COVER SHEET

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Lockhart Review into human cloning and research involving human embryos – closing the gap?

Background to the Report

On 17 June 2005, the Federal Minister for Ageing, appointed a six-member committee to conduct independent reviews of Australia's *Prohibition of Human Cloning Act 2002* (Cth) (PHCA) and the *Research Involving Human Embryos Act 2002* (Cth) (RHEA)[1]. The Committee faced the difficult task of reviewing such conceptually complex, and ethically fraught, questions as: When does human life begin?, What is the definition of a human embryo?, Should the creation of human embryos for research purposes be permitted?, Should an Australian stem cell bank be established? Those who had hoped to see a liberalisation of the laws relating to embryo research (on the grounds of potential developments in regenerative medicine) can be somewhat encouraged by the Committees recommendations, but the uncertainty of the political process and some recent cases of monumental scientific fraud in the area may make it unlikely that the Committees quite measured suggestions are implemented any time soon.

Since most of the science in relation to embryonic stem cells has developed as a consequence of the IVF revolution, laws related to IVF and embryonic stem cell research are intrinsically linked. Australia's laws relating to assisted reproductive technology (ART) and embryo research are less restrictive than those of some jurisdictions and more liberal than others. It is common practice, for example, for couples undergoing IVF treatment in Australia to have a large number of the woman's eggs fertilised and then to implant only those embryos with the greatest chance of developing into a viable pregnancy. In Italy, however, only three embryos may be created during any IVF cycle and all three must be implanted in the woman who provided the eggs.[2] In Australia, excess IVF embryos may be used for licensed research, whereas in Germany this is unlawful[3]. In the UK, both surplus embryos and those created by therapeutic cloning may be used, subject to a licence, to produce embryonic stem cells. [4] In the US the Federal government makes no attempt to regulate research involving embryos, but prohibits the use of Federal funds to extract stem cells from human embryos.

After considering 1035 written submissions and hearing personal presentations from 109 people across every State and Territory in Australia, the statutory review committee chaired by former Federal Court judge John Lockhart has recommended significant changes to the laws relating to research involving human embryos in Australia. The Report makes 50 recommendations.

Stem cells – embryonic and adult

The Committee was strongly of the view that in order for Australia to "maintain its role as a leader in the advancement of high quality and ethically sound scientific research and medical practices"[5], research into both adult and embryonic stem cells should continue without being subject to more stringent regulation, the prohibition on therapeutic cloning ought to be lifted and that a national stem cell bank ought to be formed.

The implicit support for expanding the embryonic stem cell agenda in Australia is sure to be controversial, especially the paradigmatic shift to allow for the creation of human embryos solely for research purposes. Although there has been some suggestion that researchers at Griffith University's Institute for Cellular and Molecular Therapies, and elsewhere, are predicting that adult stem cells may be of as much

benefit as embryonic cells for therapeutic purposes (thus questioning the need to use embryos), the Lockhart Committee found that "the extensive research in this area since 2001 has provided a complex and sometimes controversial picture of the plasticity of adult stem cells, and of whether any adult stem cell types can be truly regarded as pluripotent (capable of developing into virtually any other type of human cell)."[6] Some reports suggest that these adult stem cells exist in only minute numbers and are therefore difficult to isolate and purify. The DNA in adult stem cells may also be more susceptible to mutation and genetic errors due to the number of times they have replicated during the person's life. Opponents of embryonic stem cell research point out that this research has, as yet, not produced any clinically significant treatments, whereas adult stem cell therapy has been used to treat some heart conditions in clinical trials.

The Report noted that two Australian produced stem cell lines have already been deposited with the UK Stem Cell Bank and been made available to international researchers without the burden of commercial or intellectual property restrictions. The UK bank was established in 2002 and is overseen by a Steering Committee which is administered by a Management Committee comprising of members from research, academia, health care bodies, regulatory bodies and a lay member. The Lockhart Committee does not suggest how an Australian stem cell bank would be managed or regulated other than to suggest that this be done by the Australian Stem Cell Centre. Although there were vigorous submissions opposed to any sort of destructive embryonic testing and experimentation, the Committee felt that its brief to consider changes in community values and developments in technology justified its major recommendations.

Defining "human embryo"

The Committee noted that with three decades of ART research and practice behind us the time has long passed when we can be satisfied with a legal definition of a human embryo which simply involves the fertilisation of a human egg by a human sperm. A fundamental judgement needs to be made about when a fertilised egg becomes a potential life form deserving of special ethical respect and treatment. A key recommendation of the Committee was for a clearer definition of what a human embryo is. The current statutory definition catches embryos from about the age of 22 hours to about 8 weeks.[7] This is in stark contrast to the definition which many in the scientific community would prefer.

The UK's Warnock Committee were of the view that until the fourteenth day of development most cells of the embryo had the potential to develop into tissue which would not even form part of the ultimate foetus (such as placenta or the amniotic sac), and that cells which were identifiable as dedicated to the development of the foetus itself would not be determined until at least day 14 after conception.[8] Defining an embryo before this stage as a "potential life" therefore, according to the Warnock Committee" was inaccurate and misleading. Although this view would seem to have some scientific basis and rational appeal, the Lockhart Committee's proposed definition is not so courageous.[9]

The Committee suggests (Recommendation 28) adapting the NHMRC preference for two definitions of "human embryo":

(i) the first mitotic cell division when fertilisation of a human oocyte (egg) by a human sperm is complete; or

(ii) any other process that initiates organised development of a biological entity with a human nuclear genome or altered human nuclear genome that has the potential to

develop up to, or beyond, 14 days and has not yet reached eight weeks of development. (This second definition would then make it clear that an entity that is produced by cloning, without any fertilisation by a sperm, qualifies as an embryo).

Therapeutic cloning

A much more contentious issue is sure to be the Committee's decision to recommend that therapeutic cloning ought to be made lawful in certain circumstances. Cloning involves the removal of the nucleus from a human egg cell and its replacement with genetic material from another person. The embryo thus created generally contains an almost exact genetic match of the person donating the somatic cell, rather than a genetic blend of two natural parents. Predictably, the Committee recommended that the current ban on reproductive cloning under the PHCA remain, that is, that it continue to be an offence to implant any such embryo clone in a woman (Recommendation 2). The Committee does, however, recommend that it be lawful to disaggregate the inner cell mass from an embryo clone and then culture this mass to produce embryonic stem cells for research purposes. This is a significant move beyond the sort of embryonic stem cell research which is currently permitted in Australia and is really the salient feature of the Lockhart Report.

Significantly, the Report is somewhat equivocal as to whether full therapeutic cloning which involves the creation of genetic material from more than two people ought to be permitted – something which is currently expressly prohibited pursuant to PHCA. On the one hand the Committee recommends that it remain an offence to implant a woman with an embryo which contains the DNA of more than two people (Recommendation 8) but then rather weakly suggests that "consideration should be given" to the use of cytoplasmic transfer (including transfer of mitochondrial DNA), under licence, for research on mitochondrial disease and other uses to improve ART treatment.[10] Recommendation 26, however, expressly allows for the creation of human embryos containing the genetic material of more than two people. The UK Human Fertilisation and Embryology Authority this year broke new ground when it issued a licence to a research team at the University of Newcastle-upon-Tyne to use therapeutic cloning to conduct research into a mitochondrial disorder, muscular dystrophy.[11] In order to undertake this research the team were authorised to create a human embryo via SCNT containing the genetic material of three people. The research, funded by the Muscular Dystrophy Campaign, involves the transfer of the pro-nuclei from the embryo of a couple, into an unfertilised egg of the intended mother, which has had its own pro-nuclei removed.

The egg of the intended mother is unsuitable for reproductive purposes as the cytoplasm within the egg, which hosts the mitochondrial DNA of the mother, contains the gene for muscular dystrophy. This process is intended to remove the genetic defect from the mother's egg. Researchers in the US have already established that this process works for mice and the Newcastle team are hoping that the process can be replicated with human embryos. Families with a history of mitochondrial disorders may take heart at these recommendations, although the technology is in its infancy, and as noted above the Report does not go so far as to recommend that embryos created in this way be implanted.

Therapeutic cloning via SCNT, however, receives the unequivocal support of the Committee, although a strict licencing and monitoring regime is advised. Recommendation 23 calls for the licensed creation of human embryo clones for research, training and clinical applications – including the production of embryonic stem cells. In order to reduce the need for the donation of human oocytes (eggs), Recommendation 24 would allow the transfer of human somatic cell nuclei into animal oocytes. A closer reading of the Report suggests that this particular

recommendation is based squarely on the perceived need to kick-start the production of embryonic stem cell lines in Australia, and the mixing of human and animal tissue in this way is sure to stimulate significant debate in parliament if the recommendation ever makes its way into a draft Bill.

Will the recommendations be enacted?
Perhaps to foreshadow the inevitably close nature of any conscience vote on these issues in the Federal parliament next year, it is worth noting that in submissions from the States and Territories regarding therapeutic cloning, Queensland, New South Wales and Victoria supported the removal of the prohibition, but Western Australia did not seek the removal on the grounds that in a parliamentary debate there in 2004, there was no evidence of political or community support for the use of SCNT.

Given that many, if not most, institutions currently undertaking research involving human embryos are also commercial ART service providers, Recommendation 37 that "There should be no attempt to recover the cost of administration, licensing, monitoring and inspection activities associated with the legislation from researchers" seems appropriate.

The advocates for loosening the existing regulatory scheme will not have been buoyed by the recent exposure of extensive scientific fraud in other leading jurisdictions. In its influential submission to the Lockhart Review Committee, the peak research body, the Australian Stem Cell Centre, urged the committee to adopt a progressive view on embryonic stem cell research and noted that "recent advances in knowledge have exceeded expectations."[12]

The Centre then cites a number of ground breaking advances made by Professor Woo Suk Hwang from Korea, most notably his alleged proof, published in the iconic journal *Science*, that somatic cell nuclear transfer in humans was possible. This process, if perfected, would be crucial to medical research as it allows the creation, by cloning, of a human embryo which can be guaranteed to carry the genetic disease from which the person donating the somatic cell (usually a skin cell) suffers.

In late 2005, a panel set up to investigate Hwang's work found that his team had intentionally fabricated data in this, and other, research. Science withdrew the article[13] and Hwang, who was until then seen as the world's leading authority in the area, resigned his position at Seoul University and the World Stem Cell Hub.

Despite the quite measured and considered recommendations made by the Committee, we ought not to assume that they will be adopted in total, or even in part, by legislators. A number of commentators have observed that the differences in public policy between a number of developed nations has 'led to a strange jurisdictional conflict where culturally similar countries have strikingly different regulatory approaches to therapeutic cloning'. They conclude that although these countries with diverse regulatory approaches (such as the United Kingdom, United States, Canada and Australia) seem to have considered the same issues of public, policy, moral ambiguity and pragmatics (in terms of the need to keep pace with biotechnology innovations at a global level), the differences in approach seem hard to justify.[14]

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[1] Legislation Review Committee, *Prohibition of Human Cloning Act 2002* and *the Research Involving Human Embryos Act 2002*, *Final Report*, December 2005. The full report and recommendations may be accessed online at: http://www.lockhartreview.com.au/

[2] This has led to situations where Italian women are faced with a high percentage of unwanted multiple pregnancies and a dramatic rise in abortion figures. In one recent case a couple who were carriers of beta thalassemia unsuccessfully sought a court order to allow their IVF embryos to be subject to pre-implantation genetic diagnosis to be sure that only embryos without the disease were implanted, on the grounds that they would abort any foetus found to have the disease in any case. See – Veronica English 'Ethics Briefing - Italian Fertility Law' (2005), 31 *Journal of Medical Ethics* 743

[3] *Gesetz zum Schutzvon Embryonen: Embryonenschutzgesetz – EschG 1990* (Embryo Protection Act) 1(2)

[4] *Human Fertilisation and Embryology Act 1990* (UK)

[5] Legislation Review Committee, 'Lockhart Review Supports Strong Regulation Of Research Involving Human Embryos' (Press Release, 19 December 2005).

[6] Op cit at 42.

[7] *Research Involving Human Embryos Act 2002* (Cth) s.7.

[8] These cells, which will all go on to be part of the human foetus rather than the complimentary tissue required for gestation are collectively referred to as "the primitive streak". Anna McLaren, an embryologist sitting on the Warnock Committee observes that "the first two weeks after fertilisation are essentially a period of preparation for the later development of the embryo". Ann McLaren 'Why Study Human Development?', *New Scientist*, 24 April 1986, 49.

[9] The UK Parliament did not adopt the advice of the Warnock Committee either. S.1 of the *Human Fertilisation and Embryology Act 1990* (UK) defines an embryo as simply an egg which has been fertilised (which occurs with the appearance of a two cell zygote) or is "in the process of fertilisation".

[10] Admittedly to allow the implantation of an embryo which has been created with a denucleated donor egg would be to go a significant step further than what is currently permitted in the UK, but it would not involve the sort of cloning process which produces exact copies of a person. Perhaps this further step might be the only concession given to reproductive cloning that we are likely to see in coming years.

[11] Human Fertilisation and Embryology Authority, 'HFEA grants licence to Newcastle Centre at LIFE for Mitochondrial Research' (Press Release) < http://www.hfea.gov.uk/PressOffice/Archive/1126195581>

[12]Australian Stem Cell Council, 'Submission to Lockhart Review Committee' September 2005 < http://www.nscc.edu.au/file_downloads/lockhart_review/ASCC_Lockhart_Review_submission.pdf> at 23 December 2005

[13] Donald Kennedy, 11 January 2006, Editorial retraction, "Science unconditionally retracts two published papers on the basis of the final report from the Investigation Committee of Seoul National University. These are W.-S. Hwang *et al.*, *Science* **303**, 1669 (2004) and W.-S. Hwang *et al.*, *Science* **308**, 1777 (2005).
" http://www.sciencemag.org/cgi/content/abstract/1124926v1

[14] See for example - Timothy Caulfield (2003) 'The Regulation of Embryonic Stem Cell Research: A few Observations on the International Scene' 11 *Health Law Journal* 89. Commenting on the differences in community values which may inform some of the wide differences in these laws between jurisdictions, Elizabeth Finkel in her timely work - *Stem Cells: Controversy at the frontiers of science* (2005) 27 -reminds us that despite its careful scientific analysis of the issues, the UK's Warnock Committee noted the observation of David Hume that "morality is more properly felt than judged".