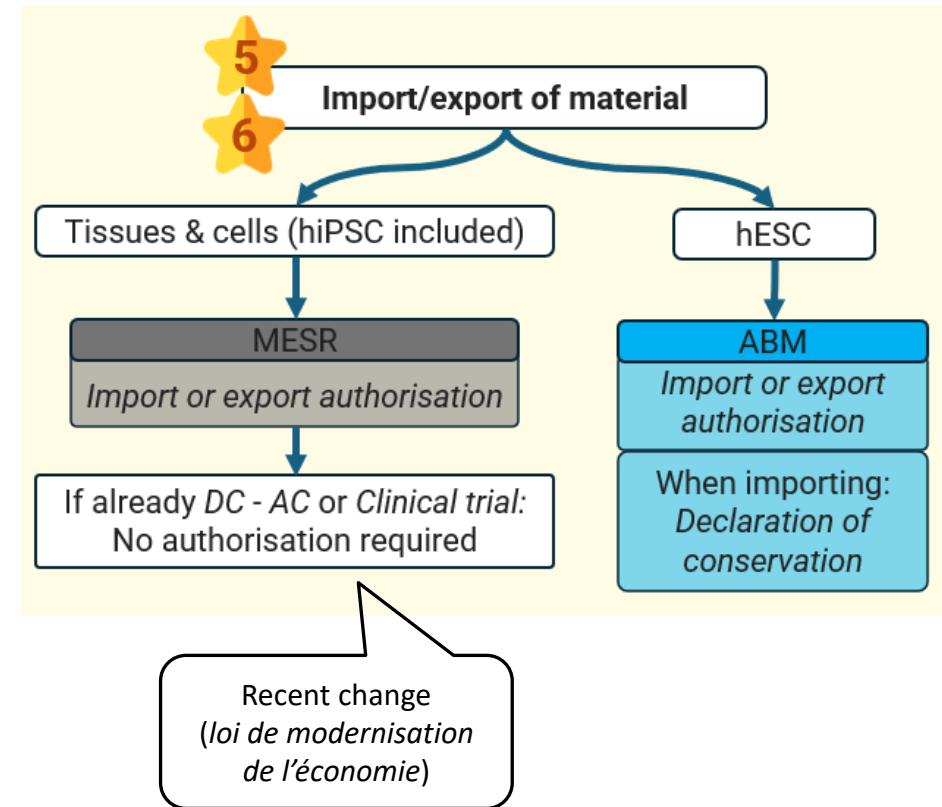
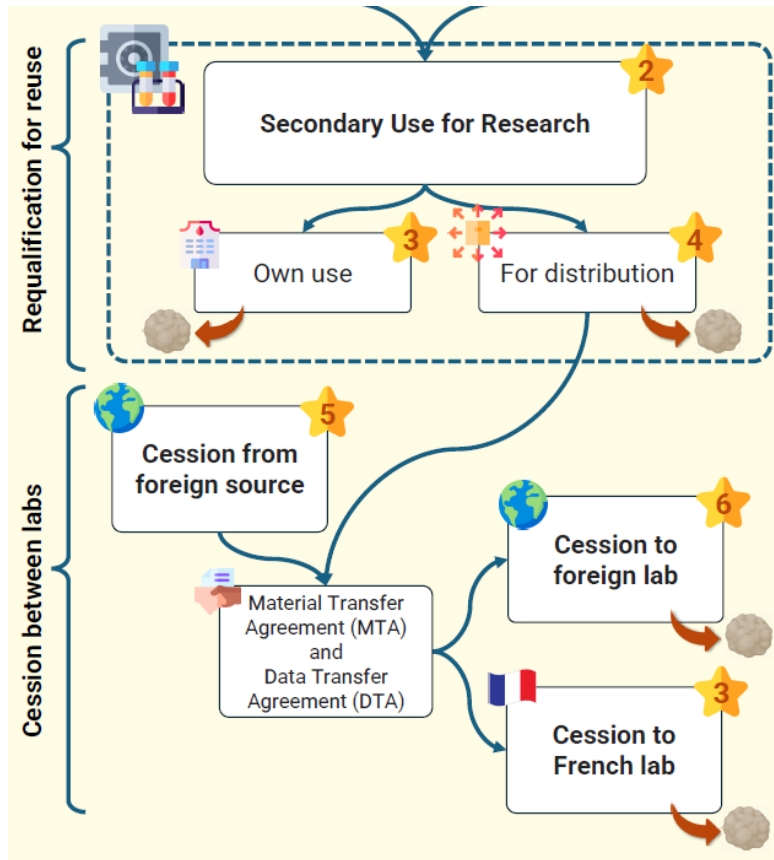
- European level
- French level

Regulatory procedures

French regulatory procedures (sample collection and storage)



French regulatory procedures (sample circulation)



OOC end-products categorisation

Clinical

OOCs as **Medical Devices** (*Regulation 2017/745*)

- MDR does not apply to product using viable derivatives of the human body. Yet, it would apply to OOCs when used to “provid[e] information by means of in vitro examination of specimens derived from the human body, including blood and tissue donations” (diagnostic purpose)

OOCs as **In Vitro Diagnostic Medical Devices** (*Regulation 2017/746*)

- Microfluidic device is the “kit, instrument, apparatus, piece of equipment, software or system” and the organoid or tissue sample is the “specimen”.

OOCs as **Advanced Therapy Medicinal Products** (*Regulation 1394/2007*)

- OOCs could be “combined ATMP” (intersection of ATMP and MD) for products administered to the patients.

Pre-Clinical

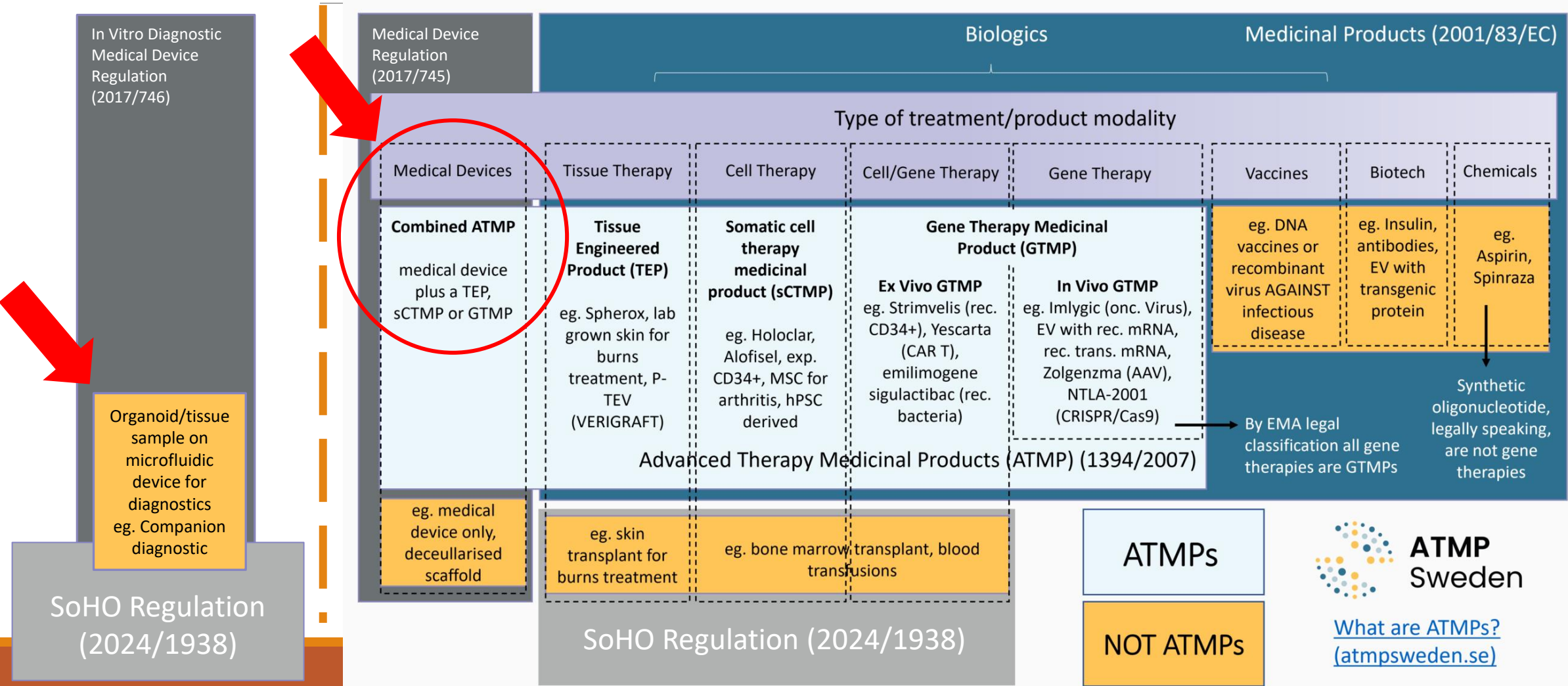
OOCs as **alternative methods**

- For regulatory toxicological testing. Requires validation according to OECD, EMA and International Committee for Harmonisation (ICH) guidelines
- Chemical testing (REACH), substances and mixtures (CLP), plant protection products, biocidal products, cosmetic products, medicinal products, veterinary medicinal products...

OOO end-products categorisation (clinical use – ATMPs and MDs)

➤ Not implanted in the human body

➤ Implanted in the human body



Support for OOC end-products categorisation

Opinion from Medical Device Coordination Group (MDCG)

Early advice from [Committee for Advanced Therapies](#) from the European Medicine Agency (EMA) (under 60 days)

EMA [Innovation Task Force](#)

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News

EU – SoHO Regulation

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

- Higher safety and quality standards, harmonised at European level. Technical norms established by expert scientific bodies
- Greater protection of donors
- Facilitate cross-border exchanges
- Most provisions will apply from **7 August 2027**, with some exceptions that will apply either earlier or later.



Impact on Biobanking activities

EU – Reform of EU pharmaceutical legislation (in progress)

[Proposal for a Regulation](#) of the European Parliament and of the Council laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency

[Proposal for a Directive](#) of the European Parliament and of the Council on the Union code relating to medicinal products for human use

- Streamline procedures, incentives for novel products, creation of regulatory sandboxes



OOO as **new approach methodologies** (NAMs) in pursuit of 3R objectives. Provide non-clinical data in support of marketing authorisation requests for medicinal products

EU – guidance documents

EMA, 3Rs Working Party (3RsWP)

Short term:

3RsWP

- Promote and support the qualification of non-animal methods by e.g. establishing acceptance criteria for specific contexts of use and active participation in qualification procedures through SAWP.
- Encourage communication between the regulators for human and veterinary medicinal products concerning possibilities for the implementation of novel 3Rs testing approaches.

2026:

3RsWP

- Finalisation of the revision of 'Reflection paper providing an overview of the current regulatory testing requirements for medicinal products for human use and opportunities for implementation of the 3Rs' [EMA/CHMP/CVMP/3Rs/742466/2015](#).
- Finalisation of the revision of 'Reflection paper providing an overview of the current regulatory testing requirements for veterinary medicinal products and opportunities for implementation of the 3Rs' [EMA/CHMP/CVMP/3Rs/164002/2016](#).
- First revision of the 'Guideline on the principles of regulatory acceptance of 3Rs testing approaches' [EMA/CHMP/CVMP/JEG-3Rs/450091/2012](#).
- Contribution to the revision of the 'Guideline on user safety for pharmaceutical veterinary medicinal products' [EMA/CVMP/543/03-Rev.1](#) (to be finalised in 2026).
- Contribution to the revision of the 'Guideline on user safety of topically administered veterinary medicinal products' [EMA/CVMP/SWP/721059/2014](#) (to be finalised in 2026).

EU – guidance documents

Joint Research Centre (JRC): “Heads on! Designing a Qualification Framework for Organ-on-Chip”, April 2024

Multiparties report: Focus Group Organ-on-Chip, “Standardization Roadmap”, July 2024.

- CEN/CENELEC, Joint Research Centre (Commission européenne), EUROoCS

EMA: “New Approach Methodologies EU-IN Horizon Scanning Report”, February 2025.

EU Reference Laboratory for alternatives to animal testing: “Non-animal methods in science and regulation: EURL ECVAM status report 2025”, Luxembourg, Publications Office, March 2026.

Editorial > ALTEX. 2024;41(2):320-323. doi: 10.14573/altex.2401231. Epub 2024 Jan 23.

Heads on! Designing a Qualification Framework for Organ-on-Chip

Monica Piergiovanni [†], Milena Mennecozzi [†], Stavroula Sampani [†], Maurice Whelan [†]

Affiliations + expand

PMID: 38414285 DOI: 10.14573/altex.2401231



International – ISO

ISO/TC 276/SC 2, Microphysiological systems and Organ-on- Chip, created in 2024

ISO/TC 276

ISO/TC 276/SC 2

Microphysiological systems and Organ-on- Chip

Scope

Standardization in the field of Microphysiological Systems (MPS) and Organ-on-Chip (OoC) that includes the following topics:

- Terminology, stakeholder environment, interdependencies in MPS and OoC
- Biological components in MPS and OoC
- Engineering in MPS and OoC, including manufacturing and designing
- Experimental design, data processing and integration of MPS and OoC studies
- Characterisation of materials and processes

ISO/TC 276/SC 2 MPS and OoC has a specific focus for MPS and OoC as a hybrid system consisting of biological components and technical components and the interaction between the two.

France – guidance document

ANSM

- Work on standardisation of OOoCs
- Proposal of regulatory prerequisites for liver-on-chip devices

National reflection on organs-on-chip for drug development: New regulatory challenges

Sonia Gomes Teixeira^a, Paul Houeto^{a,*}, Florence Gattacceca^b, Nicole Petitcollot^b, Danièle Debruyne^b, Michel Guerbet^b, Joël Guillemain^b, Isabelle Fabre^a, Gaelle Louin^a, Valérie Salomon^a

1^{er} octobre 2023, *Toxicology Letters*

“Summary of proposal preliminary regulatory requirements for liver-on-chips:

- *Justification of the concentrations of tested molecule ;*
- *Justification of the experimental protocol (and compatibility with physiological phenomena) ;*
- *Choice of measured parameters ;*
- *Choice of analytical and quantification methods ;*
- *Model validation ;*
- *Duration of the study”*

France – ministry of research

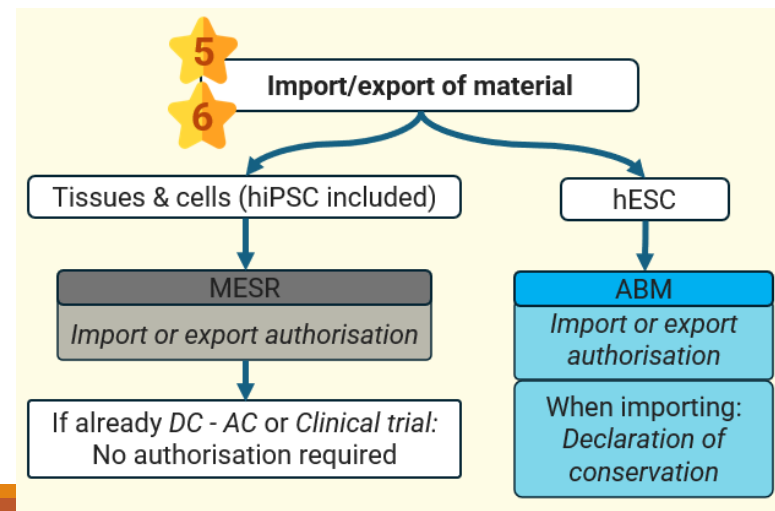
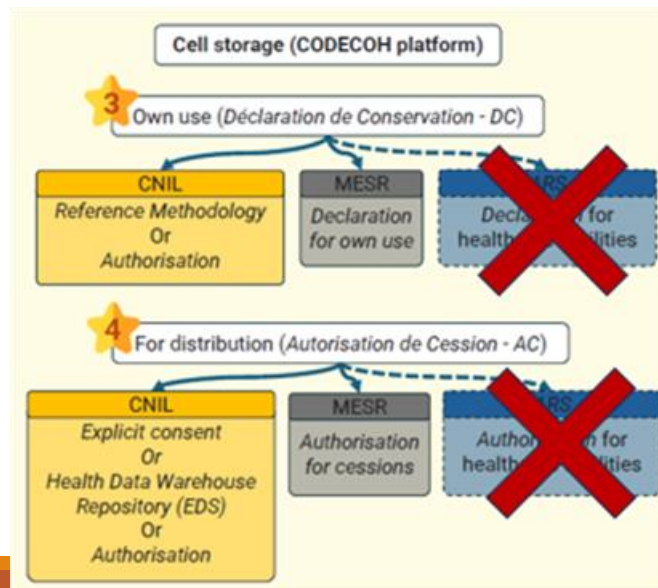
Standard contracts for public-private partnerships

1. **Contrat de collaboration de recherche : copropriété des résultats.** Ce modèle permet aux partenaires de partager la propriété des résultats issus de la recherche collaborative. Il encadre notamment la répartition des droits de propriété intellectuelle et anticipe les modalités d'exploitation conjointe des résultats.
2. **Contrat de collaboration de recherche : cession des résultats à la société.** Ce modèle prévoit une cession des droits d'exploitation des résultats à l'entreprise partenaire, en contrepartie d'un prix dont les modalités, définies par les parties selon différentes options contractuelles, dépendent du projet, des résultats obtenus et des contributions respectives. Il sécurise ainsi le transfert des innovations vers le secteur privé, tout en garantissant une juste valorisation pour l'organisme public.
3. **Contrat de développement : la propriété des résultats à « l'employeur des inventeurs/auteurs ».** Ce modèle repose sur le principe selon lequel les droits de propriété intellectuelle appartiennent à l'employeur des inventeurs ou des auteurs. Il suppose que les contributions respectives des partenaires puissent être clairement identifiées afin de déterminer, de manière objective et transparente, la titularité des droits de propriété et les modalités d'exploitation des résultats par chacun des propriétaires.

France – loi de simplification de la vie économique

27 May 2026: entry into force of the *loi de simplification de la vie économique*

- Cell storage: declaration to/authorisation from ARS for healthcare facilities no longer required
- Import/export of cells: authorisation from MESR when already DC/AC or clinical trial no longer required
- Recognition of “**Comités scientifiques et éthiques locaux**” (CSEL), distinct from CPPs and CESREES. To be clarified by decree.



France – Revision of the bioethics laws

Etats généraux de la bioéthique in 2026. Organised by the Comité Consultatif National d’Ethique (CCNE).

To be followed by reports and interviews by

- Office parlementaire d’évaluation des choix scientifiques et technologiques (OPECST),
- professional academies,
- the government...

Opportunity to get involved

Thèmes des États Généraux de la Bioéthique 2026

 Numérique et santé

 Santé et environnement

 Examens génétiques et médecine génomique

 Dons et transplantations d’organes

 Neurosciences

 Cellules souches et Organoïdes

 Procréation et embryologie

 Organisation du système de soins

 Population à travers les âges

 Outre-mer



Thank you for your attention!

CONTACT: ADRIEN.BOTTACCI@UNIV-AMU.FR

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Annexes

MDR 2017/745, definition of ‘**medical device**’ (MD):

“‘Medical device’ means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,*
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,*
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,*
- **providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,***

and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.”

Annexes

IVDMD 2017/746, definition of ‘**in vitro diagnostic medical device**’ (IVDMD), Article 2 (1-2):

- (1) ‘*medical device*’ means ‘*medical device*’ as defined in point (1) of Article 2 of Regulation (EU) 2017/745;
- (2) ‘*in vitro diagnostic medical device*’ means any medical device which is a reagent, reagent product, calibrator, control material, **kit, instrument, apparatus, piece of equipment, software or system**, whether used alone or in combination, **intended by the manufacturer to be used in vitro for the examination of specimens**, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information on **one or more of the following**:
- (a) concerning a physiological or pathological process or state;
 - (b) concerning congenital physical or mental impairments;
 - (c) concerning the predisposition to a medical condition or a disease;
 - (d) to determine the safety and compatibility with potential recipients;
 - (e) to predict treatment response or reactions;
 - (f) to define or monitoring therapeutic measures.

Specimen receptacles shall also be deemed to be in vitro diagnostic medical devices

Annexes

IVDMD 2017/746, definition of '**companion diagnostic**', Article 2 (1-2):

*(7) 'companion diagnostic' means a device which is essential for the **safe and effective use of a corresponding medicinal product** to:*

*(a) **identify**, before and/or during treatment, **patients who are most likely to benefit** from the corresponding medicinal product; or*

*(b) **identify**, before and/or during treatment, **patients likely to be at increased risk** of serious adverse reactions as a result of treatment with the corresponding medicinal product;*

Annexes

MP Directive 2001/83/EC, definition of '**Medicinal product**', Article 1 (2):

*Any substance or combination of substances **presented** for treating or preventing disease in human beings.*

*Any substance or combination of substances which may be **administered** to human beings with a view to **making a medical diagnosis or to restoring, correcting or modifying physiological functions** in human beings is likewise considered a medicinal product.*

Annexes

ATMP Regulation 1394/2007, definitions, Article 2:

‘Advanced therapy medicinal product’ means any of the following medicinal products for human use:

- a gene therapy medicinal product as defined in Part IV of Annex I to Directive 2001/83/EC,
- a somatic cell therapy medicinal product as defined in Part IV of Annex I to Directive 2001/83/EC,
- a tissue engineered product as defined in point (b)

“‘Tissue engineered product’ means a product that:

- contains or consists of engineered cells or tissues, and
- is presented as having properties for, or is used in or administered to human beings with a view to regenerating, repairing or replacing a human tissue.”

“Cells or tissues shall be considered ‘engineered’ if they fulfil at least one of the following conditions:

- the cells or tissues have been subject to substantial manipulation, so that biological characteristics, physiological functions or structural properties relevant for the intended regeneration, repair or replacement are achieved. The manipulations listed in Annex I, in particular, shall not be considered as substantial manipulations,
- the cells or tissues are not intended to be used for the same essential function or functions in the recipient as in the donor.”

“‘Combined advanced therapy medicinal product’ means an advanced therapy medicinal product that fulfils the following conditions:

- it must incorporate, as an integral part of the product, one or more medical devices within the meaning of Article 1(2)(a) of Directive 93/42/EEC or one or more active implantable medical devices within the meaning of Article 1(2)(c) of Directive 90/385/EEC, and
- its cellular or tissue part must contain viable cells or tissues, or
- its cellular or tissue part containing non-viable cells or tissues must be liable to act upon the human body with action that can be considered as primary to that of the devices referred to.”

Annexes

OOCs as alternative methods for regulatory toxicology testing:

- *Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (**REACH**)*
- *Regulation (EC) No 1272/2008 on the classification, labelling and packaging of **substances and mixtures** (CLP)*
- *Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of **plant protection products** on the market*
- *Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of **biocidal products***
- *Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on **cosmetic products***
- *Directive 2001/83/EC of the European Parliament and of the council of 6 November 2001 on the Community code relating to **medicinal products** for human use*
- *Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on **veterinary medicinal products***

Annexes

Proposal for a Regulation of the European Parliament and of the Council laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency

*“the marketing authorisation applicant and the marketing authorisation holder should take into account the principles laid down in Directive 2010/63/EU, including, where possible, use of **new approach methodologies** in place of animal testing. These can include but are not limited to: in vitro models, such as **microphysiological systems including organ-on-chips, (2D and 3D) cell culture models, organoids and human stem cells-based models**; in silico tools or read-across models.”*

Proposal for a Directive of the European Parliament and of the Council on the Union code relating to medicinal products for human use

*‘**non-clinical**’ means a study or a test conducted in vitro, in silico, or in chemico, or a non-human in vivo test related to the investigation of the safety and efficacy of a medicinal product. Such test may include simple and complex human cell-based assays, **microphysiological systems including organ-on-chip**, computer modelling, other non-human or human biology-based test methods, and animal-based tests;*