



# hESCCO: development of good practice models for hES cell derivation

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One response of the UK research community to the public sensitivity and logistical complexity of embryo donation to stem cell research has been the formation of a national network of 'human embryonic stem cell coordinators' (hESCCO). The aim of hESCCO is to contribute to the formation and implementation of national standards for hES cell derivation and banking, in particular the ethical protocols for patient information and informed consent. The hESCCO project is an innovative practical intervention within the broader attempt to establish greater transparency, consistency, efficiency and standardization of hES derivation in the UK. A major outcome of the hESCCO initiative has been the drafting and implementation of a national consent form. The lessons learned in this context may be relevant to other practitioners and regulators as a model of best practice in hES cell derivation.

Increasing interest in the potential of stem cell research within the scientific community and the general public has been occasioned by a proliferation of both practical and ethical concerns – some of which are unique to this field [1,2]. These concerns range from specific questions regarding patient information, feedback and consent, to broader principles of governance, regulation and commercialization in order to ensure the safe and responsible distribution of benefits from this promising new field [3,4]. While some stem cell research is carried out on adult and fetal tissues, which themselves give rise to specific questions of ethical regulation and governance, human embryonic stem cell (hES) research remains the most controversial area, around which there is substantial debate regarding best practice, accountability, limits to research and transparency [5]. Alongside new possibilities for the derivation of pluripotent human cell lines, such as induced pluripotent stem cell (iPS) cells derived from direct reprogramming [6,7], patients willing to donate surplus embryos to stem cell derivation efforts remain an essential component of research that must be protected by rigorous ethical guidelines.

The high ratio between the numbers of embryos needed and successful hES cell derivation for research or intended therapy is accompanied by significant public concern raised by the 'special' qualities of human embryos [8]. As a consequence of this, a high social value is placed on the maintenance of robust ethical standards for human embryo research, and a limitation or reduction of numbers of embryos used for such

research is a priority for many governments and regulatory authorities, including in the UK [9]. National coordination of hES research combined with publicly-accessible hES banking and strict oversight of both activities offer a pragmatic response to both the ethical and technical concerns raised by hES cell derivation [10]. In combination with the use of pluripotent cell lines (such as iPS cells, and those that might eventually be derived from parthenotes, from artificial gametes/embryos, triprounucleate embryos, reprogrammable fibroblasts or from umbilical cord blood), regulated donation of embryos and banking of hES cell lines offer the most socially responsible course of scientific research and ethical governance. Initiatives such as the publicly funded UK Stem Cell Bank, inaugurated in 2003, ensure that the benefits of stem cell research will be publicly accessible, and that the need for additional embryos will diminish over time (Figure 1 & 2) [10]. In order to reach the desired outcome of a national stem cell bank that can draw upon a large stock of reliable lines of sufficient diversity and quality to meet a variety of clinical requirements, improvements in the procurement and use of embryos donated specifically to stem cell research will remain a priority.

Attainment of these goals is likely to require the initial availability of significant numbers of high-quality embryos, and standardized derivation protocols and facilities that can make maximum use of these [11]. Such protocols are time-consuming to establish, laborious to standardize, and must be ethically and technically robust [12]. The obligation to maintain the highest ethical

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future  
medicine part of fsg

Figure 1. UK Stem Cell Bank.



hES cell derivation in particular, many countries share the position of lacking comprehensive, or even minimal, guidelines or standards in this comparatively new and fast-paced field [16]. Even in countries such as the UK, which has one of the most comprehensive legislative infrastructures for regulating human fertilization and embryology [17,18], hES cell derivation and banking has required the creation of new frameworks for governance [19,20]. Since 2000, the UK government has made stem cells a priority area for development and, through a series of reports, consultations and legislative amendments, has replaced the ‘legal vacuum’ that surrounded stem cell research at its outset in the late 1990s with a more robust regulatory infrastructure [21]. This process is ongoing and is also two-way [22], with the development of new standards and guidelines feeding into more overarching, and binding, regulatory infrastructures such as the recently established UK Human Tissue Authority. Responsibility for embryos used in hES cell derivation in the UK remains with the Human Fertilization and Embryology Authority (HFEA) until they are accessioned for banking, after which the Steering Committee of the bank takes responsibility for them under new regulation stipulated by the Human Tissue Authority.

In the following sections we describe further a central component of the UK strategy; namely the work of the Human Embryonic Stem Cell Coordinators’ network (hESCCO) through which greater national coordination of hES cell derivation has been achieved. Following a brief review of the regulatory context for hES cell derivation, research and banking in the UK, we turn to the formation of hESCCO, and its aims and goals, which we argue offer a set of protocols that may aid in the establishment of best practice, and greater international harmonization and standardization of hES cell derivation.

### Stem cell regulation & banking in the UK, 2003–2007

As in many other European countries, both the UK government and a majority of the general population share a positive evaluation of the potential benefits of stem cell research, and support its development, including the necessity for embryo research [23,103,104]. Although highly regulated in the UK, research involving human embryos, which now includes hES cell derivation and banking, occurs in a climate that is generally regarded as comparatively progressive, liberal and tolerant. The strategy of the UK

and quality standards for both procurement of embryos and subsequent research initiatives, while increasing the supply of embryos available for research, poses an ongoing challenge to governments and regulators, as well as for individual labs and clinics. Moreover, these challenges are increasing in number as the ethical and quality standards for stem cell research, tissue engineering and regenerative medicine progressively come under not only local, national, and European regulation, but more recent supranational initiatives towards harmonization and standardization of procedures on which successful translation will depend [13,14,102].

A crucial dimension of the challenges posed by hES cell derivation on a national scale is the need to determine appropriate guidelines, standards and regulatory policy [15]. At the same time that expectations and concerns are developing in tandem towards stem cell research in general and

Figure 2. UK Stem Cell Bank.



government has been to promote stem cell research through public funds as well as public-private partnerships, and to align the governance and regulation of this new field with existing legislation on embryo research, tissue banking and quality assurance [101]. The efforts to regulate stem cell research have resulted in a comprehensive set of measures that are aimed to promote and to protect stem cell science by ensuring public confidence in the ethical governance of this new field, while maintaining a stable environment for successful research and development, potential clinical applications, and increasing commercial investment [101].

In accordance with the conclusions of a Department of Health (DH) consultation paper, published in 2000, new regulations were introduced into Parliament to amend the 1990 Human Fertilisation and Embryology Act in order to widen the criteria for research on human embryos, including the creation of embryos through cell nuclear replacement (CNR) for research purposes. Under the Human Fertilisation and Embryology (Research Purposes) Regulations (2001), three new criteria for embryo research were added to the existing Act to widen the possibility for understanding the cellular bases of serious diseases and to permit research that might lead to their treatment – including through the method known as ‘therapeutic cloning’ (i.e., CNR).

In 2002, following the recommendations of the DH and also those contained in a special Report of the House of Lords Select Committee on Science and Technology [9], the UK Stem Cell bank was commissioned and publicly funded as

a joint endeavor between the Medical Research Council (MRC) and the Biotechnology and Biological Sciences Research Council (BBSRC, together £2.3m). 2002 also saw the first licenses granted for hES cell derivation from the HFEA, the statutory body that oversees all research concerning human embryos in the UK, and in 2003 the first UK-derived lines were announced by King’s College, London [24]. In this same year the UK stem cell bank was constructed and began its rigorous process of quality accreditation by the Medicines and Healthcare products Regulatory Agency (MHRA). In the meantime, its Steering Committee began the equally arduous process of devising means to fulfill the aims and goals of the bank in a manner that would be simultaneously consistent with existing UK and EU legislation, including the guidelines of its national research councils (e.g., MRC, BBSRC), the practices of other public tissue-banking organizations such as the National Blood Service (NBS) and the British Association of Tissue Banking (BATB), international current Good Manufacturing Practice (cGMP) and International Standards Organization (ISO) requirements, MHRA accreditation criteria, and the licensing criteria of the HFEA. By the end of 2003, the HFEA had granted eight further licenses for hES cell derivation nationwide. The bank was accredited and opened in 2004, the same year the UK Human Tissue Act came into effect, under which regulation the first UK lines were banked in 2005. The simultaneous adoption in 2004 of the EU Directive on Setting Standards of Quality and Safety for the Donation, Procurement, Testing, Processing, Storage, and Distribution of Human Tissues and Cells (widely known as the EUTCD) increased the necessity for the bank, in coordination with the UK’s increasingly numerous hES cell derivation laboratories, to reach agreed-upon standards and protocols for all aspects of derivation – from cGMP to informed consent.

### National coordination

The necessity for greater national coordination of UK hES cell line derivation prompted the MRC and the BBSRC to make available strategic research funding towards development of cooperation between hES derivation centers and assisted conception units, where couples might be contacted regarding their willingness to donate to hES research eggs and embryos unsuitable for, or surplus to, the clinical requirements of *in vitro* fertilization (IVF) or preimplantation genetic diagnosis. In particular, the

need for new consent procedures to be undertaken independently of both research and clinical personnel mandated the provision of extra staff. Seven such centers were funded across the UK in 2003, (Newcastle, York [Leeds], London/Leeds [the Bridge Centre], Sheffield, King's College London [Guy's Hospital], Roslin Institute [with Manchester], and the North of Scotland Stem Cell Initiative [Aberdeen/Dundee/Edinburgh]). Several of these centers appointed stem cell coordinators to aid in the considerable and time-consuming logistical hurdles involved in the creation of appropriate protocols for contacting and communicating regarding the numerous and complex issues involved in consent to donate eggs and embryos to hES research. In an effort to devise ethically robust procedures, and establish semistandardized national protocols for patient information and consent for embryo donation to stem cell research, additional funding was sought and approved to bring the coordinators and stem cell scientists together biannually specifically to enhance national stem cell coordination, a primary benefit of which would be increased national cooperation and consistency. In addition to the seven MRC supported units or networks, five other assisted conception or stem cell units joined the initiative at its outset: Manchester, Birmingham, Oxford, Bourn Hall Cambridge and Nottingham. A national network of stem cell coordinators was founded in 2004 with these aims in mind under the name of hESCCO (Figure 3).

Through this nationwide program of cooperation, centers encountering similar experiences, be they in meeting cGMP or drafting patient information and consent forms, could share experiences and essential information. Efficiency of scale was also gained in the effort to achieve more rapid compliance with existing and emergent legislation, and in particular the 2004 EUTCD, as well as the quality control requirements of cGMP, ISO and other accreditation criteria. In sum, national coordination offered the potential to improve the accountability and transparency of hES cell derivation and banking, by ensuring the credibility and rigor of its ethical governance, while enhancing successful scientific innovation and the potential to improve public health (Figure 4).

hESCCO meetings began in London in December 2004, attended by two members of each participating centre, so that in addition to the individual stem cell coordinators hESCCO membership included clinicians, scientists,

embryologists and social scientists. Representatives of national regulatory bodies, including the HFEA and MHRA, and of organizations with relevant tissue banking expertise, such as the NBS were invited to meetings to brief hESCCO members in response to a rapidly changing array of emergent questions concerning topics such as payment for donation, screening of donors, and changes in EU and UK policy (see further below). Members of the UK Stem Cell Bank also attended meetings, as well as representatives of the MRC, to create a highly interdisciplinary context of diverse expertise, knowledge and experience (Table 1).

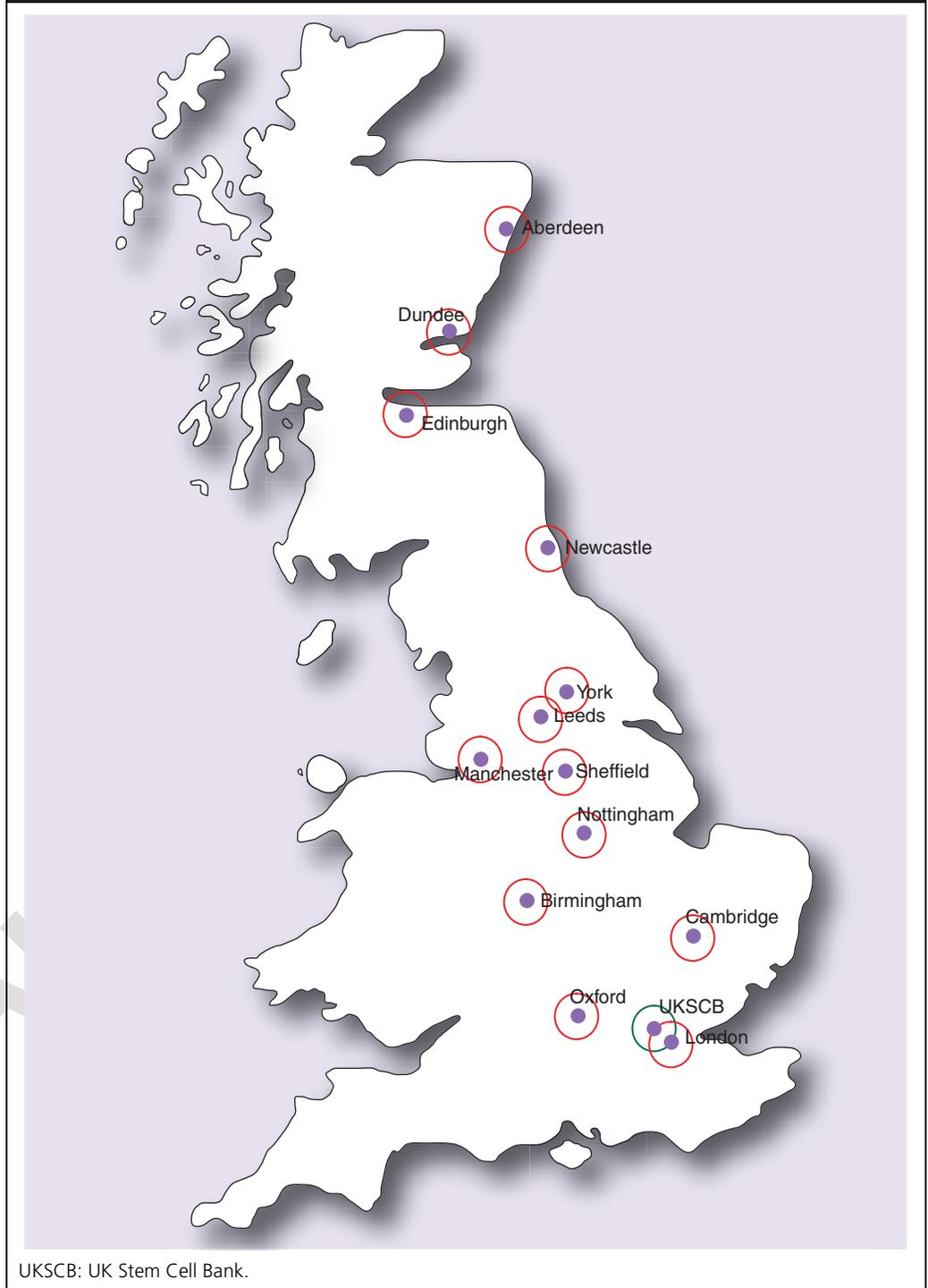
The general, overarching aims of hESCCO outlined above were linked to specific objectives, in the form of key outcomes and deliverables. In turning to a review and assessment of the achievement of these goals, our aim is to contribute to definitions of best practice that may be of relevance in other contexts of hES derivation, both nationally and internationally (Box 1).

In addition to the objectives listed below, hESCCO meetings have provided a vital opportunity to address specific technical issues of quality control, in particular where these overlap with patients' concerns – such as the point at which embryos can no longer be withdrawn from research, and the implications for IVF of hESC derivation, such as the criteria for freezing embryos at each clinic, and the potential availability of clinically derived embryos for hESC research. The contribution from the MRC towards the costs of building/renovating five cGMP-standard derivation labs linked directly to assisted conception units, in Sheffield, Manchester, London (Guy's), Newcastle and Birmingham in 2005, and the completion of the first of these in 2006 (at Sheffield), has intensified the need to develop and establish a minimum set of nationally semistandardized protocols, in spite of the difficulties of so doing. In the following sections we review which of the hESCCO goals have been accomplished, and we conclude by commenting on those that remain as future challenges.

#### A standard national hES consent form

Chief among the accomplishments of hESCCO members, whose activities are increasingly focused on the interface between IVF and stem cell research, is the development of a national consent form for embryo donation to hES research. In the post-Hwang context, as well as in the wake of the public controversy surrounding

**Figure 3. Nationwide distribution of participating hESCCO centers and the National Stem Cell Bank.**



misuse of human tissue in the Alder Hey pathology department in the UK [25], the question of accountability for robust consent procedures for embryos and human tissue, and their credibility to patients and the wider public, has gained increasing prominence [22]. While debate

regarding informed consent, patient screening, anonymisation, feedback and paid donation continue to indicate the lack of a uniform frame of reference internationally concerning best practice in the regulation of egg and embryo donation, the imperative to provide clear standards of best

**Figure 4. First Human Embryonic Stem Cell Coordinators' meeting in London.**

consenting practice is of increasing importance. Thus, in addition to the fact that consent procedures for embryo donation to stem cell research must respond with due diligence to novel sources of patient concern, such as the possibility of stem cell-derived 'artificial gametes' and more recently iPS cells, the development of such procedures is also required to conform to a new, and in some senses higher, standard. For these and other reasons, consent has become a priority issue for hESCCO, and has occupied much of its attention.

While efforts in conjunction with the UK Stem Cell Bank to develop standard national protocols for GMP and relevant aspects of derivation (such as appropriate standards of air quality, flow and monitoring) are ongoing [26], the primary deliverable of the hESCCO initiative has been the establishment of practical, legal, up-to-date, and nationally-agreed-upon criteria for informed consent procedures, as well as two new four-page consent forms (for fresh and frozen embryos). The forms are the outcome of an exhaustive consultation process involving representatives from the HFEA, the UK Stem Cell Bank, the NBS, the BATB, the DH, and the MRC.

Free and informed consent are key principles of the Human Tissue Act (2004), the HFE Act (1990), and the EU Tissue Directive (2004), as well as being a core component of best practice in clinical medicine, random-controlled trials, and any scientific research involving human subjects. For consent to be robust, legitimate and ethically sound, comprehensive information must be given in a form that is readily accessible and allows a free and informed decision to be made by potential donors [27]. In the UK, all

written (patient) information provided and consent forms have to be approved by the National Research Ethics Service [105], and for research involving embryos also by the HFEA. The HFEA requires that the donor couple must have given 'in principle consent' for the use of embryos in research using a separate form.

To respond to the additional consent issues raised by egg and embryo donation to hES cell derivation, the Steering Committee of the UK Stem Cell Bank has, in collaboration with the HFEA and the MRC, drawn up a list of 'minimum criteria' [106] that must be addressed in patient information leaflets and consent forms. Before patients give consent to donation of eggs or embryos for use in research projects to derive stem cell lines, they must be given oral information supported by relevant written material that confirms a number of criteria (Box 2).

In addition to these minimum criteria, which must be provided in the patient information leaflet accompanying the consent form, fully discussed with potential donors by an independent party who is not part of either the clinical or the research team, and considered by patients for a suitable period of time to allow reflection, each gamete or embryo provider must consent in writing to a number of criteria (Box 3).

In the establishment of minimum consent criteria, every effort was made to introduce clarity and brevity, while retaining a substantial core of necessary information. The design of the two forms, one for fresh and one for frozen eggs and embryos, was intended to maximize ease of use.

The forms are amenable to minor local variations, and publicly available as an electronic file from the hESCCO website [107], and the consent

**Table 1. Writing group on behalf of human embryonic stem cell coordinators.**

| Contributor            | Affiliation            |
|------------------------|------------------------|
| Siladitya Bhattacharya | Aberdeen               |
| Isobel Morton          | Roslin                 |
| Alison Murdoch         | Newcastle              |
| Maria Nesbitt          | Newcastle              |
| William Ledger         | Sheffield              |
| Rachel Cutting         | Sheffield              |
| Daniel Brison          | Manchester             |
| Sharon Sneddon         | Manchester             |
| Karen Arnold           | Manchester             |
| Helen Picton           | Leeds                  |
| Helen Mardon           | Oxford                 |
| Jackson Kirkman-Brown  | Birmingham             |
| Kay Elder              | Cambridge (Bourn Hall) |
| Clare Williams         | London                 |
| Madhurima Rajkhowa     | Dundee                 |
| Christopher Barratt    | Dundee                 |

form has been praised by patients and health professionals for its clarity of design and content, and consequent user-friendliness. Most importantly, the process of creating an hES consent form that is up-to-date and fit-for-purpose has aided in the

effort to establish ‘best consenting practice’ to accompany other quality markers in the stem cell area, and to ensure that consent is more than either ‘just ticking boxes’ or a ‘meaningless paper trail’.

The forms received approval from the HFEA in 2005 and have since been adopted by clinics across the UK (Figure 5).

**Box 1. Human Embryonic Stem Cell Coordinators’ Goals.**

- To establish a working national network facilitating feedback and evaluation of best practice in embryo procurement and human embryonic stem (hES) cell derivation and to provide resources for professionals involved in this area
- To achieve compliance with existing regulation, and to contribute to the formation and improvement of regulatory guidelines within the UK and in Europe
- To establish and implement semistandardized protocols for sourcing eggs and embryos (including consistent procedures for approaching patients for fresh and frozen eggs and embryos from *in vitro* fertilisation and preimplantation genetic diagnosis programs)
- To design, pilot and assess patient information and consent forms for fresh and frozen egg and embryo donation that conform to all existing guidelines related to hES derivation and to make these publicly available
- To create two websites, one public and one restricted access, which contain information regarding stem cell research and embryo donation (consent forms, database, frequently asked questions, publications, links, etc.)
- To collect data on patient perceptions of egg and embryo donation, informed consent procedures and hES research, and to publish the results of such surveys where possible
- To design, test, evaluate and standardize the protocols for a national database through which all embryos donated to hES research are tracked
- To contribute to ‘best practice’ for communication with patients concerning areas of ongoing uncertainty and concern such as feedback, commercialization, traceability, payment for donation, and the derivation of artificial gametes and embryos

**Areas of ongoing concern**

The ability to draft, pilot, revise and gain ethical approval for a consent form that is now used throughout the UK has proven a useful exercise on several fronts; for example, by facilitating confirmation of agreed minimum consent criteria, collecting information on patient perceptions to improve patient communication, and creating new mechanisms to increase transparency and accountability of the sector. This process has also confirmed the value of working at a national scale in order to make efficiency gains and clarify areas of shared uncertainty. Support is being sought to continue and expand hESCCO activities in the future.

Also of value is that the hESCCO initiative has revealed areas of concern and uncertainty that are likely to remain the subject of ongoing discussion for the foreseeable future both in the UK and elsewhere.

- Artificial gametes and restricted or conditional consent;
- Short and long-term feedback to patients;
- Remuneration of egg and embryo donors;
- Donor screening protocols.

**Box 2. Oral consent criteria.**

- The research project is directed towards the derivation of human embryonic stem cell (hES) lines.
- Very few such cell lines are derived from donated eggs or embryos at present.
- Any hES cell lines that are derived will be deposited in the UK Stem Cell bank, may be used for other projects within the UK and/or overseas, and may eventually be used for treatment.
- The research will not lead to any direct medical benefit to the donor.
- The UK stem cell bank is overseen by an independent Steering Committee, which has the responsibility to ensure legal and ethical accountability for all hES cell lines accessioned by the bank.
- Donation to research will in no way affect donors' treatment and the decision whether or not to donate is voluntary.
- Donated embryos will be anonymised, although this anonymity must, under the terms of the EU Tissue Directive, be reversible under exceptional circumstances when grave matters of public health may be at stake.
- No information emerging from tests done on the cell lines will be fed back to donors (unless under the exceptional circumstances mentioned above).
- Donors can withdraw their consent until the point that the eggs or embryos are used for research.
- Cell lines, or discoveries made using them, may be patented and used for commercial purposes, but the donors will not benefit financially from any future profit generated by their cell line.

***Conditional or restricted consent***

That it is possible for germ cell lines, or 'artificial gametes', to be derived from embryonic cell lines (and more recently iPS cells) has proven to be a concern for a small but growing number of patients. If UK-derived lines are distributed outside the UK, they could be used for reproductive purposes regardless of what UK law has to say on the subject (i.e., regardless of the ban on reproductive cloning). Patients may understandably wish to allow their embryos to be used for research or for development of new forms of medical therapy but to do so on the condition their cells will not be used to develop a new individual in years to come. The possibility of introducing conditional consent, a decision which would respond to the legitimate concerns of potential donors, is therefore one to which the HFEA has devoted serious consideration. To date it has refrained from endorsing such a practice, which would set a new precedent of 'fettering' consent to tissue donation which many regard as contrary to best practice in terms of either experimental research, tissue banking, or patients' wishes (in particular since the feasibility, and therefore authenticity, of such a guarantee of unknown duration cannot presently be reliably assured). Simply not allowing patients with these concerns to donate would reduce the number of embryos available for research into stem cell derivation and processing while also

contravening patients' wishes not to see their embryos 'go to waste'. An additional objection to making an 'exceptional case' of embryo donation as a candidate for the unprecedented use of conditional consent is that adult cells can also be used to derive gametes and embryo-like cells [6,7,28], while remaining largely unregulated. At present consent to donate embryos to hES cell research remains unrestricted and unconditional in the UK.

***Feedback to patients***

Feedback of information to patients raises issues in relation to both the short and long term. At one end of the feedback spectrum is the increasingly influential principle drawn from human rights law and bioethics that personal information belongs to the donor, and that no agency should retain identifiable information of relevance to the individual's health 'in secret', or without that individual's knowledge and consent [108]. However, information from stem cells such as possible genetic predisposition to disease may only come to light through research many years after donation, and may or may not be welcomed by a former patient, especially as the clinical implications might be unclear, unreliable or simply unknown, being derived from tissue grown *in vitro* through many cell passages. How and by whom such information would be imparted also presents difficulty. On the other hand is the requirement, under the 2004 EU Tissue Directive, that donors remain traceable through a system of reversible anonymity, so that they could be contacted in the event of a major threat to public health (the most commonly cited example being the detection of infective diseases such as BSE, which could be spread through other contaminated tissue products). Beyond this requirement, current best-practice as recommended by the UK Stem Cell Bank Code of Practice for the Use of Human Stem Cell Lines (2006) is for donors to be informed that 'no individual feedback will be given on tests performed by the UK Stem Cell Bank or research results of subsequent studies' although 'general information...including the results of research using embryonic stem cell lines will be published on the [bank's] website' [106]. Hence, while the option to be informed if their embryos have developed into cell lines has largely been foreclosed, the possibility that patients could be contacted either in the event of a public health concern, or indeed should 'test results of direct relevance to the donor or the donor's family' be

**Box 3. Written consent criteria.**

- That they consent to the use of embryos created using their gametes or embryos in a specified research project for the derivation of human embryonic stem (hES) cell lines.
- That they understand that a sample of any successfully derived hES cell line(s) will be deposited in the UK Stem Cell Bank and that these cell lines may be used in other research projects.
- That they are aware they are under no obligation to donate gametes or embryos to research and that a decision not to participate in research projects will not alter their treatment in any way.
- That they understand that they have a right to withdraw their consent without giving any reason, at any stage until the gametes and/or embryos have been used for research.
- That they understand that any cell line derived from their donated gametes/ embryos may eventually be used for treatment purposes (including cell replacement therapies) in the future, but that donors will not personally benefit from such treatment.
- That they understand that cell lines or discoveries made using them may be patented and used for commercial purposes, but that donors will not benefit financially from any future profits of such commercial activity.
- That they agree to be contacted in the future in the unlikely event that the Stem Cell Steering Committee considers that they should be contacted in relation to confirmed test results performed on stem cell lines that are of direct relevance to their own, their family's or public health.

discovered, remains open, and the more indirect feedback provided by the bank as research reports may become more detailed over time.

**Remuneration of egg & embryo donors**

In July 2006, the HFEA set a new precedent by granting a license to Newcastle University for 'egg sharing for research' – a practice designed to reduce the cost of IVF treatment in exchange for the donation of eggs and embryos to research. The Authority simultaneously announced a public consultation into the wider question of 'whether it is appropriate for women to donate their eggs for use in scientific research', and what safeguards might be needed were such a practice to become more widespread [29]. Egg sharing for research, which is unique to the UK, was approved by the HFEA on the basis of its similarity to clinical egg-sharing programs in which discounted, or free, IVF treatment is offered in exchange for donating eggs to other couples. However, egg sharing for research has been the subject of debate owing to the potential for exploitation which attaches to any kind of remuneration for tissue donation – especially the perceived 'sale' of tissue, which is widely prohibited, including by the UK Medical Research Council Ethics Guidelines. In February 2007, the HFEA reconfirmed its decision to license egg sharing for research, stating that: 'Having considered all the information on

donating eggs for research, including the risks to women and the outcomes of the public consultation, the Authority has decided that women will be allowed to donate their eggs to research, both as an altruistic donor or in conjunction with their own IVF treatment. Given that the medical risks for donating for research are no higher than for treatment, we have concluded that it is not for us to remove a woman's choice of how her donated eggs should be used.' In confirming that egg donation for research could proceed on the same remunerative basis as egg sharing for treatment, the Authority emphasized that the safeguards in place for both types of donation must continue to involve robust informed consent procedures, and that licensed clinics must ensure a 'clear separation between the researchers and people carrying out the woman's treatment, detailed information regarding the realistic outcomes of the research and the impact the donation would have and the requirement for obtaining the women's consent to be independent of the research team.' [109]

**Donor screening**

The fact that several thousand patients might receive hES cell products from a single established line poses a significant challenge for quality assurance. Which aspects of donor screening are paramount for hES cell derivation (as opposed to blood donation), and how should the screening, testing and documentation of donor characteristics be facilitated logistically, technically and ethically? The starting point for the hESCCO discussion of donor screening was an audit of existing screening for IVF. While a considerable amount of information is already gathered from patients as part of routine clinical practice – much of which overlaps with existing NBS testing is achieved in terms of HIV, Hepatitis B, and Hepatitis C screening – there is at present no requirement in the EUTCD to ask the 'lifestyle' questions routinely applied by the blood service to screen donors. To some, the paramount question of public safety can breach no slackening of the reins, while, for other perhaps more technologically confident observers, the costly and labor-intensive donor-selection processes are no longer the paradigm of either best practice or fiscal prudence, where couples are involved and when the starting and finishing material will be available for extensive re-analysis before any release for therapy. In the USA, for example,

Figure 5. Consent form cover page (fresh).

| PATIENT CONSENT TO RESEARCH  |                                   |                                  |  |
|--|-----------------------------------|----------------------------------|--|
| Derivation of human embryonic stem cell lines  |                                   |                                  |  |
| Principal Investigator:  |                                   |                                  |  |
| Other investigators:   |                                   |                                  |  |
| Ethics Committee code Number:  |                                   |                                  |  |
| HFEA Licence number:   |                                   |                                  |  |
|  | Please Initial in the boxes below |                                  |  |
|  | Male                              | Female                           |  |
| We have read and understood the information sheet about this study ( <i>insert name and version number of information sheet</i> ) and had the opportunity to discuss any concerns with a member of staff who is independent of clinical treatment. We have also had the opportunity to discuss the research project with a member of clinical staff who is independent of the research programme.        | <input type="checkbox"/>          | <input type="checkbox"/>         |  |
| We understand that we are under no obligation to take part in the study and that a decision not to participate will not alter the treatment that we would normally receive.  | <input type="checkbox"/>          | <input type="checkbox"/>         |  |
| We understand that we can withdraw our consent without giving any reason, at any stage until the embryos have been used for research.<br><i>(Embryos will be regarded as used for research after they are under the control of the researchers and they are being cultured/grown for use in research)</i>  | <input type="checkbox"/>          | <input type="checkbox"/>         |  |
| We agree to donate our embryos (made from our eggs and sperm) that are surplus/unsuitable for treatment for use in this research project.  | <input type="checkbox"/>          | <input type="checkbox"/>         |  |
| We understand that a sample of any stem cell line derived will be placed in the UK Stem Cell Bank and that the derived stem cell lines may be used in other research projects subject to regulatory approval. We understand that if a sample of a stem cell line is placed in the UK Stem Cell Bank a copy of this consent form will be given to the secretary of the Stem Cell Bank Steering Committee. | <input type="checkbox"/>          | <input type="checkbox"/>         |  |
| We understand that cell lines or discoveries made using them may be patented and used for commercial purposes, but that we will not benefit financially from this.   | <input type="checkbox"/>          | <input type="checkbox"/>         |  |
| We understand that we may be contacted in the future only in the exceptional circumstance that the Stem Cell Steering Committee considers that results obtained on any stem cell lines created from our embryos would be of direct relevance to our health, our family's health or public health.  | <input type="checkbox"/>          | <input type="checkbox"/>         |  |
| We <b>ACCEPT/DO NOT ACCEPT</b> (delete as appropriate) that in the future, subject to appropriate testing, any cell line derived from our donated embryos may be used for treatment purposes (including cell replacement therapies).   | <input type="checkbox"/>          | <input type="checkbox"/>         |  |
| Print Name:  | Sign:                             | Date:<br><i>(day/month/year)</i> |  |
| FEMALE:  |                                   |                                  |  |
| MALE:  |                                   |                                  |  |
| Verified by/Witnessed  |                                   |                                  |  |
| Your hospital address details  |                                   |                                  |  |

the FDA has emphasized that its xenotransplantation regulations are not intended to prevent the clinical use of hES cells derived using

animal products [110]. There is considerable concern regarding the EUTCDC requirement to retest living donors of embryos after 6 months,

in the same way the blood service is required to do, and the need for comprehensive lifestyle questioning, especially in fertility patients where this will have to be delivered as a couple, and may not always be answered truthfully.

### Conclusion

The hESCCO initiative has confirmed the value of a national network in the effort both to improve patient information and consent procedures, and to address questions of public dialogue, interaction and accountability. The challenge has been to develop and produce appropriate patient information protocols in a legally, ethically and technically complex arena of contemporary biomedical and bioscientific innovation. Evolving standards for best practice has required exchange of information between disparate professional communities linked to both IVF and hES cell derivation, as well as tissue culture specialists, policy-makers, regulators, social scientists and government representatives. The joint effort to solve core practical problems, such as those related to patient

feedback and donor testing, demonstrates that the advantages of greater efficiency cannot be won without also achieving a higher level of collective dialogue and coordination, in which patients appear increasingly willing to play an active role. While a number of issues remain under discussion, and are yet unresolved, the hESCCO experience demonstrates the advantages to be gained through national consultation on best practice on a range of patient-related issues, and the efficiency gains in harmonization, implementation, and standardization of these improvements that are the result of national coordination.

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