

## Appendix A – Human-animal embryos: Chronology

1. **2000:** The Sir Liam Donaldson's report, *Stem Cell Research: Medical Progress with Responsibility*, recommended, among other things, that "mixing of human adult (somatic cells) with the live eggs of any animal species should not be permitted". However, the report did not discuss the thinking behind this recommendation.
2. **2002:** The House of Lords Select Committee report on *Stem Cell Research*, took issue with the recommendation of Sir Liam Donaldson's expert group that there was a need for an outright ban on research involving inter-species embryos:

*"We are aware of reports of experiments in other countries involving the replacement of a nucleus of an animal egg with the nucleus of an adult human cell. These developments raise important issues. It would clearly be totally unacceptable to implant such an entity in a woman with a view to bringing it to term..... For any possible therapeutic applications there would also be significant concerns relating to safety, on which reassurance would be needed. However, if placing a human nucleus in an animal egg provided a way of creating human ES cells for research, some might argue that it was more acceptable to use such an entity for research, the creation of which involves no human gametes, than an embryo created by CNR."*

3. **September 2004:** Roger Pedersen gave a presentation to the HFEA Scientific and Clinical Advances Group (SCAG) on chimeras and the role they play in stem cell biology. SCAG also considered a scoping paper on chimeras which fed into subsequent consideration by the Group on definition of an embryo.
4. **March 2005:** The House of Commons Science & Technology Committee report on *Human Reproductive Technologies and the Law* recommended that new legislation was required to define the nature of inter-species embryos and make their creation legal for research purposes subject to the 14 day rule and the prohibition on implantation in a woman.
5. **September 2005:** Human-animal hybrids were identified by SCAG's 2004-5 horizon scanning process, as a medium priority issue. SCAG was informed that this issue was now being considered by DH as part of the Review of the HFE Act and that the HFEA would consider it further, as necessary, following the report of the consultation of the Act.
6. **November 2000:** The HFEA responded to the Department of Health's Review of the Act consultation. The HFEA stated:

*"The creation of human-animal hybrids is permitted until the two cell stage under the current Act and the HFEA considers that research within the constraints outlined by the Government should be permitted. As long as it can be ensured that such entities would never be implanted into a woman or allowed to develop beyond the 14 day stage, and as long as the research would fall under current research purposes, it could be argued that the ethical justification for the creation of such entities is consistent with research as it is currently allowed. Nevertheless, we recommend that the Government has proper consideration to the diversity of views on this issue. The HFEA would recommend that hybrids and chimeras are defined in the new Act."*

7. **February 2006:** The HFEA Ethics and Law Committee (ELC) and SCAG considered a scoping paper for further decision on the creation of the use of hybrid embryos in research. Scientists in the UK had publicly stated that they may wish to create hybrid embryos by fusing human cells with rabbit eggs.

The Committees agreed that, in order to advise the Authority, SCAG would be asked to look at the evidence and give a view on the scientific aspects of creating human-animal hybrids on 26<sup>th</sup> April 2006 and ELC would be asked to examine and provide a view on the legal and ethical aspects of creating human-animal hybrids.

8. **April 2006:** SCAG was asked to review the role that mitochondrial DNA plays in the development of embryos and whether embryos containing human nuclear DNA and both human and animal mitochondrial DNA would be a human embryo. If so, whether the creation of these embryos would be necessary for one of the purposes set out in Schedule 2 to the Human Fertilisation and Embryology Act 1990 as amended by the Human Fertilisation and Embryology (Research Purposes) Regulations 2001.

SCAG considered (1) any human mitochondria present would probably have a replicational advantage as they were more compatible with the genome; (ii) any egg/embryo with a human genome falls under the remit of the HFE Act; (iii) the proportion of human derived and rabbit derived proteins should be considered when deciding whether the hybrid embryos should be classed as human.

SCAG's general opinion was that these hybrids should be classed as human and the creation of these hybrids was necessary for research projects due to the lack of availability of human eggs.

9. **May 2006:** The ELC was asked to examine and provide a view on the legal and ethical aspects of creating human-animal hybrids and to consider to main questions: (i) the significance of the word 'human' in section 1(1)(a) of the Human Fertilisation and Embryology Act 1990 ('Meaning of "embryo"') (ii) how the HFEA should respond in practice should a scientist intend to create embryos artificially from human and non-human components.

The Committee agreed that an embryo containing human nuclear DNA and both human and animal mitochondrial DNA should be regarded as an 'embryo' for the purposes of the 1990 Act. The Committee agreed that the creation, keeping or use of such an embryo is capable of being regarded as necessary or desirable for one of more purposes set out in Schedule 2 of the HFEA Act (as amended), and therefore a licence committee would have the discretion whether to authorise these activities in the context of an individual licence application.

10. **July 2006:** The HFEA sought Counsel's opinion on whether a cytoplasmic hybrid is regarded as a 'human embryo' for the purposes of the Human Fertilisation and Embryology Act 1990 and whether the creation and use of such an embryo would be prohibited or licensable under the Act.
11. **November 2006:** The HFEA received two applications for research licenses for derivation of embryonic stem cells from hybrid embryos.

The HFEA's Horizon Scanning Expert Panel was asked a number of questions regarding hybrids to inform further opinion from Counsel. Respondents agreed that the hybrid embryo would contain a complete human genome, however there was no consensus on whether a hybrid embryo would be capable of implantation.

The Authority received a briefing paper in preparation for a full discussion in January 2007.

12. **December 2006:** The Government's *White Paper on Review of the Human Fertilisation and Embryology Act* stated that:

*"The extent to which the law and regulation would apply to embryos created in these circumstances is not sufficiently clear, although the law would clearly prevent such embryos being placed in a woman. In some circumstances the embryos created could be, genetically speaking, almost entirely human and therefore fall within the regulatory controls applicable to human embryos".*

The White Paper went on to propose that "revised legislation will clarify the extent to which the law and regulation applies to embryos combining human and animal material", adding that:

*“The Government will propose that the creation of hybrid and chimera embryos in vitro should not be allowed. However...the law will contain a power enabling regulations to set out the circumstances in which the creation of hybrid and chimera embryos in vitro may in future be allowed under licence for research purposes only”.*

13. **January 2007:** The HFEA sought an updated opinion from Counsel on whether hybrid embryos would fall under the remit of the HFEA. At its meeting on 10 January 2007 the Authority was advised that:

*“If the embryo contains a complete human genome and it cannot be shown definitively that the embryo does not have the normal potential to develop, it is most likely that the Court would find that this constitutes a live human embryo for the purposes of the Act. The Courts are likely to see the “hybrid” embryo in this way to ensure that this type of research falls under the scope of regulation rather than to allow it to be unregulated”.*

Presented with this opinion the Authority concluded that hybrid embryos are probably within its scope and decided to hold a full consultation on human-animal embryos to gauge public opinion on the issue.

14. **March 2007:** The House of Commons Science & Technology report on Government proposals for the regulation of hybrid and chimera embryos found that the Government’s White Paper proposals were *“too prohibitive and that the promise of future regulation was insufficient”*. Instead the Committee called for permissive legislation which would allow research using animal-human hybrid and chimera embryos through licensing, stating that:

*“In general, the creation of all types of human-animal chimera or hybrid embryos should be allowed for research purposes under licence by the regulator”.*

The Committee’s intention was that this would include true hybrids

In addressing the role of the HFEA in regulating research, the Committee said that:

*We support the decisions of the HFEA Science and Clinical Advances Group, Ethics and Law Committee and Horizon Scanning Group that an embryo containing human nuclear DNA and mitochondria of animal origin should be regarded as a human embryo for the purposes of the 1990 HFE Act.”*

On the issue of public understanding, the Committee said:

*“We welcome the HFEA proposed consultation on general principles and commend steps taken by the Authority to ensure appropriate drafting. We also commend the Government for allowing funding to be allocated towards education in this area”.*

15. **May 2007:** The Government published the *Human Tissue and Embryos (Draft) Bill*. Although the draft Bill follows the model outlined in the December 2007 White Paper, the Government issued a statement announcing its intention to accept in part the Science and Technology Committee’s recommendation of March 2007 and allow in legislation, under licence, certain categories of inter-species embryo. However, ‘true’ hybrids would remain proscribed unless permitted by regulations made by the Secretary of State.

16. **August 2007:** This issue was addressed in the report of the Joint Parliamentary Committee on the Bill. The Joint Committee recognised this as a very sensitive area and recommended that *“the creation and use of inter-species embryos for research purposes should be put to a free vote in both Houses”*. The Joint Committee recommended an alternative definition of inter-species embryos and proposed that authority should be given to the regulator:

*“To interpret and apply that definition to individual research applications, based on the principles set out in legislation”.*