

How Do In Vitro Gametogenesis And Stem Cell-based Embryo Models Challenge The Prohibition On Creating Embryos For Research Purposes?

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Introduction

- Recent scientific breakthroughs in organoid technologies have produced two major innovations: **In Vitro Gametogenesis (IVG)** and **Stem Cell-Based Embryo Models (SCBEMs)**.
- These technologies hold significant promise:**
 - Better understanding of infertility and risks to pregnancy,
 - Enhance and facilitate access to assisted reproductive technologies.
- Both raise a critical regulatory challenge:** the **gold standard** for validating their equivalence to their natural biological counterpart requires producing a viable embryo:
 - SCBEMs are challenging the distinction between “real” embryos and model embryos.
 - Validating gametes produced through IVG would require fusing them, creating an embryo.
- The **deliberate creation of human embryos for research purposes is prohibited in several jurisdictions**, most notably those that ratified the Council of Europe’s (CoE) *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (Oviedo Convention)*.
 - This prohibition is at the heart of emerging **international regulatory fragmentation** on IVG and SCBEMs (as shown with a selection of countries).

Are SCBEMs Embryos?

- Lack of global consensus**
 - ISSCR (2025 Update)**, provides a soft law baseline:
 - SCBEM and embryo research require a **specialised oversight process** (ISSCR cat. 2).
 - Transfer of SCBEMs *in utero* or ectogenesis is **prohibited**, lacking scientific rationale and raising ethical concerns (ISSCR cat. 3B).
 - Terminology update:** the “Integrated/Non-Integrated Models” distinction has been retired.
 - Equivalence?** The guidelines do not address the equivalence of SCBEMs to embryos.
- National responses on a spectrum**
 - AU:** first to act, some embryo models are assimilated to embryos, permitting their creation under a research licence.
 - FR:** refined the prohibition on creating embryos for research to protect SCBEM research.
 - NL:** amended its legislation to lift the ban on creating embryos for research and added SCBEMs within the statutory definition of embryos, unifying both under a single regulatory regime.

	Research embryo creation prohibited	Research embryo creation allowed
SCBEMs = Embryos	SCBEMs prohibited	SCBEMs allowed & under embryo research regulation 
SCBEMs ≠ Embryos	SCBEMs allowed & regulated separately 	SCBEMs allowed with various possibilities of regulation...

Testing Gametes Produced through IVG

- International guidance**
 - ISSCR:**
 - IVG for **research** (without fertilisation or generation of embryos): reportable, no specialised oversight required (ISSCR cat. 1B).
 - IVG for **reproduction**: prohibited, currently unsafe (ISSCR cat. 3A).
- National positions**
 - FR:** IVG research is allowed and reportable to the Biomedicine Agency (art. L2151-6 and -7 PHC). However, the prohibition on creating embryos for research **prevents testing IVG maturity through fertilisation**.
 - UK:** an embryo created using IVG-derived gametes would require an **embryo research licence**. Human Fertilisation and Embryology Act prohibits clinical use of *in vitro* gametes for now, as they fall outside ‘permitted gametes’ for the purpose of treatment.
 - NL:** the regulatory framework depends on the intended use: the **Embryo Act** applies if the gametes are used to create embryos, otherwise, the **Medical-scientific research with humans Act** applies.
 - USA:** research governed by a **patchwork of federal and state regulations**, with permissive, prohibitive and silent states. Clinical use of IVG requires **FDA approval**, but the legality of IVG remains uncertain depending on the state.

A middle-way out?

- Fundamental questions:** can IVG-derived gametes be equated with “natural” gametes? Can SCBEMs or embryos created through IVG be equated with “real” embryos?
- The false choice:** current regulatory frameworks force us into an all-or-nothing decision: either fully assimilating the model to the thing being modelled or fully distinguishing them.
- A potential solution:** a *sui generis* category, recognising the in-between:
 - Creates **regulatory flexibility**, leaving room for change as science evolves.
 - Decorrelate legal discussions:** distinct concepts allow for more targeted regulation.
 - Example:** the French Biomedicine Agency’s Orientation Council suggested a third regulatory pathway for SCBEMs, less restrictive than embryo research but more stringent than stem cell research.
- However, regulatory outcomes will also depend on:**
 - Institutional factors:** the scope of action of national competent authorities
 - Social factors:** public attitudes toward IVG and SCBEMs.

The Oviedo Convention

- 29 members states** of the CoE have ratified it and are directly bound (e.g. FR).
- 7 have signed but not ratified** (e.g. NL). UK and AU have not signed it.
- Key question:** How can signatory countries address requests from the scientific community for reforms that would conflict with their international commitments?
 - For existing signatories:** denounce the Convention or propose an amendment (requires five members). Both carry substantial diplomatic cost.
 - For prospective new signatories:** enter a reservation upon ratification.

Article 18§2
The creation of human embryos for research purposes is prohibited.

Conclusion

- SCBEMs and IVG do not merely test regulatory definitions.** They **reopen sensitive issues** on the governance of embryo research, leading some countries to revisit their statutory stance on *in vitro* embryo creation.
- This produces **global regulatory fragmentation** on IVG and SCBEMs, driven by diverging national positions on the prohibition of creating embryos for research purposes.

- Policymakers must **thread a fine line** to reconcile four interconnected controversies:
 - Empirical:** whether or not models have reached the complexity of the real object.
 - Ethical:** relating to the instrumental uses and commodification of gametes and embryos potentially clashing with their inherent and symbolic value.
 - Legal:** when calls from the national scientific community conflicts with their state’s international binding commitments.
 - Societal:** in preserving an open and attractive regulatory environment, while also preserving public sensibilities.