

# The legal framework for genome editing and the UK's case study

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DR ILKE TURKMENDAG  
NEWCASTLE LAW SCHOOL, NEWCASTLE UNIVERSITY  
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# Outline

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1. International legislation: declarations, conventions, reports, statements
2. Possible human rights concerns
3. Emerging themes from international legislation
4. A case study: The UK regulatory framework
  - The UK is the first country to mitochondrial replacement techniques
  - The UK also granted a licence for CRISPR/Cas9 to be tested on human embryos for research
5. How to regulate?

# International legislation

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Some of the international documents which relate to human gene editing both directly and implicitly:

- ✓ The Declaration of *Inuyama* (Council for International Organisations of Medical Science)
- ✓ Convention on Human Rights and Biomedicine 1997
- ✓ Universal Declaration on the Human Genome and Human Rights 1997 (UNESCO)
- ✓ Directive 2001/20/EC of the European Parliament and of the Council
- ✓ International Declaration on Human Genetic Data 2003 (UNESCO)
- ✓ Universal Declaration on Bioethics and Human Rights 2005 (UNESCO)
- ✓ Report of the International Bioethics Committee on the Human Genome and Human Rights (2/10/2015)
- ✓ European Group on Ethics in Science and New Technologies: Statement on Gene Editing (11/01/2016)

# The Declaration of *Inuyama* 1990

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## SAFETY FOR THE NEXT GENERATIONS

‘Some types of genetic testing or treatment not yet in prospect could raise novel issues - for example, whether limits should be placed on DNA alterations in human germ cells, because **such changes would affect future generations, whose consent cannot be obtained and whose best interests would be difficult to calculate.**’ (Para.3)

‘Before germ-line therapy is undertaken, **its safety must be very well established, for changes in germ cells would affect the descendants of patients.**’ (Para 6.)

# Convention on Human Rights and Biomedicine 1997 (Oviedo Convention)

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## **The germ line must not be edited** /Protection of **HUMAN DIGNITY**

The convention highlights that there is the need to protect the **dignity and identity** of all human beings (Art. 1), and that ‘the interests and welfare of the human being shall prevail over the sole interest of society or science.’ (Art.2).

‘any form of **discrimination against** a person on grounds of his or her genetic heritage is prohibited’ (Art.11)

‘an intervention seeking to modify the human genome may only be undertaken for preventative, diagnostic or therapeutic purposes’ only if its aim **is not to introduce any modification in the genome of any descendants**’. (Art.13).

# Universal Declaration on the Human Genome and Human Rights 1997 (UNESCO)

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## **HUMAN GENOME AS A HERITAGE/ DIVERSITY/ HUMAN DIGNITY**

According to *Art.1*, the human genome **'is the heritage of humanity.'**

*Art.2* provides that there is a need to respect diversity and a need to respect the genetic characteristics of every person.

*Art.10* : 'No research or research applications concerning the human genome, in particular in the fields of biology, genetics and medicine, **should prevail over respect for the human rights, fundamental freedoms and human dignity of individuals...**'

*Art.24* seems to suggest that **germ-line intervention could be contrary to human dignity.**

# Directive 2001/20/EC of the European Parliament and of the Council

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## PROTECTION OF GERMLINE IDENTITY

*Art.9(6)* of the Directive provides that '[n]o gene therapy trials may be carried out which result in modifications to the subject's **germ line identity**' however editing of somatic cells is allowed but only with written authorisation.

# International Declaration on Human Genetic Data 2003 (UNESCO)

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## **DISCRIMINATION BASED ON GENETIC CHARACTERISTICS**

*Art.3* highlights that a person's identity should not be reduced to **genetic characteristics as personhood is built up from other personal factors such as education and social circumstances.**

*Art.7 (a)* provides that '[e]very effort should be made to ensure that human genetic data ...are not used for purposes that **discriminate** in a way that is intended to infringe, or has the effect of infringing human rights, fundamental freedoms or human dignity...'



# Universal Declaration on Bioethics and Human Rights 2005 (UNESCO)

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## **HOLISTIC APPROACH**

*Art.8* : 'In applying and advancing scientific knowledge, medical practice and associated technologies, **human vulnerability** should be taken into account.

*Art.16* : 'The impact of life sciences on **future generations**, including on their **genetic constitution**, should be given due regard.'

*Art.17* : 'Due regard is to be given to the **interconnection between human beings and other forms of life** [...]and to the role of human beings in the protection of the environment, the biosphere and biodiversity.'

# Report of the International Bioethics Committee (2015)

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## **MORATORIUM BASED ON SAFETY AND ETHICAL CONCERNS**

Calls for international cooperation due to the human genome being the 'heritage of humanity' (Para 115)

There is a need for respect of: 'human dignity; autonomy and individual responsibility; respect for vulnerable people and personal integrity; privacy and confidentiality; equality, justice and equity; non-discrimination and non-stigmatization; respect for cultural diversity and pluralism; solidarity and cooperation; social responsibility for health; sharing of benefits; protection of future generations; protection of the environment, the biosphere and biodiversity.' (Para 116)

**'recommends a moratorium on genome editing of the human germline'** due to the safety issues as well as the ethical issues with human gene editing. (Para 118)

# European Group on Ethics in Science and New Technologies

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## Statement on Gene Editing (11/01/2016):

- There is now a debate occurring on the banning of human germ line modification due to the UK's recent regulations allowing for mitochondrial replacement as well as the rise of CRISPR-Cas9.
- Germline modification is deemed more ethically controversial than the editing of somatic cells as editing the germline can impact on further generations.
- The EGE feels that there must be a public debate on the issue due to the 'ethical, scientific and regulatory issues' which human gene editing involves.

# Human rights

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## *European Charter of Fundamental Rights (2012/C 326/02)*

- *Art.1* – ‘**Human dignity** is inviolable’
- *Art.2* - ‘In the fields of medicine and biology, the following must be respected in particular [...]’  
(b) The prohibition of **eugenic practices**, in particular those aiming at the selection of persons’
- *Art.21* – Prohibition of discrimination on any ground including genetic features, disability etc.

## *European Convention on Human Rights 1950*

- *Art.14* - Prohibition of discrimination on any ground

# Emerging themes

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Human  
dignity

Eugenics

Discrimination

Disability

Diversity

Genetic  
identity

Genetic  
determinism

Consent

Changing the  
germ line

Future  
generations

Safety

Human rights

HG as a  
heritage

Autonomy

Responsibility

# Human genome editing in the UK

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- The UK is the first country to allow germ line modification (through mitochondrial replacement)
- The UK also granted the first license: gene editing on embryos (for research purposes)
- There has not been much law on gene editing but the key reference point has been the *Human Fertilisation and Embryology Acts 1990* and *2008* for genome editing of germ cells
- *Human Tissue Act 2004* for editing somatic cells.

The Secretary of State may, in light of developments in science or medicine, **change the definition of embryo/eggs/sperm/gametes** so as to include these new developments.

*S3(5) HFEA 2008* added in *s3ZA HFEA 1990* regulates the definition of ‘permitted eggs, permitted sperm and permitted embryos’.

This provision brings the law up to date with the current technology regarding human gene editing.

# The UK's gene editing landscape for regulation

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Despite the fact that most of *s3ZA HFEA 1990* bars human gene editing resulting in permitted gametes or embryos, *s3ZA(5)* provides that regulations may provide that an egg and embryo may become permitted

‘even though the egg of embryo has had applied to it in prescribed circumstances a prescribed process designed to prevent the transmission of serious mitochondrial disease.’

This therefore allows for the editing of the germ line where specific regulations on the matter have been passed (to allow mitochondrial replacement techniques) thus opening the door for editing in specific circumstances of embryos.

# HFEA (Mitochondrial Donation) Regulations 2015

The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 opened the door for editing of the germ line under specific circumstances.

The screenshot displays the official UK legislation website, legislation.gov.uk. The page title is "The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015". The interface includes a search bar at the top right, navigation tabs for "Home", "About Us", "Browse Legislation", "New Legislation", and "Changes To Legislation", and a search box with fields for "Title", "Year", "Number", and "Type". Below the search bar, there are links for "Draft Explanatory Memorandum", "Draft Impact Assessments", and "More Resources". The main content area shows a table of contents with sections for "Introductory Text", "PART 1 Introductory Provisions", "PART 2 Permitted eggs and permitted embryos", and "PART 3 Related modifications and amendments". The "PART 2" section is expanded, showing a list of items from 3 to 9, including "Permitted egg", "Permitted egg: process", "Permitted egg: circumstances", "Permitted embryos", "Permitted embryos: process", "Permitted embryos: circumstances", and "Supplemental provision - licences".



# License for human genome editing (research)

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The committee noted that:

- CRISPR/Cas9 was a ‘highly efficient and targeted method of gene disruption, potentially superior to other techniques that were available.’ (Para 1.08)
- It is vital to use human embryos due to the fact that mouse embryos are of limited use as they do not follow the same process of development (Para 1.17)
- That such research would be useful for: developing treatments for serious diseases, increasing knowledge about the development of embryos, and promoting advances in the treatment of infertility. (Para 1.18)
- No non-permitted embryos (i.e. embryos subjected to gene editing techniques) would be placed in woman nor would an embryo be kept past the 14 day period. (Para 1.19)

# The need for public engagement

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- Self-regulation by scientists is not appropriate; the society should be guiding the development of this technology (Hurlbut 2015);
- A wide variety of individuals from all disciplines should consider the ethical, technical, and societal issues (Hildt 2016; Baltimore et al 2015).
- We must ensure a fair balance between the interests of those who support and those who do not support human gene editing (Waddington et al 2016)
- Overall, the view is that the public now should be involved in these debates.

# How to regulate: Guideline, moratorium or free for all?

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- It is noted that there is a line between the therapeutic and non-therapeutic applications (Lanphier et al 2016).
- We should **prevent restrictions being placed on the fundamentally useful basic research** with regards to CRISPR-Cas9 (Baumann 2016), and until there is a social and scientific consensus, the clinical application should be prevented (Baltimore et al 2015)
- In the meanwhile the guidelines should be constantly updated (Waddington et al 2016).
- There should be a moratorium on the **clinical use of human germline editing** (Baumann 2016).
- There is a need for a calm approach to regulation so as to prevent 'heavy-handed intervention' (Adashi and Cohen 2016).
- However, there is uncertainty as to how such a calm approach could be developed due to the various options on offer which, when combined with the ethical issues of human gene editing, each have their own difficulties and benefits.
- Most commentators emphasise that there is a need for **open public discussion** (Baltimore et al 2015).

# Bibliography

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# Thank you!

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