SENATE COMMITTEE INQUIRY

Sydney IVF Submission 1. Apparent Conflict Between Recommendations 16 & 25

Prof. Robert Jansen
Medical and Managing Director
Sydney IVF Limited

GPO Box 4383, Sydney 2001
Tel. +61 2 9229 6420
robert.jansen@sydneyivf.com

October 4, 2006

Recommendation 16

Testing of human oocytes for maturity by fertilisation up to, but not including, the first cell division or by parthenogenetic activation should be permitted for research, training and improvements in clinical practice of ART.

Recommendation 25

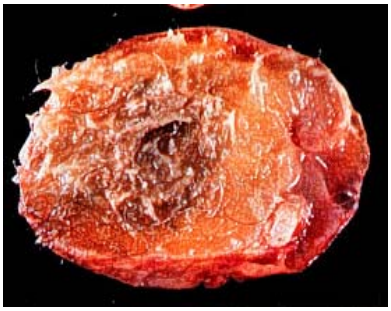
Creation of human embryos and human embryo clones by means other than fertilisation of an egg by a sperm (such as nuclear or pronuclear transfer and parthenogenesis) should be permitted, under licence, for research, training and clinical applications, including production of human embryonic stem cells, as long as the research satisfies all the criteria outlined in the amended Act and these embryos are not implanted into the body of a woman or allowed to develop for more than 14 days.

Q. Is research involving parthenogenetic activation limited to the first cell division in Rec. 16 ?

If not, and if research into parthenogentic activation is permitted for up to 14 days of development, then there is no conflict, but clarification is required.

Why the matter is important

Parthenogenesis lies behind the development of germ cell tumours, which includes the commonest ovarian tumours in Australian women (which are referred to as “dermoid cysts”, because they contain all sorts of tissues derived from stem cells, including skin and hair).



Research into understanding and preventing these tumours should not inadvertently be prohibited.

How can the legislation can be amended straightforwardly?

Recommendation 16 can be modified by removing the term “or by parthenogentic activation”, on the grounds that it is already covered in Recommendation 25.

What are the downstream collateral effects on the legislation as a whole?

I believe there are none.

The modification reflects the intention of the LRC committee and corrects ambiguous phrasing.

What questions can display this issue properly to the public?

“The most common tumour of the ovaries in Australian women are commonly known as *dermoid cysts* and I am told they are tumours of the germ cells, or eggs.

“Do the Lockhart recommendations facilitate or inhibit research into the cause of these tumours?”

SENATE COMMITTEE INQUIRY

Sydney IVF Submission 2. Conflict Between Lockhart Recommendations 19, 15 & 8

Prof. Robert Jansen
Medical and Managing Director
Sydney IVF Limited

GPO Box 4383, Sydney 2001
Tel. +61 2 9229 6420
robert.jansen@sydneyivf.com

October 4, 2006

Robert Jansen

August 25, 2006

Recommendation 19

Consideration should be given to the use of cytoplasic transfer (including transfer of mitochondrial DNA), under licence, for research on mitochondrial disease and other uses to improve ART treatment.

Recommendation 19 signals the intention of the Legislation Review Committee to deal specifically with both aspects of our submission and to enable relevant research.

Recommendation 8

Implantation into the reproductive tract of a woman of an embryo created with genetic material provided by more than two people should continue to be prohibited.

The dilemma: Mitochondrial disease cannot be treated without the transfer into an egg of cytoplasm with DNA-containing mitochondria, which means enabling an embryo created with mitochondrial genetic material from a third

person to be implanted.

Recommendation 15

Research involving fertilisation of human eggs by human sperm up to, but not including, the first cell division should be permitted for research, training and improvements in clinical practice of ART.

The dilemma

Research on mitochondrial disease is meaningless unless the manipulated egg is fertilised and develops past the point at which the embryonic genome becomes active (ie. it must develop for at least 5 to 6 days, to the stage of a blastocyst).

It forces untried treatments to be conducted on embryos intended to produce children. This is better than doing nothing for a devastating disease (see notes below), but it is second best, and it is a long way behind best practice.

Why the matter is important

There are two important, distinct reasons.

1. FAMILIES WITH MUTATIONS OF MITOCHONDRIAL DNA SUCH AS LEIGH'S DISEASE

Unlike genetic diseases from mutations in nuclear genes, through which almost all inheritance occurs, diseases caused by mutations of the tiny amount of DNA in the mitochondria affect <u>all</u> the children in the family. In the case of Leigh's disease they die within a few years of birth from brain and muscle degeneration.

Because all eggs are affected and it has not proved possible to prevent transmission by preimplantation genetic diagnosis (PGD), there is no treatment possible short of donation of mitochondria via transfer of cytoplasm from a normal, donated egg.

Families affected by mutations of mitochondrial DNA such as the mitochondrial form of Leigh's disease cannot now be helped in Australia to have disease-free children.

If less serious but nonetheless life-shortening diseases involving mitochondrial mutations are added, it is estimated that 25,000 cases per year could benefit.

Treatment is possible by infusing *cytoplasm* from an egg from a donor (the 'fleshy' part of the egg, not including the nucleus and the genetic material it contains) into the egg of the affected mother.

2. WE NEED TO KNOW WHY WOMEN NORMALLY START TO BECOME STERILE ABOUT 10 YEARS BEFORE MENOPAUSE

No research can be done in Australia at present on why, from the age of about 35, an increasing number of normal women become sterile (ie. become ncapable of having children irrespective of ART treatment). This is a natural and normal (but unexpected and frightening) phenomenon that occurs up to a decade before women reach menopause.

This research was possible in New South Wales before the 2002 legislation banned the formation of an embryo by fertilisation of an egg by a sperm after the point of conjuncture of the male and female pronucleus.

From the mid-thirties, for a steadily increasing proportion of women, the eggs can no longer produce a viable embryo; for a few years embryos form but miscarry or fail to implant. Then pregnancy inexplicably fails to occur at all – although the periods remain normal and regular.

The reason Nature has evolved – or God has intelligently designed – this phenomenon is so that women continue to produce estrogen from the ovaries while, <u>for the average woman</u>, her children are growing up and need her to be healthy. <u>Unequivocally and methodically, Nature creates and destroys human embryos to protect existing children</u>.

Research requires – and treatment may involve, under standard ethical supervision of clinical trials – infusing *cytoplasm* from an egg from a donor (the 'fleshy' part of the egg, not including the nucleus and the genetic material it contains) into the egg of the affected mother.

Consequences of enacting legislation in the manner phrased by the LRC

As with the situation that maintains the present ban entirely (see the next section), affected women are still forced to receive donated whole eggs, and thus to have the child that is, genetically, that of another woman.

Consequences of maintaining the ban on this research by leaving the present legislation effectively intact

Affected women are forced, instead, to receive donated whole eggs, and thus to have the child that is, genetically, that of another woman, whereas appropriate research permits the hope and probably the expectation that treatment may be available that enables them to have their own child.

The added mitochondrial DNA does not manifest in the fetus or child that results except for normalized metabolism. Its presence can be revealed only by highly focussed forensic DNA testing. It is otherwise medically and socially irrelevant.

In these two circumstances, women wishing to have a baby must accept donated *whole* eggs and thus have a child that is genetically not their own but that of the donor, whereas using just the cytoplasm of a donated egg would mean that they can truly have a child that (in all but a minute, forensic sense) is genetically their own.

Prohibiting the practice of cytoplasmic transfer – prohibiting medical research into this practice to see if it is safe or not – is unjust.

How can the legislation can be amended straightforwardly?

Recommendation 8 can be modified by restricting the effect of banning genetic material from three people to the genetic material of the nucleus:

> *Either*
>
> Implantation into the reproductive tract of a woman of an embryo created with **nuclear** genetic material provided by more than two people should continue to be prohibited.
>
> *or*
>
> Implantation into the reproductive tract of a woman of an embryo created with genetic material provided by more than two people, **with the exception of mitochondrial DNA**, should continue to be prohibited.

Recommendation 15 can be modified by not allowing development past the point of implantation, or by the National Health and Medical Research Council to derive on objective or popular grounds, but not on the voice of a motivated minority, namely:

> Research involving fertilisation of human eggs by human sperm **up but not including the point of implantation** should be permitted for research, training and improvements in clinical practice of ART.

And should be the subject of a licence from the NMHRC Licensing Committee.

What are the downstream collateral effects on the legislation as a whole?

I believe there are none that are not easily justifiable medically.

Socially it opens up a new way of

- Treating a small, relatively silent, but devastated number of families affected by significant mitochondrial diseases, perhaps 25,000 in Australia each year.

- Extending the reproductive span of women by a few years, thus increasing the effectiveness of IVF.

- Arousing further objection from a minority who are opposed to IVF on the basis that life starts at conception or syngamy.

What questions can display these issues properly to the public?

MITOCHONDRIAL DISEASE

"Diseases caused by mutations of the DNA in mitochondria are presently unable to be treated without requiring an affected woman to accepting, in their entirety, eggs donated by another woman, whereas in the United Kingdom they may be treated by having their own eggs receive an infusion of the fluid from the donated eggs that leaves their nuclear genes – their meaningful genome – intact.

"Do the Lockhart recommendations facilitate or inhibit research into treating these devastating diseases, which affect every child an affected woman will have, so that she can still have her own baby rather than someone else's?"

OVARIAN AGEING

"The most common cause of infertility today is the likelihood of a woman becoming infertile as a normal process up to a decade before menopause. How do the Lockhart recommendations address this issue?

"Do the Lockhart recommendations facilitate or inhibit research into this cause of infertility?"

TECHNICAL NOTE 1: MITOCHONDRIAL DNA,

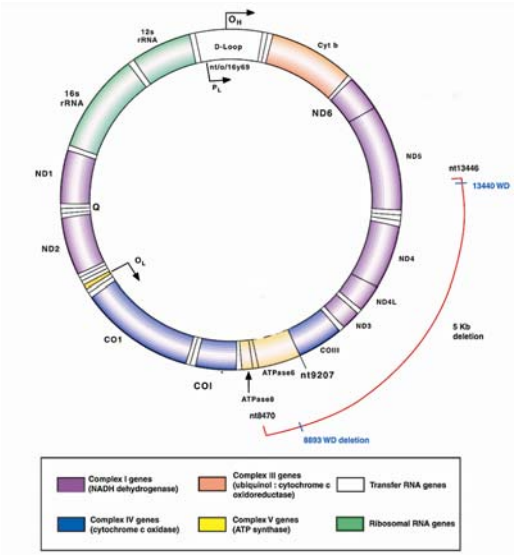
A tiny quantity of DNA is present in each of a million or so 'mitochondria' in the egg and is known as 'mitochondrial DNA' or cytoplasmic DNA – DNA that is located not in the genome in the nucleus but out in the 'fleshy' part of the egg, the cytoplasm.

This DNA is inherited entirely from the mother through the egg, and not from the father through the sperm.

Because all of us inherit all our mitochondria from our mother, a mutation present in the mitochondria of the eggs will be passed on to all of the children.

Mitochondrial chromosomes are circular, rather than stick-like, and carry 13 essential genes for metabolism. These genes are normally identical in everyone.

Mitochondrial DNA can be recognized as different only by specifically sequencing a tiny fraction of the molecule known as the "D-loop" (depicted as the pale area at 12 o'clock in the diagram), which is non-coding (ie. strictly speaking is not a gene and therefore, to take a narrow view, is not "genetic material").



TECHNICAL NOTE 2 : MITOCHONDRIAL GENE THERAPY

At fertilization, as well as inheriting two copies of each of the 30,000 or so genes that make up the nuclear genome (one copy from each parent), approximately a million little mitochondrial genomes, each with 13 genes affecting basic metabolism, are inherited through the egg's cytoplasm.

So, for the mitochondrial genome it is not a question of whether a mutant gene is present or not; rather, it is the relative amount of the abnormal gene among normal copies.

Typically a "dosage" of more than 80% mutant mitochondrial DNA means serious disease, whereas a dosage of less than 50% can mean that a woman is clinically normal. Eggs typically exaggerate the difference: they might be 10% affected or 90% affected.

Unfortunately the dosage of mutation is much the same in all of a woman's eggs, so preimplantation genetic diagnosis (PGD) or prenatal testing have little or nothing to offer in preventing transmission of mitochondrial disease.

Partial transfusion of healthy cytoplasm from the egg of a normal woman into the abnormal eggs (*cytoplasmic transfer*) causes the proportion of abnormal mitochondrial DNA to fall below the 50% or so threshold, and thus enables the birth of a baby that will not manifest the disease (and, if a female, is more likely than not, in turn, to produce eggs with a dosage of abnormal mitochondrial DNA well below the threshold). Within a few generations the abnormal mitochondrial DNA is lost from the germ line.

Sections 15 and 18 of the *Prohibtion of Human Cloning Act* had the effect of banning research into cytoplasmic transfer, on the trivial basis that forensic tests can reveal the admixture and (to stretch credulity thoroughly) thus to "confuse parenthood" to such an extent that children should be kept free from suffering this indignity!

In a variation of cytoplasmic transfer the pronuclei of fertilised eggs are exchanged: the effect is the same.

Because eggs need to be fertilised by a sperm to study the next few days of their development, it is blocked by Lockhart recommendation #15.

A clinical trial on this form of treatment involving implantation of embryos was approved in the United Kingdom during 2005, but in Australia would be blocked by Lockhart recommendation #8 if it is not modified to exclude the mitochondrial genome.

SENATE COMMITTEE INQUIRY

Sydney IVF Submission 3. Human Embryonic Stem Cells

Prof. Robert Jansen
Medical and Managing Director
Sydney IVF Limited

GPO Box 4383, Sydney 2001
Tel. +61 2 9229 6420
robert.jansen@sydneyivf.com

October 4, 2006

Sydney IVF supports the Lockhart Legislative Review Committee's recommendations regarding human embryonic stem cells in their entirety.

Detrimental practical consequences of the 2002 Legislation

1. Australia is falling out of step with the majority of OECD countries with respect to therapeutic cloning for the production of human embryonic stem cells. If this is not corrected there will be severe disadvantage caused to research into, and development of, stem cells and stem cell technology in Australia.

2. The Australian Health Ethics Committee has signalled that if therapeutic cloning remains illegal in Australia then no research must be done in Australia using imported stem cell lines produced this way. In taking this position, Australia would be at a further disadvantage among its OECD competitors. If the ban is extended to pharmaceutical companies engaged in laboratory-based drug research (research that does not involve human subjects and thus does not normally involve the NHMRC) the outcome for this industry in Australia will be catastrophic.

We wish to draw the Senate Committee's attention to the following submission we made earlier this year in an invited response to the working group formulating new National Ethical Guidelines for the Conduct of Medical Research in Australia, because it broadly yet precisely (through detailed referencing) describes the manner in which faith-based reasoning has come

to dominate the Australian Health Ethics Committee. We believe this dominance is improper and puts at risk NHMRC's reputation for objectivity.

Setting

After review by the Sydney IVF Ethics Committee[1], Sydney IVF made the following representation to the Working Group on the basis that the Second Draft still contained potentially serious tension between, on the one hand

(1) ethically proper, commercially cognizant biomedical research in the area of embryonic stem cells, and on the other

(2) ethical guidelines [2] issued by the Australian Health Ethics Committee (AHEC), which had recently become at once

(a) explicitly faith-based instead of outcomes-based, [3] and

(b) effectively compulsory in the biotech industry sector (as had been pointed out on page vii of Draft 2 of the Statement, and as emphasized also by the AHEC [2a])

It is important that the Senate be aware of this conflict, particularly the explicit priority AHEC is giving to non-outcomes-focussed ethical positions on matters related to human embryonic stem cells and research involving human embryos, which has the potential to harm the NHMRC's reputation for objectivity.

Our comments relate to Draft 2, which is the latest draft released by NHMRC:

The *Preamble* contains two anomalies, namely that

1. the statement [pp. v-vi] "Research … generates ethical dilemmas in which it is impossible to find agreement on what is right or wrong" mirrors AHEC's preamble to its guidelines [2b] but is at odds with AHEC's adopted conclusion, articulated in its submission [3] to the Lockhart committee's review of the *Research Involving Human Embryos Act (C'th) 2002* and the *Prohibition of Human Cloning Act (C'th) 2002* (the Legislation Review Committee)

2. the affirmation [p. vii] that Section 8(1) of the *National Health and Medical Research Council Act (C'th) 1992* … "requires the NHMRC to issue guidelines … precisely as developed by … AHEC)" identifies exactly the vulnerability of the *National Statement* (and indeed the NHMRC in its operations) to usurpation by a faith-based position decidedly rejected by a majority of Australians. Adoption of this subjective position is inappropriate and will compromise the objectivity the NHMRC depends on for its presently excellent credibility in our community.

Paragraph 3.7.3 (a) has the effect of asserting the permanence of statutes that were intended to be interim [4] [the *Research Involving Human Embryos Act (C'th) 2002* and the *Prohibition of Human Cloning Act (C'th) 2002*], particularly that embryos from which stem cell lines used for research (in practice, though, all embryos) must be derived

from human embryos that “were created for reproductive purposes”.

AHEC is unequivocal elsewhere [2c] that this means that embryos used for research must have been created as part of a clinical IVF program and not, for example, for the purpose of research, or even for family-based purposes such as saving the life of an extant child, including therefore embryos or embryonic stem cells produced by somatic cell nuclear transfer (“therapeutic cloning”).

The assertion conflicts with the recommendations of the Lockhart review of the legislation and its effects. [6]

NHMRC’s *Research Committee*, a principal committee that does not have the advantaged position that AHEC has under the NHMRC Act [2a], is on record as questioning this conclusion [7a] – and a call for more flexibility than the restrictive position adopted by AHEC was also made by Council of NHMRC [7b].

The Lockhart Legislation Review Committee’s recommendations, capable of approval by federal and state parliaments, would still not be able to be implemented and practised by researchers or industry because they would be contrary to AHEC’s ART guidelines and/or the National Statement, both of which are scrupulously respected by responsible researchers.

The Statement, to be authoritative in the long term, and to not invite repeated revision, should not prejudge such contentious issues.

“Autologous” in relation to tissue transfer or transfusion means transfer back to the person from whom the tissue or blood was obtained. This is too strict a requirment for human stem cells, and *Justice*, under which heading this section lies, is obstructed by this requirement.

The qualification, “except for *autologous* donation” should read “except for donation within families”.

The fact is that there is about a 25% chance (actually slightly less) [8] that a human embryonic stem cell line created from an embryo from a couple will be completely immunologically compatible with any of that couple’s children. Justice is not served if stem cells derived from such embryos are prevented from being “donated” to a child of the couple.

Please note that use on this basis within families applies only to the children of the couple; such stem cells are not genetically compatible with either parent or, for example, with any grandchildren.

The Working Party should be aware that in each instance of embryo donation for research under Sydney IVF’s Licence 309703 we require of users of resulting stem cell lines their agreement that they will never object to our retaining early-stage stem cell samples for possible future use to benefit the family that made the donation.

The Working Party should also be aware that the fact is that, for the children within families in which IVF has been used and as a result of which there are excess embryos in storage, the family has a strong interest in not ever discarding embryos.

They have a unique potential to produce stem cells compatible with one or other of their children should they ever require it as a life-saving measure.

The notion that the community is somehow morally advantaged if excess IVF embryos are discarded instead of made use of in reseach or treatment [3] is medically incomprehensible. [9]

This is not an argument for a lack of regulation and public accountability. It is an argument for using objective bases for the ethics that govern medical research.

In relation to stem cell research, it should be noted that much is planned to be carried out with the assistance of, or in commercial partnership with, organisations in countries that are significant trading partners with, or competitors of, Australia.

We reiterate that no sensible researcher in Australia advocates human reproductive cloning. The ban imposed by the *Prohibition of Human Cloning Act* – and the ban on transferring an embryo produced by nuclear transfer to a woman's uterus to produce a pregnancy recommended by the Lockhart committee report – is supported across Australia.

The *Act*, however, presently also prohibits research or clinical practice involving nuclear transfer to produce stem cells for autologous use. An example of the moral mischief of prohibiting this research is illustrative:

What is unethical here? A narrative.

It is five years from now.

Your – yes, *your* -- 20-year-old daughter or niece is dying from acute myeloid leukaemia. This is the deadliest form of leukaemia.

Unfortunately no adult stem cells free of leukaemic potential can be isolated from blood or bone marrow. Her brothers and sisters do not share her tissue groups and cannot be donors. No compatible cord blood stem cells are available from the Red Cross.

Instead, we track her ovarian cycle and, immediately before a natural ovulation, under light sedation, and taking just 5 minutes, her pre-ovulaory ovarian follicle is aspirated and an egg surrounded by follicular cells (called 'cumulus cells') are recovered with it.

The nucleus from one of the cumulus cells is transferred into the egg, as its own nucleus is removed.

The cumulus cell nucleus – like a horticultural cutting taken from a plant and placed into fertile soil – is placed into the only environment that will allow it to reprogram and divide into cells that, collectively, will look like an embryo (and in every practical way look like an embryo of just about every animal under the sun, except that there is nothing genetic here that is not your daughter). *Cont.*

A stem cell line is developed and the easiest tissue that can be differentiated from embryonic stem cells – haemopoietic cells – result. They are transfused after chemotherapy that would otherwise be fatal.

Your daughter does not die.

The table below lists the countries in which this scenario is or would be a criminal offence is given in the Table below; the Table also lists the country, fortunately if expensively, she can travel to for this treatment.

The effect of the 2002 legislation has been, and was intended, to produce a moratorium on stem cell research involving therapeutic cloning (nuclear transfer) in Australia. This research, however, has been advocated in Australia now

- by the Lockhart Legislation Review of 2005
- by a majority of the House of Representatives' Standing Committee on Legal and Constitutional Affairs in 2001
- by the 1999 Australian Health Ministers' Conference that referred the matter to the Standing Committee
- and by a clear majority of Australians according to public opinion polls.[10]

People who presently object to such stem cell research involving nuclear transfer (that is, objectors to therapeutic cloning for production of autologous stem cells) might suggest that it is only relatively undeveloped countries, perhaps with lax ethical oversight, that Australian researchers might turn to in order to remain involved in this research. Objectors might further point out that, in a well publicised vote at the United Nations during 2005, a majority of countries voted against therapeutic cloning (a result that has attracted at least superficial authority).

It is pertinent therefore to list the voting by the countries of the OECD in this regard, a result that yields a different picture – one that Australia must recognize and relate to, if we are to play a significant part in the stem-cell based revolution in clinical medicine that appears probable:

Ban nuclear transfer	*Permit nuclear transfer*	*Abstention or absence*
AUSTRALIA	BELGIUM	TURKEY
AUSTRIA	CANADA	GREECE
GERMANY	CZECH REPUBLIC	
HUNGARY	DENMARK	
IRELAND	FINLAND	
ITALY	FRANCE	
MEXICO	ICELAND	
POLAND	JAPAN	
PORTUGAL	KOREA	
SLOVAK REPUBLIC	LUXEMBOURG	
SWITZERLAND	NETHERLANDS	
UNITED STATES *	NEW ZEALAND	
	NORWAY	
	SPAIN	
	SWEDEN	
	UNITED KINGDOM	

* California and Massachusetts, both direct competitors for Australia in biotechnology, have signalled their intent actively and substantially to support human embryonic stem cell research based on nuclear transfer.

For these various reasons and experiences among Australians, we suggest that the *National Statement* should not incorporate or assume preeminence for ethical positions that are not based on experience of outcomes and which are not susceptible to verification by evidence of good or harm done.[3]

References

Ref. 1 The present and past composition of the HREC for Sydney IVF is listed in Appendix 1.

Ref. 2 *Ethical guidelines on the use of assisted reproductive technology* Australian Health Ethics Committee and NHMRC, Canberra, 2004

a. Para 1.2 Role of the NHMRC and NHMRC Act 1991.

b. Para 2.4 "AHEC has tried to be sensitive to all the relevant dimensions of ART …"

c. Para 4.1 Unacceptable Practices.

Ref. 3 *NHMRC Submission to the Legislation Review*, Appendix 2 (Submission from the Australian Health Ethics Committee), p. 32

AHEC explains here that whereas medical researchers usually rely on ethical arguments of a "teleological" kind (consequential ethics based on evidence of good or harm done), "AHEC relies on arguments of a deontological kind."

Teleology and *deontology* are defined well in the *Fontana Dictionary for Modern Thought*, an excerpt of which is attached as Appendix 2.

AHEC is misleading in implying that a deontological moral position [from the Greek *deos*, or *duty,* thus a "duty-based" moral position], while it does rest on "conformity to (an) accepted ethical principle or value", is necessarily "compromised" when consequential ethical arguments prevail.

The moral duty to relieve suffering is also a deontological ethical argument – one so powerful that it is surely immoral intentionally to ignore, let alone actively to frustrate it. Its deontological *bona fides* receives no acknowledgement by AHEC. This perfectly proper moral position is not at all at odds with the consequential, outcomes-based ethical arguments AHEC eschews.

The deontological position that AHEC takes is that the human life that requires protection by minimizing (almost at any cost brought by human suffering in the present world), namely the destruction of a human pre-implantation embryo, or the prohibition of formation of an embryo "for any purpose other than the (immediate) reproductive purpose of the couple", dates from Pius IX's papal bull *Apostolicae Sedis* of 1869, and was not (and is not now) shared by large segments of the Christian faith – let alone by those of non-Christian faiths and Australia's humanists.

On the same page of this reference, AHEC skirts this issue: "In such circumstances of community difference … it has been AHEC's view that the preferred advice is that which reflects enduring ethical traditions of thought and belief and which has clear, *if not overwhelming*, community support" [emphasis added: see Ref. 10, below].

It is important to note that not complying with this majority's wishes on religious grounds is itself unethical. Even if it were not a majority it would still be unethical in a multicultural society.

Ref. 4 The effect of the 2002 legislation has been to produce a moratorium on stem cell research involving therapeutic cloning (nuclear transfer) in Australia. This research, however, has been advocated in Australia, now

a. by the Lockhart Review in 2005

b. by a majority of the House of Representatives' Standing Committee on Legal and Constitutional Affairs in 2002 (Chaired by Kevin Andrews, MP)

c. by the 1999 Australian Health Ministers' Conference that referred the matter to the Standing Committee

d. and by a clear majority of Australians according to Morgan Gallup polls [Ref. 10]

Despite this antecedent and subsequent history, AHEC claims that the parliamentary debate of 2002 was meant somehow to settle the matter to accord with the Roman Catholic position.

Ref. 5 *NHMRC Submission to the Legislation Review*, Appendix 2 (Submission from the Australian Health Ethics Committee), p. 36

AHEC explains here that through its subcommittee known as CREGART [Committee to Review the Ethical Guidelines on ART] it sees no reason to revisit its ban on nuclear transfer, or therapeutic cloning.

> *… both CREGART and AHEC (intend) to make clear that the list at pages 10-11 of the ART guidelines 2004 both CREGART and AHEC intended to make clear that, regardless of other outcomes of the legislation review, all the practices listed (are) regarded as unethical.*

Ref. 6 *Legislation Review Committee Report* ("Lockhart Report"), Canberra, 2005
Section 17.4 Research and other activities involving human embryos under licence, [including many recommendations that contradict AHEC ethical guidelines], pp. 166-172.

Ref. 7 *NHMRC Submission to the Legislation Review*,

a. Appendix 1 (Submission from the Research Committee), p. 20

b. p. 10

Ref. 8 A person's tissue type, like his or her blood group, is determined by a set of genes inherited from each parent. Unlike blood groups, tissue groups are almost infinitely varied, being genetically determined by a set of genes on each copy of chromosome 6. The gene sets on the two chromosomes are always different (there are about 11 billion combinations of known genes possible, so the chance of the two sets being identical to each other in anything other than a brother-sister marriage is effectively zero).

Likewise the chance of one person's combination being identical to another unrelated person's combination is extremely remote.

Most times the set on each chromosome passes intact to the children. Because four combinations of chromosomes are possible, the chance of a child having an identical set of tissue types to a sibling is 1:4, or 25% … or it would be except for the phenomenon of chromosomal crossover, which can split across the set and exchange half of one set with half of the other.

The chance of a perfect match, therefore, between an embryonic stem cell line and a child within that family of the same parents is a little less than 25%.

Ref. 9 Sydney IVF has lodged two new embryo research applications [309710 and 309711], two applications that involve generating embryonic stem cell lines from proven abnormal embryos from families having IVF to prevent transmission of serious single gene defects such as Huntington disease and the other diseases for which we have performed preimplantation genetic diagnosis [see Appendix 3].

The families affected by Huntington's disease and the 100 or so others we have treated to date with IVF and preimplantation genetic diagnosis (PGD) virtually all have a fervent wish for their abnormal embryos to be applied to stem cell research to assist drug development for their particular disease. PGD today is not just about avoiding disease transmission, it is about producing stem cell systems for life-like but in vitro assay systems for screening molecules and developing inhibitory gene transcription modifiers that could be used to treat patients with the disease.

But our negotiations with the Licensing Committee have being drawn out for months because we are being asked to justify why, for example, we want to make available stem cell lines with each of the dinucleotide repeat sequence lengths in the *huntingtin* gene that causes Huntington's disease, and why we need to produce, as well, stem cell lines with the same haplotype but with the normal *huntingtin* gene. It seems that we are being asked to provide separate, literature-based justification for every mutant allele for every one of the diseases in Appendix 3 and for each disease to come, when we should be concentrating on putting the widest possible relevant range of cell lines into the hands of the people who can do the molecular research needed to alter these peoples' lives.

Ref. 10 July 2001: 52% of Australians approve therapeutic cloning
[Roy Morgan Research Finding 3421]

Dec 2001: 55% of Australians approve therapeutic cloning
[Roy Morgan Research Finding 3481].

Appendix 1. Composition of Sydney IVF's fully independent Human Research Ethics Committee, past and present

Chairs	Dr John Greenaway AM	2000–2003
	Canon Rev Dr Ivan Head	2003–present
Laywomen	Sandra Dill AM	2000–present
	Quentin Bryce AO	2000–2003
	Hon. Susan Ryan AO	2003–present
Laymen	Simon Longstaff PhD	2000–present
	John Preston	2000–2003
	Robert Ferguson	2005-present
Medical	Dr Edith Weisberg AM	2000–present
Counseling	Annette McInerney	2000–present
Religious	Rev Dr Davis McCaughey AC	2000–2003
	Canon Rev Dr Ivan Head	2003
	Rabbi Jacki Ninnio	2004–present
	Rev Peter Kurti	2004–present
Lawyer	Russell Scott AM	2000–2004
	James Lane	2005–present

Appendix 2. Lay definitions of *deontology*, *teleology* and *utilitarian* [words used by the Australian Health Ethics Committee to downplay the moral imperative of outcomes-based ethics in Reference 3] **from the *Fontana Dictionary of Modern Thought.***

deontology. Strictly, and as the title of a book allegedly by Bentham, the branch of ETHICS which inquires into the nature of moral duty and the rightness of actions; as currently used, the particular ethical theory that takes principles of duty or obligation, those that lay down what men morally ought to do, to be self-evident or self-substantiating and neither to need, nor to be susceptible of, derivation (see DEMONSTRATION) from any supposedly more fundamental moral truths, in particular from propositions or principles about the goodness of the consequences of action. The opposed view, that the rightness or wrongness of actions is determined by the goodness or badness of their consequences (whether actual, predictable, or intended) is called TELEOLOGY or consequentialism. 'Let justice be done though the heavens fall' is a deontological slogan. Kant seeks to establish deontology at the outset of his chief ethical treatise by proving that the rightness of an action is unaffected by its having, in a particular case, unfortunate consequences.

teleology (or *consequentialism*). Literally, the study of ends, goals, or purposes; more specifically, the theory that events can only be explained, and that evaluation of anything (objects, states of affairs, acts, agents) can only be justified, by consideration of the ends towards which they are directed. Teleologists contend that minds or living organisms can only be explained in a forward-looking way and that MECHANISTIC explanation in terms of efficient causes is inadequate. As an ethical doctrine (see ETHICS) teleology argues, in opposition to DEONTOLOGY, that rightness is not an intrinsic property of actions but is dependent on the goodness or badness of the consequences, whether actual, predictable, or expected, to which they give rise. There are, undoubtedly, teleological systems, i.e. complexes of events (e.g. a stock exchange or a cat stalking a bird) which take on a significant order only if seen as all directed towards some outlying purpose.

utilitarianism. In ETHICS, the theory that takes the ultimate good to be the greatest happiness of the greatest number and defines the rightness of actions in terms of their contribution to the general happiness. It follows that no specific moral principle is absolutely certain and necessary, since the RELATION between actions and their happy or unhappy consequences varies with the circumstances. Sketched by earlier philosophers, notably David Hume (1711-76), utilitarianism was made fully explicit by Jeremy Bentham (1748-1832) and, in a qualified way, by John Stuart Mill. It was widely rejected in their time for its unedifying HEDONISM (which was nevertheless altruistic). In this century it has been criticized for its commission of the supposed NATURALISTIC FALLACY. Its chief opponents are the kind of ethical INTUITIONISM that takes values to be quite distinct in nature from matters of empirical fact, and the DEONTOLOGY (often associated with that view) that holds certain kinds of conduct to be right or wrong intrinsically and quite independently of any consequences they may have.

Appendix 3. Extract from Sydney IVF's embryo research licence application #309710.
[Sydney IVF has a 50% success rate at turning a human blastocyst-stage embryo into a confirmed stem cell line, a particularly high rate internationally.]

Item A — Title of proposed use

Derivation of human embryonic stem cells for medical research from embryos identified through preimplantation genetic diagnosis to carry a genetic mutation rendering that embryo unsuitable for establishment of pregnancy.

Item B — Short statement about the nature of the proposed use

The project aims to produce human embryonic stem cell (hESC) lines with known genetic mutations from embryos identified through the clinical practice of Preimplantation Genetic Diagnosis (PGD). The stem cell lines will be used for collaborative research into the molecular biology of serious familial diseases including, but not limited to, adrenoleucodystrophy, Alzheimer disease (early onset), Batten disease, Charcot-Marie Tooth syndrome, choroideremia, chronic granulomatous disease, congenital adrenal hyperplasia, Crigler-Najjar syndrome, cystic fibrosis, Dejerine-Sottas syndrome, Diamond Blackfan disease, Duchenne muscular dystrophy, ectodermal dysplasia, facioscapulohumeral muscular dystrophy, familial adenomatous polyposis, fragile X disease, hemophilia A, hyper-IgM disase, Huntington disease, hypophosphatasia, Lowe syndrome, medullary thyroid carcinoma, MELAS (and other mitochondrial diseases), mucopolysaccharidoses, multiple endocrine neoplasia, myotonic dystrophies, neurofibromatosis, Pendred syndrome, polycystic kidney disease, polycystic kidney disease, Sandhoff disease, spinal muscular atrophy, thalassemia, tuberous sclerosis, von Hippel-Lindau disease, Wolman disease, Zellweger syndrome etc. The goal of this research is to develop many and varied, but mutation-specific, gene-transcription-modification methods to ameliorate disease expression of patients with these genetic abnormalities, to benefit the affected patients, their families, and the wider community.

Appendix 4. Extracts from NHMRC and AHEC submissions to the Lockhart Legislation Review Committee

[See separately enclosed PDF Files]