

Developing stem cell therapies

Manufacturers face serious challenges on the regulatory front and in terms of legal liability.

As the world of biomedical research continues to advance, the potential use of stem cell therapies to find reliable remedies for chronic debilitating disorders such as diabetes and Parkinson’s disease has generated substantial media attention. This article looks at the development of this research and the risks that may arise in the future from its use in new medicines.

So what are stem cells?

Stem cells are essentially primitive cells with the potential to develop into all kinds of cells

and tissue types, including bone, nerves and skin. Basically, there are three groups of stem cells as set out below:

(1) Embryonic stem cells: These can be taken from the embryo at various stage of its development	The stem cells taken from the early stages of an embryo are capable of producing any type of cell in the body (totipotent), while those taken later can develop into most – but not all – types of cells (pluripotent)
(2) Umbilical cord stem cells: The blood inside the umbilical cord has stem cells that are genetically identical to the newborn child	These stem cells are multipotent, which means they can develop into only a limited type of cells
(3) Adult stem cells: Both infants and adults have stem cells in their tissues directing their growth	These stem cells are also multipotent and can only develop into a limited type of cells

Aim of stem cell therapy

Stem cells restore tissues which are either deficient in the body or which have been damaged by injury or disease. The aim of

stem cell therapy is to replenish or replace deficient or damaged tissue that is otherwise unable to heal itself – for example, by transplanting stem cells into the damaged

area and directing them to grow new, healthy tissue, or by trying to make stem cells already in the body expand and produce more tissue.

Stem cell therapies in use

Several stem cell therapies are already being used to treat human diseases. These include umbilical cord blood stem cell transplant; adult stem cell transplant of blood stem cells; and – perhaps best-known – adult stem cell transplant of bone marrow stem cells to treat (for example) deficiency in white cells caused by cytotoxic treatment of leukaemia and other types of blood-borne cancers.

Future stem cell therapies

Scientific researchers are striving to develop stem cell therapies that are more effective, less intrusive and safer. At present, such therapies usually rely on donations from others. However, this carries the risk of rejection from the host’s immune system. In future, it may be possible for a person to use a sample of their own stem cells to regenerate tissue. This would reduce the danger of rejection.

Ethics

The ethical dilemma currently focuses principally around the use of embryonic stem cells. There are two main opposing schools of thought: those people who believe that the benefits to human beings are so great that the opportunities for research and treatment must be taken forward, and (on the other side of

the argument) those who oppose such research on the basis that embryonic stem cells are essentially human beings who cannot consent to being used. Other people take a halfway view: research on the surplus of embryos from infertility treatments is acceptable as they would otherwise be destroyed.

UK law and regulation

From April 2006, the UK regulatory framework for stem cell therapy was required to incorporate the provisions of the EU Tissue Directive 2004. This directive was designed to ensure the safety of cells and tissues that are transplanted into (or onto) the human body and applies (among other things) to cellular stem-cell-derived materials that are intended for human application. Currently, UK and Belgium are the only countries in Europe that allow the creation of embryos for the specific purpose of research.

In the UK, the primary legislation includes the following:

- the Human Fertilisation and Embryology Act 1990 (HFE Act 1990);
- the Human Fertilisation and Embryology (Disclosure of Information) Act 1992;
- the Human Reproductive Cloning Act 2001; and
- the Human Tissue Act 2004.

Applicants for research licences must justify to the Human Fertilisation and Embryology

Authority (HFEA) why embryonic stem cells are to be used rather than adult stem cells. (The HFEA was established in 1991 to enforce the provisions of the HFE Act 1990.) Applicants are also required to provide detailed information on the fate of the stem cells throughout the process, and to place a sample of all cell lines in the UK Stem Cell Bank.

On 14 December 2006, the government announced its intention to amend the HFE Act 1990 so as to clarify its policy regarding human, animal and hybrid and chimera embryos. The draft bill is expected to be presented to parliament shortly.

Manufacturers of stem cell medicines should also be aware of the Medical Devices Regulations 2002 (the MD Regulations 2002), following the recent implementation of regulation 3 of the Medical Devices (Amendment) Regulations 2007.

Regulation 3 came into force in March 2007 and provides

that the MD Regulations 2002 apply to active implantable medical devices or in vitro diagnostic medical devices, or accessories to such devices, if they:

- incorporate human blood, blood products, plasma or blood cells of human origin;
- are transplants or tissue or cells of human origin, or incorporate or are derived from such tissues or cells; or
- are transplants or tissue or cells of animal origin (other than non-viable animal tissue).

Stem cell therapy case law is beginning to emerge as well. One example is the House of Lords case of *Quintaville (on behalf of Comment on Reproductive Ethics) v Human Fertilisation and Embryology Authority* [2005] UKHL 28. In that case, the question was whether the HFEA is empowered to license tissue typing. This is a process by which embryonic cells are tested for their compatibility with the tissue of a sick sibling, with a view to planting a compatible embryo into the mother's womb and the eventual treatment of the sibling through the

donation of the baby's umbilical cord stem cells (or, failing that, with bone marrow to be taken when the newborn child is older).

The House of Lords ruled that the decision taken by the HFEA was lawful and that the HFEA can continue to issue treatment licences for families who want to conceive an IVF baby that could provide tissue-matched cord blood to help treat a sick sibling.

Looking ahead

The development of adult stem cell medicine, particularly autologous adult stem cells, continues to accelerate. Manufacturing companies are keen to produce a whole variety of adult stem cells, and patients want to be treated by them. The question then arises as to how these complex cellular products and devices can be safely characterised, stored, packaged and delivered. The regulatory system will also have to find ways of reassuring patient recipients that such products and devices are safe.

Future risks

Overall, the UK regulatory system appears to be working well, promoting safe and high-quality stem cell research for therapeutic use.

However, two crucial questions appear to have been overlooked: how will the system ensure compliance and how can manufacturers be rendered properly accountable to patients injured by stem cell therapies?

The EU Tissue Directive 2004, for example, makes no specific provision about compensation where a patient is harmed by tissue therapy. Consequently, UK claims will have to be

made on the basis of ordinary product liability laws (in particular, consumer protection legislation and common law negligence). However, this may prove difficult in the light of the Consumer Protection Act 1987's development risks defence, whereby a producer can escape liability if it shows that, at the relevant time, the state of scientific and technical knowledge was such that it could not be expected to discover the defect.

There are significant risks and challenges facing manufacturers (and insurers) who become involved in this field. For example, manufacturing companies will be responsible for ensuring that stem cell medicines do not carry viral or infectious diseases. Furthermore, as the stem cell market develops, manufacturers will have to conduct clinical trials to show clinical efficacy, as well as safety and quality. Stem cell therapy is cutting-edge technology and problems are bound to arise.

In any event, one thing is for sure. Before mobile stem cells overtake cell mobiles in terms of commercial popularity and necessity, UK manufacturing companies and their insurers need to do two things: they must seek ways of ensuring compliance with the regulatory system, and they must prepare for potential biomedical product liability claims of unknown complexity.

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