

**Briefing paper on the need to protect the future possibility of treating
infertility and other conditions by procedures that rely on the generation and
use of vitro derived gametes.**

Prepared by

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Context:

Human Fertilisation and Embryology Bill: Part 1-Amendments of the Human Fertilisation and Embryology Act 1990

Summary:

Gametes are reproductive cells – eggs and sperm. Developments in the biological sciences indicate that it is possible to make gametes from stem cells in the laboratory – called in vitro derived (IVD) gametes.

IVD gametes are thus seen as a potential cure for some forms of infertility e.g. in cases where young men have become sterile as a result of cancer treatment.

It may be several years before the use of IVD gametes in clinical trials can be initiated, but the science is already well advanced. The Embryology Bill must take account of this likely development.

The Law should not place an outright ban on the use of IVD gametes, but leave room for legislation and regulatory guidance to specify conditions where using these gametes is considered safe, ethical, and clinically necessary. The Human Fertilisation and Embryology Authority (HFEA) is best placed to oversee and regulate the research and treatment options in this area.

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(2) Background to the Legislation

The 1990 Act makes no mention of IVD gametes. The Government considered the issue of allowing use of IVD gametes under license in various consultations and concluded this would be a matter requiring primary legislation.¹

This primary legislation is now before the House.

The Embryology Bill as it was originally written permits research into the derivation of gametes from stem cells but prohibits the use of IVD gametes for treatment unless they originate from the ovary or testes. – The Bill does not allow gametes which do not originate from testes or ovaries to be "permitted gametes" for the purposes of creating a "permitted embryo" under a treatment licensed by the HFEA. Furthermore, there was no scope for further regulations in the Bill to enable such treatment to be permitted under HFEA oversight in the future.

The Lords considered these issues and many peers were convinced by the arguments made at committee stage that this provision would not adequately address the therapeutic and scientific potential of IVD gametes.

An amendment was tabled at report stage and refined for third reading in the House of Lords. The text of the amendment read as follows:

Clause 3, page 3, line 26, at end insert -
“(5A) Regulations may provide that -
(a) an egg can be a permitted egg, or
(b) a sperm can be a permitted sperm,
even though the egg or sperm has been developed from one or more human cells
in a prescribed process designed to treat infertility.

(5B) Regulations under subsection (5A) may
(a) provide that any sperm be developed from one or more cells of a genetic male
and any egg be derived from one or more cells of a genetic female.
(b) specify, or otherwise restrict, the nature of the infertility which the prescribed
process is intended to treat.”

In response, some Peers raised concerns that questions such as safety of the technology, the potential to change family structures, and the appropriateness of delegating to secondary legislation – matters that had not been adequately discussed at the Lords.

Baroness Royall of Blaisdon, Chief Whip (House of Lords) suggested:

"I trust that our commitment to look at this further in the other place and the progress made to date in initiating this process will reassure noble Lords of our intention to consider this issue fully."

The amendment was therefore withdrawn, for further consideration in the House of Commons.

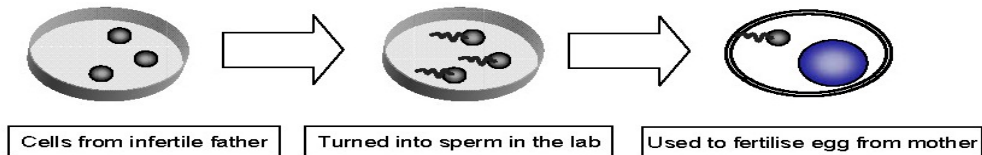
In this brief, we outline the scientific, moral and legal case for accepting the Lord's proposed amendment in the Commons.

¹ E.g. 2004 "Review of Human Reproductive Technologies and the Law" Science and Technology Committee; 2005 "Review of the Human Fertilisation and Embryology Act - A Public Consultation"; Department of Health 2005

(3) Scientific Background

Because the legislative framework in the UK has thus far been considered science-friendly, NESCI has been able to attract Professor Karim Nayernia, a world-leading researcher on IVD gametes, from Germany to the UK.

Professor Nayernia's team has derived sperm from mouse embryonic stem cells and used it to fertilise mouse eggs. Seven mouse babies were produced, six of which lived to adulthood. The team has also shown that early stages of IVD gametes can be derived from bone marrow stem cells.



There are many possible **biomedical applications** for gametes obtained from stem cells.

Fertility treatment: Chemotherapy for cancer can have a devastating effect on the gonads, sometimes rendering the patient infertile even if the tumour can be defeated. Research on IVD gametes raises the possibility of attempting to restore fertility e.g. in young men who have undergone chemotherapy. NESCI studies to help such patients have received ethical approval and are currently underway. This is the main field in which a ban on the use of IVD gametes in therapy would be immediately counterproductive.

Derivation of vitally important cell lines: If in vitro-derived sperm and egg precursor cells can be cultured as perpetual cell lines, a renewable source of gametes could be established which in turn could be used to generate a plentiful resource of stem cells for research purposes. The acute shortage of human gametes, particularly eggs, for research presents an extremely serious barrier to the development of stem cell therapies. Many –sometimes dozens or hundreds– of donor eggs are needed to derive a single cell line. It is likely that successful production of human stem cell gametes would boost research enormously and go some way towards realising the potential of stem cell therapies for the treatment of cancers, diabetes, Parkinson's disease, strokes, and other illnesses.

Genetic Research: Furthermore, the use of IVD gametes harbours significant potential as a method in research in human genetics including:

- an improved understanding of factors in inherited diseases
- an invaluable resource for investigating the origins of chromosomal abnormalities leading to birth defects such as Down syndrome. This is currently difficult to do as the early stages of meiosis are intractable.
- research into other conditions which particularly afflict the germ cells
- research into epigenetic imprinting, a next step in developing the insights presented by the Human Genome Project.

Toxicological Research: Derivation of gametes from stem cells provides a very useful system to test the effects of environmental toxins and pharmaceutical substances on germ cells in the laboratory. This could also help in reducing the necessity for extensive testing of pharmaceuticals on animals.

In summary: Research in this field is progressing rapidly. The Bill would make it impossible to implement treatments developed with this approach without the legislation returning to Parliament for further amendment. It follows that UK researchers are pursuing research projects to develop treatments for infertility and other conditions, but these treatments would become illegal in primary legislation. This has direct consequences for obtaining research funding and for future clinical trials on patients who are infertile and wish to have their own children.

(4) Policy and ethical concerns

The above clearly highlights the compelling scientific and medical case for continuing research on in vitro derived gametes. This is widely accepted and not under threat in the current bill. Questions arise if it should be possible to use the technique in **treatment**.

The Bill *unamended* would **ban** such use in all treatments, whereas the *amendment* as moved in the House of Lords would allow for the possibility of potential treatment under a regime of **continual regulatory oversight**.

If treatment was not banned **several safeguards remain**: The use of such gametes for fertility treatment would require a licence from the HFEA. The HFEA has powers to ensure that the procedures used for the creation and use of embryos for fertility treatment take account of the welfare of any child that may result. The Bill thus requires that safety issues would be the priority consideration of any treatment licence application that would use vitro derived gametes or fertility purposes. If regulation-making powers were included in the Bill then additional oversight on this issue by Parliament would be available

In the Lords concerns were raised specifically about the issues of:

family – it has been suggested that this technique could be used to alter the social understanding of a 'traditional' family, for example where homosexual couples would look toward using vitro derived gametes to create a child that is genetically related to both partners. Currently, this technique is focused on curing infertility in those whose gametes have become damaged e.g. during treatment for cancer. The amendment suggests that regulators can "specify, or otherwise restrict, the nature of the infertility which the prescribed process is intended to treat." Whether or not it is socially acceptable to develop this technique into other directions will depend not just on social attitudes but also on the clinical and moral merits of each individual case. As such, it is advisable to limit the remit in which this technique can be used in further regulations, in official guidelines and through deliberations before an ethics committee, rather than rigidly closing down all possible treatment by default. The Bill clearly sets out that any sperm must be developed from a male and any egg from a female. The Bill also allows the HFEA to restrict, the nature of the infertility which can be treated.

safety – currently, the offspring that mice produce under this technique appear to differ from 'normal' mice in a number of ways. This suggests that further tests need to be carried out on animals to ascertain that the procedure is safe to use as a therapy in humans. This is a technical question that is best left to a continual conversation between scientists, clinicians, patient groups and regulators. The HFEA will not license any procedure that has a high risk for parents or offspring. However, if the science has advanced to a stage where all parties concerned are ready to consider clinical trials, it would be a burden on patients if parliament first had to be appealed to in a lengthy process of changing the law yet again.

subsidiarity – some felt that the amendment left to Regulations an issue that should be dealt with by Parliament. We fully agree that it is important that an Act of Parliament sets frameworks and indicates directions. This will be achieved in the current Bill. However, as past developments have shown, the ethical, legal and scientific questions arising from new treatments in very individual circumstances are best delegated by Parliament to the competent authorities. This should be achieved in regulations.

It is therefore appropriate that the amendment leaves some leeway for regulations to define situations in accordance with the spirit of the Act and other relevant laws.

This information sheet is subject to an ongoing process of revision.

Please ensure you use only the most up-to-date version which can be obtained from www.nesci.ac.uk

This version expires on **Monday June 2nd 2008**.

(4) Further information

This brief has aimed at presenting the perspective of scientists and clinicians on the proposed legislation in a succinct and simple manner.

We would greatly welcome a chance to explain the underlying science and the therapeutic potential in greater detail. Please do not hesitate to contact us with any further questions or comments.

The North-East England Stem Cell Institute, a collaboration between the Universities of Durham and Newcastle, the Newcastle upon Tyne Hospitals NHS Foundation Trust and other regional partners.

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