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International Legislation: Maternal Spindle Transfer and Pro-Nuclear Transfer

The following international legal instruments may be relevant to Maternal Spindle Transfer (MST) and Pro-Nuclear Transfer (PNT). This legislation can be differentiated into two categories:

(1) **Soft Law:** which is not legally binding but which can be used by judges in international courts such as the European Court of Justice or the European Court of Human Rights to officially direct and guide their decisions and judgements.
(2) **Hard Law:** which is legally binding.

Note: The UK Government has already accepted that MST and PNT are:

(1) Germ-line Modifications[1]
(2) Germ-line Gene Therapy[2,3]

International Legislation

(1) The United Nations Education, Scientific and Cultural Organization's (UNESCO) *Universal Declaration on the Human Genome and Human Rights*

Adopted at UNESCO's 29th General Conference on 11 November 1997 (Soft Law)

Article 24 indicates that: *"'germ-line interventions'* could be considered as practices which are *'contrary to human dignity'."*[4]

[1] The UK Department of Health consultation entitled **Mitochondrial Donation** indicated that "*As the aim is that children born as a result of mitochondrial donation, and their offspring, would be free of serious mitochondrial disease, it would though be a form of germ line modification or germ line gene therapy, as recognised by reports produced by the HFEA and the Nuffield Council on Bioethics*."
UK Department of Health, Mitochondrial Donation: A consultation on draft regulations to permit the use of new treatment techniques to prevent the transmission of a serious mitochondrial disease from mother to child, February 2014, p. 13

[2] The Nuffield Council on Bioethics' Working Group concluded that "*donation treatments for mitochondrial disorders would constitute a form of germline gene therapy.*" This is because MST and PNT "*introduce a change that is incorporated into the (mitochondrial) genes of the resulting people, and so will be incorporated into the germline that they will go on to develop."*
Nuffield Council on Bioethics, Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review, Nuffield Council on Bioethics, London: 2012, p. xv.

[3] The Nuffield Council on Bioethics' Working Group further explained that using the term 'germline gene therapy' for MST and PNT *"seems appropriate because before the cell reconstruction procedure was performed and the relevant parts of the mother's and donor's egg or embryo combined, the person that would have originally resulted from their mother's egg or embryo had it been left unchanged would have had a different genetic makeup (and thus, a different germline).*"
Nuffield Council on Bioethics, Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review, Nuffield Council on Bioethics, London: 2012, p. 58.

In this regard, the **UNESCO's International Bioethics Committee** explained in 2003 that "*Germ-line interventions aim at the correction of a specific genetic abnormality in the germ cells or early embryo or at the introduction of genes that may confer to the embryo additional traits like increased resistance to certain diseases.*"[5]

In response, the **UK Government** indicated, in May 2014, that:

"Mitochondrial donation would not affect a child's nuclear DNA and therefore should not have any impact on their personal characteristics and traits; the process is solely concerned with treating an abnormality to prevent serious disease. On that basis we consider that UNESCO did not have mitochondrial donation in mind when considering practices which would be contrary to human dignity. Given that the focus of mitochondrial donation is on treating serious disease in a limited set of circumstances, we do not believe that the two proposed techniques would be contrary to human dignity."[6]

However, having discussed the UK's position relating to MST and PND with **UNESCO's International Bioethics Committee** on the 8th of September 2014 in Paris, the **Scottish Council on Human Bioethics (SCHB)** believes that the **UK Government** was misadvised to conclude that the **UNESCO's International Bioethics Committee** would not consider such procedures as being contrary to human dignity.

In July 2014, the **UK Government** also indicated that: "*UNESCO declarations are statements of principles or a common standard of achievement, which are not signed or ratified and are not legally binding*."[7]

But as already mentioned, since the UNESCO Declaration is considered as 'soft law', the judges of international courts such as the European Court of Justice or the European Court of Human Rights would be entitled to use this text to officially direct and guide their decisions and judgements.

(2) The Council of Europe's *Convention for the Protection of Human Rights and Dignity of the Human Being with Regard To The Application of Biology and Medicine*

Entered into force on the 1st of December 1999. Since the UK is one of the few countries that has not signed or ratified this Convention it only has the force of Soft Law (in the UK).

Article 13 states that:

"An intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants."

Which means, according to **paragraph 91 of the Explanatory Report** for Article 13, that:

"Interventions seeking to introduce any modification in the genome of any descendants are prohibited. Consequently, in particular genetic modifications of spermatozoa or ova for fertilisation are not allowed."

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[4] This is also supported by the World Health Organization (WHO) which reaffirms that "germ-cell therapy, where there is an intention or possibility of altering the genes passed on to the next generation, should not be permitted in the foreseeable future". World Health Organization, Fifty –First World Health Assembly, April 8, 1998, *Implementation of resolutions and decisions, A51/6 Add.1, para. 16,* http://apps.who.int/gb/archive/pdf_files/WHA51/ea6a1.pdf [accessed 20 February 2012].

[5] UNESCO International Bioethics Committee. Report of the IBC on Pre-implantation Genetic Diagnosis and Germ-line Intervention, 24 April 2003; UNESCO *International BioethicsCommittee (IBC)* Report of the IBC on Pre-implantation Genetic Diagnosis and Germ-line Intervention, 2003, http://portal.unesco.org/shs/en/files/2397/10554294261ReportfinalPGD_en.pdf/ReportfinalPGD_en.pdf

[6] Personal letter from the Department of Health to the Scottish Council on Human Bioethics dated: 13 May 2014.

[7] Mitochondrial Donation: Government response to the consultation on draft regulations to permit the use of new treatment techniques to prevent the transmission of a serious mitochondrial disease from mother to child, July 2014, p. 16.

In this regard it should be noted that, from a scientific perspective, the genome of a human being clearly includes his or her mitochondrial genome.

The **UK Government** noted, in July 2014, that: *"the UK has not signed or ratified the Convention and is therefore not legally bound by it."*[8]

The latest reason[9] given by the **UK Government**, in May 2014, for not ratifying this Convention was:

"The UK supported the original development of the Council of Europe Convention on Human Rights and Biomedicine, which covers a wide range of complex ethical and legal issues. In the UK, the complex nature of devolved responsibilities in this range of policy areas has delayed consideration of full ratification."[10]

However, since the *European Convention on Human Rights and Biomedicine* is considered as 'soft law' in the UK, the judges of international courts such as the European Court of Justice or the European Court of Human Rights would be entitled to use this text to officially direct and guide their decisions and judgements.

(3) Council of Europe *Parliamentary Assembly Written Declaration on the Creation of Embryos with Genetic Material from More than Two Progenitor Persons*

Written declaration No. 557; Doc. 13325; 3rd of October 2013 (Soft Law)

This indicates that:

"*The undersigned [34] members of the Parliamentary Assembly affirm that the creation of children with genetic material from more than two progenitor persons, as is being proposed by the United Kingdom Human Fertilisation and Embryology Authority, is incompatible with human dignity and international law*."[11]

(4) The EU *Directive on clinical trials (2001/20/EC)*[12]

Legally Binding (Hard Law)

Article 9(6) indicates that:

"No gene therapy trials may be carried out which result in modifications to the subject's germ line genetic identity."

This was implemented into UK law by the ***Medicines for Human Use (Clinical trials) Regulations 2004*** which indicates in **Article 19 (3)** that:

"The licensing authority shall not authorise a clinical trial involving products for gene therapy if the use of those products in that trial would result in modifications to any subject's germ line genetic identity."[13]

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[8] Mitochondrial Donation: Government response to the consultation on draft regulations to permit the use of new treatment techniques to prevent the transmission of a serious mitochondrial disease from mother to child, July 2014, p. 16.

[9] There have been a number of different reasons given by the UK Government over the years.

[10] Personal letter from the Department of Health to the Scottish Council on Human Bioethics dated: 13 May 2014.

[11] Council of Europe Parliamentary Assembly Written Declaration on the Creation of Embryos with Genetic Material from More than Two Progenitor Persons, http://assembly.coe.int/ASP/Doc/XrefViewPDF.asp?FileID=20204&Language=EN

[12] This will be replaced in 2016 by a new REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 April 2014: On clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC
Article 90 of this new regulation indicates that: *"No gene therapy clinical trials may be carried out which result in modifications to the subject's germ line genetic identity."*

In this regard, the **UK Government** noted, in May 2014, that: *"The Clinical Trial Directive (2001/20/EC) is limited in scope to the regulation of the conduct of "clinical trials" as defined under the Directive. Mitochondrial donation is not undertaken for investigative purposes and is not therefore a clinical trial and is not governed by the Clinical Trials Directive, including Article 9."*[14]

This means that the **UK government** is aiming to bypass the EU prohibition of Article 9(6) of the Directive and Article 19(3) of the 2004 UK Regulations relating to gene therapy trials by enabling the **Human Fertilisation and Embryology Authority (HFEA)** to go straight from animal trials to medical treatment without undertaking any clinical trials.
It can do this because, as the 2005 **House of Commons Science and Technology Committee** report entitled 'Human Reproductive Technologies and the Law' indicates, "*the HFEA has been unable to license a clinical trial; it can issue a licence for a treatment or research purposes only. It cannot issue a treatment licence unless it is satisfied either that it is for "practices designed to secure that embryos are in a suitable condition to be placed in a woman or to determine whether embryos are suitable for that purpose" and the activity is "necessary or desirable for the purpose of providing treatment services"."*[15]

The Spokesperson for the HFEA then went on to mention in this respect that "*We recognise that powers to award a clinical trials licence might have advantages for the HFEA but we would be nervous about the creation of any further bureaucratic hurdle introduced to the setting up of clinical trials."* [16]

Though the **UK Government** is legally entitled to seek to bypass EU legislation in this manner, the **Scottish Council on Human Bioethics** is very concerned that the spirit of Article 9 of the EU Directive is being ignored.
Moreover, if MST and PNT are not considered as clinical trials it would mean that expert NHS Research Ethics Committees would not be expected to assess the safety of the procedures.

(5) The EU *Charter of Fundamental Rights*

Solemnly proclaimed on 7 December 2000 (Soft Law)

Article 3 (2) stresses that:

"*In the fields of medicine and biology ... the prohibition of eugenic practices, in particular those aiming at the selection of persons"* must be respected.

In this regard, the **UK Government** indicated, in April 2014, that:

"The Government supports good practice in informed choice for all patients or parents to aid prevention of serious illness or disease and does not support human eugenic practices in the United Kingdom.
The principles set out in Article 3(2) of the Charter applies to the UK when implementing European Union law."[17]

The **UK Government** also indicated, in May 2014, that: "*The Charter is only applicable to Member States where they are implementing EU law. The regulations in question do not implement EU law and therefore the Charter does not apply.*"[18]

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[13] At present, the licensing authority in the UK is believed to be the Medicines and Healthcare Products Regulatory Agency (MHRA)

[14] Personal letter from the Department of Health to the Scottish Council on Human Bioethics dated: 13 May 2014.

[15] Paragraph 172 of the House of Commons Science and Technology Committee's "Human Reproductive Technologies and the Law", 2005.

[16] Paragraph 172 of the House of Commons Science and Technology Committee's "Human Reproductive Technologies and the Law", 2005.

[17] The Parliamentary Under-Secretary of State, Department of Health (Earl Howe), Lord Hansard, 8 Apr 2014 : Column WA267.

[18] Personal letter from the Department of Health to the Scottish Council on Human Bioethics dated: 13 May 2014.

However it is the **Scottish Council on Human Bioethics'** opinion that:

(1) Though the *EU Charter of Fundamental Rights* is not legally binding, if a case was ever to be brought before the **European Court of Justice (ECJ)** related to MST and PNT, it is inevitable that the judges of the ECJ will base their decision on Article 3 of this Charter.

(2) Though neither international nor UK legislation have defined "*eugenic practices*" they can generally be characterised as strategies or decisions aimed at effecting, in a manner which is considered to be positive, the genetic heritage of a child, a community or humanity in general.

Necessity to Involve International Partners

The **UNESCO *Universal Declaration on the Human Genome and Human Rights*** indicates that:

Article 11

"*Practices which are contrary to human dignity ... shall not be permitted. States and competent international organizations are invited to co-operate in identifying such practices and in taking, at national or international level, the measures necessary to ensure that the principles set out in this Declaration are respected*."

Article 24

"The International Bioethics Committee of UNESCO should contribute to ... the further examination of issues raised by their applications and by the evolution of the technologies in question ... It should make recommendations, in accordance with UNESCO's statutory procedures, addressed to the General Conference and give advice concerning the follow-up of this Declaration, in particular regarding the identification of practices that could be contrary to human dignity, such as germ-line interventions."

The **Scottish Council on Human Bioethics** is of the opinion that because of the UK's international responsibilities and the possibility for persons created from MST and PNT to eventually travel abroad and have their own children, it would be inappropriate for the **UK Department of Health** to consider legalising such procedures until the **UNESCO International Bioethics Committee's** report on the topic is published.