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Human stem cell-based embryo models

Overview

- Human stem cells can be used to generate models of the earliest stages of embryo development. These can be known as human stem cell-based embryo models (SCBEMs).
- SCBEMs offer the opportunity to study embryo development in ways that could not be done with human embryos. This research could have the potential to investigate factors that contribute to pregnancy loss, congenital disease, and to improve IVF outcomes amongst other conditions.
- As of February 2024, SCBEMs are not formally defined in legislation or included in the current legal definition of a human embryo and are not explicitly regulated.
- Internationally, the regulation of SCBEMs varies from no explicit regulation to different limits on its research. In 2021, the International Society for Stem Cell Research published guidelines to address the scientific, ethical, social and policy implications of this emerging technology.
- Stakeholder suggestions towards effective oversight of SCBEMs include (i) identifying similarities and differences between SCBEMs and human embryos, (ii) an independent oversight process involving experts and lay members (iii) conducting public engagement to increase public understanding and identify concerns surrounding the technology.

Background

A major scientific advance in the study of human embryo development is the generation of embryo models from pluripotent stem cells (SCBEMs).[1] SCBEMs model key features and processes of the developing embryo at early stages and could be used to investigate fundamental aspects of early development. It has been proposed that this knowledge could be used in the future to improve the understanding and outcomes of medical conditions such as early pregnancy loss, congenital diseases and *in vitro*[a] fertilisation (IVF).[2–4]

In scientific literature the terminology describing SCBEMs can vary. SCBEMs can also be referred to as artificial embryos,[5-] synthetic embryos,[6] stembryos[7], synthetic human entities with embryo-like features (SHEEFs)[8], embryo-like structures (ELS)[9], embryo models,[10] and embryoids.[11,12]

With increasing sophistication and completeness of human SCBEMs in modelling the embryo, stakeholders from academia, ethics and policy are discussing the opportunities and challenges that these scientific advances may raise.

The focus of the current debate includes how existing legislation relates to the technological progress in this area, and the wider ethical and societal implications.[5,13–20]

Types of stem cells

Stem cells are undifferentiated cells that can self-renew and grow indefinitely to produce more stem cells, and can develop into various other types of cells.[21] Stem cells can be further classified into the following:

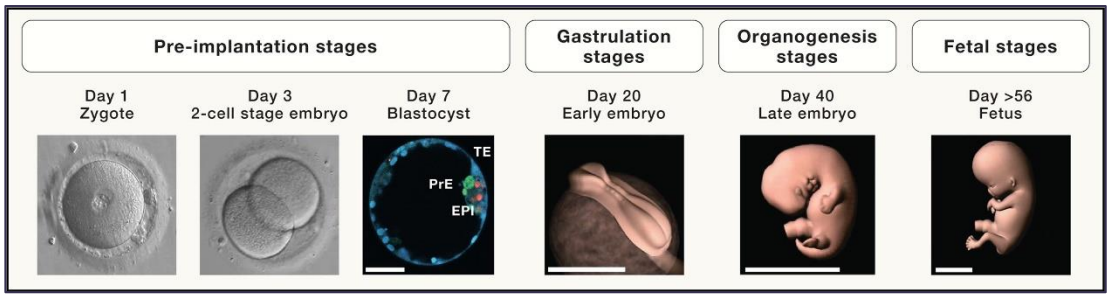
- **Embryonic stem cells (ESCs) –** stem cells that are derived from the inner part of the human embryo at a specific developmental stage that is called a blastocyst [22] (see Figure 1). ESCs are 'pluripotent' and can therefore develop into all cell types of the body (except extra-embryonic cell types).[23,24]

- **induced pluripotent stem cells (iPSCs) –** stem cells that are reprogrammed from specialised adult cells, such as skin or blood cells, to an early developmental state that may be equivalent to that of ESCs. iPSCs are also considered to be pluripotent.[21,23–25]

- **tissue-specific stem cells –** stem cells that are found in adult tissues or organs. They are also called adult stem cells or somatic stem cells. They are considered to be 'multipotent' and, can contribute to a limited range of cells, for example, blood stem cells can only form the various different cell types found in blood such as red blood cells.[23,26]

[a] Taking place outside of a living organism for example, in a test tube or petri dish.

Figure 1: Human embryonic development follows a sequence of distinct stages involving specialisation of cells that lead to the development of the fetus.[14,27]



During fertilisation, the egg and sperm fuse to form a single cell called a **zygote**. In humans, the zygote divides and differentiates to form the **blastocyst** after approximately 7 days. The blastocyst contains cells that will form the foetus (EPI, epiblast in red), and other specialised cells (called extra-embryonic cells, such as TE, trophectoderm in blue and PrE, primitive endoderm in green). After the embryo implants into the uterus, a process called **gastrulation** begins at around day 14 and lasts about a week, and this provides form to the early embryo.[28,29] This is followed by the stages of **organogenesis**, when organs begin to develop. From week 9 onwards, the term **foetus** is used.[14,27]

Source: Rivron et al. (2023) *An ethical framework for human embryology with embryo models*[14]

SCBEMs can be generated from either type of pluripotent stem cells (ESCs or iPSCs) using various methods.[30] These methods include controlling the space in which the cells grow, altering the media in which the cells are grown, grouping the cells with other cell types, such as extra-embryonic cells and/or by genetically manipulating the cells.[31–33]

Classification of SCBEMs

SCBEM is an umbrella term used to represent a range of models that vary in their complexity and completeness of modelling an embryo. These models can be categorised based on varying conditions. For instance, SCBEMs can be described based on the developmental stage of the embryo that they aim to represent.[12] The International Society for Stem Cell Research (ISSCR) guidelines (2021) classify SCBEMs based on their complexity and anticipated ability to undergo further development as inferred by the presence of relevant extra-embryonic cell types.[34]

Non-integrated SCBEMs

Non-integrated SCBEMs seek to reproduce a specific part or developmental process of the developing embryo. They do not include extra-embryonic cells and are therefore thought to lack the potential to develop into a foetus.[35–37] Non-integrated SCBEMs may include:

- models where stem cells are grown in a controlled space to trigger their self-organisation properties of early development[31]
- gastruloids, which have features of a developmental stage of the embryo called gastrulation when the body outline forms (see Figure 1)[38–40]
- models of the fluid-filled sac (the amniotic sac, within which the embryo develops inside the body)[41,42]

Integrated SCBEMs

Integrated SCBEMs model the developmental processes of the embryo along with the extra-embryonic tissue. They are thought to have the possibility of acquiring the potential to develop into a foetus, if conditions and modelling improves.[43] Integrated SCBEMs can include:

- blastoids, that represent a developmental stage of the whole embryo called the blastocyst which occurs 5-7 days after fertilisation (see Figure 1)[44–48]
- peri-gastruloids, that model post-implantation development into early organogenesis, when organs begin to develop[49]

Some scientists state that the more recent models are on a spectrum. They highlight that the proposed approach of classifying models based on the presence of extra-embryonic cells, and the subsequent interpretation of their potential to form a foetus, could be too simplistic.[50]

Potential applications of SCBEMs

Experts state that SCBEMs could allow novel forms of investigation into embryonic processes that would not be possible or practical with human embryos. [17,51–53] Hence, they are seen as a key ethical and scientific advance for understanding embryo development.[17,51–53] However, some ethicists raise concerns and questions about the feasibility of the potential applications of SCBEMs.[54]

Early pregnancy loss and IVF outcomes

Approximately 50% of fertilised human eggs fail to develop during IVF treatment.[45,55–57] Some scientists state that SCBEMs could be used to improve protocols used in IVF.[2] Even after successful implantation following natural conception, according to research taken by UK charity Tommy's, approximately 1 in 5 women experience miscarriage.[58–60] Some experts state that SCBEMs could be used to investigate periods of early embryonic development that is not possible with embryos, such as development stages beyond 14 days after fertilisation.[61,62] The knowledge produced from SCBEMs studies could help identify and reduce risks of early pregnancy loss.[2,3]

Disease modelling

In 2019, approximately 1 in 46 births in the UK were diagnosed with a congenital condition.[b] [63] Experts propose that SCBEMs could be used to investigate the origins of such congenital abnormalities.[4] Researchers are generating SCBEMs to investigate various conditions such as:

- malformations of the spine[64]
- the impact of disrupting key signals involved in the early development of the nervous system[65]

[b] Congenital abnormalities are medical conditions present from birth.

- early heart development, which could help in understanding congenital heart disease (CHD),[66] one of the leading causes of death in new-borns.[67]

In cases of rare diseases (CDP-2017-0105) where there are limited samples of tissue available for research, SCBEMs offer the opportunity to model diseases from the patients' human induced pluripotent stem cells (hiPSCs).[68]

Toxicity studies of early development

While most studies of teratogens (chemicals that cause harm to the growing embryo) are conducted on embryos of non-human animals , such as mice, these studies fail to account for species-specific responses.[69] For example, researchers have used SCBEMs to test thalidomide, a morning-sickness drug that resulted in severe birth defects in humans. They found a stronger effect of the drug on human SCBEMs compared to mouse SCBEMs.[70,71]

Large-scale drug discovery

While the efficiency of generating SCBEMs is currently very low[50], experts propose that with further optimisation of the process. SCBEMs could be produced in larger quantities and in a standardised manner,[72] which could enable the testing of multiple compounds for medicinal effects.[2,73–76]

Legislation and guidelines

In the UK, public bodies oversee research and treatment involving human embryos and some categories of stem cells, including human ESCs (see Box 1). SCBEMs are not explicitly covered by existing law or other Codes of Practices.[19,73,77] Stakeholders highlight that clarity on the explicit governance of SCBEMs is crucial for the ethical and social foundation to their continued use and to fully identify the potential benefits of SCBEMs.[77]

Human Fertilisation and Embryology Act and the Human Fertilisation and Embryology Authority (HFEA)

The Human Fertilisation and Embryology Act 1990 provided for regulation of the creation or use of embryos outside the body, the use of donated eggs or sperm in treatment, and the storage of embryos, sperm or eggs. The Human Fertilisation and Embryology Act was amended in 2008, and at present it explicitly only allows:

- the maintenance of human embryos outside the living organism (*in vitro*) up to 14 days after fertilisation or up to the first appearance of a structure called the primitive streak (PN 006)[c]

[c] The primitive streak is a transient structure that appears when the body plan of the embryo starts forming at around 14 days after fertilisation.[78]

- the sourcing of human embryonic stem cells (hESCs) from embryos generated through IVF (LLN-2018-0094) or any other process such as somatic cell nuclear transfer[d] [82]

- the use of embryos in assisted reproduction that have been created by fertilisation of a "permitted egg" with a "permitted sperm"[e] and contain no cells from other sources or have their genome edited (PN 611), with an exception for mitochondria donation (or mitochondrial replacement therapy, MRT)[f].[86–88]

The Human Fertilisation and Embryology Authority (HFEA) was established by the Act. The HFEA is an executive non-departmental public body, sponsored by the Department of Health and Social Care (DHSC). The HFEA regulates the use of human embryos in research and treatment. At present, the HFEA has stated that SCBEMs sit outside the regulatory remit of the Act.[89]

Research Ethics Committees (RECs)

In the UK, RECs review research proposals with the aim of safeguarding the rights, safety, dignity and well-being of research participants and give an opinion about whether the research is ethical.[90]

Under the Care Act 2014, RECs are governed by the United Kingdom Ethics Committee Authority (UKECA) which includes the Health Research Authority (HRA) and the devolved administrations.[90,91] For instance, HFEA requires approval from an independent REC before an application is submitted for their license.[92]

Guidelines on stem cell research

The ISSCR is an independent scientific society. Its membership includes scientists, ethicists, educators and business leaders.[93] The ISSCR publishes guidelines to address global developments in stem cell research and the associated ethical, social and policy issues.[94] In 2021, ISSCR proposed new guidelines for Stem Cell Research and Clinical Translation to address scientific advances in SCBEMs (see section Amendment of ISSCR guidelines (2021)).[95,96,43]

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[d] Somatic Cell Nuclear Transfer (SCNT) involves the transfer of the nucleus from a somatic cell (cells in the body other than stem cells or reproductive cells like the egg or sperm) into an egg whose nucleus has been removed. The remaining factors in the egg reprogram the somatic nucleus into a more naïve state to produce a cell resembling the 'zygote', that is produced upon fertilisation of the egg and sperm.[79–81]

[e] The Human Fertilisation and Embryology Act 2008, s 3ZA(2)(a) and s 3ZA(3)(a) define a **"permitted egg"** and **"permitted sperm"** as one which has been produced or extracted from the ovaries of a woman and those which have been produced or extracted from the testes of a man respectively. For instance, s3A(1) prohibits the use of female reproductive cells at any stage of maturity, including eggs, that are taken from an embryo or a foetus to provide fertility services.

[f] Mitochondria Replacement Therapy (MRT) involves the replacement of faulty/abnormal mitochondria in the egg using healthy ones from a donor before or after IVF to prevent mitochondria-associated diseases.[83–85] MRT was legalised in the UK through The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 (PN 431; CBP SN/SC/6833; Commons Insight, Mitochondrial donation in Parliament)

Box 1: Organisations relating to stem cell research and use in treatment

UK Stem Cell Bank (UKSCB)

The UKSCB and an associated Steering Committee facilitate work on human stem cell research in 3 main areas:[97]

- The UKSCB is the sole public repository for all UK-derived hESC lines and has a statutory role to provide high quality stem cells for research and clinical use.
- The UKSCB undertakes research to improve quality and derivation of hESC lines.
- The Steering Committee oversees activities and provides approval for all hESC-based work in the UK.

hESC lines derived in the UK are mandated by the HFEA to be deposited in the UKSCB, whereas the deposition of hiPSC lines is voluntary.[98,99] Thus, SCBEMs derived from hiPSCs would not be reviewed by the Steering Committee.

Human Tissue Authority (HTA)

The HTA is a non-departmental public body sponsored by the DHSC in England, Wales and Northern Ireland.[100–102] The HTA was created as a result of the Human Tissue Act 2004 (CBP-0404) and came into force in 2006. The HTA regulates and provides a license for the removal, storage and use of human tissue and cells for research, treatment (PN 641), post-mortem, education and training (excluding hair, nail, gametes and embryos).[100,101,103] However, once cell lines such as hiPSCs are established from these material, regulation of their use is excluded from the Act. [98]

Medicines and Healthcare Products Regulatory Agency (MHRA)

The MHRA regulate the manufacture, storage and distribution of research output(s) from stem cell work that could be conceived to be a medicinal product. (CDP-2023-0077, LLN-2019-0024).[104]

Challenges for governance

Inconsistent terminology

Across scientific, ethical and legal literature, different terms have been used in relation to SCBEMs. Stakeholders note that differing terms can impact public perception, lead to misinformation, and add complexity to regulating their use.[18,105,106]

For instance, SCBEMs have been described as "synthetic embryos" in numerous scientific and media reports[4–6,107–110]. However, some amongst the scientific community raise concerns about the accuracy of the term in portraying the nature of these entities..[1,14,18,111–113]

Some stakeholders also state that including the term "embryo" could mislead the public into thinking that SCBEMs at their current state are embryos.[14,111,112] Others

suggest that including the term "models" could draw attention away from the potential of integrated SCBEMs in becoming indistinguishable from embryos if and when the technology evolves.[15,16,114,115]

Overall, it is unclear at present what the consensus is on a preferred term and there is a concerted effort to address this.[19] In June 2023, the ISSCR released a statement clarifying popular use of the terms to address SCBEMs[113] following extensive media coverage of the technology.[116,117]

Determining the similarities and distinctions between a SCBEM and an embryo

Central to the discussion of regulating SCBEMs is identifying the extent of their similarity to embryos.

There have been challenges in deciding whether the same regulations that apply to embryos should also apply to SCBEMs that may in the future become indistinguishable from an embryo and acquire the potential to develop into a foetus.[62,108,118,119] A direct assessment of this potential would require the transfer of human SCBEMs into a human host, which is legally not permitted in the UK by the Human Fertilisation and Embryology Act 2008 and is prohibited by the 2021 ISSCR guidelines (see section Amendment of ISSCR guidelines (2021)).[14,34]

Some researchers propose indirect exploratory tests to find thresholds or "tipping points" beyond which a model could be considered an embryo from the legal perspective, and thus depending on the results the entities may be subject to the same or different legal protection.[14,120]

in vitro test

One proposed test includes the evaluation of a model's ability to completely or accurately develop *in vitro* for a duration that is ethically acceptable while also allowing enough time for better estimation of the model's potential.[14] However, some stakeholders highlight that there are currently no universal and established criteria to evaluate how similar a human SCBEM models is to an embryo.[10,13,14,121]

Determining the similarity of SCBEMs to human embryos is also complicated by the lack of a detailed characterisation of the human embryo.[12,18,29] Validating human SCBEMs modelling embryonic development during or after gastrulation would require the maintenance of human embryos *in vitro* to an equivalent stage beyond 14 days after fertilisation, which is currently not permitted under UK legislation.[34,122–124]

in vivo[g] test

Another proposed test could be to check if a model can produce live and healthy animals in other related species.[14] Studies in mouse, monkey and cow have reported that SCBEMs transferred into surrogate animals can, in some cases, show signs of implantation, trigger release of pregnancy hormones, initiate the formation of the sac that surrounds the embryo at early stages[h] and alter the uterine lining in preparation

[g] Taking place in a living organism.

[h] The gestational **sac** is a fluid-filled cavity surrounding the early developing embryo. It is the first structure detected in pregnancy by ultrasound.[125]

for pregnancy. However, as of yet they have not been shown capable of proceeding further along development.[126–128]

Some ethicists highlight that the criteria for evaluating SCBEMs' level of protection requires consideration of what characteristics of an embryo deem it worthy of protection (see section Moral status of the embryo).[129,130]

Lastly, given that scientific advances are taking place internationally, the variation in legal definitions of an embryo across different countries also complicates global regulation of SCBEMs. [14,18,131–134]

Determining time limits on SCBEMs

Experts highlight that determining a time limit on the *in vitro* maintenance of integrated SCBEMs is complex, as:

- there is no equivalent step to fertilisation and hence no day 0 of conception to start the counting of days[135]
- SCBEMs can develop at different rates[136]
- SCBEMs do not show linear development and can skip or show different sequences of key developmental stages[32,33]

Alternatively, some stakeholders propose setting limits based on the emergence of certain morphological features, similar to the use of the emergence of primitive streak as a limit in human embryo culture.[14,137,138]

Some scientists highlight that, at present, there is no justification to develop integrated SCBEMs to very advanced developmental stages or to high degrees of similarity to whole human embryos because:

- at these stages, integrated SCBEMs may be difficult to study due to scientific complexity and ethical concerns, which could defeat the purpose of model generation
- development of specific processes or organs can be studied using non-integrated SCBEMs and organoids,[i] which can enable investigation of specific tissue in isolation[14,50,123]

Some examples of the different approaches taken internationally are listed in Table 1.

[i] Organoids are three-dimensional *in vitro* models that are typically derived from stem cells and emulate key structures and functions of organs to diverse extents.[139]

Table 1 International comparisons of regulation on human embryos and SCBEMs

Country	Definitions of Human SCBEM vs embryo	Time limit on *in vitro* maintenance of human SCBEMs
Australia	Integrated SCBEMs fall within the definition of a human embryo.[18,140]	The Embryo Research Licensing Committee (ERLC) of the National Health and Medical Research Council restricts the maintenance of integrated SCBEMs in culture to morphological and/or molecular stages equivalent to a normally developing human embryo 14 days post fertilisation.[18,140,141]
Austria	There is no explicit regulation of SCBEMs, and research on human embryos is not practised. Research using hESCs derived outside Austrian territory is permitted.[142,143]	There is no explicit regulation of SCBEMs but the ethics committee of the Austrian Academy of Sciences has delivered licenses on a case-by-case basis.[45,142,143]
France	In September 2023, the Agence de la biomédecine's Conseil d'orientation proposed that SCBEMs cannot be considered embryos due to differences in their origin and intentionality.[144]	The Conseil proposed to allow the *in vitro* maintenance of integrated SCBEMs up to 28 days.[144]
Netherlands	In October 2023, the Health Council of Netherlands proposed that integrated SCBEMs should qualify for the same protection as human embryos.[130]	The Council proposed to allow the *in vitro* maintenance of integrated SCBEMs up to 28 days.[130]
UK (including devolved nations)	As of February 2024, there is no explicit regulation of SCBEMs.	As of February 2024, there is no explicit regulation of SCBEMs.

These countries were chosen as examples to depict the differences in regulation of SCBEMs.

Opportunities and initiatives to address regulatory gaps

Guidelines and legislative considerations

Amendment of ISSCR guidelines (2021)

In 2021, the ISSCR updated their guidelines to:

1. remove the *in vitro* maintenance of human embryos beyond 14 days from the list of prohibited activities with suggestions that the time point be reassessed following meaningful and substantial public communication and deliberations

2. classify SCBEMs into non-integrated and integrated based on the presence of extra-embryonic cell types

3. subject non-integrated SCBEMs reportable to an oversight process and integrated SCBEMs to additional review and approval through a specialised ethical and scientific process. They suggest that research with integrated SCBEMs should only proceed with a compelling scientific rationale, that the models be maintained in culture for the minimum time necessary to achieve the scientific objective and that researchers additionally comply with local laws and policies

4. prohibit the transfer of SCBEMs into the uterus of a human or animal[34]

HFEA recommendations to amend UK legislation (2023)

In November 2023, the HFEA published recommendations to update the Human Fertilisation and Embryology Act 2008. The recommendations include reform on future scientific developments and innovations under which SCBEMs are included as pressing scientific issues. For example, they propose "future proofing" scientific developments, by advocating for greater discretion to approve new developments under flexible trial mechanisms for example "regulatory sandboxes", where new products can be introduced in a controlled manner into the real world, with regular updates to Parliament.[89]

However, some ethicists voice concerns about the recommendations and suggest that the limits in the current laws be maintained.[145,146] Other stakeholders highlight the possibility of a staged-approach licensing system as implemented in Australian legislation on mitochondrial replacement therapy.[147–149]

The UK Government are currently considering the HFEA's report on priorities for law reform "and will respond in due course" (PQ 5893 [on Genetics: Screening], 7 December 2023).

Code of Practice by Governance of Stem Cell-Based Embryo Models Project (G-SCBEM)

In March 2023, Cambridge Reproduction in partnership with Progress Educational Trust launched the G-SCBEM project, which aims to address the lack of a dedicated regulatory framework to govern SCBEMs in the UK.[150–152] The working group, comprising of experts including researchers, legal scholars and bioethicists, are

developing a Code of Practice for the governance of UK-based SCBEMs research, with a draft planned to be published in early 2024.[152,153]

Code of Responsible Conduct for organoid research by HYBRIDA (2021 – 2024)

HYBRIDA is 3-year EU-funded project. It is producing a comprehensive regulatory framework, including operational guidelines and a Code of Responsible Conduct, for organoid research and related technology, including SCBEMs.[154]

A 2022 HYBRIDA report identified gaps in current international and European regulatory frameworks. A follow-up report in January 2024 included recommendations to fill these gaps.[133,134]

Wider impacts and considerations

Moral status of the embryo

Technological advances in SCBEMs and discussions relating to the protection extended to them have prompted stakeholders to revisit the long-standing deliberation on the moral status of the human embryo. The grounds for and the extent to which human embryos possess a moral status includes a range of opinions.[135]

While some see moral status as a binary concept, others view it to be developmentally emergent. Criteria such as the potential to form persons is further nuanced by discussions around the distinction between possessing an active versus passive potential.[130,155,156]

Some stakeholders including scientists and ethicists state that advances in SCBEMs are prompting the redefining of the legal definition of an embryo and its entitlement to protection.[14,157] Some ethicists propose that while the moral status of integrated SCBEMs is still unclear, they should be given the benefit of the doubt based on precautionary principle.[15]

Public engagement, awareness and perception

Public engagement is suggested to be central to the governance of SCBEMs.[20,34,43,158] Stakeholders express the need for:

- a two-way and ongoing public dialogue with representation from diverse groups[111,131]
- a consensus in the terminology of SCBEMs (see section Inconsistent terminology)[105]
- transparency in oversight process regulating SCBEMs[111,131]

Several public engagement activities have taken place or are planned (see Box 2).

Box 2: Public engagement workshops and dialogue

UK

In 2023, the Human Developmental Biology Initiative (HDBI), funded by Wellcome and UK Research and Innovation's (UKRI) Sciencewise programme, conducted a series of workshops around human embryo research, including SCBEMs. Members of the public engaged with scientists, regulators, ethicists, philosophers and people with lived experience in a deliberative dialogue.[159–161] The foundational results highlighted that many of the dialogue's participants wanted to see SCBEMs regulated and a summary of the dialogue included proposals to have more in-depth conversations regarding the novelty and complexity of SCBEMs.[162]

The G-SCBEM Oversight group is coordinating public engagement on SCBEMs through a dialogue in early 2024. It will build on the HDBI dialogue and aims to gain an understanding of public view on research using SCBEMs and their future regulation. It also plans on identifying participants' views on the draft of proposed governance framework and it aims to use this information to inform subsequent drafts (see section Code of Practice by Governance of Stem Cell-Based Embryo Models (G-SCBEM) (2023)).[163]

Europe

In November 2021, HYBRIDA conducted public workshops in Denmark, Italy and Greece to understand concerns of the general public, patients, donors, and vulnerable groups about organoid and related technology. The key recommendations from participants included prioritising informed consent, transparent research dissemination and ethical oversight.[164,165]

Members of the Wellcome-funded Future of Human Reproduction interdisciplinary research programme[166] have had a proposal accepted for a session at the 2025 European Society of Human Reproduction and Embryology (ESHRE) annual conference; ESHRE has around 9000 members in over 135 countries.[167] The lectures will explore the distinction between embryos and SCBEMs,[52] and its potential impact on the regulation of research and treatment in medically assisted reproduction.

Donor consent

In the UK, hiPSCs are not mandated to be deposited in UKSCB; they only require broad approval from Research Ethics Committees.[98,168] Therefore, ensuring informed participant consent for the use of their cells in deriving stem cell-based entities requires further discussion. For example, some experts note that clarity is required on when the right to withdraw consent begins and ends during this process. Finally, differences in regulation across jurisdictions can hinder the transfer of materials for research.[134,169]

Commercialisation and patentability

There is an increasing interest in the commercialisation of SCBEMs. For instance, there are emerging enterprises that aim to use SCBEMs for drug discovery and cell therapy.[170,171] In cell therapy (PN 567, PN 221), patients are given cells for treatment

(e.g., CAR T-cell therapy in cancer (PN 598)) or regenerative purposes (PN 620).[172–177]

Stakeholders express concerns about the equality of access if benefits were to arise from the technology (POST, Health inequalities: research and policy, PN 0553).[170,171] While EU and UK law exclude the patentability of human embryos and stem cells derived from embryos (PN 401), it is still unclear on how legislation would apply to SCBEMs and their foreseen applications.[178–180]

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