Legislative Reform Advisory Group (LRAG) Meeting notes

27 June 2022

Teleconference (Teams meeting)

Advisory Group	Present	David Archard, Nina Barnsley, Kate Brian, Emily Jackson, Gwenda Burns, Jackson Kirkman-Brown, Robin Lovell-Badge, Raj Mathur, Angela Pericleous-Smith. Peter Thompson (HFEA Chief Executive) Julia Chain (HFEA Chair)
	Apologies	Adam Balen (standing in for Eddie Morris) Tim Child Francesca Steyn
Members of the executive	Present	Laura Riley (Head of Policy- Scientific) Ana Hallgarten (Public Policy Manager) Victoria Askew (Policy Manager)

1. Welcome

1.1. The Chief Executive welcomed members to the fourth meeting of the Legislative Reform Advisory Group (LRAG) and thanked them for their involvement. The Chief Executive briefly restated the context to this important work.

2. Regulatory Processes

2.1. The Chief Executive outlined the issues in the discussion paper regarding the way in which the Act currently specifies regulatory processes and that the Act and HFEA should be able to support and encourage innovation.

2.2. The Chief Executive recommended that if amended, the Act should set out principles rather than defined processes in order for the HFEA to consider new research and/or treatments and approve or reject them in a more timely, proportionate and ideally more ‘future-proofed’ way.

2.3. There was consensus among LRAG members that:

- The use of principles rather than processes would be beneficial.
- Any principles would need to be sufficiently detailed.

3. Supporting innovation

3.1. The Chief Executive noted that the HFEA's ability to support responsible innovation within the current Act is limited. At present, in the procedure that allows HFEA authorisation of novel treatment processes, the regulatory controls are 'front-loaded', which can be problematic when some applications cannot fully evidence their safety and effectiveness until after application. At the same time, the Act has few levers that allow the HFEA to control the use of such novel processes post-approval. Taken together, this arrangement discourages innovation. The options for change presented to LRAG would allow for greater pre-approval and post-approval control, with increased flexibility in approving new developments and innovations due to the increased control later in the process.

3.2. Some LRAG members recommended that amendments to the Act should:

- Introduce a duty for HFEA to support innovation
- Support HFEA's powers to offer regulatory 'sandbox' model for appropriate new technologies or treatments
- Involve external expert body views in the assessment and monitoring process, where merited
- Protect via HFEA licencing, participants in research studies involving their own fresh sperm. These are currently unregulated by HFEA or HTA and as one in every 50 participating men could learn that they are azoospermic for example, regulatory oversight could require that appropriate information and support.

3.3. LRAG members noted that:

- 'Sandbox' models tend to be tailored to each application and require individual oversight which would create greater resource demands on the Executive than the present system
- The participation of patients in what can amount to research, but where payment is required for them to participate, is concerning. Paying to have unproven medical treatments is unusual outside of the fertility sector. To increase patient protection, LRAG members felt that it may be beneficial for HFEA in some cases to impose licence conditions stating that participants in innovative treatment that is effectively research, should not be required to pay. These areas will require careful definition and HFEA powers to require this, which may need to be explicitly provided for in the Act.

3.4. The Chief Executive asked whether the Act should be amended to offer principles for HFEA about supporting responsible innovation and authorising novel processes in the UK. Currently HFEA interpret this area from the requirements of the 2004 European Tissues and Cells Directive. LRAG members noted that EU Exit had already removed congruence with Europe in future, as any new or updated Tissues and Cell Directives will not be built into UK law.

4. Artificial Intelligence

4.1. The Chief Executive highlighted that the paper did not present concrete proposals about the rapid development of AI. The aim rather was to note different ways in which AI is being used in several fertility treatment processes in the UK. Across all heath sectors, regulatory responses and statutory responsibilities are still emerging, with a relevant government White Paper expected soon, meaning that there will be some common approaches to consider across health sectors.

4.2. LRAG members agreed that regulating AI is possibly beyond the remit of the Act and the HFEA in isolation. They recommended that HFEA contact the Ada Lovelace Institute who are working on AI governance in the health sector. It was agreed that any key work or findings from the HFEA's work on AI should be shared with LRAG.

5. The 14-day limit

5.1. The Chief Executive began by thanking the Medical Research Council and the Francis Crick Institute for their time and insights relating to the 14-day limit. They noted that, to a large extent, the 14-day limit has stood the test of time very well but as research progresses, and it is now possible to keep an embryo in vitro for longer than 14 days, it is important to consider whether this remained appropriate.

5.2. LRAG members raised that:

- The 14-day limit first proposed in the Warnock Report had gathered support for multiple reasons: Ethically, in that the 14 day limit considered the moral value of the embryo; politically, as it was considered at the time that any further limit may not have passed through Parliament; scientifically, at the time 14-days appeared sufficient for research benefits, as it was not possible to keep an embryo alive beyond 14-days nor to accurately mimic in-vivo development via embryo models.
- One member of LRAG discussed the recent proposals of the International Society for Stem Cell Research (ISSCR) guidelines to remove the 14-day limit and replace with strict case-by-case oversight of any research past 14-days where justified, as laid out in the guidelines and after extensive public engagement.
- Some members expressed disagreement with extending the 14-day limit, partly because they felt it was still an appropriate ethical limit, partly bearing in mind how some patients regard their stored embryos, and partly because they felt there could be significant public push back to any proposed extension.
- Other members agreed that either an extension to 21 or 28 days may be appropriate in the interests of increasing scientific knowledge and, in time, improving clinical options. There is a window of very early pregnancy between 14 and 28 days of embryo development which is not well researched by any other route. Researching embryo development beyond 14 days could for example, improve understanding around very early pregnancy loss where the cause lies with the embryo. Scientific benefits could include enabling more detailed research into new fertility treatments or possibilities to avoid passing on genetic disorders. These could include around mitochondrial donation, in-vitro derived gametes, and genome editing. Other areas for basic research would include around better understanding of cell differentiation, gastrulation, and the appearance of primordial germ cells.
- For those that supported it, in principle an extension would only be acceptable where there were strict regulatory conditions placed, no alternative research model was available, and

where there was a reasonable degree of public acceptance of the work going ahead, justified by high quality public dialogue. The meeting heard that scientists in the field were hopeful that the UK might take the first step given its reputation for public dialogue and the excellence of its regulatory regime.

6. In vitro-derived gametes, embryo-like entities, and stem cell based embryo models

6.1. The Chief Executive highlighted the development of these new entities, and the similar issues raised by their regulation. None are currently regulated, and some scientists are now of the view that regulating these entities may enable further innovation through the public trust that might flow from such oversight.

6.2. LRAG members concurred that the speed at which developments are taking place in this field requires assessment, and that regulation of at least some of these entities within the future Act should be considered.

6.3. It was noted that a key goal of the Warnock report was to ensure that the resulting Act would facilitate and enable science. Regulating these entities will increase public confidence. A member argued that an absence of regulation is bad for science, as it is difficult to proceed without public confidence. A balance between regulatory rules and innovation would need to be found, and any amendments will need to focus on the principles and outcomes to be controlled rather than the specific method or process used to develop these entities.

7. Use of human embryos in research: 'alternative' models

7.1. At present, the Act states that embryo research can only take place where it is both 'necessary' and 'desirable' to use human embryos.

7.2. LRAG members were broadly in favour that any future Act should consider removing the term 'necessary' and only require that it be 'desirable'.

8. Embryo selection based on Polygenic risk scores

8.1. The Chief Executive set out the permitted reasons for PGT-P testing of embryos for use in reproduction and discussed the use of polygenic risk scoring in clinical embryology in other countries.

8.2. LRAG members raised that:

- The testing regulations set out in the 2008 Act amendments are unable to adapt to new forms of testing embryos.
- The use of probability and risk calculations in genetic conditions with complex causes is problematic, as is determining the likely outcome of the interaction of genes and environment. The current lack of understanding of polygenic embryo testing and selection as a tool to reduce clinical risk means that fertility patients could be presented with unevidenced claims of clinical risk or of clinical benefit to a future child.
- There were concerns raised regarding the use of these tests, and that any permitted uses in future would require specific reasons for why this testing would be appropriate.

9. Germline genome editing

9.1. The Chief Executive set out the prohibition of nuclear germline genome editing set out in the Act and presented the options for change.

9.2. LRAG members raised that:

- Germline genome editing raises new ethical questions which may require reflection in a future Act.
- There is the possibility of future clinical benefit in strictly defined areas: if germline genome editing techniques could be used alongside mitochondrial replacement therapies in order to eliminate any carry over of mutated mitochondrial DNA, for example.
- The Act does not properly set out restrictions relating to the possible application of *epigenetic* germline genome editing, which will require consideration as research interest in this area is growing.

10. Any other business

10.1. None raised.