Gaps and overlaps: improving the current regulation of stem cells in the UK

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A failure to provide a comprehensive and cohesive regulatory system to govern stem cell research and application will hinder the development of treatments for serious diseases and undermine the UK's attempts to become a global leader in this field

Stem cells are the source cells in the human body from which all other cells develop and have the remarkable ability to heal damaged tissue and to grow new tissue and, potentially, organs. In the UK, researchers are striving to harness these capacities to develop stem cell therapies for conditions such as macular degeneration, liver disease, infertility, spinal cord injury, Parkinson disease, diabetes and many more. The government is keen to ensure the UK's global pre-eminence in this area, and in May 2004, £16.5 million of public sector funding was allocated to stem cell research.[1] In 2005, the UK Stem Cell Initiative (UKSCI) was established to develop a 10-year research and development strategy for 2006 to 2016, aiming to ensure that the UK is "the most scientifically and commercially productive location for this activity over the coming decade, and which commands the support of public and private research funders, practitioners and commercial partners".[2] The UKSCI has recommended that the government should provide increased funding of £11 million to £74 million a year over the 10 years to 2016 and set up public/private partnerships to coordinate and develop stem cell research and technology.[2]

To match the pace of scientific progress in stem cell research,[3 4] it is critical that UK law is clear, consistent and capable of application by those working in the field, from the moment of obtaining tissues from which stem cells will be derived to their use in clinical applications. Unfortunately, this is far from the case. A plethora of legislation and other guidance, both in the UK and internationally, purports to cover stem cells, although in most cases this was not the purpose underlying their creation. These include the Human Fertilisation and Embryology Act 1990 ("1990 Act"), drafted to govern IVF treatment[i]; the Human Tissue Act 2004 ("2004 Act"), which was drafted in response to the practice of non-consensual tissue retention that came to light during the Bristol and Liverpool inquiries[5 6]; the European Union Tissues and Cells Directive 2004[7] (EUTCD), which was drafted for organ donation and transplantation; and the Clinical Trials Directive 2001[8], which was drafted for drug development. Various non-binding codes of practice and guidelines to cover stem cell research have also been published by bodies such as the International Society for Stem Cell Research[9], the National Research Ethics Service[10 11], the Hinxton Group[12], Eurostem[13] and the UK Stem Cell Bank Steering Committee.[14]

Weaknesses in the UK's regulatory framework governing stem cell research and technology are apparent throughout every stage of the process of creating stem cell products. Two examples "bookend" this process, the derivation, storage and use of human embryonic stem cells (hESCs) and the regulation of stem-cell-based products.[ii]

OBTAINING AND HANDLING hESCs

The initial stages of stem cell research—that is, obtaining the stem cells and then carrying out laboratory research on them—are governed by a number of regulatory authorities, which do not seem clear about the boundaries of their jurisdiction and which are expected to interpret and apply the myriad legal provisions that govern every stage. The embryos or blastocysts[iii] from which the hESCs are derived are usually obtained from a fertility clinic and are entities that would otherwise be discarded after fertility treatment. This stage of the process is governed by the 1990 Act, which imposes very strict requirements on dealing with embryos.[iv]

Once consent has been given to make the embryos available for research, however, two different standards may apply, first in relation to their handling in the laboratory and second in relation to any subsequent uses. If the stem cells are being derived for potential human application, then specific and very high laboratory standards regarding air quality, handling, temperature and quality control are imposed.[v] In contrast, if the stem cells are being derived for research purposes only, then much lower handling standards are required.[10 15] No other statutory provisions affect research-grade stem cells and stem cell lines, and the only guidance as to how they should be stored and used comes from documents that are not legally binding, such as international guidance and the UK Stem Cell Bank Steering Committee.[9 10]

In contrast, where the stem cells are intended for human application, the Human Tissue (Quality and Safety) Regulations 2007[vi] bring them within the remit of the Human Tissue Authority (HTA). However, the stage at which the remit of the Human Fertilisation and Embryology Act (HFEA) ends and the HTA's begins has not been defined. Is it when the first stem cell is extracted from the embryo? Or when sufficient extraction has occurred that the embryo is no longer intact? Or is it when the embryo is disposed of? The HFEA and HTA, together with the Medicines and Healthcare Products Regulatory Agency (MHRA) issued a joint statement on 3 May 2007 setting out where they envisage the lines being drawn.[16] However, discrepancies remain, and this lack of clarity can only serve to damage confidence in the legal framework.

STEM-CELL-BASED PRODUCTS AND THERAPIES

Another example of the complicated and uncertain legal provisions that the scientists must navigate in their attempts to undertake stem cell research are those governing the resulting products and therapies.

Until the end of 2006, the regulatory body responsible for medicinal products in the UK, the MHRA, was insisting that it was unlikely to be responsible for such

[i] The UK government announced a review of the 1990 Act in 2004 and held a public consultation on it between August and November 2005. As a result, the Human Tissues and Embryos (Draft) Bill was published on 17 May 2007 and is intended to revise the law on assisted reproduction and embryology and to establish the Regulatory Authority for Tissue and Embryos (RATE). http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsLegislation/DH_074718 (accessed 6 Sep 2007).

[ii] There are many others—for example, hybrid embryos, artificial gametes and disposal of stem cells.

[iii] A blastocyst is a fertilised egg that has divided and is usually used when it has reached the 8-cell stage, at around 6 days post fertilisation.

[iv] For example, in relation to consent to research use in Schedule 3 and the stage of development up to which research can be carried out in sections 3(3)(a) and 4.

[v] The EUTCD, as transposed into UK law by the Human Fertilisation and Embryology Act (Amendment) Regulations 2007.

[vi] The second set of regulations transposing the EUTCD and its two technical directives into UK law.

products, as they were tissue-based therapies rather than medicinal products. The HTA was adamant that such regulation was not within its remit, either, leading to increasing concern within the scientific community that after having invested over £10 million in building state-of-the art clean-room facilities[vii] in which to develop these treatments, they had fallen into a regulatory gap. With no authority prepared to accredit or regulate them, the resulting products would be unacceptable in the global market and therefore worthless to the patient.

Hopes for clarification surfaced, however, with the approval earlier this year of the European Regulation on Advanced Therapy Medicinal Products by the European Parliament and Council of Ministers.[17] This brings stem-cell-based products squarely within the definition of medicinal products (Art 1 Directive 2001/83/EC) and therefore within the remit of the MHRA. In light of this, the MHRA has agreed to begin discussions both with the other regulators and with the scientific community to look at how its current rules and practices may or may not apply to stem-cell-based products. Nevertheless, the jurisdictional boundaries of the various regulators remain to be resolved. The MHRA will require compliance with its standards all the way back in the process of therapy development, potentially to the embryo itself, opening the area up again to regulatory gaps and overlaps.

THE FUTURE

These examples illustrate that science is as difficult to regulate now as it was 17 years ago when the 1990 Act was passed. The considerable consultation and scrutiny procedures to which the proposed amendments to the 1990 Act have been exposed indicate just how aware the government is that it needs to be extremely careful in the drafting and development of this area of law. It is, of course, very difficult for a necessarily slow and meticulous parliamentary process to keep up with a rapidly advancing scientific area that presents huge ethical and practical problems. Legislation in this field must seek to both regulate and enable scientific progress without being confusing, difficult to interpret or unnecessarily onerous. In addition, the public must have confidence that its interests are protected.

The fragmented rules on stem cells and stem cell products across Europe are deterring external investment and commercial activity. Stem cell companies in the USA prefer to stick to the US market, where the requirements of the Food and Drug Administration, however complex, are at least clearly set out and applied in a fairly uniform way.[18] The UK's current reputation in the field as a jurisdiction suitable for stem cell work, being both liberal yet appropriately regulated, is therefore endangered, which may deter international scientists from working in the UK or collaborating with UK stem cell experts. As a result, the significant sums of public money being invested in the area may be spent in vain.

Unless steps are taken to remedy this situation, the UK's position as a world leader in the field is under threat, but the solution is not to take various pieces of legislation that deal with similar areas and stretch them to cover stem cells. As we have seen, at the joins there will be gaps and areas of overlap, with regulatory authorities being unclear about where their remits begin and end. Meanwhile, scientists are trying to develop treatments that will save lives and alleviate suffering. Such developments take long enough[viii], and the law must not be the cause of further unnecessary delay. The legal regulation of stem cells must be addressed as a distinct area, and legislation that emerges must strike that elusive balance between facilitating scientific progress and providing ethical and practical safeguards.

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[vii] aboratories operating to recognised standards of good manufacturing practice (GMP), incorporating Grade B environments for derivation and culture to ensure cells are clean enough to be used therapeutically.

[viii] Centre of Excellence for Life Sciences (CELS) research indicates an approximate timeline of 23 years from initial concept to product on the market.[19]