

# **Modernising the Regulation of Fertility Treatment and Research Involving Human Embryos**

Consultation response by G-SCBEM  
13 April 2023

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## **Introduction**

The HFEA notes in its consultation document that '*Scientific advances are creating new "categories" of cells such as in vitro-derived gametes, embryo-like entities, and stem-cell-based embryo models which are outside the regulatory categories of the Act*'.

Our project – **Governance of Stem-Cell-Based Embryo Models (G-SCBEM)** – has been established specifically to develop a recommended governance framework for research involving human stem-cell-based embryo models (hereafter SCBEMs) in the UK. G-SCBEM is coordinated by **Cambridge Reproduction**, an interdisciplinary initiative at the University of Cambridge which brings together diverse researchers who have a common interest in reproduction.

Although G-SCBEM has yet to finish developing its recommended governance framework, we wish to submit this response to the present HFEA consultation in order to:

- Ask the HFEA – in the advice on law reform that it submits to the UK Government following its consultation, and also in its work more generally – to take account of our project, noting that we are developing a recommended governance framework for research involving SCBEMs.
- Make four broad preliminary recommendations. We trust that the HFEA will consider incorporating these recommendations into its own recommendations to Government.

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## **Rationale for G-SCBEM**

In consultation with experts in science, law, sociology, policy and regulation (including the HFEA's Chief Executive, Peter Thompson, who participated in two related workshops in 2022) G-SCBEM has identified various gaps, ambiguities and differences of interpretation in the current regulation of human SCBEMs. This includes SCBEMs that have been created by researchers to date, and also SCBEMs that could hypothetically be created by researchers in the future.

The resulting uncertainty is problematic for a number of reasons. Greater clarity is required in this area, so that all concerned – including researchers, their funders and institutions, relevant regulators, and the general public – can be confident in their understanding of the types of research that are possible, permissible and legitimate.

We decided that a recommended governance framework for UK research involving SCBEMs would help to address this situation. We aim to develop a framework that can:

- Provide guidance on the responsible conduct of research *in vitro* into processes of early human development using SCBEMs.
- Demonstrate responsibility, accountability and transparency on the part of researchers.
- Help to sustain and build public trust.
- Help to inform any future legislation or regulation that might apply to human SCBEMs, should this be deemed necessary.

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## **Recommendation 1**

**Future policy in this area – including any proposed revision of the Human Fertilisation and Embryology (HFE) Act – should take account of, and (where possible) take care not to contradict, the latest *Guidelines for Stem Cell Research and Clinical Translation* published by ISSCR.**

Of the guidance that already exists in this area, we believe that the latest (2021) ***Guidelines for Stem Cell Research and Clinical Translation*** published by the **International Society for Stem Cell Research (ISSCR)** at <https://www.isscr.org/guidelines> are especially important and useful.

We note that the HFEA's consultation document refers to these ISSCR *Guidelines* in relation to the current 14-day limit on research using human embryos proper. The HFEA should consider that these *Guidelines* are equally relevant to research using SCBEMs.

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## **Recommendation 2**

**Future policy in this area – including any proposed revision of the HFE Act – should, where possible, follow the definitions and terminological recommendations contained in the latest *Guidelines for Stem Cell Research and Clinical Translation* published by ISSCR.**

One respect in which the ISSCR *Guidelines* are especially helpful, is in relation to clarifying and standardising terminology in this area, which can otherwise be complex and challenging to navigate. The very term '*stem-cell-based embryo model*' is itself useful, and we are pleased to see this term used (and thereby further standardised) in the HFEA's consultation document.

The ISSCR *Guidelines* – plus related publications by the authors of the *Guidelines*, such as the article at <https://doi.org/10.1016/j.stemcr.2021.05.008> (see in particular **Table 1** in this article) – helpfully specify objects, entities and materials that do *not* constitute SCBEMs, excluding them from this category (despite certain similarities). Items excluded include human embryos proper that have been created via conventional fertilisation, human embryos created by other methods (for example parthenogenesis or nuclear transfer), and chimeric embryos (which contain both human and nonhuman cells).

The ISSCR *Guidelines* also divide SCBEMs into two subcategories, of '*integrated*' and '*non-integrated*' SCBEMs. The key distinction between these two subcategories is that '*integrated*' SCBEMs contain (or can develop) extraembryonic cell types, whereas '*non-integrated*' SCBEMs do not contain (and cannot develop) such extraembryonic cell types.

We appreciate that it is not always practical to bring the categories used in law and regulation into perfect alignment with the categories used, or emerging, in scientific research. We further appreciate that definitions in law and regulation must sometimes involve a complex interplay of scientific and non-scientific considerations (an obvious example would be the definition of '*permitted*' embryos and gametes in the Human Fertilisation and Embryology Act 2008).

These facts notwithstanding, the definitions and terminological recommendations contained in the ISSCR *Guidelines* are well articulated, and represent an attempt to establish a *lingua franca* that spans countries as well as disciplines. The recommended governance framework developed by G-SCBEM will therefore seek to employ the ISSCR terminology where it is possible to do so, and we recommend that other organisations and authorities (including the HFEA) do likewise.

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### **Recommendation 3**

**Policymakers in this area should keep open the possibility that a revised HFE Act (or the equivalent successor legislation) could refer to SCBEMs in its wording, for the purpose of clarifying that SCBEMs are *excluded* from the categories of materials to which the legislation applies (and are therefore excluded from the remit of the HFEA).**

The HFEA, discussing SCBEMs and other reproduction-related materials in its consultation document, notes that '*It may be necessary to consider whether the Act needs to be revised to include these entities, or whether these biological cells should fall under the remit of other regulators*'.

We agree that this question needs to be considered. However, we would add that in the case of SCBEMs, there is an important difference between inclusion in the *wording* of the HFE Act and inclusion in the *applicability* of the HFE Act. The best course of action may be for a revised HFE Act (or the equivalent successor legislation) to include SCBEMs in its wording, so as to clearly *exclude* SCBEMs from this law's applicability.

We say this, notwithstanding the recommendation in the ISSCR *Guidelines* (on p6) that research involving '*integrated*' SCBEMs should '*be subject to review, approval, and ongoing monitoring, as appropriate, through a specialised oversight process capable of evaluating the unique aspects of the science and the associated ethical issues*'. It is the view of G-SCBEM that a '*specialised oversight process*' should indeed be established for UK research involving SCBEMs, but that the HFEA is not necessarily best placed to assume responsibility for such a process.

G-SCBEM is currently exploring other options for establishing such a process. Possibilities include expanding the remit of the Steering Committee for the UK Stem Cell Bank and for the Use of Stem Cell Lines (whose secretariat transferred recently from the Medical Research Council to the Medicines and Healthcare Products Regulatory Agency).

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## **Recommendation 4**

**If laws and regulations are changed to permit (or facilitate the permitting of) novel reproductive technologies, it should be kept in mind that SCBEMs – while potentially very useful for testing reproductive technologies prior to clinical use – are not *themselves* likely to become a candidate reproductive technology for direct clinical use in the near future.**

After saying in its consultation document that *'It may be necessary to consider whether the Act needs to be revised to include these entities, or whether these biological cells should fall under the remit of other regulators'*, the HFEA immediately goes on to say that *'Without a flexible regime, the potential future use of any such developments for patient benefit could be limited, even when the advances in the field establish that their use is ethical and safe'*.

The latter statement may be straightforwardly true in relation to some novel reproductive technologies, but considered in relation to SCBEMs, the statement risks confusing distinct concerns. We wish to emphasise a vitally important difference between two aspects of SCBEMs.

On the one hand, research using SCBEMs – conducted in addition to (rather than in place of) research using human embryos proper – can be very helpful for studying natural human development and reproduction. Research using SCBEMs can also be helpful in testing the safety, efficacy and broader consequences of assisted conception techniques, of substances used in relation to assisted or natural conception (for example pharmaceuticals or nutritional additives taken by people wishing to conceive), and of medical interventions more generally.

Knowledge acquired from studying SCBEMs can serve such purposes for established reproductive technologies (for example, this knowledge might help to improve conventional IVF) and could also serve such purposes for reproductive technologies whose clinical use is not currently permitted (for example, this knowledge might help to assess future reproductive technologies involving *in vitro* gametogenesis and/or genome editing).

On the other hand, it is not appropriate for the time being to consider using SCBEMs *directly* in human reproduction. The novel reproductive technologies referred to in the previous paragraph are far more likely than SCBEMs to warrant consideration for direct clinical use.

It is our view that even if *'integrated'* human SCBEMs become sufficiently sophisticated for it to be feasible to use them to establish a pregnancy (at present they are not sufficiently sophisticated for this to be feasible), it would be unethical for anyone to attempt to do so in the foreseeable future.

Our view is consistent with that of ISSCR. We note that the ISSCR *Guidelines* (on p14) place *'Transfer of human stem-cell-based embryo models to the uterus of either a human or animal host'* in *'Category 3B'* (which covers activities that should remain prohibited because they *'lack a compelling scientific rationale or are widely considered to be unethical'*), rather than in the less forbidding *'Category 3A'* (which covers activities that should remain prohibited until – at minimum – outstanding issues of safety and/or ethics are addressed).

We believe that the considerations set out above will be relevant to any decision about which laws, and which bodies, are best suited to regulating human SCBEMs. We wish it to be clearly understood, and clearly conveyed, that use of human SCBEMs should be confined to the context of laboratory research for the time being.

If it were ever suggested that this situation should change, in light of some future discovery or advance, then a compelling case would have to be made and there would have to be wide-ranging public discussion of the ethical and scientific ramifications.

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### **In closing**

These are the four preliminary recommendations that G-SCBEM wishes to submit to the HFEA (and, via the HFEA, to Government).

Work on developing our recommended governance framework is ongoing, and we intend to share a draft of our framework with the HFEA (and other relevant bodies) later in 2023.

Please do not hesitate to contact us in the meantime – using the contact details we have provided in this consultation response – if you have any questions about our work, or if you would like to bring something relevant to our attention.

This consultation response was agreed by the members of the G-SCBEM Working Group, and by the G-SCBEM Principal Investigator.

#### **G-SCBEM Working Group**

- **Professor Roger Sturme**y (Professor of Reproductive Medicine, Hull York Medical School/University of Manchester) (*Chair of Working Group*)
- **Professor Bobbie Farsides** (Professor of Clinical and Biomedical Ethics, Brighton and Sussex Medical School)
- **Julian Hitchcock** (Of Counsel, Bristows LLP)
- **Professor Kathleen Liddell** (Professor of Intellectual Property and Medical Law, University of Cambridge)
- **Dr Naomi Moris** (Group Leader, Francis Crick Institute)
- **Professor Jennifer Nichols** (Professor of Embryonic Pluripotency, University of Edinburgh)
- **Dr Peter Rugg-Gunn** (Group Leader, Babraham Institute)
- **Professor Rosamund Scott** (Professor of Medical Law and Ethics and Director of the Centre of Medical Law and Ethics, King's College London)
- **Professor Austin Smith** (MRC Professor and Director of Living Systems Institute, University of Exeter)

#### **G-SCBEM Principal Investigator**

- **Professor Kathy Niakan** (Mary Marshall and Arthur Walton Professor of Reproductive Physiology, University of Cambridge; Chair, Cambridge Reproduction; Director, Centre for Trophoblast Research)